European Association of Urology

Pocket Guidelines

2020 edition

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Introduction

We are honoured to present the 2020 edition of the European Association of Urology (EAU) Guidelines, the most comprehensive, continuously updated, guidelines available for urologists and clinicians from related specialties. Produced by a dedicated Guidelines Office, involving approximately 250 international experts and endorsed by 72 national and professional societies around the world, the EAU Guidelines are internationally recognised as an excellent, high-quality resource for assisting clinicians in their everyday practice.

For the 2020 edition of the EAU Guidelines, we are proud to present the new EAU Guidelines on Sexual and Reproductive Health which consolidates the work of the former Male Infertility, Male Sexual Dysfunction and Male Hypogonadism Panels. Additionally, numerous guideline recommendations have been updated.

Going forward, the EAU Guidelines Office has a number of plans in place for the coming year, and beyond. We are delighted to announce the formation of a new EAU Guidelines Panel on Non-neurogenic Female LUTS under the leadership of Mr. C.K. Harding (Chair) and Prof.Dr. M.C. Lapitan (Vice-chair). The Panel has already begun work on producing the new guideline for publication in 2021. Additionally, the ad-hoc EAU Guidelines on Urethral Strictures, chaired by Prof.Dr. N. Lumen will also conclude their work in time for publication in 2021.

A further goal for the Guidelines Office in 2020 is a commitment to increasing patient involvement in Guidelines development. In addition, the Guidelines Office IMAGINE group will begin a two-phase programme to map practice and adherence to key Guideline recommendations across Europe.

The yearly publication of the EAU Guidelines would not be possible without the unwavering support of the EAU Executive Committee and Management team, our highly valued Guidelines Panels and young Guidelines Associates, our EAU membership and every user of the Guidelines globally. So, on behalf of the EAU Guidelines Office Board, thank you for your support and inspiration.

We hope you enjoy using the 2020 update of the EAU Guidelines!

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Level of evidence and grading systems
For each recommendation within the guidelines there is an accompanying online strength rating form, the basis of which is a modified GRADE methodology [1, 2].
Each recommendation within the 2020 Pocket Guidelines is accompanied by an online strength rating form which addresses a number of key elements, namely:

1. the overall quality of the evidence which exists for the recommendation, references used in this text are graded

according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence (see Table 1) [3];
2. the magnitude of the effect (individual or combined effects);
3. the certainty of the results (precision, consistency, heterogeneity and other statistical or study related factors);
4. the balance between desirable and undesirable outcomes;
5. the impact of patient values and preferences on the intervention;
6. the certainty of those patient values and preferences.

These key elements are the basis which panels use to define the strength rating of each recommendation. The strength of each recommendation is represented by the words 'strong' or 'weak' [4]. The strength of each recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, the quality of the evidence (including certainty of estimates), and nature and variability of patient values and preferences. The strength rating forms will be available online.

Table 1: Level of evidence*

Level	Type of evidence
1a	Evidence obtained from meta-analysis of randomised trials.
1b	Evidence obtained from at least one randomised trial.
2a	Evidence obtained from one well-designed controlled study without randomization.
2b	Evidence obtained from at least one other type of well-designed quasi-experimental study.
3	Evidence obtained from well-designed non-experimental studies, such as comparative studies, correlation studies and case reports.
4	Evidence obtained from expert committee reports or opinions or clinical experience of respected authorities.

** Modified from [3]*

References

1. Guyatt, G.H., *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, 2008. 336: 924.
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3. Phillips, B., *et al.* Oxford Centre for Evidence-based Medicine Levels of Evidence. Updated by Jeremy Howick March 2009.
4. Guyatt, G.H., *et al.* Going from evidence to recommendations. BMJ, 2008. 336: 1049.

EAU GUIDELINES ON NON-MUSCLE-INVASIVE (TaT1, CIS) BLADDER CANCER

(Limited text update March 2020)

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Introduction

The EAU Working Group has published guidelines on Non-muscle-invasive bladder cancer (NMIBC), TaT1 tumours and carcinoma *in situ* (CIS).

Staging and classification systems

The 2017 TNM (Tumour, Node, Metastasis Classification) is used for staging (Table 1). For grading, both the 1973 and 2004/2016 WHO grading classifications are used (Table 2).

Table 1: TNM Classification 2017

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Ta	Non-invasive papillary carcinoma	
Tis	Carcinoma *in situ*: 'flat tumour'	
T1	Tumour invades subepithelial connective tissue	
T2	Tumour invades muscle	
	T2a	Tumour invades superficial muscle (inner half)
	T2b	Tumour invades deep muscle (outer half)
T3	Tumour invades perivesical tissue	
	T3a	Microscopically
	T3b	Macroscopically (extravesical mass)
T4	Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall	
	T4a	Tumour invades prostate stroma, seminal vesicles, uterus or vagina
	T4b	Tumour invades pelvic wall or abdominal wall
N – Regional Lymph Nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N2	Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N3	Metastasis in common iliac lymph node(s)	

M - Distant Metastasis		
M0	No distant metastasis	
	M1a	Non-regional lymph nodes
	M1b	Other distant metastases

The prognostic value of both WHO 1973 and 2004/2016 grading systems has been confirmed. As the WHO 2004/2016 system has not yet been fully incorporated into prognostic models, long-term individual patient data using both classification systems are needed.

Carcinoma *in situ*

Carcinoma *in situ* is a flat, high-grade, non-invasive urothelial carcinoma, and classified into the following clinical types:

- Primary: isolated CIS with no previous or concurrent papillary tumours and no previous CIS;
- Secondary: CIS detected during follow-up of patients with a previous tumour that was not CIS;
- Concurrent: CIS in the presence of any other urothelial tumour in the bladder.

Table 2: WHO grading in 1973 and in 2004/2016

1973 WHO grading
Grade 1: well differentiated
Grade 2: moderately differentiated
Grade 3: poorly differentiated
2004/2016 WHO grading system *(Papillary lesions)*
Papillary urothelial neoplasm of low malignant potential (PUNLMP)
Low-grade (LG) papillary urothelial carcinoma
High-grade (HG) papillary urothelial carcinoma

Variants of urothelial carcinoma and lymphovascular invasion

Some variants of urothelial carcinoma (micropapillary, plasmocytoid, sarcomatoid) have a worse prognosis than pure HG urothelial carcinoma. The presence of lymphovascular invasion (LVI) in transurethral resection of the bladder (TURB) specimens is associated with worse prognosis.

Recommendations for bladder cancer classification	Strength rating
Use the 2017 TNM system for classification of the depth of tumour invasion (staging).	Strong
Use both the 1973 and 2004/2016 WHO grading systems.	Strong
Do not use the term "superficial bladder cancer".	Strong

Diagnosis

A comprehensive patient history is mandatory. Haematuria is the most common finding. Physical examination does not reveal NMIBC.

Recommendations for the primary assessment of non-muscle invasive bladder cancer	Strength rating
Take a patient history, focusing on urinary tract symptoms and haematuria.	Strong
Use renal and bladder ultrasound and/or computed tomography (CT)-intravenous urography during the initial work-up in patients with haematuria.	Strong

Once a bladder tumour has been detected, perform a CT urography in selected cases (e.g., tumours located in the trigone, multiple- or high-risk tumours).	Strong
Perform cystoscopy in patients with symptoms suggestive of bladder cancer or during surveillance. It cannot be replaced by cytology or by any other non-invasive test.	Strong
In men, use a flexible cystoscope, if available.	Strong
Describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities during cystoscopy. Use a bladder diagram.	Strong
Use voided urine cytology as an adjunct to cystoscopy to detect high-grade tumour.	Strong
Perform cytology on at least 25 mL fresh urine or urine with adequate fixation. Morning urine is not suitable because of the frequent presence of cytolysis.	Strong
Use the Paris system for cytology reporting.	Strong

Papillary (TaT1) tumours

The diagnosis of papillary bladder cancer ultimately depends on cystoscopic examination of the bladder and histological evaluation of the tissue resected during TURB. Transurethral resection of the bladder is a crucial procedure in the diagnosis and treatment of TaT1 tumours and should be performed systematically in individual steps (see recommendations below). A complete resection, performed by either fractioned or *en-bloc* technique, is essential to achieve a good prognosis.

The technique selected depends on the size of the lesion, its location and experience of the surgeon. In selected cases, due to the risk of tumour persistence and understaging after initial TURB, a second resection (2nd TURB) is recommended.

Carcinoma *in situ*

Carcinoma *in situ* is diagnosed by a combination of cystoscopy, urine cytology, and histological evaluation of bladder biopsies taken from suspicious areas or as mapping biopsies from normal looking mucosa (for details, please consult the extended guidelines). Carcinoma *in situ* cannot be eradicated by TURB and further treatment is mandatory.

Recommendations for transurethral resection of the bladder (TURB), biopsies and pathology report	**Strength rating**
In patients suspected of having bladder cancer, perform a TURB followed by pathology investigation of the obtained specimen(s) as a diagnostic procedure and initial treatment step.	Strong
Outpatient fulguration or laser vaporisation of small papillary recurrences can be used in patients with a history of TaG1/LG tumours.	Weak

Perform TURB systematically in individual steps: • bimanual palpation under anaesthesia. This step may be omitted in case non-invasive or early treatment for invasive disease is planned; • insertion of the resectoscope, under visual control with inspection of the whole urethra; • inspection of the whole urothelial lining of the bladder; • biopsy from the prostatic urethra (if indicated); • cold-cup bladder biopsies (if indicated); • resection of the tumour; • recording of findings in the surgery report/record; • precise description of the specimen for pathology evaluation.	Strong
Performance of individual steps	
Perform *en-bloc* resection or resection in fractions (exophytic part of the tumour, the underlying bladder wall and the edges of the resection area).	Strong
Avoid cauterisation as much as possible during TURB to avoid tissue deterioration.	Strong

Take biopsies from abnormal-looking urothelium. Biopsies from normal-looking mucosa (mapping biopsies from the trigone, bladder dome, right, left, anterior and posterior bladder wall) are recommended when cytology is positive, in case of a history of HG/G3 tumours and in tumours with non-papillary appearance. If equipment is available, perform fluorescence-guided (PDD) biopsies.	Strong
Take a biopsy of the prostatic urethra in cases of bladder neck tumour, if bladder carcinoma *in situ* is present or suspected, if there is positive cytology without evidence of tumour in the bladder, or if abnormalities of the prostatic urethra are visible. If biopsy is not performed during the initial procedure, it should be completed at the time of the second resection.	Strong
Take the biopsy from abnormal areas in the prostatic urethra and from the precollicular area (between the 5 and 7 o'clock position) using a resection loop. In primary non-muscle-invasive tumours when stromal invasion is not suspected, cold-cup biopsy with forceps can be used.	Weak
Use methods to improve tumour visualisation (fluorescence cystoscopy, narrow-band imaging) during TURB, if available.	Weak
Refer the specimens from different biopsies and resection fractions to the pathologist in separately labelled containers.	Weak

The TURB protocol must describe tumour location, appearance, size and multifocality, all steps of the procedure, as well as extent and completeness of resection.	Strong
In patients with positive cytology, but negative cystoscopy, exclude an upper tract urothelial carcinoma, CIS in the bladder (by mapping biopsies or PDD-guided biopsies) and tumour in the prostatic urethra (by prostatic urethra biopsy).	Strong
Perform a 2nd TURB in the following situations: • after incomplete initial TURB, or in case of doubt about completeness of a TURB); • if there is no muscle in the specimen after initial resection, with the exception of TaLG/G1 tumours and primary CIS; • in T1 tumours.	Strong
If indicated, perform a 2nd TURB within two to six weeks after initial resection. This 2nd TURB should include resection of the primary tumour site.	Weak
Register the pathology results of a 2nd TURB as it reflects the quality of the initial resection.	Weak
Inform the pathologist of prior treatments (intravesical therapy, radiotherapy, etc.).	Strong
The pathological report should specify tumour location, tumour grade and stage, lymphovascular invasion, unusual (variant) histology, presence of CIS, and detrusor muscle.	Strong

Predicting disease recurrence and progression

After TURB, patients should be stratified, according to prognostic factors, into risk groups which will facilitate treatment recommendations (see Table 3). For individual prediction of the risk of tumour recurrence and progression at different intervals after TURB, application of EORTC risk tables and calculator is strongly recommended: https://www.eortc.be/tools/bladdercalculator/download_disclaimer.htm.

For bacillus Calmette-Guérin (BCG)-treated patients, separate scoring models and risk groups have been created by the CUETO and the EORTC, respectively.

Recommendations for stratification of non-muscle invasive bladder cancer	Strength rating
Stratify patients into three risk groups according to Table 3.	Strong
Apply the EORTC risk tables and calculator for the prediction of the risk of tumour recurrence and progression in different intervals after transurethral resection of the bladder, in individual patients.	Strong
Use the CUETO risk tables and the EORTC risk groups for the prediction of the risk of tumour recurrence and progression in individual patients treated with bacillus Calmette-Guérin.	Strong

Table 3: Treatment recommendations in TaT1 tumours and carcinoma *in situ* according to risk stratification

Risk category	Definition	Treatment recommendation
Low-risk tumours	Primary, solitary, TaG1 (PUNLMP, LG*), < 3 cm, no CIS	One immediate instillation of intra-vesical chemotherapy after TURB.
Intermediate-risk tumours	All tumours not defined in the two adjacent categories (between the category of low and high risk).	In patients with previous low recurrence rate (≤ one recurrence per year) and expected EORTC recurrence score < 5, one immediate instillation of intra-vesical chemo-therapy after TURB. In all patients either 1-year full-dose BCG treatment (induction plus 3-weekly instillations at 3, 6 and 12 months), or instillations of chemo-therapy (the optimal schedule is not known) for a maximum of one year.

High-risk tumours	Any of the following: • T1 tumours; • G3 (HG**) tumour; • CIS; • Multiple, recurrent and large (> 3 cm) TaG1G2/LG tumours (all features must be present)*.	Intravesical full-dose BCG instillations for one to three years or radical cystectomy (in highest-risk tumours - see below).
	Subgroup of highest-risk tumours	
	T1G3/HG associated with concurrent bladder CIS, multiple and/or large T1G3/HG and/or recurrent T1G3/HG, T1G3/HG with CIS in the prostatic urethra, some forms of variant histology of urothelial carcinoma, LVI.	Radical cystectomy (RC) should be considered. In those who refuse or are unfit for RC, intravesical full-dose BCG instillations for one to three years.

**Low grade is a mixture of G1 and G2.*

*** High grade is a mixture of some G2 and all G3.*

Disease management

Adjuvant treatment

Since there is considerable risk for recurrence and/or progression of tumours after TURB, adjuvant intravesical therapy is recommended for all stages (TaT1, and CIS).

- **Immediate single post-operative instillation of chemotherapy** within six hours after TURB can reduce recurrence rate in patients with low-risk and selected intermediate-risk tumours. The difference of efficacy between individual drugs (mitomycin C, epirubicin, or doxorubicin) has not been confirmed.
- **Further chemotherapy** instillations can improve recurrence-free survival in intermediate-risk tumours, but do not prevent progression. These instillations are associated with minor side-effects.
- **Intravesical immunotherapy with BCG** (induction and maintenance) is superior to intravesical chemotherapy in reducing recurrences and in preventing or delaying progression to muscle-invasive bladder cancer.

The individual choice of further intravesical adjuvant therapy depends on the patient's risk (Table 3). In patients at highest risk of progression, RC should be considered.

Bacillus Calmette-Guérin (BCG) failure

Several categories of BCG failures, broadly defined as any disease recurrence following BCG therapy, have been proposed.

Whenever a MIBC is detected during follow-up.
BCG-refractory tumour
1. If T1G3/HG tumour is present at 3 months (LE: 3).
2. If TaG3/HG tumour is present after 3 months and/or at 6 months, after either re-induction or first course of maintenance (LE: 4).

3. If CIS (without concomitant papillary tumour) is present at 3 months and persists at 6 months after either re-induction or first course of maintenance (LE: 1b).
4. If HG tumour appears during BCG maintenance therapy*.
BCG-relapsing tumour
Recurrence of G3/HG (WHO 1973/2004) tumour after completion of BCG maintenance, despite an initial response (LE: 3).
BCG-unresponsive tumour
BCG refractory or T1Ta/HG BCG recurrence within 6 months of completion of adequate BCG exposure** or development of CIS within 12 months of completion of adequate BCG exposure (LE: 4).
BCG intolerance
Severe side effects that prevent further BCG instillation before completing treatment.

* *Patients with low-grade recurrence during or after BCG treatment are not considered to be a BCG failure.*

** *Adequate BCG is defined as the completion of at least 5 of 6 doses of an initial induction course plus at least 2 out of 6 doses of a second induction course or 2 out of 3 doses of maintenance therapy.*

Guidelines for the treatment of BCG failure

Category	Treatment options	Strength rating
BCG-unresponsive	1. Radical cystectomy (RC).	Strong
	2. Enrollment in clinical trials assessing new treatment strategies.	Weak
	3. Bladder-preserving strategies in patients unsuitable or refusing RC.	Weak

Late BCG-relapsing: T1Ta/HG recurrence > 6 months or CIS > 12 months of last BCG exposure	1. Radical cystectomy or repeat BCG course according to individual situation.	Strong
	2. Bladder-preserving strategies.	Weak
LG recurrence after BCG for primary intermediate-risk tumour	1. Repeat BCG or intravesical chemotherapy.	Weak
	2. Radical cystectomy.	Weak

General recommendations for adjuvant therapy in TaT1 tumours and for therapy of CIS	**Strength rating**
Counsel smokers with confirmed NMIBC to stop smoking.	Strong
The type of further therapy after transurethral resection of the bladder should be based on the risk groups shown in Table 3.	Strong
In patients with tumours presumed to be at low risk and in those presumed to be at intermediate risk with previous low recurrence rate (≤ one recurrence per year) and expected EORTC recurrence score < 5, one immediate chemotherapy instillation is recommended.	Strong

In patients with intermediate-risk tumours (with or without immediate instillation), one-year full-dose bacillus Calmette-Guérin (BCG) treatment (induction plus 3-weekly instillations at 3, 6 and 12 months), or instillations of chemotherapy (the optimal schedule is not known) for a maximum of one year is recommended. The final choice should reflect the individual patient's risk of recurrence and progression as well as the efficacy and side effects of each treatment modality.	Strong
In patients with high-risk tumours, full-dose intravesical BCG for one to three years (induction plus 3-weekly instillations at 3, 6, 12, 18, 24, 30 and 36 months), is indicated. The additional beneficial effect of the second and third years of maintenance should be weighed against its added costs, side-effects and problems connected with BCG shortages.	Strong
Offer transurethral resection of the prostate, followed by intravesical instillation of BCG to patients with CIS in the epithelial lining of the prostatic urethra.	Weak
Discuss immediate radical cystectomy (RC) with patients at highest risk of tumour progression.	Strong
Offer a RC to patients with BCG unresponsive tumours.	Strong

Offer patients with BCG-unresponsive tumours, who are not candidates for RC due to comorbidities, preservation strategies (intravesical chemotherapy, chemotherapy and microwave-induced hyperthermia, electromotive administration of chemotherapy, intravesical- or systemic immunotherapy; preferentially in clinical trials).	Weak
Recommendations – technical aspects for treatment	
Intravesical chemotherapy	
If given, administer a single immediate instillation of chemotherapy within 24 hours after TURB.	Weak
Omit a single immediate instillation of chemotherapy in any case of overt or suspected bladder perforation or bleeding requiring bladder irrigation.	Strong
Give clear instructions to the nursing staff to control the free flow of the bladder catheter at the end of the immediate instillation.	Strong
The optimal schedule and duration of further intravesical chemotherapy instillation is not defined; however, it should not exceed one year.	Weak
If intravesical chemotherapy is given, use the drug at its optimal pH and maintain the concentration of the drug by reducing fluid intake before and during instillation.	Strong
The length of individual instillation should be one to two hours.	Weak

BCG intravesical immunotherapy	
Absolute contraindications of BCG intravesical instillation are: • during the first two weeks after TURB; • in patients with visible haematuria; • after traumatic catheterisation; • in patients with symptomatic urinary tract infection.	Strong

Follow-up

As a result of the risk of recurrence and progression, patients with NMIBC need to be followed-up. However, the frequency and duration of cystoscopy and imaging should reflect the individual patient's degree of risk.

Recommendations for follow-up in patients after transurethral resection of the bladder	**Strength rating**
Base follow-up of TaT1 tumours and carcinoma *in situ* (CIS) on regular cystoscopy.	Strong
Patients with low-risk Ta tumours should undergo cystoscopy at three months. If negative, subsequent cystoscopy is advised nine months later, and then yearly for five years.	Weak
Patients with high-risk tumours should undergo cystoscopy and urinary cytology at three months. If negative, subsequent cystoscopy and cytology should be repeated every three months for a period of two years, and every six months thereafter until five years, and then yearly.	Weak

Patients with intermediate-risk Ta tumours should have an in-between (individualised) follow-up scheme using cystoscopy.	Weak
Regular (yearly) upper tract imaging (computed tomography-intravenous urography [CT-IVU] or IVU) is recommended for high-risk tumours.	Weak
Endoscopy under anaesthesia and bladder biopsies should be performed when office cystoscopy shows suspicious findings or if urinary cytology is positive.	Strong
During follow-up in patients with positive cytology and no visible tumour in the bladder, mapping-biopsies or PDD-guided biopsies (if equipment is available) and investigation of extravesical locations (CT urography, prostatic urethra biopsy) are recommended.	Strong
In patients initially diagnosed with TaLG/G1-2 bladder cancer, use ultrasound of the bladder during surveillance in case cystoscopy is not possible or refused by the patient.	Weak

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON UROTHELIAL CARCINOMA OF THE UPPER URINARY TRACT (UTUCs)

(Text update March 2020)

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Epidemiology

Upper urinary tract urothelial carcinomas (UTUCs) are uncommon and account for only 5-10% of urothelial carcinomas (UCs). They have a similar morphology to bladder carcinomas and nearly all UTUCs are urothelial in origin.

Recommendations	Strength rating
Evaluate patient and family history based on the Amsterdam criteria to identify patients with upper tract urothelial carcinoma.	Weak
Evaluate patient exposure to smoking and aristolochic acid.	Weak

Staging and grading systems

The UICC 2017 TNM (Tumour, Node, Metastasis Classification) for renal pelvis and ureter is used for staging (Table 1).

Tumour grade

The 2004/2016 WHO classification distinguishes between non-invasive tumours:

- papillary urothelial neoplasia of low malignant potential;
- low-grade urothelial carcinomas;
- high-grade urothelial carcinomas.

As well as flat lesions (carcinoma *in situ*) and invasive carcinoma.

Upper urinary tract tumours with low malignant potential are very rare.

Table 1: TNM Classification 2017

T - Primary tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Ta	Non-invasive papillary carcinoma
Tis	Carcinoma *in situ*
T1	Tumour invades subepithelial connective tissue
T2	Tumour invades muscularis
T3	(Renal pelvis) Tumour invades beyond muscularis into peripelvic fat or renal parenchyma (Ureter) Tumour invades beyond muscularis into periureteric fat
T4	Tumour invades adjacent organs or through the kidney into perinephric fat
N - Regional lymph nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single lymph node 2 cm or less in greatest dimension

N2	Metastasis in a single lymph node more than 2 cm, or multiple lymph nodes
M - Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis

Diagnosis

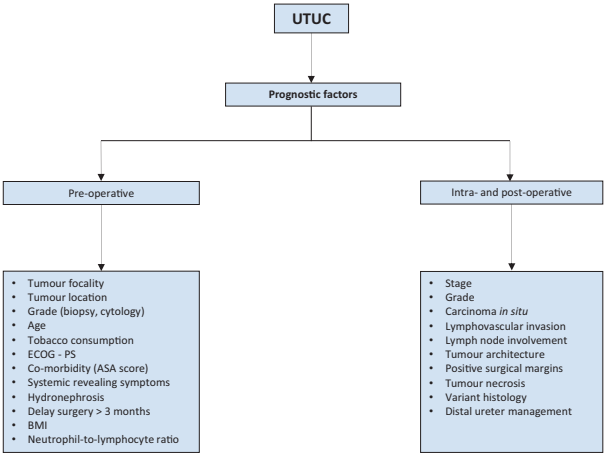
UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. In case conservative management is considered, a pre-operative ureteroscopic assessment is needed.

Recommendations	Strength rating
Perform a urethrocystoscopy to rule out bladder tumour.	Strong
Perform a computed tomography (CT) urography.	Strong
Use diagnostic ureteroscopy and biopsy if imaging and cytology are not sufficient for the diagnosis and/or risk-stratification of the tumour.	Strong
Magnetic resonance urography may be used when CT is contra-indicated.	Weak

Prognosis

Invasive UTUC usually have a very poor prognosis. The main prognostic factors are listed in Figure 1.

Figure 1: UTUC - prognostic factors

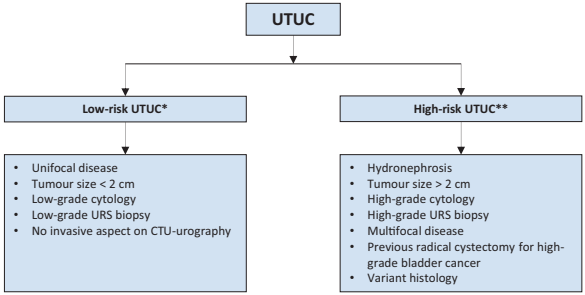


ASA = American Society of Anesthesiologists; BMI = body mass index; ECOG PS = Eastern Cooperative Oncology Group performance status; UTUC = upper urinary tract urothelial carcinoma.

Risk stratification

As tumour stage is difficult to assert clinically in UTUC, it is useful to "risk stratify" UTUC between low- and high-risk tumours to identify those patients who are more likely to benefit from kidney-sparing treatment (Figures 2 and 3).

Figure 2: Risk stratification of non-metastatic UTUC



**All of these factors need to be present.*
*** Any of these factors need to be present.*
CTU = computed tomography urography; URS = ureteroscopy; UTUC = upper urinary tract urothelial carcinoma.

Recommendation	Strength rating
Use pre-operative factors to risk-stratify patients for therapeutic guidance.	Weak

Disease management *(see also Figures 3 & 4)*

Localised disease

Kidney-sparing surgery

Kidney-sparing surgery for low-risk UTUC consists of surgery preserving the upper urinary renal unit and should be discussed in all low-risk cases, irrespective of the status of the contralateral kidney.

Kidney-sparing surgery potentially allows avoiding the morbidity associated with open radical surgery without compromising oncological outcomes and kidney function.

Kidney-sparing surgery can also be considered in select patients with serious renal insufficiency or solitary kidney (i.e. imperative indications).

Recommendations	Strength rating
Offer kidney-sparing management as primary treatment option to patients with low-risk tumours.	Strong
Offer kidney-sparing management to patients with high-risk tumours limited to the distal ureteral.	Weak
Offer kidney-sparing management to patients with solitary kidney and/or impaired renal function, providing that it will not compromise survival. This decision will have to be made on a case-by-case basis with the patient.	Strong

The instillation of bacillus Calmette-Guérin or mitomycin C in the urinary tract by percutaneous nephrostomy, or via a ureteric stent is technically feasible after kidney-sparing management, or for treatment of carcinoma *in situ*. However, the benefits have not been confirmed.

High-risk non-metastatic disease

Radical nephroureterectomy

Open nephroureterectomy (RNU) with bladder cuff excision is the standard treatment for high-risk UTUC, regardless of tumour location.

Adjuvant chemotherapy after RNU reduces the risk of recurrence by more than 50% as compared to surgery alone. In high-risk patients, neoadjuvant chemotherapy has been associated with significant downstaging at surgery and ultimately survival benefit as compared to RNU alone.

Recommendations	Strength rating
Perform radical nephroureterectomy (RNU) in patients with high-risk non-metastatic upper tract urothelial carcinoma (UTUC).	Strong
Perform open RNU in non-organ confined UTUC.	Weak
Remove the bladder cuff in its entirety.	Strong
Perform a template-based lymphadenectomy in patients with muscle-invasive UTUC.	Strong
Offer peri-operative chemotherapy to patients with muscle-invasive UTUC.	Weak
Deliver a post-operative bladder instillation of chemotherapy to lower the intravesical recurrence rate.	Strong

Metastatic disease

Radical nephroureterectomy has no benefit in metastatic (M+) disease, but may be used in palliative care. As UTUCs are urothelial tumours, platinum-based chemotherapy should provide similar results to those in bladder cancer. Currently, insufficient data are available to provide any recommendations. Radiotherapy is no longer relevant nowadays, neither as a sole treatment option, nor as an adjunct to chemotherapy.

Recommendations	Strength rating
Offer radical nephroureterectomy as a palliative treatment to symptomatic patients with resectable locally advanced tumours.	Weak

First-line treatment for cisplatin-eligible patients	
Use cisplatin-containing combination chemotherapy with GC, MVAC, preferably with G-CSF, HD-MVAC with G-CSF or PCG.	Strong
Do not offer carboplatin and non-platinum combination chemotherapy.	Strong
First-line treatment in patients unfit for cisplatin	
Offer checkpoint inhibitors pembrolizumab or atezolizumab depending on PD-L1 status.	Weak
Offer carboplatin combination chemotherapy if PD-L1 is negative.	Strong
Second-line treatment	
Offer checkpoint inhibitor (pembrolizumab) to patients with disease progression during or after platinum-based combination chemotherapy for metastatic disease.	Strong
Offer checkpoint inhibitor (atezolizumab) to patients with disease progression during or after platinum-based combination chemotherapy for metastatic disease.	Strong
Only offer vinflunine to patients for metastatic disease as second-line treatment if immunotherapy or combination chemotherapy is not feasible. Alternatively, offer vinflunine as third- or subsequent-treatment line.	Strong

GC = gemcitabine plus cisplatin; G-CSF = granulocyte colony-stimulating factor; HD-MVAC = high-dose methotrexate, vinblastine, adriamycin plus cisplatin; PD-L1 = programmed death ligand 1; PCG = paclitaxel, cisplatin, gemcitabine.

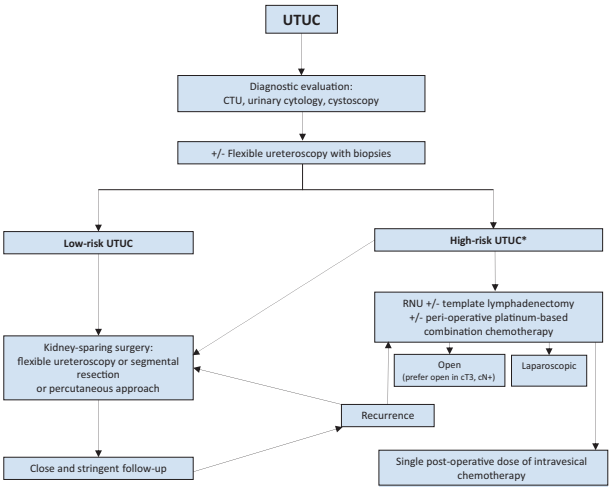
Follow-up after initial treatment

In all cases, there should be strict follow-up after radical management to detect metachronous bladder tumours, as well as invasive tumours, local recurrence and distant metastases. When kidney-sparing surgery is performed, the ipsilateral upper urinary tract requires careful follow-up due to the high risk of recurrence.

Recommendations	Strength rating
After radical nephroureterectomy	
Low-risk tumours	
Perform cystoscopy at three months. If negative, perform subsequent cystoscopy nine months later and then yearly, for five years.	Weak
High-risk tumours	
Perform cystoscopy and urinary cytology at three months. If negative, repeat subsequent cystoscopy and cytology every three months for a period of two years, and every six months thereafter until five years, and then yearly.	Weak
Perform computed tomography (CT) urography and chest CT every six months for two years, and then yearly.	Weak
After kidney-sparing management	
Low-risk tumours	
Perform cystoscopy and CT urography at three and six months, and then yearly for five years.	Weak
Perform ureteroscopy (URS) at three months.	Weak

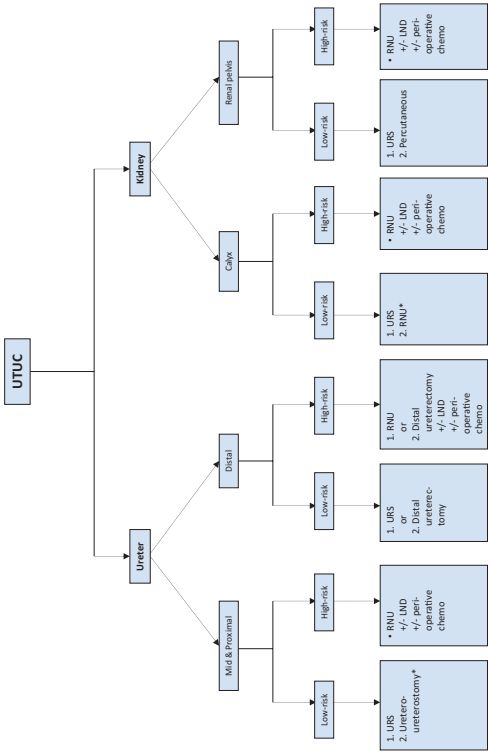
High-risk tumours	
Perform cystoscopy, urinary cytology, CT urography and chest CT at three and six months, and then yearly.	Weak
Perform URS and urinary cytology *in situ* at three and six months.	Weak

Figure 3: Proposed flowchart for the management of UTUC



** In patients with a solitary kidney, consider a more conservative approach.*
CTU = computed tomography urography;
RNU = nephroureterectomy; UTUC = upper urinary tract urothelial carcinoma.

Figure 4: Surgical treatment according to location and risk status



1 = first treatment option; 2 = secondary treatment option.
**In case not amendable to endoscopic management.*
LND = lymph node dissection; RNU = radical nephroureterectomy; URS = ureteroscopy;
UTUC = upper urinary tract urothelial carcinoma.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON MUSCLE-INVASIVE AND METASTATIC BLADDER CANCER

(Limited text update March 2020)

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Introduction

Optimal treatment strategies for Muscle-invasive Bladder Cancer (MIBC) require the involvement of a specialist multidisciplinary team and a model of integrated treatment strategies to avoid fragmentation of patient care.

Staging and grading systems

The 2017 TNM (Tumour, Node, Metastasis Classification) is used for staging (Table 1). For grading, the 1973 and 2004/2016 WHO grading classifications are used.

Table 1: TNM Classification 2017

T - Primary Tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Ta	Non-invasive papillary carcinoma	
Tis	Carcinoma *in situ*: 'flat tumour'	
T1	Tumour invades subepithelial connective tissue	
T2	Tumour invades muscle	
	T2a	Tumour invades superficial muscle (inner half)
	T2b	Tumour invades deep muscle (outer half)
T3	Tumour invades perivesical tissue	
	T3a	Microscopically
	T3b	Microscopically (extravesical mass)
T4	Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall	
	T4a	Tumour invades prostate stroma, seminal vesicles, uterus or vagina
	T4b	Tumour invades pelvic wall or abdominal wall
N – Regional Lymph Nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N2	Metastasis in multiple lymph nodes in the true pelvis (hypogastric, obturator, external iliac, or presacral)	
N3	Metastasis in a common iliac lymph node(s)	

M - Distant Metastasis		
M0	No distant metastasis	
	M1a	Non-regional lymph nodes
	M1b	Other distant metastasis

Pathology of MIBC

Determination of morphological subtypes can be helpful in assessing the prognosis and treatment options of high-grade urothelial carcinomas (UCs) (grade II or grade III) as discussed in these guidelines. The following differentiations are used:

1. urothelial carcinoma (more than 90% of all cases);
2. urothelial carcinomas with partial squamous and/or glandular or trophoblastic differentiation
3. micropapillary or microcystic UC;
4. nested variant (including large nested variant);
5. lymphoepithelioma-like;
6. plasmocytoid, signet ring, diffuse,
7. some UCs with small-cell carcinomas;
9. sarcomatoid carcinomas;
10. poorly differentiated.

Recommendations for the assessment of tumour specimens	Strength rating
Record the depth of invasion (categories pT2a and pT2b, pT3a and pT3b or pT4a and pT4).	Strong
Record margins with special attention paid to the radial margin, prostate, ureter, urethra, peritoneal fat, uterus and vaginal top.	
Record the total number of lymph nodes (LNs), the number of positive LNs and extranodal spread.	
Record lymphatic or blood vessel invasion.	
Record the presence of carcinoma *in situ*.	

Recommendations for the primary assessment of presumably invasive bladder tumours*	Strength rating
Describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities during cystoscopy. Use a bladder diagram.	Strong
Take a biopsy of the prostatic urethra in cases of bladder neck tumour, when bladder carcinoma *in situ* is present or suspected, when there is positive cytology without evidence of tumour in the bladder, or when abnormalities of the prostatic urethra are visible.	Strong
Take a biopsy at the time of the second resection, if no biopsy was taken during the initial procedure.	Strong

In women undergoing subsequent orthotopic neobladder construction, obtain procedural information (including histological evaluation) of the bladder neck and urethral margin, either prior to, or at the time of cystoscopy.	Strong
In the pathology report, specify the grade, depth of tumour invasion, and whether the lamina propria and muscle tissue are present in the specimen.	Strong

* *For general information on the assessment of bladder tumours, see the EAU Guidelines on Non-muscle-invasive Bladder Cancer.*

Recommendations for staging of MIBC	**Strength rating**
In patients with confirmed MIBC, use computed tomography (CT) of the chest, abdomen and pelvis as the optimal form of staging.	Strong
Perform a CT urography for upper tract evaluation and for staging.	Strong
For upper tract evaluation, use diagnostic ureteroscopy and biopsy only in cases where additional information will impact treatment decisions.	Strong
Use magnetic resonance urography when CT urography is contraindicated for reasons related to contrast administration or radiation dose.	Strong
Use CT or magnetic resonance imaging (MRI) for staging locally advanced or metastatic disease in patients in whom radical treatment is considered.	Strong

Use CT to diagnose pulmonary metastases. Computed tomography and MRI are generally equivalent for diagnosing local disease and distant metastases in the abdomen.	Strong

Prognosis

Recommendations for the use of comorbidity scales	Strength rating
Base the decision on bladder-sparing treatment or radical cystectomy in elderly/frail patients with invasive bladder cancer on tumour stage and comorbidity.	Strong
Assess comorbidity by a validated score, such as the Charlson Comorbidity Index. The American Society of Anesthesiologists score should not be used in this setting.	Strong

Disease Management

Recommendations for treatment failure of non-muscle-invasive bladder cancer	Strength rating
Discuss immediate radical treatment (radical cystecomy [RC]) with patients at the highest risk of progression (i.e. high grade, multifocality, carcinoma *in situ*, and tumour size, as outlined in the EAU Guidelines for Non-muscle-invasive Bladder Cancer).	Strong
Offer RC to patients with BCG-unresponsive tumours.	Strong

Offer patients with BCG-unresponsive tumours, who are not candidates for RC due to comorbidities, preservation strategies (intravesical chemotherapy, chemotherapy and microwave-induced hyperthermia, electromotive administration of chemotherapy, intravesical- or systemic immunotherapy; preferably within clinical trials).	Weak

Neoadjuvant therapy

Neoadjuvant cisplatin-containing combination chemotherapy (NAC) improves overall survival (5-8% at five years), irrespective of the type of definitive treatment used. Currently, no tools are available to select patients who have a higher probability of benefitting from NAC. Response after two cycles of treatment is related to outcome. In the future, genetic markers in a personalised medicine setting, might facilitate the selection of patients for NAC and differentiate responders from non-responders.

Checkpoint inhibitors have shown significant benefit in patients with unresectable and metastatic bladder cancer in the salvage setting and in platinum-ineligible PD-L1+ patients as first-line treatment, but data are still immature.

Recommendations for neoadjuvant therapy	**Strength rating**
Offer neoadjuvant chemotherapy (NAC) for T2-T4a, cN0M0 bladder cancer. In this case, always use cisplatin-based combination therapy.	Strong

Do not offer NAC to patients who are ineligible for cisplatin-based combination chemotherapy.	Strong
Only offer neoadjuvant immunotherapy to patients within a clinical trial setting.	Strong

Recommendations for pre- and post-operative radiotherapy in MIBC	Strength rating
Do not offer pre-operative radiotherapy (RT) for operable MIBC since it will only result in down-staging, but will not improve survival.	Strong
Do not offer pre-operative RT when subsequent radical cystectomy with urinary diversion is planned.	Strong

Radical cystectomy and urinary diversion

Contraindications for orthotopic bladder substitution are positive margins at the level of urethral dissection, positive margins anywhere on the bladder specimen (in both sexes), if the primary tumour is located at the bladder neck or in the urethra (in women), or if tumour extensively infiltrates the prostate (in men).

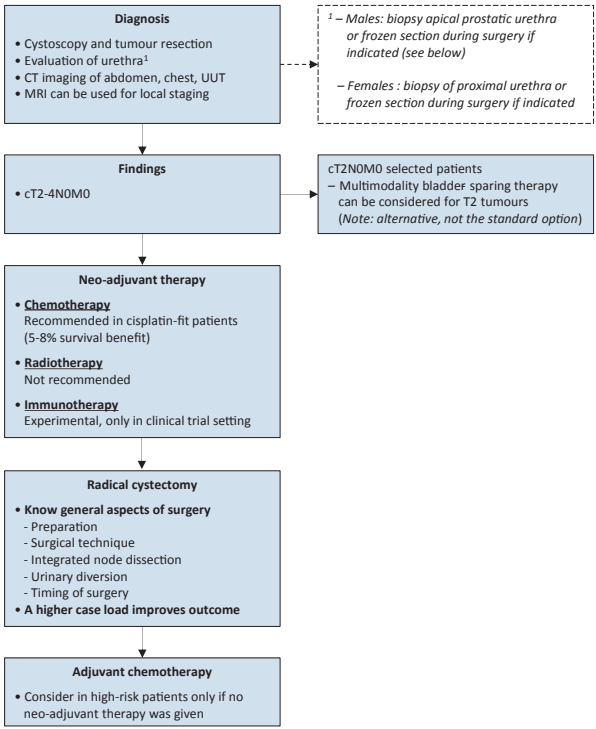
Recommendations for radical cystectomy and urinary diversion	Strength rating
Do not delay radical cystectomy (RC) for > 3 months as it increases the risk of progression and cancer-specific mortality.	Strong
Perform at least 10, and preferably > 20, RCs per hospital/per year.	Strong

Before RC, fully inform the patient about the benefits and potential risks of all possible alternatives. The final decision should be based on a balanced discussion between the patient and the surgeon.	Strong
Do not offer an orthotopic bladder substitute diversion to patients who have a tumour in the urethra or at the level of urethral dissection.	Strong
Do not offer sexual-preserving radical cystectomy to men as standard therapy for MIBC.	Strong
Offer sexual-preserving techniques to men motivated to preserve their sexual function since the majority will benefit.	Strong
Select men for sexual-preserving techniques based on: • organ-confined disease; • absence of any kind of tumour at the level of the prostate, prostatic urethra or bladder neck.	Strong
Do not offer pelvic organ-preserving radical cystectomy to women as standard therapy for MIBC.	Strong
Offer sexual-preserving techniques to women motivated to preserve their sexual function since the majority will benefit.	Weak
Select women for sexual-preserving techniques based on: • organ-confined disease; • absence of tumour in bladder neck or urethra.	Strong

Pre-operative bowel preparation is not mandatory. “Fast track” measurements may reduce the time to bowel recovery.	Strong
Offer pharmacological prophylaxis, such as low molecular weight heparin to RC patients, starting the first day post-surgery, for a period of 4 weeks.	Strong
Offer RC in T2-T4a, N0M0, and high-risk non-muscle-invasive bladder cancer.	Strong
Perform a lymph node dissection as an integral part of RC.	Strong
Do not preserve the urethra if margins are positive.	Strong

Recommendations for laparoscopic/ robotic-assisted laparoscopic cystectomy	**Strength rating**
Inform the patient of the advantages and disadvantages of open radical cystectomy (ORC) and robot-assisted radical cystectomy (RARC) to allow selection of the proper procedure.	Strong
Select experienced centres, not specific techniques, both for RARC and ORC.	Strong

Figure 1: Flow chart for the management of T2-T4a N0M0 urothelial bladder cancer



CT = computed tomography; MRI = magnetic resonance imaging; UUT = upper urinary tract.

Bladder-sparing treatments for localised disease

Transurethral resection of bladder tumour

Transurethral resection of bladder tumour alone is only possible as a therapeutic option if tumour growth is limited to the superficial muscle layer and if restaging biopsies are negative for residual tumour.

External beam radiotherapy

External beam radiotherapy alone should only be considered as a therapeutic option when the patient is unfit for cystectomy or a multimodality bladder-preserving approach.

Radiotherapy can also be used to stop bleeding from the tumour when local control cannot be achieved by transurethral manipulation due to extensive local tumour growth.

Chemotherapy and best supportive care

Complete and partial local responses have been reported with cisplatin-based chemotherapy as primary therapy for locally advanced tumours in highly selected patients.

Multimodality treatment

In a highly selected patient population, long-term survival rates of multimodality treatment are comparable to those of early cystectomy. Delaying surgery can compromise survival rates.

Recommendations for bladder-sparing treatments for localised disease	Strength rating
Do not offer transurethral resection of bladder tumour alone as a curative treatment option as most patients will not benefit.	Strong
Do not offer radiotherapy alone as primary therapy for localised bladder cancer.	Strong
Do not offer chemotherapy alone as primary therapy for localised bladder cancer.	Strong
Offer surgical intervention or multi-modality treatments (MMT) as primary curative therapeutic approaches since they are more effective than radiotherapy alone.	Strong
Offer MMT as an alternative to selected, well-informed and compliant patients, especially for whom radical cystectomy is not an option.	Strong

Surgically non-curable tumours

Palliative radical cystectomy for metastatic disease

Primary radical cystectomy (RC) in T4b bladder cancer is not a curative option. If there are symptoms, RC may be a therapeutic/palliative option. Intestinal or non-intestinal forms of urinary diversion can be used, with or without palliative cystectomy.

Recommendations	Strength rating
Offer radical cystectomy as a palliative treatment to patients with inoperable locally advanced tumours (T4b).	Weak
Offer palliative cystectomy to patients with symptoms.	Weak

Adjuvant chemotherapy

Recommendation	Strength rating
Offer adjuvant cisplatin-based combination chemotherapy to patients with pT3/4 and/or pN+ disease if no neoadjuvant chemotherapy has been given.	Strong
Only offer immunotherapy with a check-point inhibitor in a clinical trial setting.	Strong

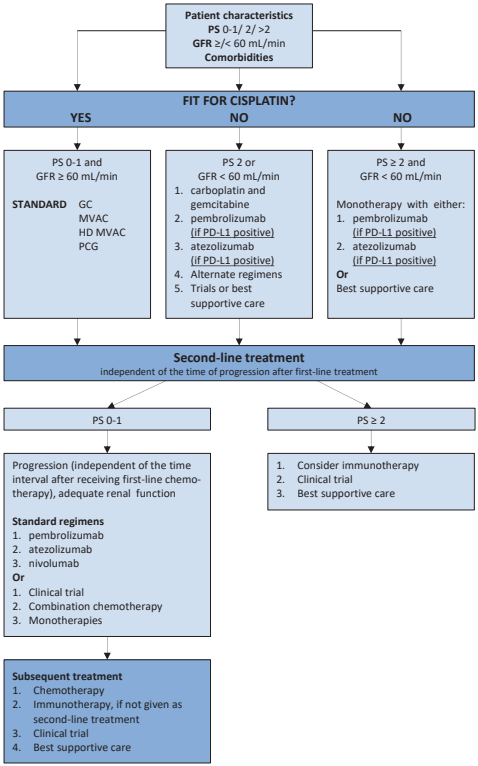
Metastatic disease

Recommendations	Strength rating
First-line treatment for cisplatin-eligible patients	
Use cisplatin-containing combination chemotherapy with GC, MVAC, preferably with G-CSF, HD-MVAC with G-CSF or PCG.	Strong
Do not offer carboplatin and non-platinum combination chemotherapy.	Strong
First-line treatment in patients ineligible (unfit) for cisplatin	
Offer checkpoint inhibitors pembrolizumab or atezolizumab to PD-L1-positive patients.	Strong

Offer carboplatin combination chemotherapy if PD-L1 is negative.	Strong
Second-line treatment	
Offer checkpoint inhibitor pembrolizumab to patients progressing during, or after, platinum-based combination chemo-therapy for metastatic disease. Alternatively, offer treatment within a clinical trial setting.	Strong
Offer zoledronic acid or denosumab for supportive treatment in case of bone metastases.	Weak
Only offer vinflunine to patients for metastatic disease as subsequent-line treatment if immunotherapy, or combination chemotherapy, or FGFR3-inhibitor therapy, or inclusion in a clinical trial is not feasible.	Weak

GC = gemcitabine plus cisplatin; G-CSF = granulocyte colony-stimulating factor; FGFR = fibroblast growth factor receptor; HD-MVAC = high-dose methotrexate, vinblastine, adriamycin plus cisplatin; PCG = paclitaxel, cisplatin, gemcitabine.

Figure 2: Flow chart for the management of metastatic urothelial cancer



GC = gemcitabine plus cisplatin; GFR = glomerular filtration rate; HD MVAC = high-dose methotrexate, vinblastine, adriamycin plus cisplatin; MVAC = methotrexate, vinblastine, adriamycin plus cisplatin; PCG = paclitaxel, cisplatin, gemcitabine; PS = performance status.

Health-related quality-of-life (HRQoL)

Important determinants of (subjective) quality of life are a patient's personality, coping style and social support.

Recommendation	Strength rating
Use validated questionnaires to assess HRQoL in patients with MIBC.	Strong
Offer a continent urinary diversion unless a patient's comorbidities, tumour variables and coping abilities present clear contraindications.	Strong
Pre-operative patient information, patient selection, surgical techniques, and careful post-operative follow-up are the cornerstones for achieving good long-term results.	Strong
Provide clear and exhaustive information on all potential benefits and side-effects, allowing patients to make informed decisions. Encourage patients to actively participate in the decision-making process.	Strong

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EAU GUIDELINES ON PRIMARY URETHRAL CARCINOMA

(Limited text update March 2020)

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Epidemiology

Primary Urethral Carcinoma is a rare cancer, accounting for < 1% of all genitourinary malignancies. The age-standardised ratio is 1.1 per million inhabitants (1.6/million in men and 0.6/million in women, with a male to female ratio of 2.9:1).

Aetiology

Predisposing factors include urethral strictures, chronic irritation after intermittent catheterisation/urethroplasty, external beam irradiation therapy, radioactive seed implantation, chronic urethral inflammation following sexually transmitted diseases (especially human papilloma virus) and lichen sclerosus.

Staging and Grading systems

The 2017 TNM classification (8th edition) is used for the staging of urethral carcinoma. Of note, a separate staging system exists for urothelial carcinoma (UC) of the prostatic urethra.

T - Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Urethra (male and female)	
Ta	Non-invasive papillary, polypoid, or verrucous carcinoma
Tis	Carcinoma *in situ*
T1	Tumour invades subepithelial connective tissue
T2	Tumour invades any of the following: corpus spongiosum, prostate, periurethral muscle
T3	Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina, bladder neck (extraprostatic extension)
T4	Tumour invades other adjacent organs (invasion of the bladder)
Urothelial (transitional cell) carcinoma of the prostate	
Tis pu	Carcinoma *in situ*, involvement of prostatic urethra
Tis pd	Carcinoma *in situ*, involvement of prostatic ducts
T1	Tumour invades subepithelial connective tissue (for tumours involving prostatic urethra only)
T2	Tumour invades any of the following: prostatic stroma, corpus sponsiosum, periurethral muscle
T3	Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule, bladder neck (extraprostatic extension)
T4	Tumour invades other adjacent organs (invasion of the bladder or rectum)
N - Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single lymph node
N2	Metastasis in multiple lymph nodes

M - Distant Metastasis	
M0	No distant metastasis
M1	Distant metastasis

Histopathology

Urothelial carcinoma of the urethra is the predominant histological type in men with primary urethral carcinoma followed by squamous cell carcinoma and adenocarcinoma.

In women, recent studies report higher rates of adenocarcinoma rather than UC. Specimen handling should follow the general rules as published by the International Collaboration on Cancer Reporting.

Recommendation for staging and grading	LE	Strength rating
Use the 2017 TNM classification and 2004/2016 WHO grading systems for pathological staging and grading of primary urethral carcinoma.	3	Strong

Diagnosis

Diagnosis of primary urethral carcinoma is based on clinical examination, urine cytology, urethroscopy with biopsy and cross-sectional imaging for the assessment of the primary tumour, lymph nodes (LNs) and distant organs. Patients with clinically enlarged inguinal or pelvic LNs often exhibit pathological LN metastasis.

Recommendations	LE	Strength rating
Use urethrocystoscopy with biopsy and urinary cytology to diagnose urethral carcinoma.	3	Strong
Assess the presence of distant metastases by computed tomography of the thorax and abdomen/pelvis.	3	Strong
Use pelvic magnetic resonance imaging to assess the local extent of urethral tumour and regional lymph node enlargement.	3	Strong

Prognosis

The majority of patients are diagnosed late, with local symptoms due to advanced disease and the prognosis is poor.

Risk factors for survival include age, race, tumour stage, grade, nodal stage, presence of distant metastasis, histological type, tumour size, tumour location, concomitant bladder cancer and the type and modality of treatment.

Disease management

Localised disease in males

Distal urethral tumours exhibit significantly improved survival rates compared with proximal tumours. Therefore, optimising treatment of distal urethral carcinoma has become the focus of clinicians to improve functional outcome and quality of life, while preserving oncological safety. Penis-preserving surgery for tumours confined to the corpus spongiosum (stage ≤ T2) using various reconstructive techniques has been investigated. In distal urethral tumours performing a partial urethrectomy with a minimal safety margin does not increase the risk of local recurrence when complete circumferential assessment of the margins shows no evidence of disease.

Recommendations	LE	Strength rating
Offer distal urethrectomy as an alternative to penile amputation in localised distal urethral tumours, if surgical margins are negative.	3	Weak
Ensure complete circumferential assessment of the proximal urethral margin if penis-preserving surgery is intended.	3	Strong

Localised disease in females

In women with distal tumours, urethra-sparing surgery and local radiotherapy (RT) present alternatives to primary urethrectomy but are associated with increased risk of tumour recurrence and local toxicity.

Recommendations	LE	Strength rating
Offer urethra-sparing surgery, as an alternative to primary urethrectomy, to women with distal urethral tumours, if negative surgical margins can be achieved intra-operatively.	3	Weak
Offer local radiotherapy as an alternative to urethral surgery to women with localised urethral tumours, but discuss local toxicity.	3	Weak

Multi-modal therapy in advanced disease in both genders

Multi-modal therapy in primary urethral carcinoma consists of definitive surgery plus chemotherapy with the option of additional RT. Multimodal therapy is often under-utilised in locally advanced disease. It confers an overall survival benefit in primary urethral carcinoma of urothelial origin.

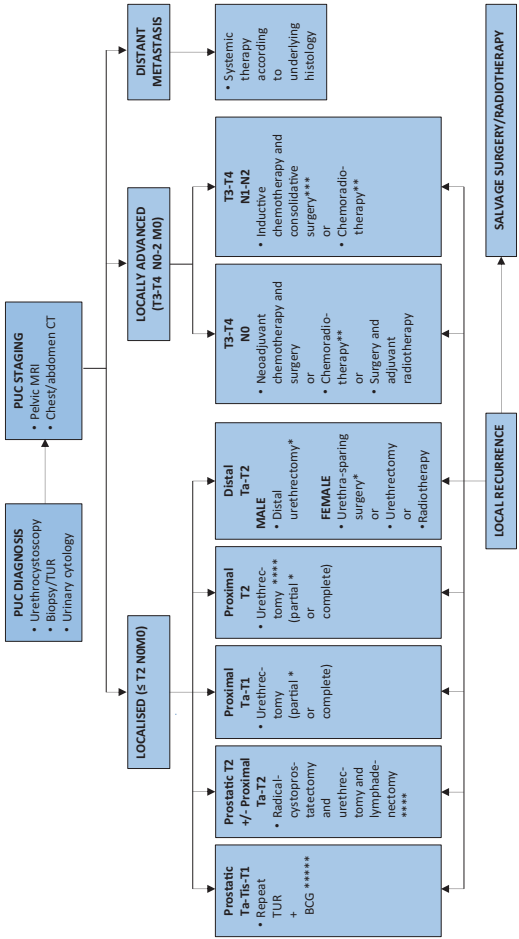
Recommendations	LE	Strength rating
Discuss treatment of patients with locally advanced urethral carcinoma within a multidisciplinary team of urologists, radio-oncologists and oncologists.	3	Strong
In locally advanced urethral carcinoma, use cisplatin-based chemotherapeutic regimens with curative intent prior to surgery.	3	Weak
In locally advanced squamous cell carcinoma of the urethra, offer the combination of curative radiotherapy (RT) with radiosensitising chemo-therapy for definitive treatment and genital preservation.	3	Weak
Offer salvage surgery or RT to patients with urethral recurrence after primary treatment.	3	Weak

Treatment of urothelial carcinoma of the prostate

Local conservative treatment with extensive transurethral resection (TUR) and subsequent bacillus Calmette-Guérin (BCG) instillation is effective in patients with Ta or Tis prostatic urethral carcinoma. Patients undergoing TUR of the prostate for prostatic urethral carcinoma prior to BCG treatment show superior complete response rates compared to those who do not.

Recommendations	LE	Strength rating
Offer a urethra-sparing approach with transurethral resection (TUR) and bacillus Calmette-Guérin (BCG) to patients with non-invasive urethral carcinoma or carcinoma *in situ* of the prostatic urethra and prostatic ducts.	3	Strong
Perform a TUR of the prostate prior to treatment with BCG to improve response to BCG.	3	Weak
In patients not responding to BCG, or in patients with extensive ductal or stromal involvement, perform a cystoprostatectomy with extended pelvic lymphadenectomy.	3	Strong

Figure 1: Management of primary urethral carcinoma



* Ensure complete circumferential assessment if penis-preserving/urethra-sparing surgery or partial urethrectomy is intended.
** Squamous cell carcinoma.
*** Regional lymphadenectomy should be considered in clinically enlarged lymph nodes.
**** Consider neoadjuvant chemotherapy.
***** In extensive or BCG-unresponsive disease: consider (primary) cystoprostatectomy +/- urethrectomy + lymphadenectomy.

BCG = bacillus Calmette-Guérin; CT = computed tomography; MRI = magnetic resonance imaging; PUC = primary urethral carcinoma; TUR = transurethral resection.

Follow-up

Given the low incidence of primary urethral cancer, follow-up has not been systematically investigated. Therefore, it seems reasonable to tailor surveillance regimens according to patients' individual risk factors. In patients undergoing urethra-sparing surgery, it seems prudent to advocate a more extensive follow-up with urinary cytology, urethrocystoscopy and cross-sectional imaging despite the lack of specific data.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU-EANM-ESTRO-ESUR-SIOG GUIDELINES ON PROSTATE CANCER

(Text update March 2020)

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Introduction

Prostate cancer (PCa) is a complex disease, in which disease characteristics, age, comorbidities and individual patient preference will impact treatment choice. All available management options need to be discussed, in full, with the patient.

Epidemiology and Risk Prevention

Prostate cancer is the second most common cancer in males. It is a major health concern, especially in developed countries due to the greater proportion of elderly men in the general population, and the potential risk of over-treatment following early diagnosis. There are three well-established risk factors for PCa: increasing age, ethnic origin, and genetic predisposition. There is currently no high-level evidence that preventative measures may reduce the risk of PCa.

Classification and Staging Systems

The 2017 Tumour Node Metastasis (TNM) classification is used for staging (Table 1).

Table 1: 2017 TNM classification

T - Primary Tumour (stage based on digital rectal examination [DRE] only)		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
T1	Clinically inapparent tumour that is not palpable	
	T1a	Tumour incidental histological finding in 5% or less of tissue resected
	T1b	Tumour incidental histological finding in more than 5% of tissue resected
	T1c	Tumour identified by needle biopsy (e.g. because of elevated PSA)
T2	Tumour that is **palpable** and confined within prostate	
	T2a	Tumour involves one half of one lobe or less
	T2b	Tumour involves more than half of one lobe, but not both lobes
	T2c	Tumour involves both lobes
T3	Tumour extends through the prostatic capsule	
	T3a	Extracapsular extension (unilateral or bilateral)
	T3b	Tumour invades seminal vesicle(s)
T4	Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles, and/or pelvic wall	
N - Regional (pelvic) Lymph Nodes[1]		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	Regional lymph node metastasis	

M - Distant Metastasis[2]	
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

[1] *Metastasis no larger than 0.2 cm can be designated pNmi.*
[2] *When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.*

Pathological staging (pTNM) is based on histopathological tissue assessment and largely parallels the clinical TNM, except for clinical stage T1c and the T2 substages. All histopathologically confirmed organ-confined PCas after radical prostatectomy (RP) are pathological stage T2 and the current UICC no longer recognises pT2 substages.

Table 2: EAU risk groups for biochemical recurrence of localised and locally advanced prostate cancer

Definition			
Low-risk	**Intermediate-risk**	**High-risk**	
PSA < 10 ng/mL and GS < 7 (ISUP grade 1) and cT1-2a	PSA 10-20 ng/mL or GS 7 (ISUP grade 2/3) or cT2b	PSA > 20 ng/mL or GS > 7 (ISUP grade 4/5) or cT2c	any PSA any GS (any ISUP grade) cT3-4 or cN+
Localised			**Locally advanced**

GS = Gleason score; ISUP = International Society for Urological Pathology; PSA = prostate-specific antigen.

The International Society of Urological Pathology (ISUP) World Health Organization (WHO) 2014 grade groups have been adopted which allow patients to better understand the behaviour of their diagnosed prostate carcinoma, while separating GS 7 adenocarcinoma into two prognostically very distinct categories; grade group 2 for GS 7(3+4) and grade group 3 for GS 7(4+3) (see Table 3).

Table 3: ISUP 2014 grade

Gleason score	ISUP grade
2-6	1
7(3+4)	2
7(4+3)	3
8(4+4 or 3+5 or 5+3)	4
9-10	5

Recommendations for screening and early detection	Strength rating
Do not subject men to prostate-specific antigen (PSA) testing without counselling them on the potential risks and benefits.	Strong
Offer an individualised risk-adapted strategy for early detection to a well-informed man and a life-expectancy of at least 10 to 15 years.	Weak
Offer early PSA testing to well-informed men at elevated risk of having PCa: • men > 50 years of age; • men > 45 years of age and a family history of PCa; • men of African descent > 45 years of age; • men carrying *BRCA2* mutations > 40 years of age.	Strong

Offer a risk-adapted strategy (based on initial PSA level), with follow-up intervals of 2 years for those initially at risk: • men with a PSA level of > 1 ng/mL at 40 years of age; • men with a PSA level of > 2 ng/mL at 60 years of age; Postpone follow-up to 8 years in those not at risk.	Weak
Stop early diagnosis of PCa based on life expectancy and performance status; men who have a life-expectancy of < 15 years are unlikely to benefit.	Strong

Diagnostic Evaluation

Clinical diagnosis

Prostate cancer is usually suspected on the basis of DRE and/or PSA levels. Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate biopsy cores, specimens from transurethral resection of the prostate (TURP), or prostatectomy for benign prostatic enlargement.

The decision whether to proceed with further diagnostic or staging work-up is guided by which treatment options are available to the patient, taking the patient's life expectancy into consideration. Diagnostic procedures that will not affect the treatment decision can usually be avoided.

Guidelines for diagnostic imaging	Strength rating
Recommendations for all patients	
Do not use multi-parametric magnetic resonance imaging (mpMRI) as an initial screening tool.	Strong

Adhere to PI-RADS guidelines for mpMRI acquisition and interpretation and evaluate mpMRI results in multidisciplinary meetings with pathological feedback.	Strong
Recommendations in biopsy-naïve patients	
Perform mpMRI before prostate biopsy.	Strong
When mpMRI is positive (i.e. PI-RADS ≥ 3), combine targeted and systematic biopsy.	Strong
When mpMRI is negative (i.e., PI-RADS ≤ 2), and clinical suspicion of PCa is low, omit biopsy based on shared decision making with the patient.	Weak
Recommendations in patients with prior negative biopsy	
Perform mpMRI before prostate biopsy.	Strong
When mpMRI is positive (i.e. PI-RADS ≥ 3), perform targeted biopsy only.	Weak
When mpMRI is negative (i.e., PI-RADS ≤ 2), and clinical suspicion of PCa is high, perform systematic biopsy based on shared decision making with the patient.	Strong

Pathology of prostate biopsies

A biopsy pathology report includes the type of carcinoma and parameters describing its extent (e.g. proportion of positive cores, percentage or mm of carcinoma involvement per core) as well as Gleason score (GS) per biopsy site and global GS. Reporting of a RP specimen includes type of carcinoma, global ISUP grade, pathological stage and surgical margin status

Recommendations for the clinical diagnosis	Strength rating
Perform transrectal prostate needle biopsies under antibiotic protection.	Strong
Use a local anaesthetic by peri-prostatic infiltration for prostate needle biopsies.	Strong

Do not offer non-targeted transition zone sampling at initial biopsies due to low detection rates.	Weak
Ensure that prostate core biopsies from different sites are submitted separately for processing and pathology reporting.	Strong

Guidelines for staging of PCa

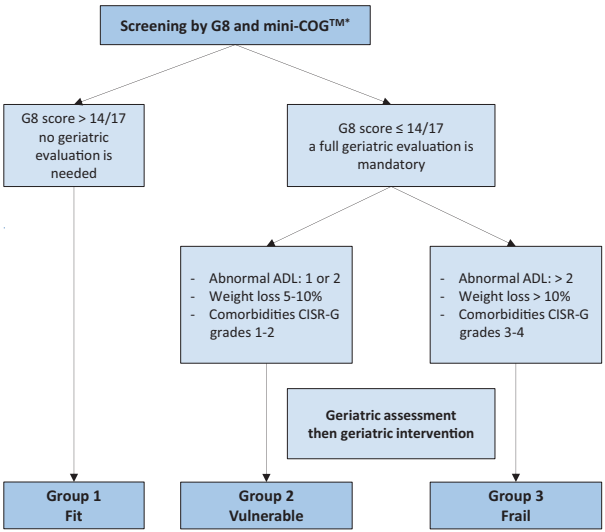
Any risk group staging	**Strength rating**
Use pre-biopsy mpMRI for staging information.	Weak
Low-risk localised PCa	
Do not use additional imaging for staging purposes.	Strong
Intermediate-risk PCa	
In ISUP grade ≥ 3, include at least a cross-sectional abdominopelvic imaging and bone-scan for metastatic screening.	Weak
High-risk localised PCa/locally advanced PCa	
Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.	Strong

Evaluating health status and life expectancy

Recommendations	**Strength rating**
Use individual life expectancy, health status, and comorbidity in PCa management.	Strong
Use the Geriatric-8 and mini-COG tools for health status screening.	Strong
Perform a full specialist geriatric evaluation in patients with a G8 score ≤ 14.	Strong

Consider standard treatment in vulnerable patients with reversible impairments (after resolution of geriatric problems) similar to fit patients, if life expectancy is > 10 years.	Weak
Offer adapted treatment to patients with irreversible impairment.	Weak
Offer symptom-directed therapy alone to frail patients.	Strong

Figure 1: Decision tree for health status screening (men > 70 years)*



Mini-COG™ = Mini-COG™ cognitive test; ADLs = activities of daily living; CIRS-G = Cumulative Illness Rating Score - Geriatrics; CGA = comprehensive geriatric assessment.

*For Mini-COG™, a cut-off point of ≤ 3/5 indicates a need to refer the patient for full evaluation of potential dementia.
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Disease Management

Deferred treatment

Many men with localised PCa will not benefit from definitive treatment and 45% of men with PSA-detected PCa may be candidates for deferred management.

In men with comorbidity and a limited life expectancy, treatment of localised PCa may be deferred to avoid loss of quality of life (QoL).

General guidelines for active treatment of PCa

Recommendations	Strength rating
Inform patients that no active treatment modality has shown superiority over any other active management options or deferred active treatment in terms of overall- and PCa-specific survival for clinically localised disease.	Strong
Offer a watchful waiting policy to asymptomatic patients with a life expectancy < 10 years (based on comorbidities).	Strong
Inform patients that all active treatments have side effects.	Strong
Surgical treatment	
Inform patients that no surgical approach (open-, laparoscopic- or robotic radical prostatectomy) has clearly shown superiority in terms of functional or oncological results.	Weak

When a lymph node dissection (LND) is deemed necessary, perform an extended LND template for optimal staging.	Strong
Do not perform nerve-sparing surgery when there is a risk of ipsilateral extracapsular extension (based on cT stage, ISUP grade, nomogram, multiparametric magnetic resonance imaging).	Weak
Do not offer neoadjuvant androgen deprivation therapy before surgery.	Strong
Radiotherapeutic treatment	
Offer intensity-modulated radiation therapy (IMRT) or volumetric arc external-beam radiotherapy (VMAT) for definitive treatment of PCa by external-beam radiation therapy.	Strong
Offer moderate hypofractionation (HFX) with IMRT/VMAT, including image-guided radiation therapy to the prostate, to carefully selected patients with localised disease.	Strong
Ensure that moderate HFX adheres to radiotherapy protocols from trials with equivalent outcome and toxicity, i.e. 60 Gy/20 fractions in 4 weeks or 70 Gy/28 fractions in 6 weeks.	Strong
Active therapeutic options outside surgery and radiotherapy	
Only offer cryotherapy and high-intensity focused ultrasound within a clinical trial setting or well-designed prospective cohort study.	Strong
Only offer focal therapy within a clinical trial setting or well-designed prospective cohort study.	Strong

Guidelines for first-line treatment of various disease stages

Recommendations		Strength rating
Low-risk disease		
Active surveillance (AS)	Offer AS to patients with a life expectancy > 10 years and low-risk disease.	Strong
	If a patient has had upfront multiparametric magnetic resonance imaging (mpMRI) followed by systematic and targeted biopsies there is no need for confirmatory biopsies.	Weak
	Patients with intraductal and cribiform histology on biopsy should be excluded from AS.	Strong
	If required, perform mpMRI before a confirmatory biopsy.	Strong
	Take both targeted biopsy (of any PI-RADS $\geq$ 3 lesion) and systematic biopsy if confirmatory biopsy performed.	Strong
	Perform serum prostate-specific antigen (PSA) assessment every 6 months.	Strong
	Perform digital rectal examination (DRE) every 12 months.	Strong

	Repeat biopsy should be performed if there is evidence of PSA progression, clinical progression on DRE or radiological progression on mpMRI.	Strong
	During follow-up, if mpMRI is negative (i.e., PI-RADS ≤ 2), and clinical suspicion of PCa progression is low (e.g. low PSA velocity, long PSA doubling time [DT]), omit biopsy based on shared decision making with the patient.	Weak
	Counsel patients about the possibility of needing further treatment in the future.	Strong
Active treatment	Offer surgery and radiotherapy (RT) as alternatives to AS to patients suitable for such treatments and who accept a trade-off between toxicity and prevention of disease progression.	Weak
Pelvic lymph node dissection (PLND)	Do not perform a PLND (estimated risk for pN+ ≤ 5%).	Strong

Radiotherapy	Offer low-dose rate (LDR) brachytherapy to patients with low-risk PCa, without a previous transurethral resection of the prostate (TURP), with a good International Prostatic Symptom Score (IPSS) and a prostate volume < 50 mL.	Strong
	Use intensity-modulated radiation therapy (IMRT) with a total dose of 74-80 Gy or moderate hypofractionation (60 Gy/20 fx in 4 weeks, or 70 Gy/28 fx in 6 weeks), without androgen deprivation therapy (ADT).	Strong
Other options	Only offer whole gland treatment (such as cryotherapy, high-intensity focused ultrasound [HIFU], etc.) or focal treatment within a clinical trial setting or well-designed prospective cohort study.	Strong
Intermediate-risk disease		
Active surveillance	Offer AS to highly selected patients (< 10% Gleason pattern 4) accepting the potential increased risk of further metastases.	Weak
Radical prostatectomy (RP)	Offer RP to patients with intermediate-risk disease and a life expectancy > 10 years.	Strong
	Offer nerve-sparing surgery to patients with a low risk of extracapsular disease.	Strong

Extended pelvic lymph node dissection (ePLND)	Perform an ePLND in intermediate-risk disease if the estimated risk for positive LNs exceeds 5%.	Strong
Radiotherapy	Offer LDR brachytherapy to selected patients; patients without a previous TURP, with a good IPSS and a prostate volume < 50 mL.	Strong
	For EBRT, use a total dose of 76-78 Gy or moderate hypofractionation (60 Gy/20 fx in 4 weeks or 70 Gy/28 fx in 6 weeks), in combination with short-term neoadjuvant plus concomitant ADT (4 to 6 months).	Strong
	In patients not willing to undergo ADT, use an escalated dose of EBRT (76-80 Gy) or a combination with brachytherapy.	Weak
Other therapeutic options	Only offer whole-gland ablative therapy (such as cryotherapy, HIFU, etc.) or focal ablative therapy for intermediate-risk disease within a clinical trial setting or well-designed prospective cohort study.	Strong
	Do not offer ADT monotherapy to intermediate-risk asymptomatic men unable to receive any local treatment.	Weak

High-risk localised disease		
Radical prostatectomy (RP)	Offer RP to selected patients with high-risk localised PCa, as part of a potential multi-modal therapy.	Strong
Extended pelvic lymph node dissection	Perform an ePLND in high-risk PCa.	Strong
	Do not perform a frozen section of nodes during RP to decide whether to proceed with, or abandon, the procedure.	Strong
Radiotherapy	In patients with high-risk localised disease, use ERBT with 76-78 Gy in combination with long-term ADT (2 to 3 years).	Strong
	In patients with high-risk localised disease, use EBRT with brachytherapy boost (either HDR or LDR), in combination with long-term ADT (2 to 3 years).	Weak
Other options	Do not offer either whole gland or focal therapy to high-risk patients.	Strong
	Do not use ADT monotherapy in asymptomatic patients.	Strong
Locally-advanced disease		
Radical prostatectomy	Offer RP to highly selected patients with cT3b-T4 N0 or any cN1 disease only as part of multi-modal therapy.	Strong

Extended pelvic lymph node dissection	Perform an ePLND in high-risk PCa.	Strong
Radiotherapy	In patients with locally advanced cN0 disease, offer RT in combination with long-term ADT.	Strong
	Offer long-term ADT for at least 2 years.	Weak
Other options	Do not offer whole gland treatment or focal treatment to high-risk patients.	Strong
	Only offer ADT monotherapy to those patients unwilling or unable to receive any form of local treatment if they have a PSA-DT < 12 months, and either a PSA > 50 ng/mL, a poorly-differentiated tumour or troublesome local disease-related symptoms.	Strong
	Offer patients with cN1 disease a local treatment (either RP or EBRT) plus long-term ADT.	Weak
Adjuvant treatment after radical prostatectomy		
	Do not prescribe adjuvant ADT in pN0 patients.	Strong
	Offer adjuvant EBRT to the surgical field to highly selected patients.	Strong

	Discuss three management options with patients with pN+ disease after an ePLND, based on nodal involvement characteristics: 1. Offer adjuvant ADT; 2. Offer adjuvant ADT with additional radiotherapy; 3. Offer observation (expectant management) to a patient after eLND and ≤ 2 nodes with microscopic involvement, and a PSA < 0.1 ng/mL and absence of extranodal extension.	Weak
Non-curative or palliative treatments in a first-line setting		
Localised disease		
Watchful waiting (WW)	Offer WW to asymptomatic patients not eligible for local curative treatment and those with a short life expectancy.	Strong
Localised advanced disease		
Watchful waiting	Offer a deferred treatment policy using ADT monotherapy to M0 asymptomatic patients with a PSA-DT > 12 months, a PSA < 50 ng/mL and well-differentiated tumour, who are unwilling or unable to receive any form of local treatment.	Strong

Persistent PSA after RP	
Offer a prostate-specific membrane antigen (PSMA) positron emission tomography (PET) scan to men with a persistent PSA > 0.2 ng/mL to exclude metastatic disease.	Weak
Treat men with no evidence of metastatic disease with salvage radiotherapy and additional hormonal therapy.	Weak

Follow-up after treatment with curative intent

- After RP, PSA should be undetectable (< 0.1 ng/mL). A PSA of > 0.1 ng/mL after RP is a signal of residual prostate tumour tissue. After an undetectable PSA is obtained following RP, a PSA > 0.4 ng/mL and rising, best predicts further metastases.
- After RT, an increase in PSA > nadir + 2 ng/mL best predicts further metastases.
- Palpable nodules and increasing serum PSA are often signs of local recurrence.

Recommendations for follow-up	Strength rating
Routinely follow up asymptomatic patients by obtaining at least a disease-specific history and serum prostate-specific antigen (PSA) measurement. These should be performed at 3, 6 and 12 months after treatment, then every 6 months until 3 years, and then annually.	Strong
At recurrence, only perform imaging to detect local recurrence if the outcome will affect treatment planning.	Strong

Only offer bone scans and other imaging modalities to men with biochemical recurrence or symptoms suggestive of progression without signs of biochemical relapse.	Strong

Guidelines for metastatic disease, second-line and palliative treatments

Recommendations	Strength rating
Metastatic disease in a first-line setting	
Offer immediate systemic treatment with androgen deprivation therapy (ADT) to palliate symptoms and reduce the risk for potentially serious sequelae of advanced disease (spinal cord compression, pathological fractures, ureteral obstruction) to M1 symptomatic patients.	Strong
Offer luteinising hormone-releasing hormone (LHRH) antagonists, especially to patients with an impending spinal cord compression or bladder outlet obstruction.	Weak
Offer surgery and/or local radiotherapy (RT) to any patient with M1 disease and evidence of impending complications such as spinal cord compression or pathological fracture.	Strong
Offer immediate systemic treatment also to M1 patients asymptomatic from their tumour.	Weak

Discuss deferred ADT with well-informed M1 patients asymptomatic from their tumour since it lowers the treatment-related side-effects, provided the patient is closely monitored.	Weak
Offer short-term administration of an older generation androgen receptor (AR) antagonist to M1 patients starting LHRH agonist to reduce the risk of the 'flare-up' phenomenon.	Weak
Do not offer AR antagonists monotherapy to patients with M1 disease.	Strong
Offer ADT combined with chemotherapy (docetaxel) to patients whose first presentation is M1 disease and who are for docetaxel.	Strong
Offer ADT combined with abiraterone acetate plus prednisone or apalutamide or enzalutamide to patients whose first presentation is M1 disease and who are fit enough for the regimen.	Strong
Offer ADT combined with prostate RT to patients whose first presentation is M1 disease and who have low volume of disease by CHAARTED criteria.	Strong
Do not offer ADT combined with any local treatment (RT/surgery) to patients with high volume (CHAARTED criteria) M1 disease outside of clinical trials (except for symptom control).	Strong

Recommendations for imaging in biochemical recurrence	Strength rating
Prostate-specific antigen (PSA) recurrence after radical prostatectomy	
Perform prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform fluciclovine PET/CT or choline PET/CT imaging if the results will influence subsequent treatment decisions.	Weak
PSA recurrence after radiotherapy	
Perform prostate mpMRI to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	Weak
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	Strong

Recommendations for second-line therapy after treatment with curative intent		Strength rating
Biochemical recurrence after treatment with curative intent		
Biochemical recurrence after radical prostatectomy (RP)	Offer PSA monitoring to patients with biochemical recurrence with low-risk features at relapse who may not benefit from intervention.	Weak
	Offer salvage radiotherapy (SRT) to patients with a PSA rise from the undetectable range. Once the decision for SRT has been made, SRT (at least 66 Gy) should be given as soon as possible.	Strong
	Offer hormonal therapy in addition to SRT to men with biochemical recurrence.	Weak
Biochemical recurrence after RT	Treat highly selected patients with localised PCa and a histologically proven local recurrence with salvage RP (SRP).	Weak
	Salvage RP should only be performed in experienced centres.	Weak
	Only offer salvage high intensity focused ultrasound, salvage cryosurgical ablation and salvage brachytherapy to patients with proven local recurrence within a clinical trial setting or well-designed prospective cohort study.	Strong

Systemic salvage treatment	Do not offer ADT to M0 patients with a PSA-DT > 12 months.	Strong
Life-prolonging treatments of castration-resistant disease		
Ensure that testosterone levels are confirmed to be < 50 ng/dL, before diagnosing castration-resistant PCa (CRPC).		Strong
Counsel, manage and treat patients with metastatic CRPC (mCRPC) in a multidisciplinary team.		Strong
Treat patients with mCRPC with life-prolonging agents. Base the choice of first-line treatment on the performance status (PS), symptoms, comorbidities, location and extent of disease, patient preference, and on the previous treatment for hormone-sensitive metastatic PCa (HSPC) (alphabetical order: abiraterone, cabazitaxel, docetaxel, enzalutamide, radium-223, sipuleucel-T).		Strong
Cytotoxic treatments of castration-resistant disease		
Offer patients with mCRPC who are candidates for cytotoxic therapy docetaxel with 75 mg/m^2 every 3 weeks.		Strong
Offer patients with mCRPC and progression following docetaxel chemotherapy further life-prolonging treatment options, which include abiraterone, cabazitaxel, enzalutamide and radium-223.		Strong
Base further treatment decisions of mCRPC on pre-treatment PS, response to previous treatment, symptoms, comorbidities, extent of disease and patient preference.		Strong
Offer cabazitaxel to patients previously treated with docetaxel and progressing within 12 months of treatment with abiraterone or enzalutamide.		Strong

Supportive care of castration-resistant disease	
Offer bone protective agents to patients with mCRPC and skeletal metastases to prevent osseous complications.	Strong
Monitor serum calcium and offer calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonates.	Strong
Treat painful bone metastases early on with palliative measures such as EBRT and adequate use of analgesics.	Strong
In patients with spinal cord compression start immediate high-dose corticosteroids and assess for spinal surgery followed by irradiation. Offer radiation therapy alone if surgery is not appropriate.	Strong
Non-metastatic castrate-resistant disease	
Offer apalutamide, darolutamide or enzalutamide to patients with M0 CRPC and a high risk of developing metastasis (PSA-DT < 10 months) to prolong time to metastases.	Strong

Follow-up after treatment with life-prolonging treatments

Recommendations for follow-up during hormonal treatment	**Strength rating**
Evaluate patients at 3 to 6 months after the initiation of treatment.	Strong
The follow-up strategy must be individualised based on stage of disease, prior symptoms, prognostic factors and the treatment given.	Strong

In patients with stage M0 disease, schedule follow-up at least every 6 months. As a minimum requirement, include a disease-specific history, serum prostate-specific antigen (PSA) determination, as well as liver and renal function in the diagnostic work-up.	Strong
In patients with stage M1 disease, schedule follow-up every 3 to 6 months. As a minimum requirement, include an initial FRAX-score assessment, disease-specific history, digital rectal examination (DRE), serum PSA, haemoglobin, serum creatinine and alkaline phosphatase measurements in the diagnostic work-up. The testosterone level should be checked, especially during the first year. Pay attention to symptoms associated with metabolic syndrome as a side effect of androgen deprivation therapy (ADT). Phospholipid profiles and glucose levels should be checked and treated if abnormal.	Strong
Counsel patients (especially with M1b status) about the clinical signs suggestive of spinal cord compression.	Strong
When disease progression is suspected, adapt/individualise follow up.	Strong
In patients with suspected progression, assess the testosterone level. By definition, castration-resistant PCa requires a testosterone level < 50 ng/dL (< 1 mL/L).	Strong
Do not offer routine imaging to otherwise stable asymptomatic patients.	Strong

Quality of Life

Treating PCa can affect an individual both physically and mentally, as well as his close relations and his work or vocation. These multifaceted issues all have a bearing on his perception of 'quality of life (QoL)'. Prostate cancer care should not be reduced to focusing on the organ in isolation. Taking QoL into consideration relies on understanding the patient's wishes and preferences so that optimal treatment can be discussed. There is clear evidence of unmet needs and ongoing support requirements for some men after diagnosis and treatment for PCa.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON RENAL CELL CARCINOMA

(Limited update March 2020)

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Epidemiology

The use of imaging techniques such as ultrasound (US) and computed tomography (CT) has increased the detection of asymptomatic renal cell carcinoma (RCC). The peak incidence of RCC occurs between 60 and 70 years of age, with a 3 : 2 ratio of men to women. Aetiological factors include lifestyle factors, such as smoking, obesity and hypertension. Having a first-degree relative with RCC is associated with a significantly increased risk of RCC.

Staging system

The current UICC 2017 TNM (Tumour Node Metastasis) classification is recommended for the staging of RCC (Table 1).

Table 1: The 2017 TNM staging classification system

T - Primary Tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Tumour ≤ 7 cm or less in greatest dimension, limited to the kidney
	T1a Tumour ≤ 4 cm or less
	T1b Tumour > 4 cm but ≤ 7 cm
T2	Tumour > 7 cm in greatest dimension, limited to the kidney
	T2a Tumour > 7 cm but ≤ 10 cm
	T2b Tumours > 10 cm, limited to the kidney
T3	Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia
	T3a Tumour grossly extends into the renal vein or its segmental (muscle-containing) branches, or tumour invades perirenal and/or renal sinus fat (peripelvic fat), but not beyond Gerota fascia
	T3b Tumour grossly extends into the vena cava below diaphragm
	T3c Tumour grossly extends into vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)
N - Regional Lymph Nodes	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)

M - Distant metastasis			
M0	No distant metastasis		
M1	Distant metastasis		
TNM stage grouping			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

A help desk for specific questions about TNM classification is available at http://www.uicc.org/tnm.

Clinical Diagnosis

Many renal masses remain asymptomatic until late disease stages. The classic triad of flank pain, visible haematuria, and palpable abdominal mass is rare and correlates with aggressive histology and advanced disease.

Paraneoplastic syndromes are found in approximately 30% of patients with symptomatic RCCs. A few symptomatic patients present with symptoms caused by metastatic disease, such as bone pain or persistent cough.

Imaging

Computed tomography imaging, before and after intravenous contrast, can verify the diagnosis and provide information on the function and morphology of the contralateral kidney and assess tumour extension, including extra-renal spread, venous involvement, and enlargement of lymph nodes (LNs) and adrenals.

Abdominal US and magnetic resonance imaging (MRI) are supplements to CT. Contrast-enhanced US can be helpful in specific cases (e.g., chronic renal failure with a relative contraindication for iodinated or gadolinium-based contrast

media, complex cystic masses, and differential diagnosis of peripheral vascular disorders such as infarction and cortical necrosis).

Magnetic resonance imaging can be used in patients with possible venous involvement, or allergy to intravenous contrast. Chest CT is the most accurate for chest staging and is recommended in the primary work-up of patients with suspected RCC.

In younger patients who are worried about the radiation exposure of frequent CT scans, MRI may be offered as alternative for follow-up imaging.

Biopsy

Percutaneous renal tumour biopsies are used:

- to obtain histology of radiologically indeterminate renal masses;
- to select patients with small renal masses for active surveillance;
- to obtain histology before, or simultaneously with, ablative treatments;
- to select the most suitable form of medical and surgical strategy in the setting of metastatic disease.

In patients with any sign of impaired renal function, a renal scan and total renal function evaluation using estimated glomerular filtration rate should always be undertaken to optimise the treatment decision.

Renal biopsy is not indicated for comorbid and frail patients who can be considered only for conservative management (watchful waiting) regardless of biopsy results.

Recommendations	Strength rating
Use multi-phasic contrast-enhanced computed tomography (CT) of abdomen and chest for the diagnosis and staging of renal tumours.	Strong
Use magnetic resonance imaging to better evaluate venous involvement, reduce radiation or avoid intravenous CT contrast medium.	Weak
Use non-ionising modalities, mainly contrast-enhanced ultrasound, for further characterisation of small renal masses, tumour thrombus and differentiation of unclear renal masses.	Strong
Do not routinely use bone scan and/or positron-emission tomography CT for staging of renal cell carcinoma.	Weak
Perform a renal tumour biopsy before ablative therapy and systemic therapy without previous pathology.	Strong
Perform a percutaneous biopsy in select patients who are considering active surveillance.	Weak
Use a coaxial technique when performing a renal tumour biopsy.	Strong
Do not perform a renal tumour biopsy of cystic renal masses.	Strong
Use a core biopsy technique rather than fine needle aspiration for histological characterisation of solid renal tumours.	Strong

Histological diagnosis

A variety of renal tumours exist, and about 15% are benign. All kidney lesions require examination for malignant behaviour.

Histopathological classification

The new WHO/ISUP classification will replace the Fuhrman nuclear grade system but will need validation.

The three most common RCC subtypes, with genetic and histological differences, are: clear-cell RCC (cc-RCC) (80-90%), papillary RCC (10-15%), and chromophobe RCC (4-5%). The various RCC types have different clinical courses and responses to therapy.

Prognostic factors

In all RCC types, prognosis worsens with stage and histopathological grade. Histological factors include tumour grade, RCC subtype, sarcomatoid features, microvascular invasion, tumour necrosis, and invasion of the perirenal fat and collecting system. Clinical factors include performance status, local symptoms, cachexia, anaemia, platelet count, neutrophil/lymphocyte ratio, C-reactive protein and albumin.

Recommendations	Strength rating
Use the current Tumour, Node, Metastasis classification system.	Strong
Use grading systems and classify renal cell carcinoma type.	Strong
Use prognostic systems in the metastatic setting.	Strong
In localised disease, use integrated prognostic systems or nomograms to assess risk of recurrence.	Strong

Disease Management

Treatment of localised RCC

Localised RCCs are best managed with partial nephrectomy (PN) rather than radical nephrectomy (RN), irrespective of the surgical approach. Partial nephrectomy is unsuitable in some patients with localised RCC due to:

- locally advanced tumour growth;
- unfavourable tumour location;
- significant health deterioration.

If pre-operative imaging and intra-operative findings are normal, routine adrenalectomy is not indicated.

Lymphadenectomy should be restricted to staging because the survival benefit of extended LN dissection is unclear in patients with localised disease. In patients who have RCCs with tumour thrombus and no metastatic spread, prognosis is improved after nephrectomy and complete thrombectomy.

Nephron-sparing surgery versus radical nephrectomy

Based on current available oncological and quality of life outcomes, localised RCC is best managed by nephron-sparing surgery (NSS) rather than RN, irrespective of the surgical approach. Before routine nephrectomy, tumour embolisation has no benefit. In patients unfit for surgery with massive haematuria or flank pain, embolisation can be a beneficial palliative approach.

Recommendations	Strength rating
Offer surgery to achieve cure in localised renal cell cancer.	Strong
Offer partial nephrectomy to patients with T1 tumours.	Strong
Do not perform ipsilateral adrenalectomy if there is no clinical evidence of invasion of the adrenal gland.	Strong
Offer an extended lymph node dissection to patients with adverse clinical features, including a large diameter of the primary tumour.	Weak
Offer embolisation to patients unfit for surgery presenting with massive haematuria or flank pain.	Weak

Radical- and partial nephrectomy techniques

Summary of evidence	LE
Laparoscopic RN has lower morbidity than open nephrectomy.	1b
Short-term oncological outcomes for T1-T2a tumours are equivalent for laparoscopic- and open RN.	2a
Partial nephrectomy can be performed, either by open-, pure laparoscopic- or robot-assisted approach, based on surgeon's expertise and skills.	2b
Partial nephrectomy is associated with a higher percentage of positive surgical margins compared to RN.	3

Recommendations	Strength rating
Offer laparoscopic radical nephrectomy (RN) to patients with T2 tumours and localised masses not treatable by partial nephrectomy (PN).	Strong
Do not perform minimally invasive RN in patients with T1 tumours for whom a PN is feasible by any approach, including open.	Strong
Do not perform minimally invasive surgery if this approach may compromise oncological-, functional- and peri-operative outcomes.	Strong

Alternatives to surgery

Surveillance

Elderly and comorbid patients with incidental small renal masses have a low RCC-specific mortality and significant competing-cause mortality. In selected patients with advanced age and/or comorbidities, active surveillance (AS) is appropriate to initially monitor small renal masses, followed, if required, by treatment for progression. The concept of AS differs from the concept of watchful waiting. Watchful waiting is reserved for patients whose comorbidities contraindicate any subsequent active treatment and who do not require follow-up imaging, unless clinically indicated.

Cryoablation and radiofrequency ablation

Currently there are no data showing oncological benefit of cryoablation or radiofrequency ablation (RFA) techniques over PN.

Recommendation	Strength rating
Offer active surveillance, radiofrequency ablation or cryoablation to frail and/or comorbid patients with small renal masses.	Weak
When radiofrequency ablation, cryoablation and active surveillance are offered, inform patients about the higher risk of local recurrence and/or tumour progression.	Weak

Treatment of locally advanced RCC

Management of clinically positive lymph nodes (cN+)

In the presence of clinically positive LNs (cN+), LND is always justified but the extent of LND is still controversial.

Low level data suggest that tumour thrombus in the setting of non-metastatic disease should be excised. Adjunctive procedures such as tumour embolisation or inferior vena cava filter do not appear to offer any benefits in the treatment of tumour thrombus.

In patients unfit for surgery, or with non-resectable disease, embolisation can control symptoms, including visible haematuria or flank pain. At present there is no evidence for the use of adjuvant therapy following surgery.

Treatment of advanced/metastatic RCC

Management of RCC with venous tumour thrombus

Recommendations	Strength rating
In patients with clinically enlarged lymph nodes (LNs), perform LN dissection for staging purposes or local control.	Weak
Remove the renal tumour and thrombus in case of venous involvement in non-metastatic disease.	Strong

Cytoreductive nephrectomy

Tumour nephrectomy is curative only if all tumour deposits are excised. This includes patients with the primary tumour in place and single- or oligometastatic resectable disease. For most patients with metastatic disease, cytoreductive nephrectomy (CN) is palliative and systemic treatments are necessary.

Summary of evidence	LE
Deferred CN with pre-surgical sunitinib in intermediate-risk patients with cc-metastatic RCC (mRCC) shows a survival benefit in secondary endpoint analyses and selects out patients with inherent resistance to systemic therapy.	2b
Sunitinib alone is non-inferior compared to immediate CN followed by sunitinib in patients with MSKCC intermediate and poor risk who require systemic therapy with vascular endothelial growth factor receptor (VEGFR)-tyrosine kinase inhibitor (TKI).	1a
Cytoreductive nephrectomy for patients with simultaneous complete resection of a single metastasis or oligometastases may improve survival and delay systemic therapy.	3
Patients with MSKCC or IMDC poor risk (≥ 4 risk factors) do not benefit from local therapy.	1a

Recommendations	Strength rating
Do not perform cytoreductive nephrectomy (CN) in MSKCC poor-risk patients.	Strong
Do not perform immediate CN in MSKCC intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy with vascular endothelial growth factor receptor (VEGFR)-tyrosine kinase inhibitor (TKI).	Weak
Start systemic therapy without CN in MSKCC intermediate-risk patients who have an asymptomatic synchronous primary tumour and require systemic therapy with VEGFR-TKI.	Weak
Discuss delayed CN in MSKCC intermediate-risk patients under VEGFR-TKI therapy who derive long-term sustained benefit and/or minimal residual metastatic burden.	Weak
Perform immediate CN in patients with good performance who do not require systemic therapy.	Weak
Perform immediate CN in patients with oligometastases when complete local treatment of the metastases can be achieved.	Weak

IMDC = International Metastatic RCC Database Consortium; MSKCC = Memorial Sloan-Kettering Cancer Center.

Local therapy of metastases in metastatic RCC

A systematic review of the local treatment of metastases from RCC in any organ was undertaken. The heterogeneity of the data will only allow for cautious recommendations.

Summary of evidence	LE
All studies included in a Panel systematic review were retrospective, non-randomised comparative studies, resulting in a high risk of bias associated with non-randomisation, attrition, and selective reporting.	3
With the exception of brain and possibly bone metastases, metastasectomy remains by default the only local treatment for most sites.	3
Retrospective comparative studies consistently point towards a benefit of complete metastasectomy in mRCC patients in terms of OS, CSS and delay of systemic therapy.	3
Radiotherapy to bone and brain metastases from RCC can induce significant relief from local symptoms (e.g. pain).	3

Recommendations	Strength rating
To control local symptoms, offer ablative therapy, including metastasectomy, to patients with metastatic disease and favourable disease factors and in whom complete resection is achievable.	Weak
Offer stereotactic radiotherapy for clinically relevant bone- or brain metastases for local control and symptom relief.	Weak

Systemic therapy for advanced/metastatic RCC

Chemotherapy

Recommendation	Strength rating
Do not offer chemotherapy to patients with metastatic renal cell carcinoma.	Strong

Immunotherapy

Interferon-α monotherapy and combined with bevacizumab, has been superceded as standard treatment by targeted therapy of advanced cc-mRCC.

Immune checkpoint inhibition of programmed death receptor (PD-1) and ligand (PD-L1) inhibition have been investigated in mRCC. Randomised data support the use of nivolumab (a PD-1 inhibitor) in VEGF-refractory disease. The combination of two immune checkpoint inhibitors: ipilimumab and nivolumab showed superior survival in intermediate- and poor-risk patients while the combination of pembrolizumab and axitinib showed survival advantage for patients in all risk groups.

Summary of evidence	LE
Interferon-α monotherapy is inferior to VEGF-targeted therapy or mammalian target of rapamycin (mTOR) inhibition in mRCC.	1b
Nivolumab leads to superior OS compared to everolimus in patients failing one or two lines of VEGF-targeted therapy.	1b
The combination of nivolumab and ipilimumab in treatment-naïve patients with cc-mRCC of IMDC intermediate and poor risk demonstrated OS and ORR benefits compared to sunitinib.	1b
The combination of pembrolizumab and axitinib in treatment-naïve patients with cc-mRCC across all IMDC risk groups demonstrated OS and ORR benefits compared to sunitinib.	1b
Currently, PD-L1 expression is not used for patient selection.	2b
Axitinib can be continued if immune-related adverse events results in cessation of axitinib and pembrolizumab. Re-challeange with immunotherapy requires expert support.	4
Patients who do not receive the full 4 doses of ipilimumab due to toxicity should continue on single-agent nivolumab, where safe and feasible. Re-challange with combination therapy requires expert support.	4
Treatment past progression can be justified but requires close scrutiny and the support of an expert multidisciplinary team.	1b

Nivolumab plus ipilimumab and pembrolizumab plus axitinib should be administered in centres with experience of immune combination therapy and appropriate supportive care within the context of a multidisciplinary team.	4
The combination of nivolumab and ipilimumab in the intention-to-treat population of treatment-naive unselected patients with cc-mRCC leads to superior survival compared to sunitinib.	2b
Due to the exploratory nature of PD-L1 tumour expression, the small sample size, the lack of OS data and the premature results in this subpopulation, definitive conclusions cannot be drawn relative to the usefulness of PD-L1 expression.	2b
Nivolumab plus ipilimumab was associated with 15% grade 3-5 toxicity and 1.5% treatment-related deaths.	1b

Recommendations	**Strength rating**
Offer pembrolizumab plus axitinib to treatment-naïve patients with any IMDC-risk clear-cell metastatic renal cell carcinoma (cc-mRCC).	Strong
Offer ipilimumab plus nivolumab to treatment-naïve patients with IMDC intermediate- and poor-risk cc-mRCC.	Strong
Administer nivolumab plus ipilimumab and pembrolizumab plus axitinib in centres with experience of immune combination therapy and appropriate supportive care within the context of a multidisciplinary team.	Weak

Patients who do not receive the full 4 doses of ipilimumab due to toxicity should continue on single-agent nivolumab, where safe and feasible.	Weak
Offer axitinib as subsequent treatment to patients who experience treatment-limiting immune-related adverse events after treatment with the combination of axitinib and pembrolizumab.	Weak
Treatment past progression can be justified but requires close scrutiny and the support of an expert multidisciplinary team.	Weak
Do not re-challange patients who stopped immune checkpoint inhibitors because of toxicity without expert guidance and support from a multidisciplinary team.	Strong
Offer nivolumab after one or two lines of vascular endothelial growth factor-targeted therapy in mRCC.	Strong
Offer sunitinib or pazopanib to treatment-naïve patients with IMDC favourable-, intermediate-, and poor-risk cc-mRCC who cannot receive or tolerate immune checkpoint inhibition.	Strong
Offer cabozantinib to treatment-naïve patients with IMDC intermediate- and poor-risk cc-mRCC who cannot receive or tolerate immune checkpoint inhibition.	Strong*

* *While this is based on a randomised phase II trial, cabozantinib (weak) looks at least as good as sunitinib in this population. This justified the same recommendation under exceptional circumstances.*

IMDC = International Metastatic RCC Database Consortium.

Targeted therapies

At present, several targeting drugs have been approved for the treatment of mRCC.

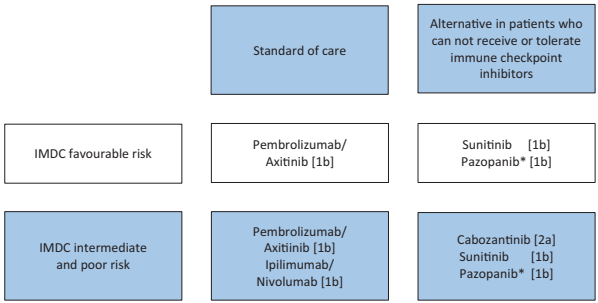
Summary of evidence	LE
Single agent VEGF-targeted therapy has been superseded by immune checkpoint-based combination therapy.	1b
Pazopanib is non-inferior to sunitinib in front-line mRCC.	1b
Cabozantinib in intermediate- and poor-risk treatment-naïve cc-RCC leads to better response rates and PFS but not OS when compared to sunitinib.	2b
Tivozanib has been EMA approved, but the evidence is still considered inferior over existing choices in the front-line setting.	3
Single-agent VEGF-targeted therapies are preferentially recommended after front-line PD-L1-based combinations. Re-challenge with treatments already used should be avoided.	3
Single-agent cabozantinib or nivolumab are superior to everolimus after one or more lines of VEGF-targeted therapy.	1b
Everolimus prolongs PFS after VEGF-targeted therapy when compared to placebo. This is no longer widely recommended before third-line therapy.	1b
Both mTOR inhibitors and VEGF-targeted therapies have limited activity in non-cc-mRCC. There is a non-significant trend for improved oncological outcomes for sunitinib over everolimus.	2a

Lenvatinib in combination with everolimus improved PFS over everolimus alone in VEGF-refractory disease. Its role after immune checkpoint inhibitors is uncertain. There is a lack of robust data on this combination making its recommendation challenging.	2a

Recommendations	**Strength rating**
Offer nivolumab or cabozantinib for immune checkpoint inhibitor-naive vascular endothelial growth factor receptor (VEGFR)-refractory clear-cell metastatic renal cell carcinoma (cc-mRCC).	Strong
Sequencing the agent not used as second-line therapy (nivolumab or cabozantinib) for third-line therapy is recommended.	Weak
Offer VEGF-tyrosine kinase inhibitors as second-line therapy to patients refractory to nivolumab plus ipilimumab or axitinib plus pembrolizumab.	Weak
Offer cabozantinib after VEGF-targeted therapy in cc-mRCC.	Strong
Sequence systemic therapy in treating mRCC.	Strong

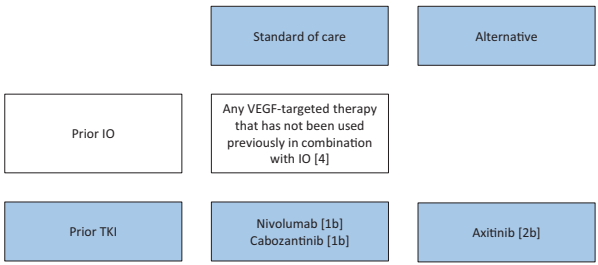
IMDC = International Metastatic RCC Database Consortium.

Figure 1: Updated EAU Guidelines recommendations for the treatment of first-line and following lines in clear-cell metastatic renal cancer.



IMDC = International Metastatic RCC Database Consortium.
**pazopanib for intermediate-risk disease only.*
[1b] = based on one randomised controlled phase III trial.
[2a] = based on one randomised controlled phase II trial.

Figure 2: Guidelines Recommendations for later-line therapy



IO = immunotherapy; TKI = tyrosine kinase inhibitors;
VEGF = vascular endothelial growth factor.

[1b] = based on one randomised controlled phase III trial.
[2b] = subgroup analysis of a randomised controlled phase III trial.
[4] = expert opinion.

Recurrent RCC

Locally recurrent disease can occur either after nephrectomy, PN, or after ablative therapy. After nephron-sparing treatment approaches the recurrence may be intra-renal or regional, e.g. venous tumour thrombi or retroperitoneal LN metastases. Isolated local recurrence in the true renal fossa after RN is rare.

Patients can benefit from a complete surgical resection of local recurrent disease. In cases where complete surgical removal is not feasible due to advanced tumour growth and pain, palliative treatments including radiation treatment can be considered.

Surveillance following surgery for RCC

The aim of surveillance is to detect either local recurrence or metastatic disease while the patient is still surgically curable. Surveillance after treatment for RCC allows the urologist to assess:

- postoperative complications;
- renal function;
- local recurrence;
- recurrence in the contralateral kidney;
- development of metastases.

Depending on the availability of new effective treatments, more intensive follow-up schedules may be required, particularly as there is a higher local recurrence rate after cryotherapy and RFA. At present there is no evidence-based standard for the follow-up of patients with RCC, or for the optimal duration of follow-up. An example of a surveillance

algorithm monitoring patients after treatment for RCC that recognises not only the patient's risk profile but also treatment efficacy is provided in Table 2. For patients with metastatic disease, individualised follow-up is indicated.

Table 2: Proposed surveillance schedule following treatment for RCC, taking into account patient risk profile andtreatment efficacy (expert opinion [LE: 4])

Risk profile	Surveillance				
	6 mo	**1 y**	**2 y**	**3 y**	**> 3 y**
Low	US	CT	US	CT	CT once every 2 years; counsel about recurrence risk of ~10%
Intermediate / High	CT	CT	CT	CT	CT once every 2 years

CT = computed tomography of chest and abdomen, alternatively use magnetic resonance imaging for the abdomen; US = ultrasound of abdomen, kidneys and renal bed.

Summary of evidence and recommendations for surveillance following RN or PN orablative therapies in RCC

Summary of evidence	LE
Surveillance can detect local recurrence or metastatic disease while the patient is still surgically curable.	4
After NSS, there is an increased risk of recurrence for larger (> 7 cm) tumours, or when there is a positive surgical margin.	3
Patients undergoing surveillance have a better OS than patients not undergoing surveillance.	3
Repeated CT scans do not reduce renal function in chronic kidney disease patients.	3

Recommendations	Strength rating
Base follow-up after RCC on the risk of recurrence.	Strong
Intensify follow-up in patients after nephron-sparing surgery for tumours > 7 cm or in patients with a positive surgical margin.	Weak
Base risk stratification on pre-existing classification systems such as the University of California Los Angeles integrated staging system or the SSIGN score.	Strong

SSIGN = (Mayo Clinic) stage, size, grade, and necrosis score.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON TESTICULAR CANCER

(Limited text update March 2020)

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Epidemiology , eatiology and pathology

Compared with other types of cancer, testicular cancer (TC) is relatively rare accounting for approximately 1-1.5% of all cancers in men. At diagnosis, 1-2% are bilateral and the predominant histology is Germ Cell Tumour (GCT). Peak incidence is in the third decade of life for non-seminoma and mixed GCTs, and fourth decade for pure seminoma. Epidemiological risk factors for the development of TC are components of testicular dysgenesis syndrome, which encompasses cryptorchidism, hypospadias, decreased spermatogenesis evidenced by sub- or infertility, familial history of testicular tumours among first-grade relatives, and the presence of a contralateral tumour, or germ cell neoplasia *in situ* (GCNIS).

Histological classification

The recommended pathological classification is the 2016 update of the World Health Organization (WHO).

Staging and Classification systems

Staging systems

The 2016 Tumour, Node, Metastasis (TNM) classification of the International Union Against Cancer (UICC) is recommended to assess the anatomical extent of the disease (Table 2).

Table 1: TNM classification for testicular cancer (adapted from UICC, 2016, 8th edn.)

T - Primary Tumour[1]	
pTX	Primary tumour cannot be assessed (see note 1)
pT0	No evidence of primary tumour (e.g. histological scar in testis)
pTIS	Intratubular germ cell neoplasia (carcinoma *in situ*)
pT1	Tumour limited to testis and epididymis[2] without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis*
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica lbuginea with involvement of tunica vaginalis**
pT3	Tumour invades spermatic cord with or without vascular/lymphatic invasion**
pT4	Tumour invades scrotum with or without vascular/ lymphatic invasion
N - Regional Lymph Nodes - Clinical	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 2 cm in greatest dimension

N2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour		
N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
Pn - Regional Lymph Nodes - Pathological			
pNX	Regional lymph nodes cannot be assessed		
pN0	No regional lymph node metastasis		
pN1	Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension		
pN2	Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence or extranodal extension of tumour		
pN3	Metastasis with a lymph node mass more than 5 cm in greatest dimension		
M - Distant Metastasis			
MX	Distant metastasis cannot be assessed		
M0	No distant metastasis		
M1	Distant metastasis**		
	M1a Non-regional lymph node(s) or lung metastasis		
	M1b Distant metastasis other than non-regional lymph nodes and lung		
S - Serum tumour markers (Pre-chemotherapy)			
SX	Serum marker studies not available or not performed		
S0	Serum marker study levels within normal limits		
	LDH (U/l)	**hCG (mIU/mL)**	**AFP (ng/mL)**
S1	< 1.5 x N and	< 5,000 and	< 1,000
S2	1.5-10 x N or	5,000-50,000 or	1,000-10,000
S3	> 10 x N or	> 50,000 or	> 10,000

N indicates the upper limit of normal for the LDH assay. LDH = lactate dehydrogenase; hCG = human chorionic gonadotrophin; AFP = alpha-fetoprotein.

** AJCC eighth edition subdivides T1 Pure Seminoma by T1a and T1b depending on size no greater than 3 cm or greater than 3 cm in greatest dimension.*

*** AJCC eight edition considers the hilar soft tissue invasion as pT2, while the discontinuous involvement of then spermatic cord is considered as pM1.*

[1] Except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchidectomy; see pT. In other circumstances, TX is used if no radical orchidectomy has been performed.

[2] The current "carcinoma in situ" nomenclature is replaced by GCNIS

The International Germ Cell Cancer Collaborative Group (IGCCCG) defined a prognostic factor-based staging system for metastatic germ cell cancer that includes 'good' and 'intermediate' prognosis seminoma and 'good', 'intermediate', and 'poor' prognosis non-seminomatous germ cell tumour (NSGCT) (Table 2).

The IGCCG for metastatic Testicular Cancer

A prognostic factor-based staging system is widely used for metastatic TC based on identification of clinically independent adverse factors.

Table 2: Prognostic-based staging system for metastatic germ cell cancer (IGCCCG)*

Good-prognosis group	
Non-seminoma *(56% of cases* 5-year PFS 89% 5-year survival 92%	*All of the following criteria:* • Testis/retro-peritoneal primary • No non-pulmonary visceral metastases • AFP < 1,000 ng/mL • hCG < 5,000 IU/L (1,000 ng/mL) • LDH < 1.5 x ULN
Seminoma (90% of cases) 5-year PFS 82% 5-year survival 86%	*All of the following criteria:* • Any primary site • No non-pulmonary visceral metastases • Normal AFP • Any hCG • Any LDH
Intermediate-prognosis group	
Non-seminoma *(28% of cases)* 5-year PFS 75% 5-year survival 80%	*Any of the following criteria:* • Testis/retro-peritoneal primary • No non-pulmonary visceral metastases • AFP 1,000 - 10,000 ng/mL or • hCG 5,000 - 50,000 IU/L or • LDH 1.5 - 10 x ULN

Seminoma (10% of cases) 5-year PFS 67% 5-year survival 72%	*All of the following criteria:* • Any primary site • Non-pulmonary visceral metastases • Normal AFP • Any hCG • Any LDH
Poor-prognosis group	
Non-seminoma (16% of cases) 5-year PFS 41% 5-year survival 48%	*Any of the following criteria:* • Mediastinal primary • Non-pulmonary visceral metastases • AFP > 10,000 ng/mL or • hCG > 50,000 IU/L (10,000 ng/mL) or • LDH > 10 x ULN
Seminoma	No patients classified as poor prognosis

** Pre-chemotherapy serum tumour markers should be assessed immediately prior to the administration of chemotherapy (same day).*

PFS = progression-free survival; AFP = alpha-fetoprotein; hCG = human chorionic gonadotrophin; LDH = lactate dehydrogenase.

Diagnostic evaluation

The diagnosis of TC is based on:

1. ***Physical examination***
   Testicular cancer usually presents as a unilateral testicular scrotal mass detected by the patient, or as an incidental ultrasound (US) finding. Around 1% of patients presenting with gynecomastia have a germ cell or sex cord/gonadal tumour of the testes and 11% present with back and flank

pain. When there is suspicion of TC, physical exploration must include abdominal and supraclavicular exploration.

2. Imaging

a. Ultrasound

High frequency (>10 MHz) testicular US should be used to confirm a testicular tumour even in the presence of clinically evident testicular lesion. Testicular US is also recommended for all men with retroperitoneal or visceral masses and/or without elevated serum human chorionic gonadotropin (hCG) or alpha-fetoprotein (AFP) in the absence of a palpable testicular mass.

b. Computerised tomography

Contrast enhanced computerised tomography (CECT) is the most sensitive means to evaluate the thorax, abdomen and pelvis for TC staging. Contrast enhanced computerised tomography is recommended in all patients for staging before orchidectomy, but may be postponed until histopathological confirmation of malignancy. Brain imaging by CECT is recommended in patients with NSGCT, multiple lung metastases and poor-prognosis IGCCCG risk group (for patients with hCG values >5,000 UI/L), or if clinical symptoms are present.

c. Magnetic resonance imaging

Magnetic resonance imaging (MRI) has similar accuracy to CECT in the detection of retroperitoneal nodal enlargement. However, there are no indications for routine use of MRI for TC staging unless CT is contraindicated because of allergy to iodine contrast media.

MRI has a primary role in the detection of brain metastasis because it is more sensitive than CECT.

d. *Fluorodeoxyglucose- positron emission tomography*
There is no evidence to support the use of fluorodeoxy-glucose-positron emission tomography (FDG-PET) for initial staging and routine follow-up of TC.

e. *Bone scan*
There is no evidence to support the use of bone scan for staging of TC.

3. Serum tumour markers

Serum tumour markers (AFP, β-hCG and LDH,) should be determined before, and after orchidectomy until normalisation. Normal serum markers levels do not exclude the presence of TC, whilst persistence, or increase of elevated serum tumour markers following orchidectomy indicates the likely presence of metastatic disease. Tumour markers should be routinely used for follow-up.

4. Inguinal exploration and initial management

Orchidectomy including division of the spermatic cord at the internal inguinal ring represents the standard of care in patients with TC.

- Testis sparing surgery (TSS) may be attempted in patients with a solitary testis to preserve fertility and hormonal function. It should only be offered together with frozen section examination (FSE).
- Testicular prosthesis should be offered to all patients receiving unilateral or bilateral orchidectomy.
- Routine contralateral biopsy for diagnosis of GCNIS should be discussed with the patient and is recommended in 'high-risk' patients (testicular volume < 12 mL, a history of cryptorchidism and age < 40 years).

5. Pathological examination of the testis

Following orchidectomy, the pathological examination of the testis should include a number of investigations:

1. macroscopic features: side, testis size, maximum tumour size, and macroscopic features of the epididymis, spermatic cord, and tunica vaginalis;
2. sampling: a 1 cm^2 section for every cm^2 of maximum tumour diameter, including normal macroscopic parenchyma (if present), albuginea and epididymis, with selection of suspected areas;
3. at least one proximal and one distal section of spermatic cord plus any suspected area;
4. microscopic features and diagnosis: histological type (specify individual components and estimate amount as percentage) according to WHO 2016;
    - presence or absence of peri-tumoural venous and/or lymphatic invasion;
    - presence or absence of albuginea, tunica vaginalis, rete testis, epididymis or spermatic cord invasion;
    - presence or absence of GCNIS in non-tumour parenchyma;
    - in cases of rete testis invasion, attention should be paid to distinguishing between the pagetoid involvement and stromal invasion;
5. pT category according to TNM 2016;
6. immunohistochemical studies: in seminoma and mixed GCT, AFP and hCG.

6. Screening

There are no high-level evidence studies supporting screening programs. In the presence of clinical risk factors, and a family history of TC, family members and the patient should be informed about the importance of physical self-examination.

7. Impact on fertility and fertility-associated issues

Sperm abnormalities and Leydig cell dysfunction are frequently found in patients with TCs prior to orchidectomy. Furthermore, treatment for TC, including orchidectomy, may have a negative impact on reproductive function. As such, all patients should be offered semen preservation

Recommendations for diagnosis and staging of testicular cancer	**Strength rating**
Discuss sperm banking with all men prior to starting treatment for testicular cancer (TC).	Strong
Perform bilateral testicular ultrasound (US) in all patients with suspicion of TC.	Strong
Perform physical examination including clavicular, cervical, axillary and inguinal lymph nodes, breast and testicles.	Strong
Measure serum determination of tumour markers both before and after orchidectomy taking into account half-life kinetics.	Strong
Perform orchidectomy and pathological examination of the testis to confirm the diagnosis and to define the local extension (pT category). In a life-threatening situation due to extensive metastasis, start chemotherapy before orchidectomy.	Strong
Perform contrast enhanced computerised tomography scan (chest, abdomen and pelvis) in patients with diagnosis of TC. If iodine allergy or other limiting factors, perform abdominal and pelvic magnetic resonance imaging (MRI).	Strong

Perform MRI of the brain if facilities available (or brain CECT if not available) in patients with multiple lung metastases or high β-hCG values or those in the poor-prognosis IGCCCG risk group.	Strong
Do not use positron-emission tomography CT or bone scan for staging.	Strong
Encourage patients with testicular germ cell cancers to perform self-examination and to inform first-degree male relatives of the need for self-examination.	Strong
Discuss testis-sparing surgery with frozen section examination in patients with a high-likelihood of having a benign testicular tumour and which are suitable for enucleation.	Strong
Offer biopsy of the contralateral testis and discuss its consequences with patients at high-risk for contralateral germ cell neoplasia *in situ*.	Strong

Prognosis

Table 3: Pathological risk-factors for occult metastatic disease in Stage I TC

Histological type	Seminoma	Non seminoma
Pathological risk-factors	• Tumour size • Invasion of the rete testis	• Lympho-vascular invasion in peri-tumoural tissue

Disease management

1. Stage I Germ cell Tumours

GCNIS, when diagnosed, can be treated by local radiotheray (18-20 Gy in fractions of 2 Gy) or orchidectomy.

Recommendations for the treatment of stage I seminoma	Strength rating
Fully inform the patient about all available management options, including surveillance or adjuvant chemotherapy after orchidectomy, as well as treatment specific recurrence rates and acute and long-term side effects.	Strong
Offer surveillance as a management option if facilities are available and the patient is compliant.	Strong
Offer one course at area under curve (AUC) 7, if carboplatin chemotherapy is considered.	Strong
Do not perform adjuvant treatment in patients at very low risk (no risk factors).	Strong
Do not routinely perform adjuvant radio-therapy. This option should be reserved for selected patients not suitable for surveillance and with contraindications to chemotherapy.	Strong

Recommendations for the treatment of stage I non-seminomatous germ cell tumour	Strength rating
Inform patients with stage I non-seminomatous germ cell tumour (NSGCT) about all adjuvant treatment options after orchidectomy (surveillance, adjuvant chemotherapy, and retroperitoneal lymph node dissection [RPLND]) including treatment-specific recurrence rates as well as acute and long-term side effects.	Strong
In patients with stage I NSGCT, offer surveillance or risk-adapted treatment based on lymphovascular invasion.	Strong
If patients are not willing to undergo surveillance, offer one course of cisplatin, etoposide, bleomycin (BEP) as an adjuvant treatment alternative since it has proven to be superior to RPLND in terms of recurrence rates.	Strong

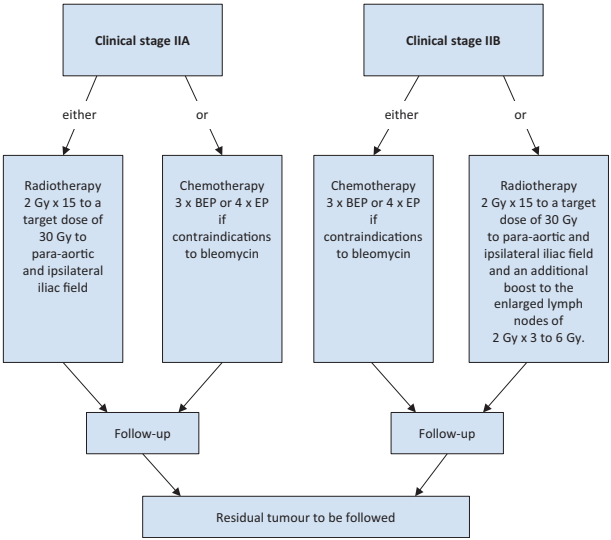
Recommendations for risk-adapted treatment for clinical stage I based on vascular invasion	Strength rating
Stage IA (pT1, no vascular invasion): low risk	
Offer surveillance if the patient is willing and able to comply.	Strong
In low-risk patients not willing (or unsuitable) to undergo surveillance, offer adjuvant chemotherapy with one course of cisplatin, etoposide, bleomycin (BEP).	Strong

Stage IB (pT2-pT4): high risk	
Offer primary chemotherapy with one course of BEP, or surveillance and discuss the advantages and disadvantages.	Strong
Offer surveillance to patients not willing to undergo adjuvant chemotherapy.	Strong
Offer nerve-sparing retroperitoneal lymph node dissection to highly selected patients only; those with contraindication to adjuvant chemotherapy and unwilling to accept surveillance.	Strong
Primary retroperitoneal lymph node dissection should be advised in men with teratoma with somatic-type malignancy.	Weak

2. Metastatic Germ cell Tumours

Clinical S1 (CS1) stage patients with peristently elevated serum tumours markers require repeated imaging including US examination of contralateral testis and abdominal and extrabdominal sites. They should be treated according to IGCCCG prognostic groups.

Figure 1: Treatment options in patients with seminoma clinical stage IIA and B



BEP = cisplatin, etoposide, bleomycin; EP = etoposide and cisplatin.

Recommendations for the treatment of metastatic germ cell tumours	Strength rating
Treat low-volume non-seminomatous germ cell tumour (NSGCT) stage IIA/B with elevated markers like "good- or intermediate-prognosis" advanced NSGCT, with three or four cycles of cisplatin, etoposide, bleomycin (BEP).	Strong

In stage IIA/B NSGCT without marker elevation, exclude marker negative embryonal carcinoma by obtaining histology by either retroperitoneal lymph node dissection or biopsy. If not possible, repeat staging after six weeks of surveillance before making a final decision on further treatment.	Strong
In metastatic NSGCT with an "intermediate prognosis", treat with four cycles of standard BEP.	Strong
In metastatic NSGCT with a "poor prognosis", treat with one cycle of BEP, (or cisplatin, etoposide and ifosfamide [PEI] in case of poor lung function), followed by tumour marker assessment after three weeks. In case of a favourable marker decline, continue BEP (or PEI) up to a total of four cycles. In case of an unfavourable decline, initiate chemotherapy intensification.	Weak
Perform surgical resection of residual masses after chemotherapy in NSGCT in the case of visible residual masses and when serum levels of tumour markers are normal or normalising.	Strong
In Clinical stage IIA seminoma, offer radiotherapy or chemotherapy and inform the patient of potential long-term side effects of both treatment options.	Strong
Offer initial chemotherapy in seminoma stage IIB (BEP x 3 or EP x 4, in good prognosis) as an alternative to radiotherapy.	Strong

Treat seminoma stage IIC and higher, with primary chemotherapy according to the same principles used for NSGCT.	Strong

Relapse after chemotherapy

The treatment of relapsed GCT after chemotherapy is typically salvage chemotherapy. For patients at first relapse with good prognostic features (initial achievement of complete response/partial remission negative markers [CR/PRm] and gonadal primary tumour) four cycles of standard-dose salvage chemotherapy are proposed. For patients with poor prognostic factors (extragonadal primary and/or incomplete response to first-line chemotherapy) and for all patients with subsequent (second or more) relapse, high-dose chemotherapy with autologous stem cell support is recommended.

Follow-up

The primary aim of follow-up in the first five years is the timely diagnosis of recurrent disease in order to be able to treat the patient with curative intent with the least aggressive therapy.

The following factors should be taken into account:

a) Follow-up must be tailored to the individual patient with a schedule acceptable to the patient, the clinician, and the health care system.
b) The interval of follow-up visits and the clinical investigations to be performed at each visit should depend on the risk of relapse, in general, as well as the likely sites of relapse in an individual patient.
c) When possible, an effort should be made to minimise any risks associated with ionising radiation exposure.
d) The increased risk of second malignancy (in the primary site and in other tissues that may have been exposed to the same carcinogens, or in which there is epidemiological evidence of increased risk) should also guide the selection of tests.

Table 4: Recommended minimal follow-up for seminoma stage I on active surveillance or after adjuvant treatment (carboplatin or radiotherapy)[1]

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	2 times	2 times	2 times	Once	Further management according to survivorship care plan
Chest X-ray	-	-	-	-	
Abdominopelvic computed tomography/ magnetic resonance imaging	2 times	2 times	Once at 36 months	Once at 60 months	

Table 5: Recommended minimal follow-up for non-seminoma stage I on active surveillance[1]

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times**	4 times	2 times	1-2 times	Further management according to survivorship care plan
Chest X-ray	1-2 times	2 times	Once, in case of LVI+	At 60*** months if LVI+	
Abdominopelvic computed tomography/magnetic resonance imaging	1-2 times	At 24*** months	Once at 36 months*	Once at 60 months*	

LVI = lymphovascular invasion

[1] Recommendations based upon ESMO Testicular seminoma and non-seminoma consensus meeting outcomes.

** Recommended by 50% of the consensus group members.*

*** In case of high risk (LVI+) a minority of the consensus group members recommended six times.*

****In case of high risk (LVI+) a majority of the consensus group members recommended an additional CT at eighteen months.*

Table 6: Recommended minimal follow up after adjuvant treatment or complete remission for advanced disease (excluded: poor prognosis and no remission[1])

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times	4 times	2 times	2 times	Further management according to survivorship care plan**
Chest X-ray	1-2 times	Once	Once	Once	
Abdominopelvic computed tomography/ magnetic resonance imaging	1-2 times	At 24 months	Once at 36 months	Once at 60 months	
Thorax CT	*	*	*	*	

[1] Recommendations based upon European Society for Medical Oncology (ESMO)Testicular seminoma and non-seminoma consensus meeting outcomes.

* Same time points as abdomino-pelvic CT/MRI in case of pulmonary metastases at diagnosis.

** In case of teratoma in resected residual disease: the patient should remain with the uro-oncologist.

Quality of life and long-term toxicities after cure

Patients diagnosed with TC are usually between 18 and 40 years of age at diagnosis, and life expectancy after cure extends over several decades. Patients should be informed before treatment of common long-term toxicities before any treatment is planned.

During follow-up, patients should be screened and treated for known risk factors such as high blood pressure, hyper-lipidaemia and testosterone deficiency. When follow-up by the clinical expert is discontinued, a written cancer survivorship plan addressing late toxic effects, lifestyle recommendations, recurrence risk, and cancer-specific follow-up might be helpful.

Included among the long-term toxicity and secondary effects of TC treatment are: second malignant neoplasms, leukemia, infections, pulmonary and cardiovascular complications, Raynaud-like phenomena, neuro- nephro- and ototoxiciy, impaired cognitive function, hypogonadism and fatigue as well as quality of life issues.

Testicular Stromal Tumours

Testicular stromal tumours are rare; however, Leydig cell and Sertoli cell tumours are of clinical relevance.

Leydig cell tumours

Approximately 10% of Leydig tumours are malignant presenting the following features:

- large size (> 5 cm);
- older age;
- cytologic atypia and DNA aneuploidy;
- increased mitotic activity (> 3 per 10 high-power field [HPF]) and increased MIB-1 expression;
- necrosis;
- vascular invasion infiltrative margins;
- extension beyond the testicular parenchyma.

The tumour presents as a painless enlarged testis or as an incidental US finding accompanied in, up to 80% of cases, by hormonal disorders. Serum tumour markers are negative and approximately 30% of patients present with gynaecomastia. These tumours are often treated by inguinal orchidectomy because they are misinterpreted as GCTs. In patients with symptoms of gynaecomastia, hormonal disorders, or atypical imaging on US, a partial orchidectomy (+ frozen section) should be considered until final histology is available. In the case of histological signs of malignancy and orchidectomy. Adjuvant RPLND is not justified in CSI disease without high risk features. Retroperitoneal lymph node dissection is an

option in stage IIA to achieve long term cure.

Sertoli cell tumours

Sertoli cell tumours are malignant in 10 - 22% of cases. Morphological signs of malignancy are:

- large size (> 5 cm);
- increased mitotic activity (> 5 per 10 HPF);
- pleomorphic nuclei with nucleoli;
- necrosis and/or vascular invasion.

Sertoli cell tumours present either as an enlarged testis or as incidental US finding. Hormonal disorders are infrequent and serum tumour markers are negative. Ultrasonographically, they generally appear as hypoechoic and cannot be safely distinguished from germ-cell tumour except for the subtype large cell calcifying form which is usually associated with genetic syndromes (Carney's complex, Peutz-Jeghers syndrome). Sertoli cell tumours are often interpreted as germ-cell tumours and an orchidectomy is performed.

Organ-sparing surgery should be considered (with caution), but in the case of histological signs of malignancy, orchidectomy. Adjuvant RPLND is not justified in CSI disease without high risk features. Retroperitoneal lymph node dissection is an option in stage IIA to achieve long term cure.

Conclusions

Most testis tumours are diagnosed at an early stage. Staging is the cornerstone of treatment. Following orchidectomy, excellent cure rates are achieved for those early stages irrespective of the treatment policy adopted, although pattern and relapse rates are closely linked to the treatment modality chosen. In metastatic disease a multidisciplinary therapeutic approach offers an acceptable survival. Follow-up schedules should be tailored to initial staging and treatment.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON PENILE CANCER

(Text update March 2018)

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Introduction and epidemiology

The incidence of penile cancer increases with age, peaking during the sixth decade of life. However, the disease does occur in younger men. There are significant geographical variations within Europe as well as worldwide. Penile cancer is common in regions with a high prevalence of human Papilloma virus (HPV), which may account for the global incidence variation, as the worldwide HPV prevalence varies considerably. There is at present no recommendation for the use of HPV vaccination in boys.

Risk factors

Recognised aetiological and epidemiological risk factors for penile cancer are:

Risk factors	Relevance
Phimosis	Odds ratio 11-16 vs. no phimosis
Chronic penile inflammation (balanoposthitis related to phimosis), lichen sclerosus	Risk
Sporalene and ultraviolet A phototherapy for various dermatological conditions such as psoriasis	Incidence rate ratio 9.51 with > 250 treatments
Smoking	Five-fold increased risk (95% Confidence interval: 2.0-10.1) vs. non-smokers
HPV infection, condylomata acuminata	22.4% in verrucous squamous cell carcinoma 36-66.3% in basaloid-warty
Rural areas, low socio-economic status, unmarried	
Multiple sexual partners, early age of first intercourse	Three to five-fold increased risk of penile cancer

Pathology

Different variants of squamous cell carcinoma (SCC) accounts for more than 95% of cases of malignant penile disease. Table 1 lists premalignant lesions and Table 2 lists the pathological subtypes of penile carcinomas.

Table 1: Premalignant penile lesions (precursor lesions)

Lesions sporadically associated with squamous cell carcinoma (SCC) of the penis: • Bowenoid papulosis of the penis (HPV related) • Lichen sclerosus
Premalignant lesions (up to one-third transform to invasive SCC): • Penile intraepithelial lesions • Giant condylomata (Buschke-Löwenstein) • Bowen's disease • Paget's disease (intradermal ADK)

Table 2: Histological subtypes of penile carcinomas, their frequency and outcome

Subtype	Frequency (% of cases)	Prognosis
Common squamous cell carcinoma (SCC)	48-65	Depends on location, stage and grade
Basaloid carcinoma	4-10	Poor prognosis, frequently early inguinal nodal metastasis
Warty carcinoma	7-10	Good prognosis, metastasis rare
Verrucous carcinoma	3-8	Good prognosis, no metastasis
Papillary carcinoma	5-15	Good prognosis, metastasis rare
Sarcomatoid carcinoma	1-3	Very poor prognosis, early vascular metastasis
Mixed carcinoma	9-10	Heterogeneous group

Pseudohyperplastic carcinoma	< 1	Foreskin, related to lichen sclerosis, good prognosis, metastasis not reported
Carcinoma cuniculatum	< 1	Variant of verrucous carcinoma, good prognosis, metastasis not reported
Pseudoglandular carcinoma	< 1	High-grade carcinoma, early metastasis, poor prognosis
Warty-basaloid carcinoma	9-14	Poor prognosis, high metastatic potential (higher than in warty, lower than in basaloid SCC)
Adenosquamous carcinoma	< 1	Central and peri-meatal glans, high-grade carcinoma, high metastatic potential but low mortality
Mucoepidermoid carcinoma	< 1	Highly aggressive, poor prognosis
Clear cell variant of penile carcinoma	1-2	Exceedingly rare, associated with human papilloma virus, aggressive, early metastasis, poor prognosis, outcome is lesion-dependent, frequent lymphatic metastasis

Biopsy

Doubtful penile lesions should be biopsied and histological verification obtained before local treatment. Histological confirmation is necessary to guide management when:

- there is doubt about the exact nature of the lesion (e.g. carcinoma *in situ*, metastasis or melanoma);
- treatment with topical agents, radiotherapy or laser surgery is planned.

Recommendations for the pathological assessment of tumour specimens	Strength rating
The pathological evaluation of penile carcinoma specimens must include an assessment of the HPV status.	Strong
The pathological evaluation of penile carcinoma specimens must include a diagnosis of the squamous cell carcinoma subtype.	Strong
The pathological evaluation of penile carcinoma surgical specimens must include an assessment of surgical margins including the width of the surgical margin.	Strong

Staging and classification systems

The 2016 UICC, Tumour Node Metastasis (TNM) classification should be used for staging and classification (Table 3). The T1 category is stratified into two prognostically different risk groups. The classification T2 denotes invasion of the corpus spongiosum and T3 invasion of the corpora cavernosa, recognising that these two invasion patterns differ prognostically. The current pN1 group consists of one or two inguinal lymph node metastases, pN2 is more than two uni- or bilateral metastatic nodes, and pN3 any pelvic nodes, uni- or bilateral and any extranodal extension.

Table 3: 2016 TNM clinical and pathological classification of penile cancer

Clinical classification		
T - Primary tumour		
TX	Primary tumour cannot be assessed	
T0	No evidence of primary tumour	
Tis	Carcinoma *in situ*	
Ta	Non-invasive verrucous carcinoma*	
T1	Tumour invades subepithelial connective tissue	
	T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated
	T1b	Tumour invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated
T2	Tumour invades corpus spongiosum with or without invasion of the urethra	
T3	Tumour invades corpus cavernosum with or without invasion of the urethra	
T4	Tumour invades other adjacent structures	
N - Regional lymph nodes		
NX	Regional lymph nodes cannot be assessed	
N0	No palpable or visibly enlarged inguinal lymph nodes	
N1	Palpable mobile unilateral inguinal lymph node	
N2	Palpable mobile multiple or bilateral inguinal lymph nodes	
N3	Fixed inguinal nodal mass *or* pelvic lymphadenopathy, unilateral or bilateral	
M - Distant metastasis		
M0	No distant metastasis	
M1	Distant metastasis	

Pathological classification	
The pT categories correspond to the clinical T categories	
The pN categories are based upon biopsy or surgical excision	
pN - Regional Lymph Nodes	
pNX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in one or two inguinal lymph nodes
pN2	Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3	Metastasis in pelvic lymph node(s), unilateral *or* bilateral or extranodal extension of regional lymph node metastasis
pM - Distant Metastasis	
pM1	Distant metastasis microscopically confirmed
G - Histopathological Grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

**Verrucous carcinoma not associated with destructive invasion.*

Diagnostic evaluation and staging

Penile cancer can be cured in over 80% of all cases if diagnosed early. Once metastatic spread has occurred, it is a life-threatening disease with poor prognosis. Local treatment, although potentially life-saving, can be mutilating and devastating for the patient's psychological well-being.

Physical Examination

Careful palpation of both groins for enlarged inguinal lymph nodes must be part of the initial physical examination of patients with penile cancer.

Imaging

- Ultrasound (US) can give information about infiltration of the corpora.
- Magnetic resonance imaging (MRI) with an artificially induced erection can help to exclude tumour invasion of the corpora cavernosa if preservation of the penis is planned.
- In case of non-palpable inguinal nodes, current imaging techniques are not reliable in detecting micrometastases.
- A pelvic computed tomography (CT) scan can be used to assess pelvic lymph nodeIn case of positive inguinal nodes, CT of the abdomen and pelvis and a chest X-ray are recommended; a thoracic CT will be more sensitive than an X-ray.

Recommendations for the diagnosis and staging of penile cancer	Strength rating
Primary tumour	
Perform a physical examination, record morphology, extent and invasion of penile structures.	Strong
Obtain a penile Doppler ultrasound or MRI with artificial erection in cases with intended organ-sparing surgery.	Weak
Inguinal lymph nodes	
Perform a physical examination of both groins, record the number, laterality and characteristics of inguinal nodes and: • If nodes are not palpable, offer invasive lymph node staging in intermediate- and high-risk patients; • If nodes are palpable, stage with a pelvic computed tomography (CT) or positron emission tomography (PET)/CT.	Strong
Distant metastases	
In N+ patients, obtain an abdominopelvic CT scan and chest X-ray/thoracic CT for systemic staging. Alternatively, stage with a PET/CT scan.	Strong
In patients with systemic disease or with relevant symptoms, obtain a bone scan.	

Disease management

Treatment of the primary penile cancer lesion aims to remove the tumour completely while preserving as much of the penis as possible without compromising radicality.

Recommendations for stage-dependent local treatment of penile carcinoma		
Primary tumour	**Use organ-preserving treatment whenever possible**	**Strength rating**
Tis	Topical treatment with 5-fluorouracil or imiquimod for superficial lesions with or without photodynamic control.	Strong
	Laser ablation with carbon dioxide (CO_2) or neodymium: yttrium-aluminium-garnet (Nd:YAG) laser.	
	Glans resurfacing.	
Ta, T1a (G1, G2)	Wide local excision with circumcision, CO_2 or Nd:YAG laser with circumcision.	Strong
	Laser ablation with CO_2 or Nd:YAG laser.	
	Glans resurfacing.	
	Glansectomy with reconstruction.	
	Radiotherapy for lesions < 4 cm.	
T1b (G3) and T2	Wide local excision plus reconstruction.	Strong
	Glansectomy with circumcision and reconstruction.	
	Radiotherapy for lesions < 4 cm in diameter.	
T3	Partial amputation with reconstruction or radiotherapy for lesions < 4 cm in diameter.	Strong

T3 with invasion of the urethra	Partial penectomy or total penectomy with perineal urethrostomy.	Strong
T4	Neoadjuvant chemotherapy followed by surgery in responders or palliative radiotherapy.	Weak
Local recurrence	Salvage surgery with penis-sparing in small recurrences or partial amputation.	Weak
	Large or high-stage recurrence: partial or total amputation.	

Management of inguinal lymph nodes

The treatment of regional lymph nodes is crucial for the survival of the patient. A surveillance strategy carries considerable risk as regional lymph node recurrence dramatically reduces the chance of long-term survival. Invasive staging by modified inguinal lymphadenectomy or dynamic sentinel node biopsy is recommended for penile cancers pT1G1 and higher.

Recommendations for treatment strategies for nodal metastases		
Regional lymph nodes	**Management of regional lymph nodes is fundamental in the treatment of penile cancer**	**Strength rating**
No palpable inguinal nodes (cN0)	Tis, Ta G1, T1G1: surveillance.	Strong
	> T1G2: invasive lymph node staging by either bilateral modified inguinal lymphadenectomy or dynamic sentinel node biopsy.	Strong
Palpable inguinal nodes (cN1/cN2)	Radical inguinal lymphadenectomy.	Strong
Fixed inguinal lymph nodes (cN3)	Neoadjuvant chemotherapy followed by radical inguinal lymphadenectomy in responders.	Weak
Pelvic lymph nodes	Ipsilateral pelvic lymphadenectomy if two or more inguinal nodes are involved on one side (pN2) or if extracapsular nodal metastasis (pN3) reported.	Strong
Adjuvant chemotherapy	In pN2/pN3 patients after radical lymphadenectomy.	Strong
Radiotherapy	Not recommended for nodal disease except as a palliative option.	Strong

Recommendations for chemotherapy in penile cancer patients	Strength rating
Offer patients with pN2-3 tumours adjuvant chemotherapy after radical lymphadenectomy (three to four cycles of cisplatin, a taxane and 5-fluorouracil or ifosfamide).	Strong
Offer patients with non-resectable or recurrent lymph node metastases neoadjuvant chemotherapy (four cycles of a cisplatin- and taxane-based regimen) followed by radical surgery.	Weak
Offer palliative chemotherapy to patients with systemic disease.	Weak

Follow-up

Follow-up after curative treatment in penile carcinoma, as in any malignant disease, is important for two reasons:

- early detection of recurrence allows for potentially curative treatment;
- the detection and management of treatment-related complications.

Local recurrence does not significantly reduce long-term survival if successfully treated, while inguinal nodal recurrence leads to a drastic reduction in the probability of long-term disease-specific survival.

Recommendations for follow-up in penile cancer					
	Interval of follow-up		Examinations and investigations	Minimum duration of follow-up	Strength rating
	Years one to two	Years three to five			
Recommendations for follow-up of the primary tumour					
Penile-preserving treatment	Three months	Six months	Regular physician or self-examination. Repeat biopsy after topical or laser treatment for penile intraepithelial neoplasia.	Five years	Strong
Amputation	Three months	One year	Regular physician or self-examination.	Five years	Strong
Recommendations for follow-up of the inguinal lymph nodes					
Surveillance	Three months	Six months	Regular physician or self-examination.	Five years	Strong
pN0 at initial treatment	Three months	One year	Regular physician or self-examination. Ultrasound with fine-needle aspiration biopsy optional.	Five years	Strong
pN+ at initial treatment	Three months	Six months	Regular physician or self-examination. Ultrasound with fine-needle aspiration cytology optional, computed tomography/magnetic resonance imaging optional.	Five years	Strong

Quality of life

Overall, nearly 80% of penile cancer patients of all stages can be cured. Partial penectomy has negative consequences for the patients' self-esteem and sexual function. Organ preserving treatment allows for better quality of life and sexual function and should be offered to all patients whenever feasible. Referral to centres with experience is recommended and psychological support is very important for penile cancer patients.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON NON-NEUROGENIC MALE LUTS INCLUDING BENIGN PROSTATIC OBSTRUCTION

(Limited text update March 2020)

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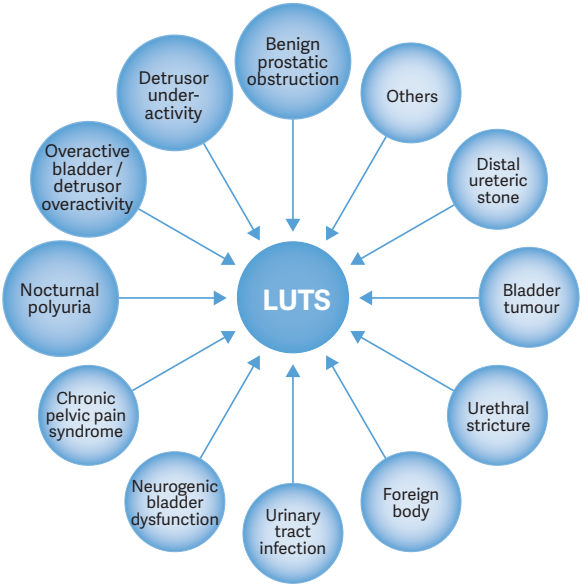
Introduction

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic obstruction (BPO), detrusor overactivity/overactive bladder (OAB), or nocturnal polyuria in men ≥ 40 years. The multifactorial aetiology of LUTS is illustrated in Figure 1.

Figure 1: Causes of male lower urinary tract symptoms (LUTS)



Diagnostic Evaluation

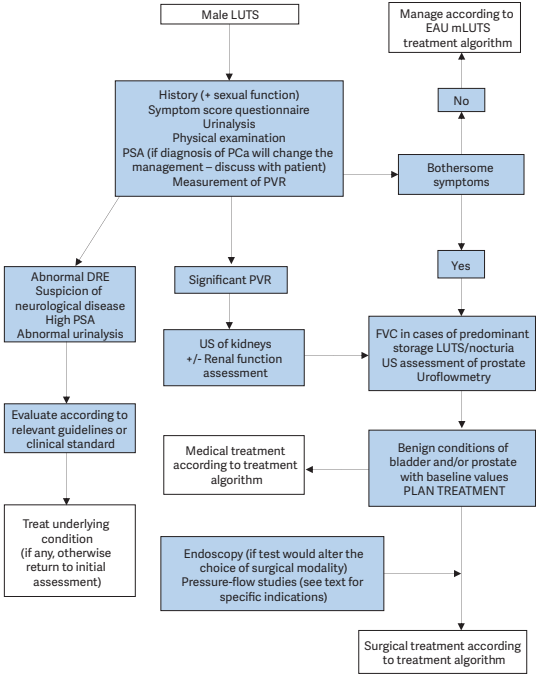
The high prevalence and the underlying multifactorial pathophysiology of male LUTS mean that an accurate assessment of LUTS is critical to provide best evidence-based care. Clinical assessment of LUTS aims to differentially diagnose and to define the clinical profile. A practical algorithm has been developed (Figure 2).

Recommendations for the diagnostic evaluation of male LUTS	Strength rating
Take a complete medical history from men with LUTS.	Strong
Use a validated symptom score questionnaire including bother and quality of life assessment during the assessment of male LUTS and for re-evaluation during and/or after treatment.	Strong
Use a bladder diary to assess male LUTS with a prominent storage component or nocturia.	Strong
Tell the patient to complete a bladder diary for at least three days.	Strong
Perform a physical examination including digital rectal examination in the assessment of male LUTS.	Strong
Urinalysis and prostate-specific antigen (PSA)	
Use urinalysis (by dipstick or urinary sediment) in the assessment of male LUTS.	Strong
Measure PSA if a diagnosis of prostate cancer will change management.	Strong
Measure PSA if it assists in the treatment and/or decision making process.	Strong
Renal function, post-void residual and uroflowmetry	
Assess renal function if renal impairment is suspected based on history and clinical examination, or in the presence of hydronephrosis, or when considering surgical treatment for male LUTS.	Strong
Measure post-void residual in the assessment of male LUTS.	Weak

Perform uroflowmetry in the initial assessment of male LUTS.	Weak
Perform uroflowmetry prior to medical or invasive treatment.	Strong
Imaging and urethrocystoscopy	
Perform ultrasound of the upper urinary tract in men with LUTS.	Weak
Perform imaging of the prostate when considering medical treatment for male LUTS, if it assists in the choice of the appropriate drug.	Weak
Perform imaging of the prostate when considering surgical treatment.	Strong
Perform urethrocystoscopy in men with LUTS prior to minimally invasive/surgical therapies if the findings may change treatment.	Weak
Pressure-flow studies (PFS)	
Perform PFS only in individual patients for specific indications prior to invasive treatment or when evaluation of the underlying pathophysiology of LUTS is warranted.	Weak
Perform PFS in men who have had previous unsuccessful (invasive) treatment for LUTS.	Weak
Perform PFS in men considering invasive treatment who cannot void > 150 mL.	Weak
Perform PFS when considering surgery in men with bothersome predominantly voiding LUTS and Q_{max} > 10 mL/s.	Weak

Perform PFS when considering invasive therapy in men with bothersome, predominantly voiding LUTS with a post-void residual > 300 mL.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged > 80 years.	Weak
Perform PFS when considering invasive treatment in men with bothersome, predominantly voiding LUTS aged < 50 years.	Weak
Non-invasive tests in diagnosing bladder outlet obstruction	
Do not offer non-invasive tests, as an alternative to PFS, for diagnosing bladder outlet obstruction in men.	Strong

Figure 2: Assessment algorithm of LUTS in men aged 40 years or older



DRE = digital-rectal examination; FVC = frequency volume chart; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PSA = prostate specific antigen; PVR = post-void residual; US = ultrasound.
Note: Readers are strongly recommended to read the full text that highlights the current position of each test in detail.

Disease Management

Conservative and pharmacological treatment

Watchful waiting is suitable for mild-to-moderate uncomplicated LUTS. It includes education, re-assurance, lifestyle advice, and periodic monitoring.

Recommendations for the conservative and pharmacological management of male LUTS	Strength rating
Conservative management	
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	Strong
Offer men with LUTS lifestyle advice prior to, or concurrent with, treatment.	Strong
Pharmacological management	
Offer α1-blockers to men with moderate-to-severe LUTS.	Strong
Use 5α-reductase inhibitors (5-ARIs) in men who have moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Counsel patients about the onset of action (three to six months) of 5-ARIs.	Strong
Use muscarinic receptor antagonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Strong
Do not use antimuscarinic overactive bladder medications in men with a post-void residual (PVR) volume > 150 mL.	Weak
Use phosphodiesterase type 5 inhibitors in men with moderate-to-severe LUTS with or without erectile dysfunction.	Strong

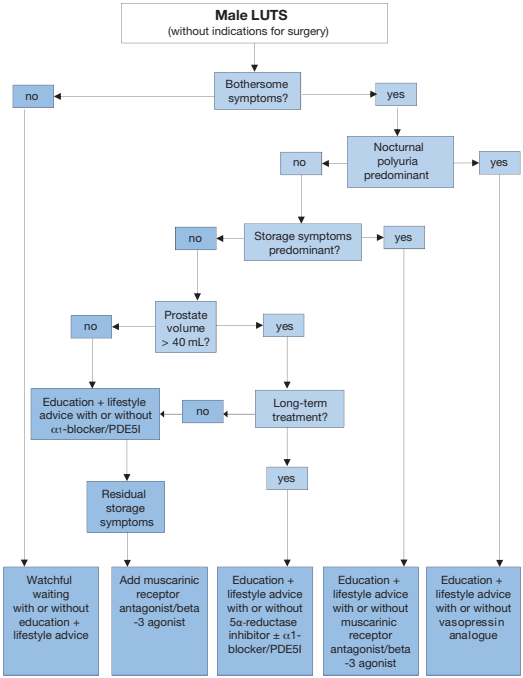
Use beta-3 agonists in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	Weak
Offer combination treatment with an α1-blocker and a 5-ARIs to men with moderate-to-severe LUTS and an increased risk of disease progression (e.g. prostate volume > 40 mL).	Strong
Use combination treatment of a α1-blocker with a muscarinic receptor antagonist in patients with moderate-to-severe LUTS if relief of storage symptoms has been insufficient with monotherapy with either drug.	Strong
Do not prescribe combination treatment of an α1-blocker with a muscarinic receptor antagonist in men with a PVR volume > 150 mL.	Weak

Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without pharmacological treatment. A flowchart illustrating conservative and pharmacological treatment choices according to evidence-based medicine and patients' profiles is provided in Figure 3.

Figure 3: Treatment algorithm of male LUTS using medical and/or conservative treatment options.

Treatment decisions depend on results assessed during initial evaluation. Note that patients' preferences may result in different treatment decisions.



PDE5I = phosphodiesterase type 5 inhibitor.
Note: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

Surgical treatment

Prostate surgery is usually required when patients have experienced recurrent or refractory urinary retention, overflow incontinence, recurrent urinary tract infections, bladder stones or diverticula, treatment-resistant visible haematuria due to BPH/BPE, or dilatation of the upper urinary tract due to BPO, with or without renal insufficiency (absolute operation indications, need for surgery). Surgery is usually needed when patients have had insufficient relief of LUTS or post-void residual after conservative or pharmacological treatments (relative operation indications).

Recommendations for surgical treatment of male LUTS	Strength rating
Offer transurethral incision of the prostate to surgically treat moderate-to-severe LUTS in men with prostate size < 30 mL, without a middle lobe.	Strong
Offer bipolar or monopolar transurethral resection of the prostate (TURP) to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Strong
Offer bipolar transurethral vaporisation of the prostate as an alternative to monopolar TURP to surgically treat moderate-to-severe LUTS in men with prostate size of 30-80 mL.	Weak
Offer open prostatectomy in the absence of endoscopic enucleation to treat moderate-to-severe LUTS in men with prostate size > 80 mL.	Strong

Laser treatments of the prostate	
Offer laser enucleation of the prostate using Ho:YAG laser (HoLEP) to men with moderate-to-severe LUTS as an alternative to TURP or open prostatectomy.	Strong
Offer 80-W 532-nm Potassium-Titanyl-Phosphate (KTP) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer 120-W 532-nm Lithium Borat (LBO) laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer 180-W 532-nm LBO laser vaporisation of the prostate to men with moderate-to-severe LUTS with a prostate volume of 30-80 mL as an alternative to TURP.	Strong
Offer laser vaporisation of the prostate using 80-W KTP, 120 or 180-W LBO for the treatment of patients receiving antiplatelet or anticoagulant therapy with a prostate volume < 80 mL.	Weak
Offer 120-W 980 nm diode laser vaporisation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP.	Weak
Offer 120-W 980 nm or 1,318 nm diode laser enucleation of the prostate to men with moderate-to-severe LUTS as a comparable alternative to TURP or bipolar enucleation.	Weak

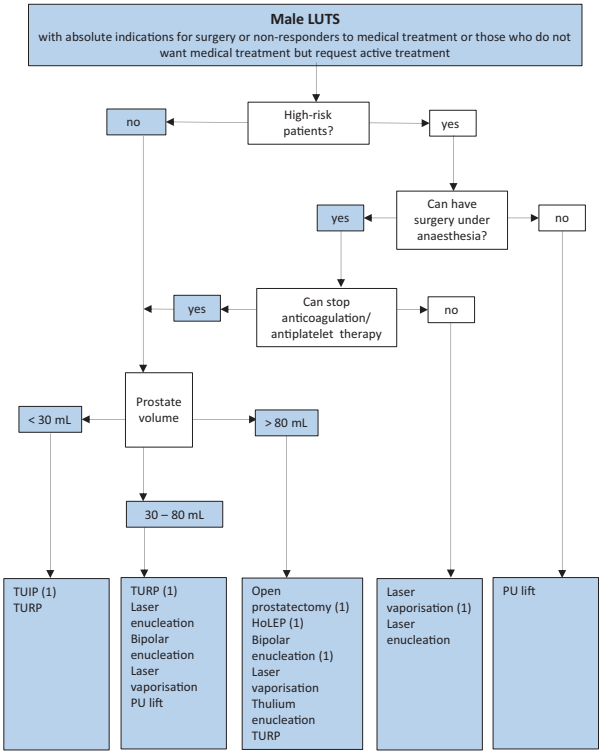
Offer laser enucleation of the prostate using Tm:YAG vapoenucleation (ThuVEP) and Tm:YAG laser assisted anatomical enucleation (ThuLEP) to men with moderate-to-severe LUTS as alternatives to TURP and HoLEP.	Weak
Offer ThuVEP to patients receiving anticoagulant or antiplatelet therapy.	Weak
Offer laser resection of the prostate using Tm:YAG laser (ThuVARP) as an alternative to TURP.	Strong
Offer ThuVARP to patients receiving anticoagulant or antiplatelet therapy.	Weak
Prostatic urethral lift	
Offer Prostatic urethral lift (Urolift®) to men with LUTS interested in preserving ejaculatory function, with prostates < 70 mL and no middle lobe.	Strong
Intra-prostatic injections	
Do not offer intraprostatic Botulinum toxin-A injection treatment to patients with male LUTS.	Strong

Summary surgical treatment

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, patient's preference/willingness to accept surgery-associated side effects, availability of the surgical armamentarium, and experience of the surgeon. Figure 4 illustrates surgical treatment choices according to the patient's profile.

Figure 4: Treatment algorithm of bothersome LUTS refractory to conservative/medical treatment or in cases of absolute operation indications.

The flowchart is stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



Laser vaporisation includes GreenLight, thulium, and diode laser vaporisation; Laser enucleation includes holmium and thulium laser enucleation.
HoLEP = holmium laser enucleation; TUIP = transurethral incision of the prostate; TURP = transurethral resection of the prostate and PU = prostatic urethral.

Techniques Under Investigation

A recommendation is given for Aquablation and Prostatic Artery Embolisation (PAE); however, these two techniques should still be considered as under investigation in order to better define their position in the armamentarium of invasive therapies for BPO and to better define the subgroups of patients who will benefit most from them.

Recommendations for techniques under investigation	Strength rating
Offer Aquablation* to patients with moderate-to-severe LUTS and prostates between 30 – 80 mL as an alternative to transurethral resection of the prostate (TURP).	Weak
Inform patients about the risk of bleeding and the lack of long-term follow up data.	Strong
Offer prostatic artery embolisation (PAE)* to men with moderate-to-severe LUTS who wish to consider minimally invasive treatment options and accept less optimal objective outcomes compared with TURP.	Weak
Perform PAE only in units where the work up and follow up is performed by urologists working collaboratively with trained interventional radiologists for the identification of PAE suitable patients.	Strong

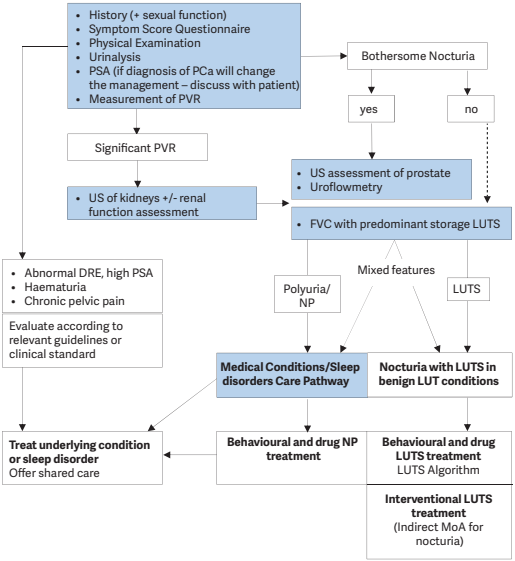
** Technique remains under investigation*

Management of Nocturia in Men with LUTS

Diagnostic assessment

Evaluation is outlined in Figure 5.

Figure 5: Evaluation of nocturia in non-neurogenic male LUTS



Assessment must establish whether the patient has polyuria, LUTS, sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment with a frequency volume chart, (indicated by the dotted line), depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered.
DRE = digital rectal examination; NP = nocturnal polyuria; MoA = mechanism of action; PVR = post-void residual; PSA = prostate-specific antigen; US = ultrasound; FVC = frequency volume chart.

Medical conditions and sleep disorders shared care pathway

Table 1: Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

UROLOGICAL CONTRIBUTION	*SHARED CARE*	*MEDICAL CONTRIBUTION*
Diagnosis of LUTD • Urological/ LUTS evaluation • Nocturia symptom scores • Bladder diary		**Diagnosis of conditions causing NP** • Evaluate patient's known conditions • Screening for sleep disorders • Screening for potential causes of polyuria*

Conservative management Behavioural therapy • Fluid/sleep habits advice • Drugs for storage LUTS • (Drugs for voiding LUTS) • ISC/ catherisation **Interventional therapy** • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS	**Conservative management** • Antidiuretic • Diuretics • Drugs to aid sleep	**Management** • Initiation of therapy for new diagnosis • Optimised therapy of known conditions * Potential causes of polyuria NEPHROLOGICAL DISEASE • Tubular dysfunction • Global renal dysfunction CARDIOVASCULAR DISEASE • Cardiac disease • Vascular disease ENDOCRINE DISEASE • Diabetes insipidus/mellitus • Hormones affecting diuresis/natriuresis NEUROLOGICAL DISEASE • Pituitary and renal innervation • Autonomic dysfunction RESPIRATORY DISEASE • Obstructive sleep apnoea BIOCHEMICAL • Altered blood oncotic pressure

Recommendations for treatment of nocturia	Strength rating
Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	Weak
Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.	Weak
Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65 years of age.	Weak
Offer low dose desmopressin for men > 65 years of age with nocturia at least twice per night due to nocturnal polyuria.	Weak
Screen for hyponatremia at baseline, day three and day seven, one month after initiating therapy and periodically during treatment. Measure serum sodium more frequently in patients > 65 years of age and in patients at increased risk of hyponatremia.	Strong
Discuss with the patient the potential clinical benefit relative to the associated risks from the use of desmopressin, especially in men > 65 years of age.	Strong
Offer α1-adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.	Weak

Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.	Weak
Offer 5α-reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate (> 40 mL).	Weak
Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.	Weak

Follow-up

Recommended follow-up strategy:

- Patients managed with watchful waiting should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α1-blockers, muscarinic receptor antagonists, beta-3 agonists, phospodiesterase 5 inhibitors, or a combination should be reviewed four to six weeks after drug initiation. If patients gain symptomatic relief, without troublesome side effects, drug therapy may be continued. Patients should be reviewed at six months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving 5α-reductase inhibitors should be reviewed after twelve weeks and six months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day three and seven and after one month and, if serum sodium concentration has remained normal, every three months subsequently; the follow-up sequence should be restarted after dose escalation.

- Patients after prostate surgery should be reviewed four to six weeks after catheter removal to evaluate treatment response and side effects. If patients have symptomatic relief and there are no side effects, further assessment is not necessary.

Recommendations for follow-up	Strength rating
Follow-up all patients who receive conservative, medical or surgical management.	Weak
Define follow-up intervals and examinations according to the specific treatment.	Weak

Readers are strongly recommended to read the full version of the Guidelines where the efficacy, safety and considerations for each treatment are presented.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON URINARY INCONTINENCE

(Limited text update March 2018)

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Introduction

This pocket version aims to synthesise the important clinical messages described in the full text and is presented as a series of 'action based recommendations' with a strength rating.

Diagnostic Evaluation

History and physical examination

The history should include details of the type, timing and severity of urinary incontinence (UI), associated voiding and other urinary symptoms. The history should allow UI to be categorised into stress urinary incontinence (SUI), urgency urinary incontinence (UUI) or mixed urinary incontinence (MUI).

It should also identify patients who need rapid referral to an appropriate specialist. These include patients with associated pain, haematuria, a history of recurrent urinary tract infection (UTI), pelvic surgery (particularly prostate surgery) or radiotherapy, constant leakage suggesting a fistula, voiding difficulty or suspected neurological disease. The patient should also be asked about other ill health and for the details of current medications, as these may impact on symptoms of UI.

Questionnaires

Recommendation	Strength rating
Use a validated and appropriate questionnaire when standardised assessment is required.	Strong

Voiding diaries

Recommendations	Strength rating
Ask patients with UI to complete a voiding diary.	Strong
Use a diary duration of at least three days.	Strong

Urinalysis and urinary tract infection

Recommendations	Strength rating
Perform urinalysis as a part of the initial assessment of a patient with UI.	Strong
If a symptomatic urinary tract infection is present with UI, reassess the patient after treatment.	Strong
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve UI.	Strong

Post-voiding residual volume

Recommendations	Strength rating
When measuring post-void residual (PVR) urine volume, use ultrasound.	Strong
Measure (PVR) in patients with UI who have voiding symptoms.	Strong

Measure (PVR) when assessing patients with complicated UI.	Strong
Monitor PVR in patients receiving treatments that may cause or worsen voiding dysfunction, including surgery for SUI.	Strong

Urodynamics

Recommendations	Strength rating
(NB: Concerning only neurologically intact adults with UI)	
When performing urodynamics in patients with UI adhere to 'Good Urodynamic Practice' standards as described by the International Continence Society: • attempt to replicate the patient's symptoms; • check recordings for quality control; • interpret results in the context of the clinical problem; • remember there may be physiological variability within the same individual.	Strong
Do not routinely carry out urodynamics when offering treatment for uncomplicated SUI.	Strong
Perform urodynamics if the findings may change the choice of invasive treatment.	Weak
Do not use urethral pressure profilometry or leak point pressure to grade severity of incontinence.	Strong

Pad testing

Recommendations	Strength rating
Use a pad test of standardised duration and activity protocol.	Strong
Use a pad test when quantification of UI is required.	Weak

Imaging

Recommendation	Strength rating
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of UI.	Strong

Disease Management

Conservative management

In clinical practice, it is a convention that non-surgical therapies are tried first because they usually carry the least risk of harm. Conventional medical practice encourages the use of simple, relatively harmless, interventions before resorting to those associated with higher risks.

Simple medical interventions

Correction of underlying disease/cognitive impairment

Urinary incontinence, especially in the elderly, has been associated with multiple comorbid conditions including:

- cardiac failure;
- chronic renal failure;
- diabetes;
- chronic obstructive pulmonary disease;
- neurological disease including stroke and multiple sclerosis;
- general cognitive impairment;
- sleep disturbances, e.g. sleep apnoea;

- depression;
- metabolic syndrome.

Adjustment of medication

Although changing drug regimens for underlying disease may be considered as a possible early intervention for UI, there is very little evidence of benefit. There is also a risk that stopping or altering medication may result in more harm than benefit.

Recommendations	Strength rating
Take a drug history from all patients with UI.	Strong
Review any new medication associated with the development or worsening of UI.	Weak

Constipation

Studies have shown strong associations between constipation and UI. Constipation can be improved by behavioural, physical and medical treatments.

Recommendation	Strength rating
Advise adults with UI who also suffer from constipation about bowel management, in line with good medical practice.	Strong

Containment (pads etc.)

Recommendations	Strength rating
Inform adults with UI and/or their carers regarding available treatment options before deciding on containment alone.	Strong
Offer incontinence pads and/or containment devices for management of UI.	Strong

Lifestyle interventions

Examples of lifestyle factors that may be associated with UI

include obesity, smoking, level of physical activity and diet. Modification of these factors may improve UI.

Recommendations	Strength rating
Encourage overweight and obese adults with UI to lose weight and maintain weight loss.	Strong
Advise adults with UI that reducing caffeine intake may improve symptoms of urgency and frequency but not incontinence.	Strong
Review type and amount of fluid intake in patients with UI.	Weak
Provide smoking cessation strategies to patients with UI who smoke.	Strong

Behavioural and physical therapies

Recommendations	Strength rating
Offer prompted voiding for adults with incontinence, who are cognitively impaired.	Strong
Offer bladder training as a first-line therapy to adults with UUI or MUI.	Strong
Offer supervised intensive pelvic floor muscle training (PFMT), lasting at least three months, as a first-line therapy to women with SUI or MUI (including the elderly and post-natal).	Strong
Offer instruction on PFMT to men undergoing radical prostatectomy to speed-up recovery from UI.	Strong
Ensure that PFMT programmes are as intensive as possible.	Strong

Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of SUI.	Strong
Do not offer magnetic stimulation for the treatment of UI or overactive bladder in women.	Strong
Consider percutaneous tibial nerve stimulation as an option for improvement of UUI in women who have not benefited from antimuscarinic medication.	Strong

Conservative therapy in MUI

Recommendation	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak

Pharmacological Management

Antimuscarinics

Recommendations	Strength rating
Offer antimuscarinic drugs for adults with UUI who failed conservative treatment.	Strong
Consider extended release formulations of antimuscarinics drugs, whenever possible.	Strong
If an antimuscarinic treatment proves ineffective, consider dose escalation or offering an alternative antimuscarinic formulation, or mirabegron, or a combination.	Strong

Encourage early review (of efficacy and side effects) of patients on antimuscarinic medication for UUI.	Strong

Mirabegron

Recommendation	Strength rating
Offer antimuscarinic drugs or mirabegron to adults with UUI who failed conservative treatment.	Strong

Antimuscarinic drugs in the elderly

Recommendation	Strength rating
Use long-term antimuscarinic treatment with caution in elderly patients especially those who are at risk of, or have, cognitive dysfunction.	Strong

Drugs for SUI

Recommendations	Strength rating
Offer Duloxetine in selected patients with symptoms of SUI when surgery is not indicated.	Strong
Initiate and withdraw duloxetine using dose titration because of high risk of adverse events.	Strong

Oestrogen

Recommendations	Strength rating
Offer long-term vaginal oestrogen therapy to post-menopausal women with UI and symptoms of vulvo-vaginal atrophy.	Strong
In women with a history of breast cancer, the treating oncologist should be consulted.	Weak
Discuss alternative hormone replacement therapies with women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening UI.	Strong
Advise women who are taking systemic oestradiol who suffer from UI that stopping the oestradiol is unlikely to improve their UI.	Strong

Desmopressin

Recommendations	Strength rating
Consider offering desmopressin to patients requiring occasional short-term relief from daytime UI and inform them that this drug is not licensed for this indication.	Strong
Monitor plasma sodium levels in patients on desmopressin.	Strong
Do not use desmopressin for long-term control of UI.	Strong

Drug treatment in MUI

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak
Offer antimuscarinic drugs or beta 3 agonists to patients with urgency-predominant MUI.	Strong
Consider offering duloxetine to patients with MUI unresponsive to other conservative treatments and who are not seeking cure.	Strong

Surgical Management

The section considers surgical options for the following situations:

- Women with uncomplicated SUI; this means no history of previous surgery, no neurological lower urinary tract dysfunction (LUTD), no bothersome genitourinary prolapse, and those not considering further pregnancy.
- Women with complicated SUI. Neurogenic LUTD is reviewed in the EAU Guidelines on Neuro-urology.
- Associated genitourinary prolapse has been included in these Guidelines in terms of treating the incontinence, but no attempt has been made to comment on treatment of prolapse itself.
- Men with SUI, mainly those with post-prostatectomy incontinence without neurological disease affecting the lower urinary tract.
- Patients with refractory DO (detrusor overactivity) incontinence.

Women with uncomplicated SUI

Recommendations	Strength rating
Offer a mid-urethral sling, colposuspension or autologous fascial sling to women with uncomplicated SUI.	Strong
Inform women of the unique complications associated with each individual procedure.	Strong
Inform women who are being offered a single-incision sling that long-term efficacy remains uncertain.	Strong
Inform older women with SUI about the increased risks associated with surgery, including the lower probability of success.	Weak
Inform women that any vaginal surgery may have an impact on sexual function, which is generally positive.	Weak
Only offer new devices, for which there is no level 1 evidence base, as part of a structured research programme.	Strong
Only offer adjustable mid-urethral sling as a primary surgical treatment for SUI as part of a structured research programme.	Strong
Offer bulking agents to women with SUI who request a low-risk procedure with the understanding that repeat injections are likely and long-term durability is not established.	Strong

Women with complicated SUI

Recommendations	Strength rating
Management of complicated SUI should only be offered in expert centres*.	Weak
Base the choice of surgery for recurrent SUI on careful evaluation of the individual patient including multichannel urodynamics and imaging as appropriate.	Weak
Inform women with recurrent SUI that the outcome of a surgical procedure, when used as a second-line treatment, is generally inferior to its use as a first-line treatment, both in terms of reduced efficacy and increased risk of complications.	Weak
Consider secondary synthetic sling, colposuspension or autologous sling as first options for women with complicated SUI.	Weak
Inform women receiving artificial urinary sphincter (AUS) or Adjustable Compression device (ACT©) that although cure is possible, even in expert centres, there is a high risk of complications, mechanical failure, or a need for explantation.	Weak

** Expert centres refers to the comments on surgeon volume in the introduction to the surgical chapter.*

Women with both stress urinary incontinence and pelvic organ prolapse

Recommendations for women requiring surgery for bothersome pelvic organ prolapse who have symptomatic or unmasked SUI.	**Strength rating**
Offer simultaneous surgery for pelvic organ prolapse and SUI.	Strong
Inform women of the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	Strong
Recommendations for women requiring surgery for bothersome pelvic organ prolapse without symptomatic or unmasked SUI.	
Inform women that there is a risk of developing *de novo* SUI after prolapse surgery.	Strong
Warn women that the benefit of surgery for SUI may be outweighed by the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	Strong

Urethral diverticulum

Recommendation	Strength rating
Symptomatic urethral diverticula should be completely surgically removed.	Strong

Men with SUI

Recommendations	Strength rating
Offer duloxetine only to hasten recovery of continence after prostate surgery but inform the patient about the possible adverse events and that its use is off label for this indication in most European countries.	Weak
Only offer bulking agents to men with mild post-prostatectomy UI who desire temporary relief of UI symptoms.	Weak
Do not offer bulking agents to men with severe post-prostatectomy UI.	Weak
Offer fixed slings to men with mild-to-moderate* post-prostatectomy UI.	Weak
Warn men that severe UI, prior pelvic radiotherapy or urethral stricture surgery, may worsen the outcome of fixed male sling surgery.	Weak
Offer artificial urinary sphincter (AUS) to men with moderate-to-severe post-prostatectomy incontinence.	Weak
Implantation of AUS or ProACT© for men should only be offered in expert centres.	Weak

Warn men receiving AUS or ProACT© that, although cure can be achieved, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	Weak
Do not offer non-circumferential compression device (ProACT®) to men who have had pelvic radiotherapy.	Weak

** The terms mild and moderate post-prostatectomy UI remain undefined.*

Surgical interventions for refractory detrusor overactivity

Intravesical injection of botulinum toxin A

Recommendations	Strength rating
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with UUI refractory to conservative therapy (such as pelvic floor muscle training and/or drug treatment).	Strong
Warn patients of the limited duration of response, risk of urinary tract infection and the possible prolonged need to self-catheterise (ensure that they are willing and able to do so).	Strong

Sacral nerve stimulation (neuromodulation)

Recommendation	Strength rating
Offer sacral nerve modulation to patients who have UUI refractory to antimuscarinic therapy.	Strong

Cystoplasty/urinary diversion

Recommendations	Strength rating
Offer augmentation cystoplasty to patients with UI who have failed all other treatment options.	Weak
Inform patients undergoing augmentation cystoplasty of the high risk of having to perform clean intermittent self-catheterisation (ensure they are willing and able to do so) and that they need lifelong surveillance.	Weak
Do not offer detrusor myectomy as a treatment for UI.	Weak
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of UI and who will accept a stoma and have been warned about the possible small risk of malignancy.	Weak

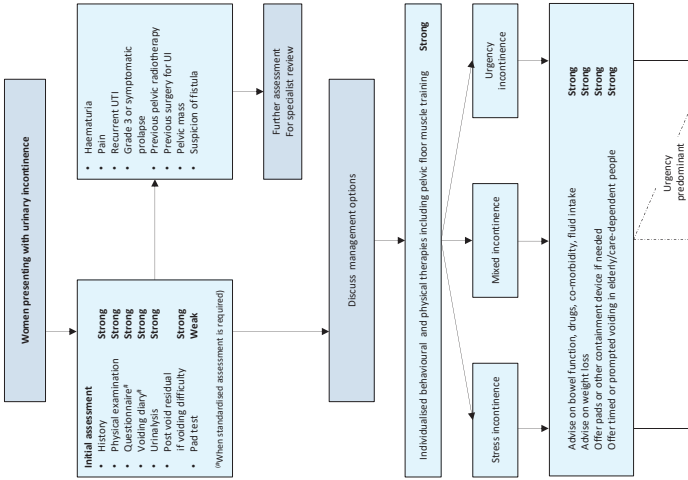
Surgery in patients with MUI

Recommendations	Strength rating
Treat the most bothersome symptom first in patients with MUI.	Weak
Warn patients with MUI that surgery is less likely to be successful than surgery for SUI alone.	Strong
Inform women with MUI that one single treatment may not cure UI; it may be necessary to treat other components of the incontinence problem as well as the most bothersome symptom.	Strong

Surgery for UI in the elderly

Recommendation	Strength rating
Inform older women with UI about the increased risks associated with surgery (including onabotulinum toxin A injection), together with the lower probability of benefit.	Weak

Figure 1: Women presenting with urinary incontinence



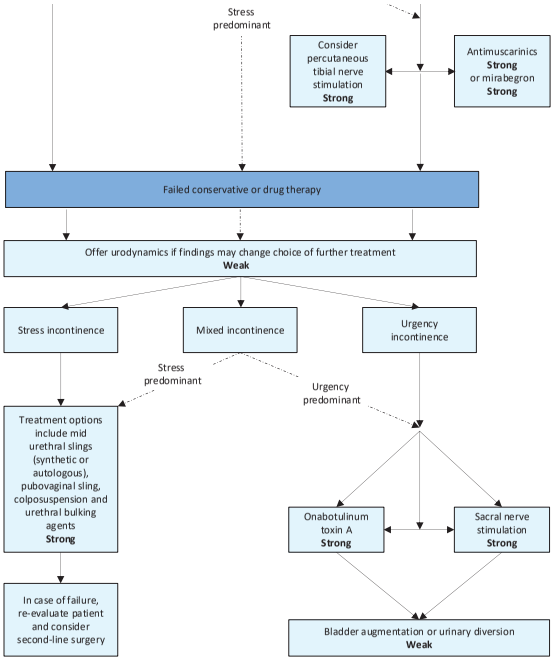
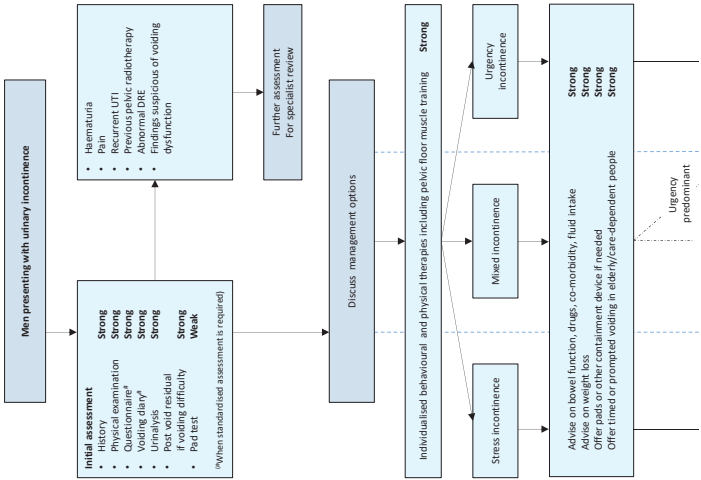
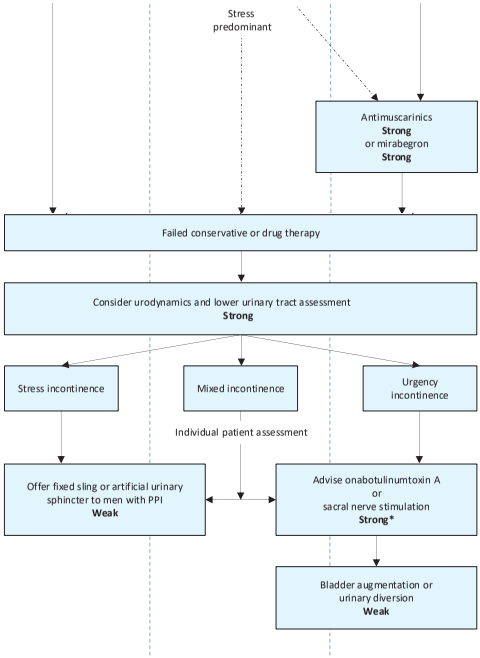

Stress predominant
Consider percutaneous tibial nerve stimulation **Strong**
Antimuscarinics **Strong** or mirabegron **Strong**
Failed conservative or drug therapy
Offer urodynamics if findings may change choice of further treatment **Weak**
Stress incontinence
Mixed incontinence
Urgency incontinence
Stress predominant
Urgency predominant
Treatment options include mid urethral slings (synthetic or autologous), pubovaginal sling, colposuspension and urethral bulking agents **Strong**
In case of failure, re-evaluate patient and consider second-line surgery
Onabotulinum toxin A **Strong**
Sacral nerve stimulation **Strong**
Bladder augmentation or urinary diversion **Weak**

Figure 2: Men presenting with urinary incontinence





*Available evidence refers mainly to women

Non Obstetric Urinary Fistula*

Recommendations	Strength rating
General	
Surgeons undertaking complex pelvic surgery should be competent at identifying, preserving and repairing the ureter.	Weak
Do not routinely use ureteric stents as prophylaxis against injury during routine gynaecological surgery.	Weak
Suspect ureteric injury or fistula in patients following pelvic surgery if a fluid leak or pelvicalyceal dilatation occurs post-operatively or if drainage fluid contains high levels of creatinine.	Weak
Suspect uretero-arterial fistula in patients presenting with haematuria with a history of relevant surgery.	Weak
Use three dimensional imaging techniques to diagnose and localise urinary fistulae.	Weak
Manage upper urinary tract fistulae by conservative or endoluminal technique where such expertise and facilities exists.	Weak
Surgical principles	
Surgeons involved in fistula surgery should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	Weak
Attention should be given as appropriate to skin care, nutrition, rehabilitation, counselling and support prior to, and following, fistula repair.	Weak

If a vesicovaginal fistula is diagnosed within six weeks of surgery, consider indwelling catheterisation for a period of up to twelve weeks after the causative event.	Weak
Tailor the timing of fistula repair to the individual patient and surgeon requirements once any oedema, inflammation, tissue necrosis, or infection, are resolved.	Weak
Where concurrent ureteric re-implantation or augmentation cystoplasty are required, the abdominal approach is necessary.	Weak
Ensure that the bladder is continuously drained following fistula repair until healing is confirmed (expert opinion suggests: 10-14 days for simple and/or post-surgical fistulae; 14-21 days for complex and/or post-radiation fistulae).	Weak
Where urinary and/or faecal diversions are required, avoid using irradiated tissue for repair.	Weak
Use interposition grafts when repair of radiation associated fistulae is undertaken.	Weak
In patients with intractable UI from radiation-associated fistula, where life expectancy is very short, consider performing ureteric occlusion.	Weak
Repair persistent ureterovaginal fistula by an abdominal approach using open, laparoscopic or robotic techniques according to availability and competence.	Weak

Consider palliation by nephrostomy tube diversion and endoluminal distal ureteric occlusion for patients with ureteric fistula associated with advanced pelvic cancer and poor performance status.	Weak
Urethrovaginal fistulae should preferably be repaired by a vaginal approach.	Weak

** These recommendations are derived from the ICUD 2013 review and have not been fully validated by the EAU Guidelines Office methodology.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON NEURO-UROLOGY

(Limited text update March 2020)

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Introduction

Neuro-urological disorders can cause a variety of long-term complications; the most dangerous being damage of renal function. Treatment and intensity of follow-up examinations are based on the type of neuro-urological disorder and the underlying cause.

Terminology

The terminology used and the diagnostic procedures outlined in this document follow those published by the International Continence Society.

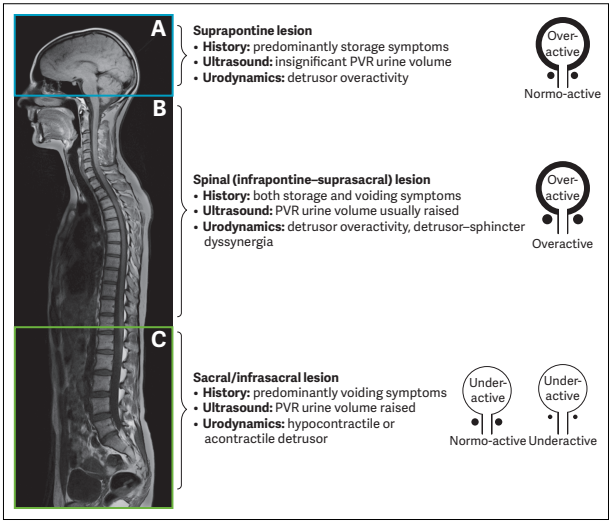
Risk factors and epidemiology

All central and peripheral neurological disorders carry a high risk of causing functional disturbances of the urinary tract.

Classification

The pattern of lower urinary tract (LUT) dysfunction following neurological disease is determined by the site and nature of the lesion. A very simple classification system, for use in daily clinical practice, to decide on the appropriate therapeutic approach is provided in Figure 1.

Figure 1: Patterns of lower urinary tract dysfunction following neurological disease



The pattern of LUT dysfunction following neurological disease is determined by the site and nature of the lesion. Panel A denotes the region above the pons, panel B the region between the pons and sacral cord and panel C the sacral cord and infrasacral region. Figures on the right show the expected dysfunctional states of the detrusor-sphincter system. Figure adapted from Panicker et al. with permission from Elsevier. PVR = post-void residual.

Diagnostic evaluation

Early diagnosis and treatment are essential in both congenital and acquired neuro-urological disorders, even in the presence of normal neurological reflexes. Neuro-urological disorders

can be the presenting feature of neurological pathology and early intervention can prevent irreversible deterioration of the lower and upper urinary tract.

Patient assessment

Diagnosis of neuro-urological disorders should be based on a comprehensive assessment of neurological and non-neurological conditions. Initial assessment should include a detailed history, physical examination, and urinalysis.

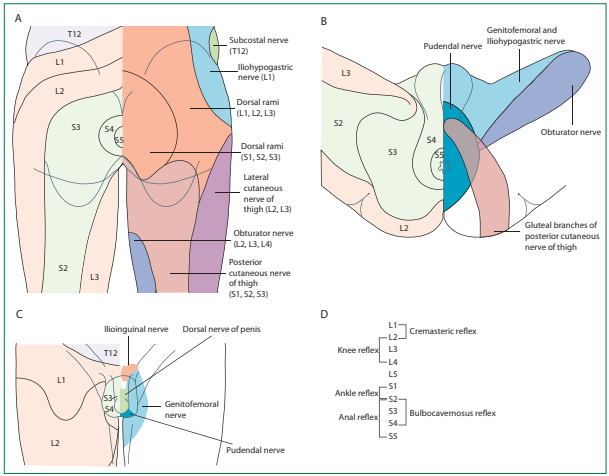
History

An extensive general and specific history is mandatory and should concentrate on past and present symptoms, disorders of the urinary tract as well as bowel, sexual and neurological function. Special attention should be paid to possible warning signs and symptoms (e.g. pain, infection, haematuria, fever) that warrant further investigation.

Physical examination

The neurological status should be described as completely as possible. All sensations and reflexes in the urogenital area must be tested, including detailed testing of the anal sphincter and pelvic floor functions (Figure 2). Availability of this clinical information is essential for the reliable interpretation of subsequent diagnostic investigations.

Figure 2: Lumbosacral dermatomes, cutaneous nerves, and reflexes



The physical examination includes testing sensations and reflexes mediated through the lower spinal cord. Abnormal findings would suggest a lesion affecting the lumbosacral segments; mapping out distinct areas of sensory impairment helps to further localise the site of lesion. Distribution of dermatomes (areas of skin mainly supplied by a single spinal nerve) and cutaneous nerves over the perianal region and back of the upper thigh (A), the perineum (B), male external genitalia (C) and root values of lower spinal cord reflexes (D). Figure adapted from Panicker et al., with parts A-C adapted from Standring, both with permission from Elsevier.

Recommendations for history taking and physical examination

Recommendations	Strength rating
History taking	
Take an extensive general history, concentrating on past and present symptoms.	Strong
Take a specific history for each of the four mentioned functions - urinary, bowel, sexual and neurological.	Strong
Pay special attention to the possible existence of alarm signs (e.g. pain, infection, haematuria, fever) that warrant further specific diagnosis.	Strong
Assess quality of life when evaluating and treating the neuro-urological patient.	Strong
Use available validated tools including the Qualiveen and I-QoL for urinary symptoms and the QoL-BM for bowel dysfunction in multiple sclerosis and spinal cord injury patients. In addition, generic (SF-36 or KHQ) questionnaires can be used.	Strong
Use MSISQ-15 and MSISQ-19 to evaluate sexual function in multiple sclerosis patients.	Strong
Physical examination	
Acknowledge individual patient disabilities when planning further investigations.	Strong
Describe the neurological status as completely as possible, sensations and reflexes in the urogenital area must all be tested.	Strong

Test the anal sphincter and pelvic floor functions.	Strong
Perform urinalysis, blood chemistry, bladder diary, residual and free flowmetry, incontinence quantification and urinary tract imaging.	Strong

I-QoL = Incontinence Quality of Life Instrument; OoL-BM = Quality of Life Bowel Management scoring tool; KHQ = King's Health Questionnaire; SF-36 = Short Form 36-item Health Survey Questionnaires; MSISQ 15/19 = Multiple Sclerosis Intimacy and Sexuality Questionnaire 15/19 question version.

Urodynamic tests

Bladder diaries are considered a valuable diagnostic tool in patients with neuro-urological disorders. A bladder diary should be recorded for at least two to three days. Uroflowmetry and ultrasound assessment of post-void residual should be repeated at least two or three times in patients able to void. Invasive urodynamic studies comprise mandatory assessment tools to determine the exact type of neuro-urological disorder. Video-urodynamics combines filling cystometry and pressure flow studies with radiological imaging. Currently, video-urodynamics is considered to provide the most comprehensive information for evaluating neuro-urological disorders.

Recommendations for urodynamics and uro-neurophysiology

Recommendations	Strength rating
Perform a urodynamic investigation to detect and specify lower urinary tract (dys-)function, use same session repeat measurement as it is crucial in clinical decision making.	Strong
Non-invasive testing is mandatory before invasive urodynamics is planned.	Strong
Use video-urodynamics for invasive urodynamics in neuro-urological patients. If this is not available, then perform a filling cystometry continuing into a pressure flow study.	Strong
Use a physiological filling rate and body-warm saline.	Strong

Treatment

The primary aims and their prioritisation when treating neuro-urological disorders are:

1. protection of the upper urinary tract;
2. improvement of urinary continence;
3. restoration of (parts of) LUT function;
4. improvement of the patient's quality of life (QoL).

Further considerations are the patient's disability, cost-effectiveness, technical complexity, and possible complications.

Conservative treatment

Assisted bladder emptying

Triggered reflex voiding is not recommended as there is a risk

of pathologically elevated bladder pressures. Only in the case of absence, or surgically reduced outlet obstruction, may it be an option.

Caution: bladder compression techniques to expel urine (Credé) and voiding by abdominal straining (Valsalva manoeuvre) create high pressures and are potentially hazardous; therefore, their use should be discouraged.

Rehabilitation

In selected patients, pelvic floor muscle exercises, pelvic floor electro-stimulation, and biofeedback might be beneficial.

External appliances

Social continence for the incontinent patient can be achieved using an appropriate method of urine collection.

Medical therapy

A single, optimal, medical therapy for patients with neuro-urological symptoms is not yet available. Muscarinic receptor antagonists are the first-line choice for treating neuro-urological disorders.

Recommendations for drug treatment

Recommendations	Strength rating
Use antimuscarinic therapy as the first-line medical treatment for neurogenic detrusor overactivity.	Strong
Prescribe α-blockers to decrease bladder outlet resistance.	Strong
Do not prescribe parasympathomimetics for underactive detrusor.	Strong

Recommendations for minimal invasive treatment

Recommendations	Strength rating
Catheterisation	
Use intermittent catheterisation, whenever possible aseptic technique, as a standard treatment for patients who are unable to empty their bladder.	Strong
Thoroughly instruct patients in the technique and risks of intermittent catheterisation.	Strong
Avoid indwelling transurethral and suprapubic catheterisation whenever possible.	Strong
Intravesical drug treatment	
Offer intravesical oxybutynin to neurogenic patients with detrusor overactivity and poor tolerance to the oral route.	Strong
Botulinum toxin	
Use botulinum toxin injection in the detrusor to reduce neurogenic detrusor overactivity in multiple sclerosis or spinal cord injury patients if antimuscarinic therapy is ineffective.	Strong
Bladder neck incision is effective in a fibrotic bladder neck.	Strong

Surgical treatment

Recommendations for surgical treatment

Recommendations	Strength rating
Perform bladder augmentation in order to treat refractory neurogenic detrusor overactivity.	Strong
Place an autologous urethral sling in female patients with neurogenic stress urinary incontinence who are able to self-catheterise.	Strong
Insert an artificial urinary sphincter in male patients with neurogenic stress urinary incontinence.	Strong

Urinary tract infections (UTI)

Patients with neuro-urological disorders, especially those with spinal cord injury, may have other signs and symptoms in addition to, or instead of, traditional signs and symptoms of a UTI in able-bodied individuals.

Recommendations for the treatment of UTI

Recommendations	Strength rating
Do not screen for or treat asymptomatic bacteriuria in patients with neuro-urological disorders.	Strong
Avoid the use of long-term antibiotics for recurrent urinary tract infections (UTIs).	Strong

In patients with recurrent UTI, optimise treatment of neuro-urological symptoms and remove foreign bodies (e.g. stones, indwelling catheters) from the urinary tract.	Strong
Individualise UTI prophylaxis in patients with neuro-urological disorders as there is no optimal prophylactic measure available.	Strong

Sexual function and fertility

Patients with neurological disease often suffer from sexual dysfunction, which frequently impairs QoL.

Recommendations for erectile dysfunction and male fertility

Recommendations	Strength rating
Prescribe oral phosphodiesterase type 5 inhibitors as first-line medical treatment in neurogenic erectile dysfunction (ED).	Strong
Give intracavernous injections of vaso-active drugs (alone or in combination) as second-line medical treatment in neurogenic ED.	Strong
Offer mechanical devices such as vacuum devices and rings to patients with neurogenic ED.	Strong
Perform vibrostimulation and transrectal electroejaculation for sperm retrieval in men with spinal cord injury.	Strong

Perform microsurgical epididymal sperm aspiration, testicular sperm extraction and intracytoplasmic sperm injection after failed vibrostimulation and/or transrectal electroejaculation in men with spinal cord injury.	Strong
Counsel men with spinal cord injury at or above Th 6 and fertility clinics about the potentially life-threatening condition of autonomic dysreflexia.	Strong

Recommendations on female sexuality and fertility

Recommendations	Strength rating
Do not offer medical therapy for the treatment of neurogenic sexual dysfunction in women.	Strong
Take a multidisciplinary approach, tailored to individual patient's needs and preferences, in the management of fertility, pregnancy and delivery in women with neurological diseases.	Strong

Follow-up

Neuro-urological disorders are often unstable and the symptoms may vary considerably, even within a relatively short period. Regular follow-up is therefore necessary.

Recommendations for follow-up

Recommendations	Strength rating
Assess the upper urinary tract at regular intervals in high-risk patients.	Strong
Perform a physical examination and urine laboratory every year in high-risk patients.	Strong
Any significant clinical changes should instigate further, specialised, investigation.	Strong
Perform urodynamic investigation as a mandatory baseline diagnostic intervention in high-risk patients at regular intervals.	Strong

Summary

Neuro-urological disorders present a multifaceted pathology. Extensive investigation and a precise diagnosis are required before the clinician can initiate individualised therapy. Treatment must take into account the patient's medical and physical condition and expectations with regard to his/her future social, physical, and medical situation.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON SEXUAL AND REPRODUCTIVE HEALTH

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Guidelines Associates: L. Boeri, P. Capogrosso, N.C. Çilesiz, A. Cocci, K. Dimitropoulos, M. Gül, G. Hatzichristodoulou, V. Modgil, U. Milenkovic, G. Russo, T. Tharakan

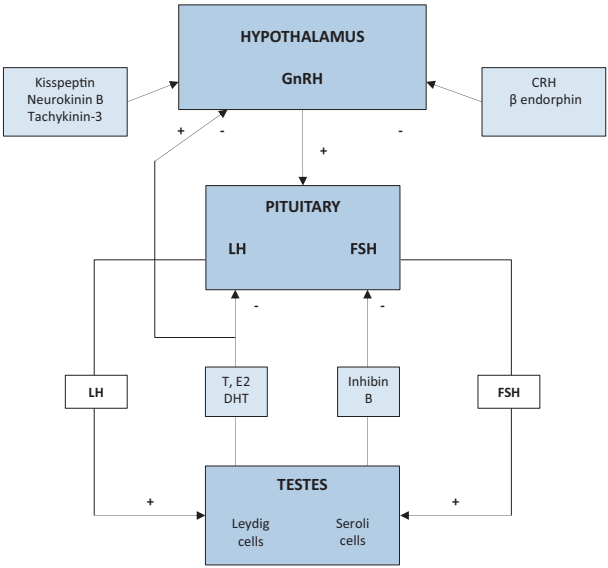
Introduction

The EAU Working Group has published guidelines on Male Sexual and Reproductive Health, combining the former guideline on Male Sexual Dysfunction, Male Infertility and Male Hypogonadism. For priapism refer to the 2018 Male Sexual Dysfunction Guidelines and the 2018 version of the pocket guideline.

Male Hypogonadism

Male Hypogonadism, also known as Testosterone Deficiency, is a disorder associated with decreased functional activity of the testes, with decreased production of androgens and/or impaired sperm production. It may adversely affect multiple organ functions and quality of life (QoL). The prevalence increases with age.

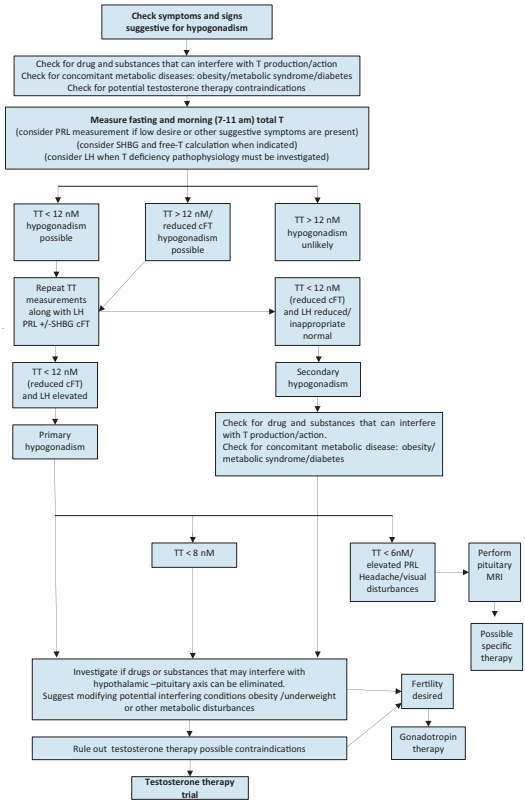
Figure 1: Physiology of testosterone production



GnRH = gonadotropin releasing hormone; LH = luteinising hormone; FSH = follicular stimulating hormone; T = testosterone; E2 = 7-β-estradiol; DHT = dehydroepiandrosterone; CRH = corticotrophin releasing hormone.

Diagnostic evaluation of Late-Onset Hypogonadism

Figure 2: Diagnostic evaluation of Late-Onset Hypogonadism



TT = total testosterone; cFT = calculated free testosterone; PRL = prolactin; SHBG = sex hormone-binding globulin; LH = luteinising hormone; MRI = magnetic resonance imaging.

Recommendations for the diagnostic evaluation of Late-onset Hypogonadism

Recommendations	Strength rating
Check for concomitant diseases, drugs and substances that can interfere with testosterone production/action.	Strong
Total testosterone must be measured in the morning (7.00 and 11.00 hours) and in the fasting state, with a reliable method.	Strong
Repeat total testosterone on at least two separate occasions when below 12 nmol/L and before starting testosterone therapy.	Strong
12 nmol/L total testosterone (3.5 ng/mL) represents a reliable threshold to diagnose late-onset hypogonadism (LOH).	Strong
Consider sex hormone-binding globulin and free-testosterone calculation when indicated.	Strong
Calculated free-testosterone < 225 pmol/L has been suggested as a possible cut off for diagnosis of LOH.	Weak
Analyse luteinising hormone and follicle-stimulating hormone serum levels to differentiate between primary hypogonadism and secondary hypogonadism.	Strong
Consider prolactin (PRL) measurement if low desire (or other suggestive signs/ symptoms) and low or low-normal testosterone is present.	Strong

Perform pituitary magnetic resonance imaging (MRI) in secondary hypogonadism, with elevated PRL or specific symptoms of a pituitary mass and/or presence of other anterior pituitary hormone deficiencies.	Strong
Perform pituitary MRI in secondary severe hypogonadism (total testosterone < 6 nmol/L).	Weak

Recommendations for screening men for Late-onset Hypogonadism

Recommendations	Strength rating
Screen for late-onset hypogonadism (LOH) (including in type 2 diabetes) only in symptomatic men.	Strong
Do not use structured interviews and self-reported questionnaires for systematic screening for LOH as they have low specificity.	Strong

Recommendations for disease management

Recommendations	Strength rating
The use of testosterone therapy in eugonadal men is not indicated.	Strong
Use testosterone therapy as first-line treatment in symptomatic hypogonadal patients with milder erectile dysfuntion (ED).	Strong
Use the combination of phosphodiesterase type 5 inhibitors and testosterone therapy in more severe forms of ED as it may result in better outcomes.	Weak

Use conventional medical therapies for treating severe depressive symptoms and osteoporosis.	Strong
Do not use testosterone therapy to improve body composition, reduce weight and benefit cardio-metabolic profile.	Weak
Do not use testosterone therapy for improving cognition vitality and physical strength in aging men.	Strong

Recommendations for LOH choice of treatment	**Strength rating**
Treat, when indicated, organic causes of hypogonadism (e.g., pituitary masses, hyperprolactinemia, etc.).	Strong
Improve lifestyle and reduce weight (e.g., obesity); withdraw, when possible, concomitant drugs which can impair testosterone production; treat comorbidities before starting testosterone therapy.	Weak
Fully inform the patient about expected benefits and side-effects of any treatment option. Select the testosterone preparation in a joint decision process, only with a fully informed patient.	Strong
The aim of testosterone therapy is to restore serum testosterone concentration to the average normal range for young men.	Weak
Use testosterone gels rather than long-acting depot administration when starting initial treatment, so that therapy can be adjusted or stopped in the case of treatment-related adverse side effects.	Weak

Recommendations on risk factors in testosterone treatment	Strength rating
Fully counsel symptomatic hypogonadal men who have been surgically treated for localised prostate cancer (PCa) and who are currently without evidence of active disease considering testosterone therapy, emphasising the benefits and lack of sufficient safety data on long-term follow up.	Weak
Restrict treatment to patients with a low risk for recurrent PCa (i.e., Gleason score < 8; pathological stage T1-2; pre-operative PSA < 10 ng/mL) and should start after at least one year follow-up with a PSA level < 0.01 ng/mL.	Weak
Safety data on the use of testosterone therapy in men treated for breast cancer are unknown.	Strong
Assess for cardiovascular risk factors before commencing testosterone therapy.	Strong
Assess men with known cardiovascular disease (CVD) for cardiovascular symptoms before testosterone therapy and with close clinical assessment and evaluation during treatment.	Strong
Treat men with hypogonadism and pre-existing CVD, venous-thromboembolism or chronic cardiac failure, who require testosterone therapy with caution, by careful clinical monitoring and regular measurement of haematocrit (not exceeding 54%) and testosterone levels.	Weak

Exclude a family history of venous-thromboembolism before commencing testosterone therapy.	Strong
Monitor testosterone, haematocrit at three, six and twelve months after testosterone therapy initiation, and thereafter annually. A haematocrit more than 54% should require testosterone therapy withdrawal and phlebotomy. Re-introduce testosterone therapy at a lower dose once the haematocrit has normalised and consider switching to topical testosterone preparations.	Strong

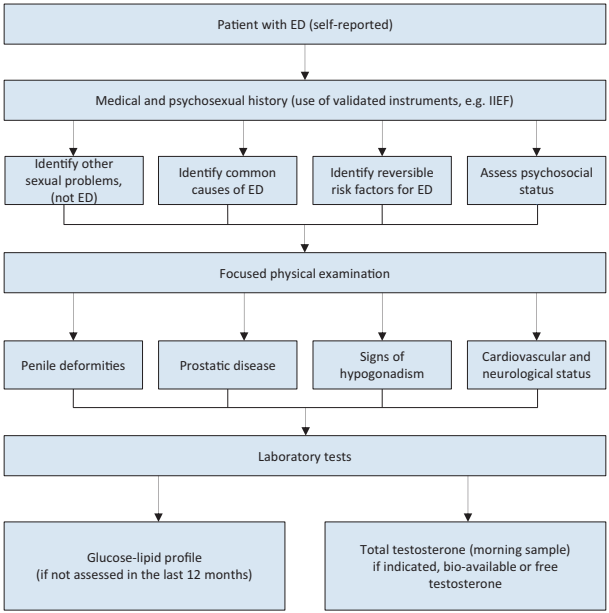
Erectile dysfunction

Introduction

Erectile dysfunction is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance. Erectile dysfunction may affect physical and psychosocial health and may have a significant impact on the QoL of sufferers and their partners. There is increasing evidence that ED can also be an early manifestation of coronary artery and peripheral vascular disease; therefore, ED should not be regarded only as a QoL issue, but also as a potential warning sign of CVD.

Diagnostic evaluation

Figure 3: Minimal diagnostic evaluation (basic work-up) in patients with erectile dysfunction



ED = erectile dysfunction; IIEF = International Index of Erectile Function.

Table 1: Cardiac risk stratification (based on 2nd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardio-myopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

Table 2: Indications for specific diagnostic tests

Primary ED (not caused by acquired organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative revascularisation surgery or angioplasty.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital penile curvature).
Patients with complex psychiatric or psychosexual disorders.
Patients with complex endocrine disorders.
Specific tests may be indicated at the request of the patient or their partner.
Medico-legal reasons (e.g., implantation of penile prosthesis to document end stage ED, sexual abuse).

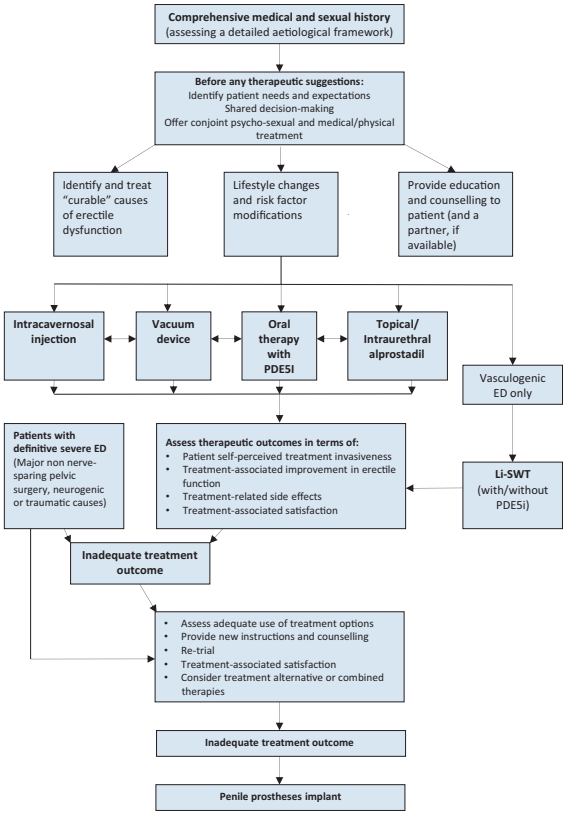
Table 3: Specific diagnostic tests

Nocturnal Penile Tumescence and Rigidity (NTPR) using Rigiscan®
Vascular studies: - Intracavernous vasoactive drug injection - Penile dynamic duplex ultrasonography - Penile dynamic infusion cavernosometry and cavernosography - Internal pudendal arteriography
Specialised endocrinological studies
Specialised psycho-diagnostic evaluation

Recommendations for the diagnosis of erectile dysfunction

Recommendations	Strength rating
Take a comprehensive medical and sexual history in every patient presenting for erectile dysfunction (ED). Consider psychosexual development, including life stressors, cultural aspects, and cognitive/thinking style of the patient regarding their sexual performance.	Strong
Use a validated questionnaire related to ED to assess all sexual function domains (e.g., International Index of Erectile Function [IIEF]) and the effect of a specific treatment modality.	Strong
Include a focused physical examination in the initial assessment of men with ED to identify underlying medical conditions and comorbid genital disorders that may be associated with ED.	Strong
Assess routine laboratory tests, including glucose and lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	Strong
Include specific diagnostic tests in the initial evaluation of ED in the presence of the conditions presented in Table 1.	Strong

Figure 4: Management algorithm for erectile dysfunction



ED = erectile dysfunction; PDE5Is = phosphodiesterase type 5 inhibitors ; Li-SWT = low-intensity shockwave treatment.

Table 4: Summary of the key pharmacokinetic data for the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Parameter	Sildenafil, 100 mg	Tadalafil, 20 mg	Vardenafil, 20 mg	Avanafil, 200mg
C_{max}	560 µg/L	378 µg/L	18.7 µg/L	5.2 µg/L
T_{max} (median)	0.8-1 hours	2 hours	0.9 hours	0.5-0.75 hours
T1/2	2.6-3.7 hours	17.5 hours	3.9 hours	6-17 hours
AUC	1,685 µg.h/L	8,066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bio-availability	41%	NA	15%	8-10%

** Fasted state, higher recommended dose. Data adapted from EMA statements on product characteristics.*

C_{max} = maximal concentration; T_{max} = time-to-maximum plasma concentration; T1/2 = plasma elimination halftime; AUC = area under curve or serum concentration time curve.

Table 5: Common adverse events of the four PDE5 inhibitors currently EMA-approved to treat erectile dysfunction*

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil, 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon

Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	None
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

** Adapted from EMA statements on product characteristics.*

Table 6: Penile prostheses models available on the market

Semi-rigid prostheses	**Inflatable prostheses**	
	Two-piece	**Three-piece**
AMS Tactra™ [Boston Scientific]	AMS Ambicor™ [Boston Scientific]	Titan™ [Coloplast]
Genesis™ [Coloplast]		Titan OTR NB™ (Narrow base) [Coloplast]
		Titan Zero Degree™
Tube™ [Promedon]		AMS 700 CX™ [Boston Scientific]
ZSI 100™ [Zephyr]		AMS 700 LGX™ [Boston Scientific]
Virilis II™ [Subrini]		AMS 700 CXR™ [Boston Scientific]
		ZSI 475™ [Zephyr]

Recommendations for the treatment of erectile dysfunction

Recommendations	Strength rating
Assess all patients for inadequate/incorrect information about the mechanism of action and the ways in which drugs should be taken, as they are the main causes of a lack of response to phosphodiesterase type 5 inhibitors (PDE5Is).	Weak
Use Cognitive Behaviour Therapy as psychological approach (include the partner) combined with medical treatment to maximise treatment outcomes.	Strong
Discuss with patients undergoing radical prostatectomy (any technique) about the risk of sexual changes other than erectile dysfunction (ED), including libido reduction, changes in orgasm, anejaculation, Peyronie's like disease and penile size changes.	Strong
Initiate lifestyle changes and risk factor modification prior to or at the same time as initiating erectile dysfunction (ED) treatments.	Strong
Treat a curable cause of ED first, when found.	Weak
Use PDE5Is as first-line therapeutic option.	Strong
Use topical/intraurethral alprostadil as an alternative first-line therapy in well-informed patients who do not wish or are not suitable for oral vasoactive therapy. Use topical/ intraurethral alprostadil as an alternative therapy to intracavernous injections in patients who prefer a less-invasive therapy.	Weak

Use low intensity shockwave treatment (LI-SWT) in patients with mild vasculogenic ED or as an alternative first-line therapy in well-informed patients who do not wish or are not suitable for oral vasoactive therapy or desire a curable option.	Weak
Use LI-SWT in vasculogenic ED patients who are poor responders to PDE5Is.	Weak
Use vacuum erection devices as a first-line therapy in well-informed patients with infrequent sexual intercourse and comorbidities requiring non-invasive, drug-free management of ED.	Weak
Use intracavernous injections as an alternative first-line therapy in well-informed patients or as second-line therapy.	Strong
Use implantation of a penile prosthesis if other treatments fail or based upon patient preference.	Strong
Data is inadequate to support the use of any specific regimen for penile rehabilitation after radical prostatectomy.	Strong
Pro-erectile treatments should start at the earliest opportunity after radical prostatectomy/pelvic surgery and other curative treatments for prostate cancer.	Weak

Disorders of ejaculation

Introduction

Ejaculation is a complex physiological process, which is composed of emission and expulsion and is mediated by interwoven neurological and hormonal pathways. Any condition that interferes with these pathways may cause a wide range of ejaculatory disorders.

Table 7: Spectrum of ejaculatory disorders

Premature ejaculation
Retarded or delayed ejaculation
Anejaculation
Painful ejaculation
Retrograde ejaculation
Anorgasmia
Haemospermia

Diagnostic evaluation

Recommendations for the diagnostic evaluation of premature ejaculation

Recommendations	Strength rating
Perform the diagnosis and classification of premature ejaculation (PE) based on medical and sexual history, which should include assessment of intravaginal ejaculatory latency time (IELT) (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	Strong

Use of stopwatch-measured IELT is not compulsory in clinical practice.	Weak
Use patient-reported outcomes in daily clinical practice.	Weak
Include physical examination in the initial assessment of PE to identify anatomical abnormalities that may be associated with PE or other sexual dysfunctions, particularly erectile dysfunction.	Strong
Do not perform routine laboratory or neuro-physiological tests. They should only be directed by specific findings from history or physical examination.	Strong

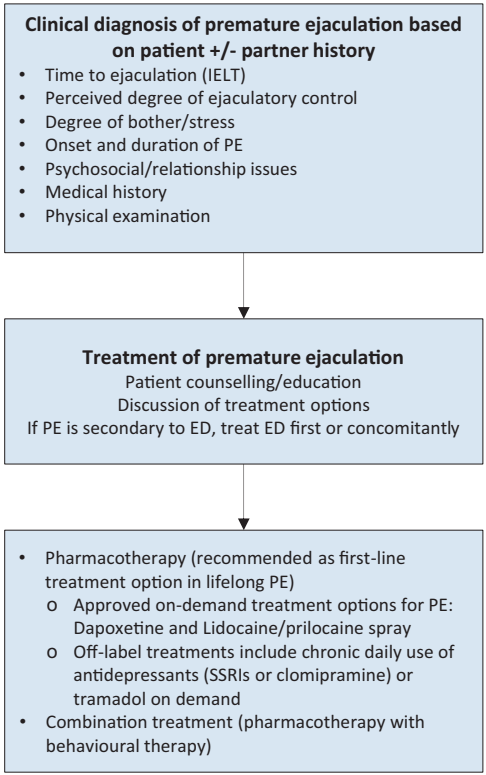
Disease management

Recommendations for the treatment of premature ejaculation

Recommendations	Strength rating
Treat erectile dysfunction (ED), other sexual dysfunction or genitourinary infection (e.g., prostatitis) first.	Strong
Use either dapoxetine or the lidocaine/prilocaine spray as first-line treatments for lifelong premature ejaculation (PE).	Strong
Use off-label topical anaesthetic agents as a viable alternative to oral treatment with selective serotonin re-uptake inhibitor (SSRIs).	Strong
Use tramadol on-demand as a weak alternative to SSRIs.	Weak

Use PDE5Is alone or in combination with other therapies in patients with PE (without ED).	Strong
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired PE.	Weak

Figure 5: Management of premature ejaculation*



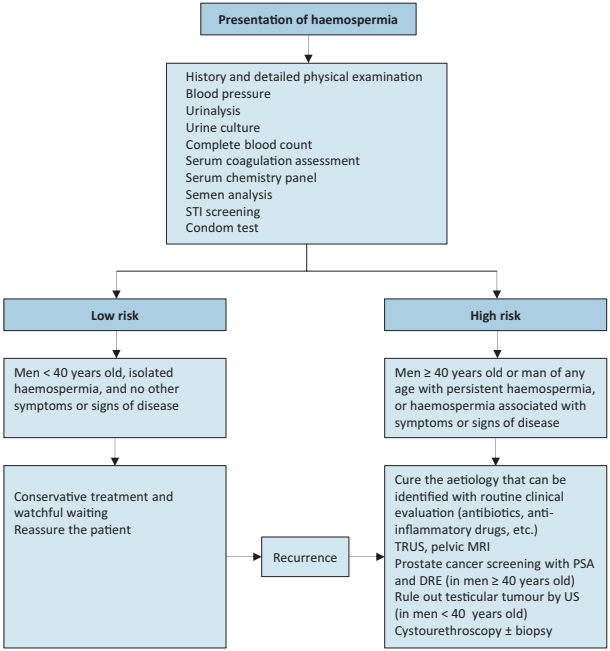
* Adapted from Lue *et al*. 2004.

ED = erectile dysfunction; PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; SSRI = selective serotonin receptor inhibitor.

Recommendations for the management of recurrent haemospermia

Recommendations	Strength rating
Perform a full medical and sexual history with detailed physical examination.	Strong
Men ≥ 40 years of age with persistent haemospermia should be screened for prostate cancer.	Weak
Consider non-invasive imaging modalities (TRUS, MRI) in men ≥ 40 years of age or men of any age with persistent or refractory heamospermia.	Weak
Consider invasive methods such as cystoscopy and vesiculoscopy when the non-invasive methods are inconclusive.	Weak

Figure 6: Management algorithm for haemospermia



STI = sexually transmitted infections; PSA = prostate-specific antigen; DRE = digital rectal examination; US = ultrasonography; TRUS = transrectal ultrasonography; MRI = magnetic resonance imaging.

Low Sexual Desire

Introduction

It has been always a challenge to define sexual desire because of its complex nature and it can be conceptualised in many different ways. According to the ICD-10, lack or loss of sexual desire should be the principal problem and no other sexual problems accompanying it such as erectile dysfunction (ED). In the Diagnostic and Statistical Manual of Mental Disorders-V, male hypoactive sexual desire disorder was defined as "*the persistent or recurrent deficiency (or absence) of sexual or erotic thoughts or fantasies and desire for sexual activity*".

The judgment of deficiency is made by the clinician, taking into account other factors that may affect sexual function, such as age and socio-cultural factors in an individual's life. According to fourth International Consultation on Sexual Medicine (ICSM-IV), the definition of male hypoactive sexual desire disorder was proposed as a *"persistent or recurrent deficiency or absence of sexual or erotic thoughts or fantasies and desire for sexual activity (clinical principle)".*

Table 8: The list of common causes of low sexual desire in men

Androgen deficiency
Hyperprolactinemia
Anger and anxiety
Depression
Relationship conflict
Stroke
Antidepressant therapy
Epilepsy
Post-traumatic stress syndrome
Renal failure
Coronary disease and heart failure

Ageing
HIV
Body-building and eating disorders
Erectile dysfunction
Prostatitis/chronic pelvic pain syndrome

Psychological intervention

Findings on treatment efficacy for psychological intervention are scarce. Accordingly, recommendations must be interpreted with caution. Psychological interventions with a focus on cognitive and behavioural strategies may be beneficial for low sexual desire (LSD) in men. Since both members of a couple may experience age-related changes concurrently and nterdependently, it could be helpful to address the sexual health needs of the aging couple (thus including LSD) as a whole rather than treating the individual patient.

Disease management

Recommendations for the treatment of low sexual desire

Recommendations	Strength rating
Perform the diagnosis and classification of low sexual desire (LSD) based on medical and sexual history, which could include validated questionnaires.	Weak
Include physical examination in the initial assessment of LSD to identify anatomical abnormalities that may be associated with LSD or other sexual dysfunctions, particularly erectile dysfunction.	Weak
Perform laboratory tests to rule out endocrine disorders.	Strong

Modulate chronic therapies which can negatively impact toward sexual desire.	Weak
Replace testosterone if LSD is associated with signs and symptoms of testosterone deficiency.	Strong

Penile curvature

Introduction

Congenital penile curvature (CPC) results from disproportionate development of the tunica albuginea of the corporal bodies and is not associated with urethral malformation. In the majority of cases the curvature is ventral but, can be lateral and rarely dorsal.

Diagnostic evaluation

Taking a medical and sexual history is usually sufficient to establish the diagnosis of CPC. Patients usually present after reaching puberty as the curvature becomes more apparent with erections, and a severe curvature can make intercourse difficult or impossible. Physical examination during erection (autophotograph or after intracavernosal injection of vasoactive drugs) is useful to document curvature and exclude other pathologies.

Disease management

The treatment of this disorder is surgical correction deferred until after puberty. Surgical treatments for congenital penile curvature generally share the same principles as in Peyronie's disease (presented in detail in the next section). Nesbit's procedure with excision of an ellipse of the tunica albuginea is the optimum surgical treatment but many other techniques have been described and employed. Plication techniques are widely used including techniques producing a de-rotation of the corporal bodies. Most of the time, dissection and

mobilisation of the penile dorsal neurovascular bundle are required in order to avoid loss of sensation and ischaemia to the glans penis.

Recommendation for the treatment of congenital penile curvature	Strength rating
Use plication techniques with or without neurovascular bundle dissection (medial/lateral) for satisfactory curvature correction, although there is currently no optimum surgical technique.	Strong

Peyronie's disease

An insult (repetitive microvascular injury or trauma) to the tunica albuginea is the most widely accepted hypothesis on the aetiology of the disease. Abnormal wound healing leads to the remodelling of connective tissue into a fibrotic plaque. Penile plaque formation can result in curvature which, if severe, may impair penetrative sexual intercourse. The most commonly associated comorbidities and risk factors are diabetes, hypertension, dyslipidemias, ischaemic cardiopathy, autoimmune diseases, ED, smoking, excessive consumption of alcohol, low testosterone and pelvic surgery (e.g., radical prostatectomy).

Two phases of the disease can be distinguished. The first is the active inflammatory phase, which may be associated with painful erections and a palpable nodule or plaque in the tunica of the penis; typically, but not invariably, a penile curvature begins to develop. The second is the fibrotic phase with the formation of hard, palpable plaques that can calcify, with stabilisation of the disease and development of the penile deformity.

Diagnostic evaluation

The aim of the initial evaluation is to obtain information on the presenting symptoms and their duration (e.g., pain on erection, palpable nodules, deformity, length and girth and erectile function). It is important to obtain information on the distress caused by the symptoms and the potential risk factors for ED and PD.

Recommendations for the diagnostic evaluation of Peyronie's disease

Recommendations	Strength rating
Take a medical and sexual history of patients with Peyronie's disease (PD), include duration of the disease, pain on erection, penile deformity, difficulty in vaginal intromission due to disabling deformity and erectile dysfunction (ED).	Strong
Take a physical examination, including assessment of palpable plaques, stretched or erect penile length, degree of curvature (self-photography, vacuum-assisted erection test or pharmacological-induced erection) and any other related diseases (e.g. Dupuytren's contracture, Ledderhose disease) in patients with PD.	Strong
Use the intracavernous injection (IC) method to provide an objective assessment of penile curvature with an erection in the diagnostic work-up of PD.	Weak
Use the PD specific questionnaire especially in clinical trials, but mainstream usage in daily clinical practice is not mandatory.	Weak

Do not use ultrasound (US), computerised tomography or magnetic resonance imaging to assess plaque size and deformity in everyday clinical practice.	Weak
Use Doppler US only in the case of diagnostic evaluation of ED, to ascertain penile haemodynamic and vascular anatomy.	Weak

Disease management

Non-operative treatment

Table 9: Conservative treatments for Peyronie's disease

Oral treatments
Non-steroidal anti-inflammatory drugs (NSAIDs)
Phosphodiesterase type 5 inhibitors (PDE5Is)
Intralesional treatments
Verapamil
Nicardipine
Clostridium collagenase
Interferon α2B
Hyaluronic acid
Botulinum toxin
Topical treatments
H-100 gel
Extracorporeal shockwave treatment

Other
Traction devices
Multimodal treatment

Recommendations for the conservative treatment of Peyronie's disease

Recommendations	Strength rating
Offer conservative treatment to patients not fit for surgery or when surgery is not acceptable to the patient.	Strong
Discuss with patients all the available treatment options and expected results before starting any treatment.	Strong
Do not offer oral treatment with vitamin E, potassium para-aminobenzoate (potaba), tamoxifen, pentoxifiline, colchicine and acetyl esters of carnitine to treat Peyronie's disease (PD).	Strong
Non-steroidal anti-inflammatory drugs can be used to treat penile pain in the acute phase of PD.	Strong
Extracorporeal shockwave treatment (ESWT) can be used to treat penile pain in the acute phase of PD.	Weak
Phosphodiesterase type 5 inhibitors can be used to treat concomitant erectile dysfunction or if the deformity results in difficulty in penetrative intercourse in order to optimise penetration.	Weak
Intralesional therapy with interferon alpha-2b may be offered in patients with stable curvature dorsal or lateral > 30° seeking a minimal invasive procedure.	Strong

Intralesional therapy with collagenase of *clostridium histolyticum* may be offered in patients with stable PD and dorsal or lateral curvature > 30°, who request non-surgical treatment, although the placebo effects are high.	Strong
Do not offer intralesional treatment with steroids to reduce penile curvature, plaque size or pain.	Strong
Do not offer ESWT to improve penile curvature and reduce plaque size.	Strong
Penile traction devices and vacuum devices may be offered to reduce penile deformity or as part of a multimodal therapy approach, although outcome data is limited.	Weak

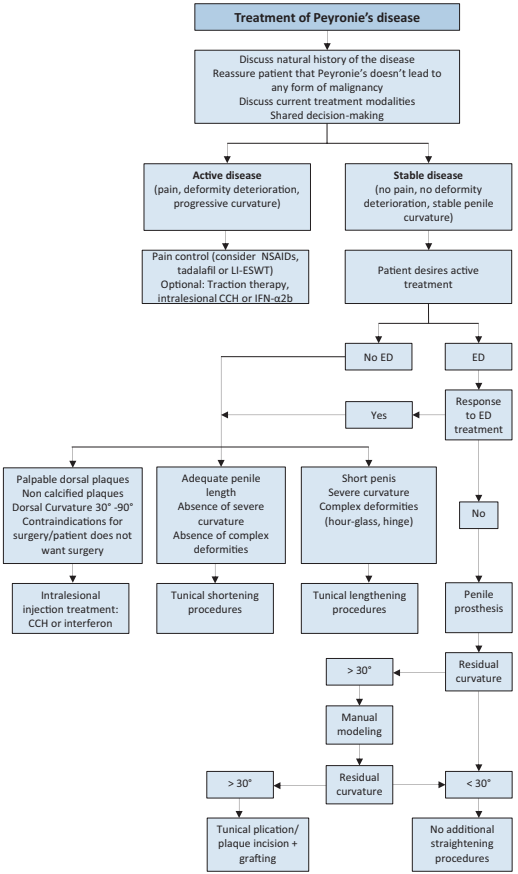
Surgical treatment

Recommendations for the surgical treatment

Recommendations	Strength rating
Perform surgery only when Peyronie's disease (PD) has been stable for at least three months (without pain or deformity deterioration), which is usually the case after twelve months from the onset of symptoms, and intercourse is compromised due to deformity.	Strong
Prior to surgery, assess penile length, curvature severity, erectile function (including response to pharmacotherapy in case of erectile dysfunction [ED]) and patient expectations.	Strong

Use tunical shortening procedures as the first treatment option for congenital penile curvature and for PD with adequate penile length and rigidity, non-severe curvature and absence of complex deformities (hour-glass, hinge). The type of procedure used is dependent on surgeon and patient preference, as no procedure has proven superior to its counterparts.	Weak
Use tunical lengthening procedures for patients with PD and normal erectile function, without adequate penile length, severe curvature or presence of complex deformities (hour-glass, hinge). The type of graft used is dependent on the surgeon and patient factors, as no graft has proven superior to its counterparts.	Weak
Use the sliding techniques with caution, as there is a significant risk of life changing complications (e.g., glans necrosis).	Strong
Do not use synthetic grafts in PD reconstructive surgery.	Strong
Use penile prosthesis implantation, with or without any additional procedure (modeling, plication, incision or excision with or without grafting), in PD patients with ED not responding to pharmacotherapy.	Strong

Figure 7 : Treatment algorithm for Peyronie's disease



ED = erectile dysfunction; Li-ESWT= low-intensity extracorporeal shockwave treatment; US = ultrasound.

Male infertility

Introduction

'Infertility is the inability of a sexually active, non-contraceptive couple to achieve spontaneous pregnancy in one year' (World Health Organization [WHO] 2000).

Diagnostic evaluation

A focused evaluation of the male patient must always be undertaken and should include: a medical and reproductive history; physical examination; semen analysis – with strict adherence to WHO reference values for human semen characteristics, and hormonal evaluation. Other investigations (e.g., genetic analysis and imaging) may be required depending on the clinical features and findings on semen analysis.

Semen analysis

A comprehensive andrological examination is always indicated if the semen analysis shows abnormalities when compared to reference values (Table 10).

Table 10: Lower reference limits (5th centiles and their 95% CIs) for semen characteristics

Parameter	Lower reference limit (range)
Semen volume (mL)	1.5 (1.4-1.7)
Total sperm number (10^6/ejaculate)	39 (33-46)
Sperm concentration (10^6/mL)	15 (12-16)
Total motility (PR + NP)	40 (38-42)
Progressive motility (PR, %)	32 (31-34)
Vitality (live spermatozoa, %)	58 (55-63)

Sperm morphology (normal forms, %)	4 (3.0-4.0)
Other consensus threshold values	
pH	> 7.2
Peroxidase-positive leukocytes (10^6/mL)	< 1.0
Optional investigations	
MAR test (motile spermatozoa with bound particles, %)	< 50
Immunobead test (motile spermatozoa with bound beads, %)	< 50
Seminal zinc (µmol/ejaculate)	≥ 2.4
Seminal fructose (µmol/ejaculate)	≥ 13
Seminal neutral glucosidase (mU/ejaculate)	≤ 20

CIs = confidence intervals; MAR = mixed antiglobulin reaction; NP = non-progressive; PR = progressive (a+b motility).

Recommendations for the diagnostic work-up of male infertility

Recommendations	Strength rating
Include a parallel assessment of the fertility status, including ovarian reserve, of the female partner during the diagnosis and management of the infertile male, since this might determine decision making in terms of timing and therapeutic strategies (e.g., ART vs. surgical intervention).	Strong
A complete medical history, physical examination and semen analysis are the essential components of male infertility evaluation.	Strong

Prader's orchidometer-derived testis volume is a reliable surrogate of ultrasound-measured testis volume in everyday clinical practice.	Weak
Perform semen analyses according to the WHO Laboratory Manual for the Examination and Processing of Human Semen (5th edn) indications and reference criteria.	Strong
Perform a full andrological assessment in all men with couple infertility, particularly when semen analysis is abnormal in at least two consecutive tests.	Strong
In cases of oligozoospermia and azoospermia, a hormonal evaluation should be performed, including a serum total testosterone and Follicle-Stimulating Hormone (FSH)/Luteinising Hormone.	Weak
Offer standard karyotype analysis and genetic counselling to all men with azoospermia and oligozoospermia (spermatozoa < 10 million/mL) for diagnostic purposes.	Strong
Do not test for Y-chromosome micro-deletions in men with pure obstructive azoospermia as spermatogenesis will be normal.	Strong
Y-chromosome microdeletion testing may be offered in men with sperm concentrations of < 5 million sperm/mL, but should be mandatory in men with sperm concentrations of ≤ 1 million sperm/mL.	Strong

Testicular sperm extraction (TESE) (any type) should not be attempted in patients with complete deletions that include the aZFa and aZFb regions, since they are a poor prognostic indicator for retrieving sperm at surgery.	Strong
Inform men with Yq microdeletion and their partners who wish to proceed with intracytoplasmic sperm injection (ICSI) that microdeletions will be passed to sons, but not to their daughters.	Strong
In men with structural abnormalities of the vas deferens (unilateral or bilateral absence with no renal agenesis), test the male and his partner for cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations, which should include common point mutations and the 5T allele.	Strong
Provide genetic counselling in all couples with a genetic abnormality found on clinical or genetic investigation and in patients who carry a (potential) inheritable disease.	Strong
For men with Klinefelter Syndrome offer long-term endocrine follow-up and appropriate medical treatment.	Strong
Do not routinely use reactive oxygen species testing in the diagnosis and management of the male partner of an infertile couple.	Weak
Sperm DNA fragmentation testing should be performed in the assessment of couples with recurrent pregnancy loss from natural conception and ART or men with unexplained infertility.	Strong

Perform scrotal ultrasound (US) in patients with infertility, as there is a higher risk of testis cancer.	Weak
A multidisciplinary team discussion concerning invasive diagnostic modalities (e.g., US-guided testis biopsy with frozen section versus radical orchidectomy versus surveillance) should be considered in infertile men with US-detected indeterminate testicular lesions, especially if additional risk factors for malignancy are present.	Weak
Perform transrectal US if a partial or complete distal obstruction is suspected.	Strong
Consider imaging for renal abnormalities in men with structural abnormalities in the vas deferens and no evidence of CFTR abnormalities.	Strong

Special Conditions and Relevant Clinical Entities

Crytorchidism

Cryptorchidism is the most common congenital abnormality of the male genitalia; at one year of age nearly 1% of all full-term male infants have cryptorchidism. Approximately 30% of undescended testes are non-palpable and may be located within the abdominal cavity.

Recommendations	Strength rating
Do not use hormonal treatment for cryptorchidism in post-pubertal men.	Strong

If undescended testes are corrected in adulthood, perform simultaneous testicular biopsy, for the detection of intratubular germ cell neoplasia *in situ* (formerly carcinoma *in situ*).	Strong
Men with unilateral undescended testis and normal hormonal function/spermatogenesis should be offered orchidectomy.	Strong
Men with unilateral or bilateral undescended testis with biochemical hypogonadism and/or or spermatogenic failure (i.e., infertility) may be offered unilateral or bilateral orchidopexy, if technically feasible.	Weak

Germ cell malignancy and male infertility

Testicular germ cell tumour (TGCT) is the most common malignancy in Caucasian men aged 15-40 years, and affects approximately 1% of sub-fertile men. Overall, sperm, cryopreservation is considered standard practice in all patients with cancer and not only those with testicular cancer. As such, it is important to stress that all men with cancer must be offered sperm cryopreservation prior to the therapeutic use of gonadotoxic agents or ablative surgery which may impair spermatogenesis or ejaculation (i.e., chemotherapy; radiation therapy; retroperitoneal surgery). Men with TGCT have decreased semen quality, even before cancer treatment.

Recommendations	Strength rating
Men with testicular microcalcification (TM) should learn to perform self-examination even without additional risk factors, as this may result in early detection of testicular germ cell tumour (TGCT).	Weak

Do not perform testicular biopsy, follow-up scrotal ultrasound (US), measure biochemical tumour markers, or abdominal or pelvic computed tomography, in men with isolated TM without associated risk factors (e.g., infertility, cryptorchidism, testicular cancer, and atrophic testis).	Strong
Testicular biopsy may be offered in infertile men with TM, who belong to one of the following higher risk groups: spermatogenic failure (infertility), bilateral TM, atrophic testes (less than 12 mL), history of undescended testes and TGCT.	Weak
If there are suspicious findings on physical examination or US in patients with TM with associated lesions, perform inguinal surgical exploration with testicular biopsy or offer orchidectomy after multi-disciplinary meeting and discussion with the patient.	Strong
Men treated for TGCT are at increased risk of developing hypogonadism, sexual dysfunction and cardiovascular risk. Men should be managed in a multidisciplinary team setting with a dedicated late effects clinic.	Weak
Sperm cryopreservation should be performed prior to planned orchidectomy, since men with testis cancer may have significant semen abnormalities (including azoospermia).	Weak

Men with testis cancer and azoospermia or severe abnormalities in their semen parameters may be offered onco-testicular sperm extraction (TESE) at the time of radical orchidectomy.	Weak

Varicocele

Varicocele is a common genital abnormality, which may be associated with the following andrological conditions:

- male subfertility;
- failure of ipsilateral testicular growth and development;
- symptoms of pain and discomfort;
- hypogonadism.

Recommendations	Strength rating
Treat varicocele in adolescents with ipsilateral reduction in testicular volume and evidence of progressive testicular dysfunction.	Weak
Do not treat varicocele in infertile men who have normal semen analysis and in men with a subclinical varicocele.	Weak
Treat infertile men with a clinical varicocele, abnormal semen parameters and otherwise unexplained infertility in a couple where the female partner has good ovarian reserve to improve fertility rates.	Strong
Varicocelectomy may be considered in men with raised DNA fragmentation with otherwise unexplained infertility or who have suffered from failed assisted reproductive techniques, including recurrent pregnancy loss, failure of embryo-genesis and implantation failure.	Weak

Male accessory gland infections and infertility

Infections of the male urogenital tract are potentially curable causes of male infertility. The WHO considers urethritis, prostatitis, orchitis and epididymitis to be male accessory gland infections (MAGIs). Semen analysis clarifies whether the prostate is involved as part of a generalised MAGI and provides information regarding sperm quality. In addition, leukocyte analysis allows differentiation between inflammatory and non-inflammatory chronic pelvic pain syndrome.

Recommendations	Strength rating
Treating male accessory gland infections (MAGIs) may improve sperm quality, although it does not necessarily improve the probability of increasing conception.	Weak
Data is insufficient to conclude whether antibiotics and antioxidants for the treatment of infertile men with leukocyto-spermia may improve fertility outcomes.	Weak
Refer sexual partners of patients with accessory sex gland infections that are known or suspected to be caused by sexually transmitted diseases for evaluation and treatment.	Strong

Non-Invasive Male Infertility Management

Idiopathic male infertility and OATS

Oligo-astheno-teratozoospermia (OAT) is a clinical condition, with a reduced number of spermatozoa in the ejaculate, which is also characterised by a reduced motility and morphology; often referred to as OAT syndrome (OATS).

Recommendations	Strength rating
In men with idiopathic oligo-astheno-teratozoospermia, life-style changes including weight loss and increased physical activity, smoking cessation and alcohol intake reduction can improve sperm quality and the chances of conception.	Weak
No clear recommendation can be made for treatment of patients with idiopathic infertility using antioxidants, although anti-oxidant use may improve semen parameters.	Weak
No conclusive recommendations on the use of selective oestrogen receptor modulators in men with idiopathic infertility can be drawn.	Weak
No conclusive recommendations on the use of either steroidal (testolactone) or non-steroidal (anastrozole and letrozole) aromatase inhibitors in men with idiopathic infertility can be drawn, even before testis surgery.	Weak

Hormonal therapy

Recommendations	Strength rating
Hypogonadotropic hypogonadism (secondary hypogonadism), including congenital causes, should be treated with combined human chorionic gonadotropin (hCG) and follicle-stimulating hormone (FSH) (recombinant FSH; highly purified FSH) or pulsed gonadotropin releasing hormone (GnRH) via pump therapy to stimulate spermatogenesis.	Strong
In men with hypogonadotropic hypogonadism, induce spermatogenesis by an effective drug therapy (hCG; human menopausal gonadotropins; recombinant FSH; highly purified FSH).	Strong
The use of GnRH therapy is more expensive and does not offer any advantages when compared to gonadotropins for the treatment of hypogonadotropic hypogonadism.	Strong
In men with idiopathic oligozoospermia and FSH values within the normal range, FSH treatment may ameliorate spermatogenesis outcomes.	Weak
No conclusive recommendations can be given on the use of high dose FSH in men with idiopathic infertility prior (m)TESE and therefore cannot be routinely advocated.	Weak
Do not use testosterone therapy for the treatment of male infertility.	Strong

Provide testosterone therapy for symptomatic patients with primary and secondary hypogonadism who are not considering parenthood.	Strong
In the presence of hyperprolactinaemia dopamine agonist therapy may improve spermatogenesis.	Weak

Invasive Male Infertility Management

Obstructive azoospermia

Obstructive azoospermia (OA) is the absence of spermatozoa in the sediment of a centrifuged sample of ejaculate due to obstruction. Obstructive azoospermia is less common than non-obstructive azoospermia (NOA) and occurs in 20-40% of men with azoospermia. Men with OA usually have a normal FSH, testes of normal size and epididymal enlargement or distension. Of clinical relevance, men with late maturation arrest may present with normal gonadotrophins and testis size and may be only be distinguished from OA at the time of surgical exploration. The vas deferens may be absent bilaterally (CBAVD) or unilaterally (CUAVD). Obstruction in primary infertile men is more frequently present at the epididymal level.

Recommendations	Strength rating
Perform microsurgical vasovasostomy or epididymovasostomy for azoospermia caused by epididymal or vasal obstruction in men with female partners of good ovarian reserve.	Strong

Use sperm retrieval techniques, such as microsurgical epididymal sperm aspiration (MESA), testicular sperm extraction (TESE) and percutaneous techniques (PESA, TESA) either as an adjunct to reconstructive surgery, or if the condition is not amenable to surgical repair, or when the ovarian reserve of the partner is limited or patient preference is not to undertake a surgical reconstruction and the couple prefer to proceed to ICSI treatment directly.	Strong

Non-obstructive azoospermia

Non-obstructive azoospermia (NOA) is defined as the absence of sperm in semen analysis after centrifugation, with usually a normal ejaculate volume. This finding should be confirmed on at least two consecutives semen analyses. The severe deficit in spermatogenesis observed in NOA patients is often a consequence of primary testicular dysfunction or may be related to a dysfunction of the hypothalamus-pituitary-gonadal (HPG) axis.

Recommendations	Strength rating
Patients with non-obstructive azoospermia (NOA) should undergo a comprehensive assessment, including detailed medical history, hormonal profile and genetic tests to investigate the underlying aetiology and associated comorbidities. Genetic counselling is mandatory in couples with genetic abnormalities prior to any assisted reproductive technology (ART) protocols.	Strong

Surgery for sperm retrieval can be performed in men who are candidates for ART (i.e., intracytoplasmic sperm injection). In patients with complete AZFa and AZFb microdeletions surgery is contra-indicated since the chance of sperm retrieval is zero.	Strong
Fine needle aspiration (FNA) and testicular sperm aspiration (TESA) should not be considered the treatments of choice in patients with NOA, given the lower probability of positive sperm retrieval compared to conventional testicular sperm extraction (cTESE) and microdissection TESE (mTESE).	Weak
Fine needle aspiration as a prognostic procedure prior to definitive testicular sperm extraction (any type) in patients with NOA is not recommended for use in routine clinical practice.	Weak
Conventional TESE or mTESE are the techniques of choice for retrieving sperm in patients with NOA.	Weak
No pre-operative biochemical and clinical variables may be considered sufficient and reliable predictors of positive sperm retrieval at surgery in patients with NOA.	Weak
No conclusive recommendations on the routine use of medical therapy (e.g., recombinant follicle-stimulating hormone (FSH); highly purified FSH; human chorionic gonadotrophin (hCG); aromatase inhibitors or selective oestrogen receptor modulators [SERMs]) in patients with NOA can be drawn and are not therefore currently recommended routinely before TESE.	Weak

This short booklet is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON PRIAPISM

(Limited text update March 2018)

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Introduction

Priapism is a pathological condition representing a true disorder of penile erection that persists for more than four hours and is beyond or unrelated to sexual interest or stimulation. Erections lasting up to four hours are defined by consensus as 'prolonged'. Priapism may occur at all ages.

Classification

Ischaemic priapism is a persistent erection marked by rigidity of the corpora cavernosa and by little or no cavernous arterial inflow, although often proximally there is a compensated high velocity picture with little blood flow distally. The patient typically complains of penile pain and clinical examination reveals a rigid erection.

Non-ischaemic priapism is a persistent erection caused by unregulated cavernous arterial inflow. The patient typically reports an erection that is not fully rigid and is not associated with pain although fully rigid erections may still occur with sexual stimulation.

Stuttering (recurrent or intermittent) priapism is a distinct condition that is characterised by repetitive and painful episodes of prolonged erections. Erections are often

self-limited with intervening periods of detumescence. These are analogous to repeated episodes of ischaemic (or low flow) priapism. The duration of the erectile episodes is generally shorter than in ischaemic priapism. The frequency and/or duration of these episodes is variable and a single episode can sometimes progress into a full-blown ischaemic priapism.

Ischaemic (Low-Flow or Veno-Occlusive) Priapism

Diagnostic Evaluation

Table 1: Key points when taking the history of priapism

Duration of erection
Presence and severity of pain
Previous episodes of priapism and method of treatment
Current erectile function, especially the use of any erectogenic therapies prescription or nutritional supplements
Medications and recreational drug use
Sickle cell disease, haemoglobinopathies, hypercoagulable states
Trauma to the pelvis, perineum, or penis

Table 2: Key findings in priapism

	Ischaemic priapism	Non-ischaemic priapism
Corpora cavernosa fully rigid	Usually	Seldom
Penile pain	Usually	Seldom
Abnormal penile blood gas	Usually	Seldom
Haematological abnormalities	Sometimes	Seldom
Recent intracavernosal injection	Sometimes	Sometimes
Perineal trauma	Seldom	Usually

Table 3: Typical blood gas values

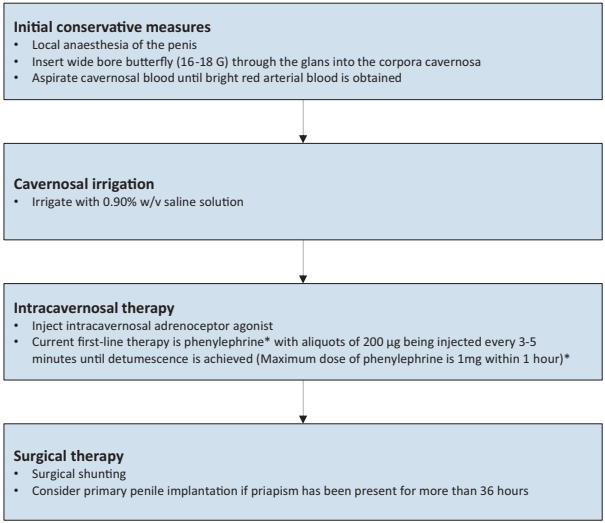
Source	pO_2 (mmHg)	pCO_2 (mmHg)	pH
Normal arterial blood (room air) [similar values are found in arterial priapism]	> 90	< 40	7.40
Normal mixed venous blood (room air)	40	50	7.35
Ischaemic priapism (first corporal aspirate)	< 30	> 60	< 7.25

Recommendations for the diagnosis of ischaemic priapism	Strength rating
Take a comprehensive history to establish the diagnosis which can help to determine the priapism subtype.	Strong
Include a physical examination of the genitalia, the perineum and the abdomen in the diagnostic evaluation.	Strong
For laboratory testing, include complete blood count, white blood count with blood cell differential, platelet count and coagulation profile. Direct further laboratory testing based on history, clinical and laboratory findings. In children with priapism, perform a complete evaluation of all possible causes.	Strong
Analyse the blood gas parameters from blood aspirated from the penis to differentiate between ischaemic and non-ischaemic priapism.	Strong
Perform colour duplex ultrasound of the penis and perineum for the differentiation between ischaemic and non-ischaemic priapism as an alternative or adjunct to blood gas analysis.	Strong
In cases of prolonged ischaemic priapism, use magnetic resonance imaging of the penis to predict smooth muscle viability and confirm erectile function restoration.	Strong
Perform selected pudendal arteriogram when embolisation is planned for the management of non-ischaemic priapism.	Strong

Disease Management

The treatment is sequential and the physician should move on to the next stage if the treatment fails.

Figure 1: Treatment of ischaemic priapism



** The dose of phenylephrine should be reduced in children. It can result in significant hypertension and should be used with caution in men with cardiovascular disease. Monitoring of pulse, blood pressure and electrocardiogram (ECG) is advisable in all patients during administration and for 60 minutes afterwards. Its use is contraindicated in men with a history of cerebro-vascular disease and significant hypertension.*

Table 4: Medical treatment of ischaemic priapism

Drug	Dosage/Instructions for use
Phenylephrine	• Intracavernous injection of 200 µg every three to five minutes. • Maximum dosage is 1 mg within one hour. • Lower doses are recommended in children and patients with severe cardiovascular disease.
Etilephrine	• Intracavernosal injection at a concentration of 2.5 mg in 1-2 mL normal saline.
Methylene blue	• Intracavernous injection of 50-100 mg, left for five minutes. It is then aspirated and the penis compressed for an additional five minutes.
Adrenaline	• Intracavernous injection of 2 mL of 1/100,000 adrenaline solution up to five times over a twenty minute period.
Terbutaline	• Oral administration of 5 mg for prolonged erections lasting more than 2.5 hours, after intracavernous injection of vasoactive agents.

Recommendations for the treatment of ischaemic priapism	Strength rating
Start management of ischaemic priapism as early as possible (within four to six hours) and follow a stepwise approach.	Strong

First, decompress the corpora cavernosa by penile aspiration until fresh red blood is obtained.	Weak
In priapism secondary to intracavernous injections of vasoactive agents, replace blood aspiration with intracavernous injection of a sympathomimetic drug as the first step.	Strong
In priapism that persists despite aspiration, proceed to the next step, which is intra-cavernous injection of a sympathomimetic drug.	Strong
In cases that persist despite aspiration and intracavernous injection of a sympathomi-metic drug, repeat these steps several times before considering surgical intervention.	Strong
Treat ischaemic priapism due to sickle cell anaemia in the same fashion as idiopathic ischaemic priapism. Provide other supportive measures (intravenous hydration, oxygen administration with alkalisation with bicarbonates, blood exchange transfusions), but do not delay initial treatment to the penis.	Strong
Proceed to surgical treatment only when blood aspiration and intracavernous injection of sympathomimetic drugs have failed or for priapism events lasting < 72 hours.	Strong
Perform distal shunt surgical procedures first followed by proximal procedures in case of failure.	Strong
Consider insertion of a penile prosthesis if priapism episode is > 36 hours after onset, or in cases for which all other interventions have failed.	Strong

Non-ischaemic (High-Flow or Arterial) Priapism

Diagnostic Evaluation

History

A comprehensive history is also mandatory in the diagnosis of non-ischaemic priapism and follows the same principles as described in Table 1.

Recommendations for the diagnosis of non-ischaemic priapism

The same recommendations as for ischaemic priapism apply.

Disease Management

Recommendations for the treatment of non-ischaemic priapism	Strength rating
Because non-ischaemic priapism is not an emergency, perform definitive management at the discretion of the treating physician.	Weak
Manage conservatively with the use of site specific perineal compression as the first step, especially in children. Consider androgen deprivation therapy only in adults.	Weak
Perform superselective arterial embolisation, using temporary material.	Strong
Repeat the procedure with temporary or permanent material for recurrent non-ischaemic priapism following selective arterial embolisation.	Weak
Reserve selective surgical ligation of a fistula as a final treatment option when embolisation has failed.	Weak

Stuttering (Recurrent or Intermittent) Priapism

Diagnostic Evaluation

History

A comprehensive history is mandatory and follows the same principles as described in Table 1.

Disease Management

Recommendations for the treatment of stuttering priapism	Strength rating
Manage each acute episode similar to that for ischaemic priapism.	Weak
Use hormonal therapies (mainly gonadotropin-receptor hormone agonists or antagonists) and/or anti-androgens for the prevention of future episodes in patients with frequent relapses. Do not use them before sexual maturation is reached.	Weak
Initiate treatment with phosphodiesterase type 5 inhibitors only when the penis is in its flaccid state.	Strong
Use digoxin, α-adrenergic agonists, baclofen, gabapentin or terbutaline only in patients with very frequent and uncontrolled relapses.	Weak
Use intracavernous self-injections at home of sympathomimetic drugs for the treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.	Weak

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON UROLOGICAL INFECTIONS

(Limited text update March 2020)

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Introduction

The European Association of Urology (EAU) Urological Infections Guidelines Panel has compiled these clinical guidelines to provide medical professionals with evidence-based information and recommendations for the prevention and treatment of urological tract infections (UTIs). These guidelines also aim to address the important public health aspects of infection control and antimicrobial stewardship.

Important notice:
On March 11, 2019 the European Commission implemented stringent regulatory conditions regarding the use of fluoroquinolones due to their disabling and potentially long-lasting side effects. This legally binding decision is applicable in all EU countries. National authorities have been urged to enforce this ruling and to take all appropriate measures to promote the correct use of this class of antibiotics.

Antimicrobial Stewardship

Stewardship programmes have two main sets of actions. The first set mandates use of recommended care at the patient level conforming to guidelines. The second set describes strategies to achieve adherence to the mandated guidance.

These include persuasive actions such as education and feedback together with restricting availability linked to local formularies. The important components of antimicrobial stewardship programmes are:

- regular training of staff in best use of antimicrobial agents;
- adherence to local, national or international guidelines;
- regular ward visits and consultation with infectious diseases physicians and clinical microbiologists;
- audit of adherence and treatment outcomes;
- regular monitoring and feedback to prescribers of their performance and local pathogen resistance profiles.

Asymptomatic Bacteriuria

Asymptomatic bacteriuria in an individual without urinary tract symptoms is defined by a mid-stream sample of urine showing bacterial growth ≥ 10^5 cfu/mL in two consecutive samples in women and in one single sample in men.

Recommendations	Strength rating
Do not screen or treat asymptomatic bacteriuria in the following conditions: • women without risk factors; • patients with well-regulated diabetes mellitus; • post-menopausal women; • elderly institutionalised patients; • patients with dysfunctional and/or reconstructed lower urinary tracts; • patients with renal transplants; • patients prior to arthoplasty surgeries; • patients with recurrent urinary tract infections.	Strong

Screen for and treat asymptomatic bacteriuria prior to urological procedures breaching the mucosa.	Strong
Screen for and treat asymptomatic bacteriuria in pregnant women with standard short course treatment.	Weak

Uncomplicated Cystitis

Uncomplicated cystitis is defined as acute, sporadic or recurrent cystitis limited to non-pregnant women with no known relevant anatomical and functional abnormalities within the urinary tract or comorbidities.

Recommendations for the diagnostic evaluation of uncomplicated cystitis	**Strength rating**
Diagnose uncomplicated cystitis in women who have no other risk factors for complicated urinary tract infections based on: • a focused history of lower urinary tract symptoms (dysuria, frequency and urgency); • the absence of vaginal discharge or irritation.	Strong
Use urine dipstick testing for diagnosis of acute uncomplicated cystitis.	Weak
Urine cultures should be done in the following situations: • suspected acute pyelonephritis; • symptoms that do not resolve or recur within four weeks after the completion of treatment; • women who present with atypical symptoms; • pregnant women.	Strong

In uncomplicated cystitis a fluoroquinolone should only be used when it is considered inappropriate to use other antibacterial agents that are commonly recommended for the treatment of these infections.

Recommendations for antimicrobial therapy for uncomplicated cystitis	Strength rating
Prescribe fosfomycin trometamol, pivmecillinam or nitrofurantoin as first-line treatment for uncomplicated cystitis in women.	Strong
Do not use aminopenicillins or fluoroquinolones to treat uncomplicated cystitis.	Strong

Table 1: Suggested regimens for antimicrobial therapy in uncomplicated cystitis

Antimicrobial	Daily dose	Duration of therapy	Comments
First-line women			
Fosfomycin trometamol	3 g SD	1 day	Recommended only in women with uncomplicated cystitis
Nitrofurantoin macrocrystal	50-100 mg four times a day	5 days	
Nitrofurantoin monohydrate/ macrocrystals	100 mg b.i.d	5 days	
Nitrofurantoin macrocrystal prolonged release	100 mg b.i.d	5 days	
Pivmecillinam	400 mg t.i.d	3-5 days	

Alternatives			
Cephalosporins (e.g. cefadroxil)	500 mg b.i.d	3 days	Or comparable
If the local resistance pattern for E. coli is < 20%			
Trimethoprim	200 mg b.i.d	5 days	Not in the first trimenon of pregnancy
Trimethoprim-sulphamethoxazole	160/800 mg b.i.d	3 days	Not in the last trimenon of pregnancy
Treatment in men			
Trimethoprim-sulphamethoxazole	160/800 mg b.i.d	7 days	Restricted to men, fluoroquinolones can also be prescribed in accordance with local susceptibility testing.

SD = single dose; b.i.d = twice daily; t.i.d = three times daily.

Recurrent UTIs

Recurrent UTIs (rUTIs) are recurrences of uncomplicated and/or complicated UTIs, with a frequency of at least three UTIs/year or two UTIs in the last six months.

Recommendations for the diagnostic evaluation and treatment of rUTIs	Strength rating
Diagnose recurrent UTI by urine culture.	Strong
Do not perform an extensive routine work-up (e.g cystoscopy, full abdominal ultrasound) in women younger than 40 years of age with recurrent UTI and no risk factors.	Weak
Advise patients on behavioural modifications which might reduce the risk of recurrent UTI.	Weak
Use vaginal oestrogen replacement in post-menopausal women to prevent recurrent UTI.	Weak
Use immunoactive prophylaxis to reduce recurrent UTI in all age groups.	Strong
Use continuous or post-coital antimicrobial prophylaxis to prevent recurrent UTI when non-antimicrobial interventions have failed. Counsel patients regarding possible side effects.	Strong
For patients with good compliance self-administered short term antimicrobial therapy should be considered.	Strong

Uncomplicated Pyelonephritis

Uncomplicated pyelonephritis is defined as pyelonephritis limited to non-pregnant, pre-menopausal women with no known relevant urological abnormalities or comorbidities.

Recommendations for the diagnostic evaluation of uncomplicated pyelonephritis	Strength rating
Perform urinalysis (e.g. using a dipstick method), including the assessment of white and red blood cells and nitrite, for routine diagnosis.	Strong
Perform urine culture and antimicrobial susceptibility testing in patients with pyelonephritis.	Strong
Perform imaging of the urinary tract to exclude urgent urological disorders.	Strong

Recommendations for the treatment of uncomplicated pyelonephritis	Strength rating
Treat patients with uncomplicated pyelonephritis not requiring hospitalisation with short course fluoroquinolones as first-line treatment.	Strong
Treat patients with uncomplicated pyelonephritis requiring hospitalisation with an intravenous antimicrobial regimen initially.	Strong
Switch patients initially treated with parenteral therapy, who improve clinically and can tolerate oral fluids, to oral antimicrobial therapy.	Strong
Do not use nitrofurantoin, oral fosfomycin, and pivmecillinam to treat uncomplicated pyelonephritis.	Strong

Table 2: Suggested regimens for empirical oral antimicrobial therapy in uncomplicated pyelonephritis			
Antimicrobial	**Daily dose**	**Duration of therapy**	**Comments**
Ciprofloxacin	500-750 mg b.i.d	7 days	Fluoroquinolone resistance should be less than 10%.
Levofloxacin	750 mg q.d	5 days	
Trimethoprim sulphamethoxazol	160/800 mg b.i.d	14 days	If such agents are used empirically, an initial intravenous dose of a long-acting parenteral antimicrobial (e.g. ceftriaxone) should be administered.
Cefpodoxime	200 mg b.i.d	10 days	
Ceftibuten	400 mg q.d	10 days	

b.i.d = twice daily; q.d = every day.

Table 3: Suggested regimens for empirical parenteral antimicrobial therapy in uncomplicated pyelonephritis		
Antimicrobials	**Daily dose**	**Comments**
First-line treatment		
Ciprofloxacin	400 mg b.i.d	
Levofloxacin	750 mg q.d	
Cefotaxime	2 g t.i.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Ceftriaxone	1-2 g q.d	Lower dose studied, but higher dose recommended.
Second-line treatment		
Cefepime	1-2 g b.i.d	Lower dose studied, but higher dose recommended.
Piperacillin/ tazobactam	2.5-4.5 g t.i.d	
Gentamicin	5 mg/kg q.d	Not studied as monotherapy in acute uncomplicated pyelonephritis.
Amikacin	15 mg/kg q.d	

Last-line alternatives		
Imipenem/ cilastatin	0.5 g t.i.d	Consider only in patients with early culture results indicating the presence of multi-drug resistant organisms.
Meropenem	1 g t.i.d	
Ceftolozane/ tazobactam	1.5 g t.i.d	
Ceftazidime/ avibactam	2.5 g t.i.d	
Cefiderocol	2 g t.i.d	
Meropenem-vaborbactam	2 g t.i.d	
Plazomicin	15 mg/kg o.d	

b.i.d = twice daily; t.i.d = three times daily; q.d = every day; o.d = once daily.

Complicated UTIs

A complicated UTI occurs in an individual in whom factors related to the host (e.g. underlying diabetes or immunosuppression) or specific anatomical or functional abnormalities related to the urinary tract (e.g. obstruction, incomplete voiding due to detrusor muscle dysfunction) are believed to result in an infection that will be more difficult to eradicate than an uncomplicated infection.

Recommendations for the treatment of complicated UTIs	Strength rating
Use the combination of: • amoxicillin plus an aminoglycoside; • a second generation cephalosporin plus an aminoglycoside; • a third generation cephalosporin intravenously as empirical treatment of complicated UTI with systemic symptoms.	Strong
Only use ciprofloxacin provided that the local resistance percentages are < 10% when: • the entire treatment is given orally; • patients do not require hospitalisation; • patient has an anaphylaxis for beta-lactam antimicrobials.	Strong
Do not use ciprofloxacin and other fluoroquinolones for the empirical treatment of complicated UTI in patients from urology departments or when patients have used fluoroquinolones in the last six months.	Strong
Manage any urological abnormality and/or underlying complicating factors.	Strong

Catheter-associated UTIs

Catheter-associated UTI refers to UTIs occurring in a person whose urinary tract is currently catheterised or has been catheterised within the past 48 hours.

Recommendations for diagnostic evaluation of CA-UTI	Strength rating
Do not carry out routine urine culture in asymptomatic catheterised patients.	Strong
Do not use pyuria as sole indicator for catheter-associated (CA-UTI).	Strong
Do not use the presence or absence of odorous or cloudy urine alone to differentiate catheter-associated asymptomatic bacteriuria from CA-UTI.	Strong

Recommendations for disease management and prevention of CA-UTI	Strength rating
Treat symptomatic CA-UTI according to the recommendations for complicated UTI.	Strong
Take a urine culture prior to initiating antimicrobial therapy in catheterised patients in whom the catheter has been removed.	Strong
Do not treat catheter-associated asymptomatic bacteriuria in general.	Strong
Treat catheter-associated asymptomatic bacteriuria prior to traumatic urinary tract interventions (e.g. transurethral resection of the prostate).	Strong
Replace or remove the indwelling catheter before starting antimicrobial therapy.	Strong
Do not apply topical antiseptics or antimicrobials to the catheter, urethra or meatus.	Strong
Do not use prophylactic antimicrobials to prevent catheter-associated UTIs.	Strong
The duration of catheterisation should be minimal.	Strong

Recommendations for antibiotic prophylaxis following indwelling bladder catheter removal	Strength rating
Do not routinely use antibiotic prophylaxis to prevent clinical UTI after urethral catheter removal.	Weak

Urosepsis

Urosepsis is defined as life threatening organ dysfunction caused by a dysregulated host response to infection originating from the urinary tract and/or male genital organs.

Recommendations for the diagnosis and treatment of urosepsis	Strength rating
Perform the quickSOFA score to identify patients with potential sepsis.	Strong
Take a urine culture and two sets of blood cultures before starting antimicrobial treatment.	Strong
Administer parenteral high dose broad spectrum antimicrobials within the first hour after clinical assumption of sepsis.	Strong
Adapt initial empiric antimicrobial therapy on the basis of culture results.	Strong
Initiate source control including removal of foreign bodies, decompression of obstruction and drainage of abscesses in the urinary tract.	Strong
Provide immediate adequate life-support measures.	Strong

Table 4: Suggested regimens for antimicrobial therapy for urosepsis		
Antimicrobials	**Daily dose**	**Duration of therapy**
Cefotaxime	2 g t.i.d	7-10 days Longer courses are appropriate in patients who have a slow clinical response
Ceftazidime	1-2 g t.i.d	
Ceftriaxone	1-2 g q.d	
Cefepime	2 g b.i.d	
Piperacillin/tazobactam	4.5 g t.i.d	
Ceftolozane/tazobactam	1.5 g t.i.d	
Ceftazidime/avibactam	2.5 g t.i.d	
Gentamicin*	5 mg/kg q.d	
Amikacin*	15 mg/kg q.d	
Ertapenem	1 g q.d	
Imipenem/cilastatin	0.5 g t.i.d	
Meropenem	1 g t.i.d	

** Not studied as monotherapy in urosepsis*
b.i.d = twice daily; t.i.d = three times daily; q.d = every day.

Urethritis

Inflammation of the urethra presents usually with lower urinary tract symptoms and must be distinguished from other infections of the lower urinary tract. The following recommendations are based on a review of several European national guidelines and are aligned with the Center for Disease Control's guidelines on sexual transmitted diseases.

Recommendations for the diagnostic evaluation and antimicrobial treatment of urethritis	Strength rating
Perform a Gram stain of urethral discharge or a urethral smear to preliminarily diagnose gonococcal urethritis.	Strong
Perform a validated nucleic acid amplification test (NAAT) on a first-void urine sample or urethral smear prior to empirical treatment to diagnose chlamydial and gonococcal infections.	Strong
Delay treatment until the results of the NAATs are available to guide treatment choice in patients with mild symptoms.	Strong
Perform a urethral swab culture, prior to initiation of treatment, in patients with a positive NAAT for gonorrhoea to assess the antimicrobial resistance profile of the infective strain.	Strong
Use a pathogen directed treatment based on local resistance data.	Strong
Sexual partners should be treated maintaining patient confidentiality.	Strong

Table 5: Suggested regimens for antimicrobial therapy for urethritis		
Pathogen	**Antimicrobial**	**Alternative regimens**
Gonococcal Infection:	Ceftriaxone: 1 g i.m. or i.v., SD Azithromycin: 1 g p.o., SD	• Cefixime 400 mg p.o., SD plus Azithromycin 1 g p.o., SD In case of cephalosporin allergy: • Gentamicin 240 mg i.m SD plus Azithromycin 2 g p.o., SD • Gemifloxacin 320 mg p.o., SD plus Azithromycin 2 g p.o., SD • Spectinomycin 2 g i.m., SD • Fosfomycin trometamol 3 g p.o., on days 1, 3 and 5 In case of azithromycin allergy, in combination with ceftriaxone or cefixime: • Doxycycline 100 mg b.i.d, p.o., 7 days
Non-Gonococcal infection (non-identified pathogen)	Doxycycline: 100 mg b.i.d, p.o., 7-10 days	Azithromycin 500 mg p.o., day 1, 250 mg p.o., 4 days

Chlamydia trachomatis	Azithromycin: 1.0-1.5 g p.o., SD OR Doxycycline: 100 mg b.i.d, p.o., for 7 days	• Levofloxacin 500 mg p.o., q.d., 7 days • Ofloxacin 200 mg p.o., b.i.d., 7 days
Mycoplasma genitalium	Azithromycin: 500 mg p.o., day 1, 250 mg p.o., 4 days	In case of macrolide resistance: • Moxifloxacin 400 mg q.d., 7-14 days
Ureaplasma urealyticum	Doxycycline: 100 mg b.i.d, p.o., 7 days	Azithromycin 1.0-1.5 g p.o., SD
Trichomonas vaginalis	Metronidazole: 2 g p.o., SD Tinidazole: 2 g p.o., SD	Metronidazole 500 mg p.o., b.i.d., 7 days
Persistent non-gonococcal urethritis		
After first-line doxycycline	Azithromycin: 500 mg p.o., day 1, 250 mg p.o., 4 days plus Metronidazole: 400 mg b.i.d. p.o., 5 days	If macrolide resistant *M. genitalium* is detected moxifloxacin should be substituted for azithromycin
After first-line azithromycin	Moxifloxacin: 400 mg p.o. q.d., 7–14 days plus Metronidazole: 400 mg b.i.d. p.o., 5 days	

SD = single dose; b.i.d = twice daily; q.d = everyday; p.o. = orally, i.m. = intramuscular.

Bacterial Prostatitis

Bacterial prostatitis is a clinical condition caused by bacterial pathogens. It is recommended that urologists use the classification suggested by the National Institute of Diabetes, Digestive and Kidney Diseases of the National Institutes of Health, in which bacterial prostatitis, with confirmed or suspected infection, is distinguished from chronic pelvic pain syndrome.

Recommendations for the diagnosis of bacterial prostatitis	Strength rating
Do not perform prostatic massage in acute bacterial prostatitis (ABP).	Strong
Take a mid-stream urine dipstick to check nitrite and leukocytes in patients with clinical suspicion of ABP.	Weak
Take a mid-stream urine culture in patients with ABP symptoms to guide diagnosis and tailor antibiotic treatment.	Weak
Take a blood culture and a total blood count in patients presenting with ABP.	Weak
Perform accurate microbiological evaluation for atypical pathogens such as *Chlamydia trachomatis* or Mycoplasmata in patients with chronic bacterial prostatitis (CBP).	Weak
Perform the Meares and Stamey 2- or 4-glass test in patients with CBP.	Strong
Perform transrectal ultrasound in selected cases to rule out the presence of prostatic abscess.	Weak
Do not routinely perform microbiological analysis of the ejaculate alone to diagnose CBP.	Weak

Recommendations for the disease management of bacterial prostatitis	Strength rating
Acute bacterial prostatitis	
Treat acute bacterial prostatitis according to the recommendations for complicated UTI.	Strong
Chronic bacterial prostatitis (CBP)	
Prescribe a fluoroquinolone (e.g. ciprofloxacin, levofloxacin) as first-line treatment for CBP.	Strong
Prescribe a macrolide (e.g. azithromycin) or a tetracycline (e.g. doxycycline) if intracellular bacteria have been identified as the causative agent of CBP.	Strong
Prescribe metronidazole in patients with *Trichomonas vaginalis* CBP.	Strong

Table 6: Suggested regimens for antimicrobial therapy for chronic bacterial prostatitis

Antimicrobial	Daily dose	Duration of therapy	Comments
Floroquinolone	Optimal oral daily dose	4-6 weeks	
Doxycycline	100 mg b.i.d	10 days	Only for *C. trachomatis* or mycoplasma infections
Azithromycin	500 mg once daily	3 weeks	Only for *C. trachomatis* infections
Metronidazole	500 mg t.i.d.	14 days	Only for *T. vaginalis* infections

b.i.d = twice daily; t.i.d = three times daily.

Acute Infective Epididymitis

Acute epididymitis is clinically characterised by pain, swelling and increased temperature of the epididymis, which may involve the testis and scrotal skin. It is generally caused by migration of pathogens from the urethra or bladder. Torsion of the spermatic cord (testicular torsion) is the most important differential diagnosis in boys and young men.

Recommendations for the diagnosis and treatment of acute infective epididymitis	**Strength rating**
Obtain a mid-stream urine and a first voided urine for pathogen identification by culture and nucleic acid amplification test.	Strong
Initially prescribe a single antibiotic or a combination of two antibiotics active against *Chlamydia trachomatis* and Enterobacteriaceae in young sexually active men; in older men without sexual risk factors only Enterobacteriaceae have to be considered.	Strong
If gonorrhoeal infection is likely give single dose ceftriaxone 500 mg intramuscularly in addition to a course of an antibiotic active against *C. trachomatis*.	Strong
Adjust antibiotic agent when pathogen has been identified and adjust duration according to clinical response.	Weak
Follow national policies on reporting and tracing/treatment of contacts for sexually transmitted infections.	Strong

Fournier's Gangrene

Fournier's gangrene is an aggressive and frequently fatal polymicrobial soft tissue infection of the perineum, peri-anal

region, and external genitalia. It is an anatomical sub-category of necrotising fasciitis with which it shares a common aetiology and management pathway.

Recommendations for the disease management of Fournier's Gangrene	Strength rating
Start treatment for Fournier's gangrene with broad-spectrum antibiotics on presentation, with subsequent refinement according to culture and clinical response.	Strong
Commence repeated surgical debridement for Fournier's gangrene within 24 hours of presentation.	Strong
Do not use adjunctive treatments for Fournier's gangrene except in the context of clinical trials.	Weak

Table 7: Suggested regimens for antimicrobial therapy for Fournier's Gangrene of mixed microbiological aetiology

Antimicrobial	Dosage
Piperacillin-tazobactam plus Vancomycin	4.5 g every 6-8 h IV 15 mg/kg every 12 h
Imipenem-cilastatin	1 g every 6-8 h IV
Meropenem	1 g every 8 h IV
Ertapenem	1 g once daily
Gentamicin	5 mg/kg daily
Cefotaxime plus metronidazole or clindamycin	2 g every 6 h IV 500 mg every 6 h IV 600-900 mg every 8 h IV
Cefotaxime plus fosfomycine plus metronidazole	2 g every 6 h IV 5 g every 8 h IV 500 mg every 6 h IV

IV = intravenous.

Peri-Procedural Antibiotic Prophylaxis

The available evidence enabled the panel to make recommendations concerning urodynamics, cystoscopy, stone procedures (extracorporeal shockwave lithotripsy, ureteroscopy and per-cutaneous neprolithotomy), transurethral resection of the prostate, transurethral resection of the bladder and prostate biopsy. For nephrectomy and prostatectomy the scientific evidence was too weak to allow the panel to make recommendations either for or against antibiotic prophylaxis.

Recommendations for peri-procedural antibiotic prophylaxis	Strength rating
Do not use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following: • urodynamics; • cystoscopy; • extracorporeal shockwave lithotripsy.	Strong
Use antibiotic prophylaxis to reduce the rate of symptomatic urinary infection following ureteroscopy.	Weak
Use single dose antibiotic prophylaxis to reduce the rate of clinical urinary infection following percutaneous nephrolithotomy.	Strong
Use antibiotic prophylaxis to reduce infectious complications in men undergoing transurethral resection of the prostate.	Strong
Use antibiotic prophylaxis to reduce infectious complications in high-risk patients undergoing transurethral resection of the bladder.	Weak
Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy.	Strong
Use antimicrobial prophylaxis in men prior to transrectal prostate biopsy.	Strong

Note: As stated in section 3.14.1.4 of the full text guideline the panel have decided not to make recommendations for specific

agents for particular procedures, those listed below represent possible choices only. Urologists should choose a specific antimicrobial based on their knowledge of local pathogen prevalence for each type of procedure, their antibiotic susceptibility profiles and virulence.

Table 8: Suggested regimens for antimicrobial prophylaxis prior to urological procedures

Procedure	Prophylaxis recommended	Antimicrobial
Urodynamics	No	
Cystoscopy	No	
Extracorporeal shockwave lithotripsy	No	
Ureteroscopy	Yes	Trimethoprim Trimethoprim-sulphamethoxazole Cephalosporin group 2 or 3 Aminopenicillin plus a beta-lactamase inhibitor
Percutaneous nephrolithotomy	Yes (single dose)	
Transurethral resection of the prostate	Yes	
Transurethral resection of the bladder	Yes in patients who have a high risk of suffering post-operative sepsis.	
Transrectal prostate biopsy	Yes	Fluoroquinolones if permitted Cephalosporins, fosfomycin, aminoglycosides, if fluoroquinolones are not permitted

This short booklet text is based on the more comprehensive AU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON UROLITHIASIS

(Limited text update March 2020)

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Aetiology and classification

Urinary stones can be classified according to the following aspects: aetiology of stone formation, stone composition (mineralogy), stone size, stone location, and X-ray characteristics of the stone. The recurrence risk is basically determined by the disease or disorder causing the stone formation.

Risk groups for stone formation

The risk status of stone formers is of particular interest because it defines the probability of recurrence or regrowth, and is imperative for pharmacological treatment (Table 1).

Table 1: High-risk stone formers

General factors
Early onset of urolithiasis (especially children and teenagers)
Familial stone formation
Brushite-containing stones ($CaHPO_4.2H_2O$)
Uric acid and urate-containing stones
Infection stones
Solitary kidney (the kidney itself does not particularly increase the risk of stone formation, but prevention of stone recurrence is of more importance)

Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome
Nephrocalcinosis
Polycystic kidney disease (PKD)
Gastrointestinal diseases (i.e. jejuno-ileal bypass, intestinal resection, Crohn's disease, malabsorptive conditions, enteric hyperoxaluria after urinary diversion) and bariatric surgery
Sarcoidosis
Spinal cord injury, neurogenic bladder
Increased levels of vitamin D
Genetically determined stone formation
Cystinuria (type A, B and AB)
Primary hyperoxaluria (PH)
Renal tubular acidosis (RTA) type I
2,8-Dihydroxyadeninuria
Xanthinuria
Lesch-Nyhan syndrome
Cystic fibrosis
Drug-induced stone formation
Anatomical abnormalities associated with stone formation
Medullary sponge kidney (tubular ectasia)
Ureteropelvic junction (UPJ) obstruction
Calyceal diverticulum, calyceal cyst
Ureteral stricture
Vesico-uretero-renal reflux
Horseshoe kidney
Ureterocele
Environmental factors
High ambient tempertures
Chronic lead and cadmium exposure

Diagnostic Evaluation

Diagnostic imaging

Standard evaluation of a patient includes taking a detailed medical history and physical examination. The clinical diagnosis should be supported by appropriate imaging.

Recommendation	Strength rating
Immediate imaging is indicated with fever or solitary kidney, and when diagnosis is doubtful.	Strong

Ultrasound (US) should be used as the primary diagnostic imaging tool, although pain relief, or any other emergency measures, should not be delayed by imaging assessments.

Kidney-ureter-bladder (KUB) urography should not be performed if non-contrast-enhanced computed tomography (NCCT) is being considered, but KUB urography can differentiate between radiolucent and radiopaque stones and should be used for comparison during follow up.

Recommendation for radiologic examinations of patients with acute flank pain/suspected ureteral stones	Strength rating
Use non-contrast-enhanced computed tomography to confirm stone diagnosis in patients with acute flank pain, following initial ultrasound assessment.	Strong

Recommendation for radiologic examination of patients with renal stones	Strength rating
Perform a contrast study if stone removal is planned and the anatomy of the renal collecting system needs to be assessed.	Strong

Diagnostics: Metabolism-related

Each emergency patient with urolithiasis needs a succinct biochemical work-up of urine and blood; no difference is made between high- and low-risk patients.

Recommendations: basic laboratory analysis - emergency stone patients	Strength rating
Urine	
Dipstick test of spot urine sample: • red cells; • white cells; • nitrites; • approximate urine pH; • urine microscopy and/or culture.	Weak
Blood	
Serum blood sample: • creatinine; • uric acid; • (ionised) calcium; • sodium; • potassium; • blood cell count; • C-reactive protein.	Weak
Perform a coagulation test (partial thromboplastin time and international normalised ratio) if intervention is likely or planned.	Strong

Examination of sodium, potassium, C-reactive protein (CRP), and blood coagulation time can be omitted if no intervention is planned in non-emergency stone patients. Patients at high risk for stone recurrences should undergo a more specific analytical programme (see section on Metabolic Evaluation).

Recommendations related to non-emergency stone analysis	Strength rating
Perform stone analysis in first-time formers using a valid procedure (X-ray diffraction or infrared spectroscopy).	Strong
Repeat stone analysis in patients presenting with: • recurrent stones despite drug therapy; • early recurrence after complete stone clearance; • late recurrence after a long stone-free period because stone composition may change.	Strong

Diagnosis for special groups/conditions

Pregnancy

Recommendations	Strength rating
Use ultrasound as the preferred method of imaging in pregnant women.	Strong
In pregnant women, use magnetic resonance imaging as a second-line imaging modality.	Strong
In pregnant women, use low-dose computed tomography as a last-line option.	Strong

Children

Recommendations	Strength rating
Complete a metabolic evaluation based on stone analysis, in all children.	Strong
Collect stone material for analysis to classify the stone type.	Strong
Perform ultrasound (US) as first-line imaging modality in children when a stone is suspected; it should include the kidney, fluid-filled bladder and the ureter.	Strong
Perform a kidney-ureter-bladder radiography (or low-dose non-contrast-enhanced computed tomography) if US will not provide the required information.	Strong

In children, the most common non-metabolic disorders facilitating stone formation are vesico-ureteral reflux, ureteropelvic junction obstruction (UPJ), neurogenic bladder, and other voiding difficulties.

The radiation dose for intravenous urography (IVU) is comparable to that for voiding cysto-urethrography, but the need for contrast medium injection is a major drawback.

Disease Management

Acute treatment of a patient with renal colic

Pain relief is the first therapeutic step in patients with an acute stone episode.

Recommendations	Strength rating
Offer a non-steroidal anti-inflammatory as the first drug of choice; e.g. metamizol* (dipyrone); alternatively paracetamol or, depending on cardiovascular risk factors, diclofenac**, indomethacin or ibuprofen***.	Strong
Offer opiates (hydromorphine, pentazocine or tramadol) as a second choice.	Weak
Offer renal decompression or uretero-scopic stone removal in case of analgesic refractory colic pain.	Strong

** Maximum single oral dose recommended 1,000 mg, total daily dose up to 5,000 mg, not recommended last 3 months of pregnancy and breastfeeding (EMA, Dec. 2018).*

*** Affects glomerular filtration rate (GFR) in patients with reduced renal function.*

**** Recommended to counteract recurrent pain after ureteral colic.*

Administration of daily α-blockers seems to reduce colic episodes, although controversy remains in the published literature.

If analgesia cannot be achieved medically, drainage, using stenting or percutaneous nephrostomy or stone removal, should be performed.

Management of sepsis and anuria in the obstructed kidney

The obstructed, infected, kidney is a urological emergency.

Recommendations	Strength rating
Urgently decompress the collecting system in case of sepsis with obstructing stones, using percutaneous drainage or ureteral stenting.	Strong
Delay definitive treatment of the stone until sepsis is resolved.	Strong

In exceptional cases, with severe sepsis and/or the formation of abscesses, an emergency nephrectomy may become necessary.

Recommendations – Further measures	Strength rating
Collect (again) urine for antibiogram test following decompression.	Strong
Start antibiotics immediately (+ intensive care, if necessary).	Strong
Re-evaluate antibiotic regimen following antibiogram findings.	Strong

Medical expulsive therapy (MET)

Medical expulsive therapy should only be used in informed patients. Treatment should be discontinued if complications develop (infection, refractory pain, deterioration of renal function).

Medical expulsive therapy, using α-blockers, seems to be efficacious treating patients with ureteric stones that are amenable to conservative management. Patients benefitting most might be those with larger (distal) stones.

There is no or insufficient evidence to support the use of phosphodiesterase type 5 inhibitor (PDE-5i) or corticosteroids in combination with α-blockers as a standard adjunct to active stone removal.

Recommendation for medical expulsive therapy (MET)	Strength rating
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm.	Strong

Chemolytic dissolution of stones

Oral chemolysis of stones or their fragments can be useful in uric acid stones. It is based on alkalinisation of urine by application of alkaline citrate or sodium bicarbonate. The pH should be adjusted to 7.0-7.2.

Percutaneous irrigation chemolysis is rarely used any more.

Recommendations – Oral chemolysis of uric acid stones	Strength rating
Inform the patient how to monitor urine-pH by dipstick and to modify the dosage of alkalising medication according to urine pH, as changes in urine pH are a direct consequence of such medication.	Strong
Carefully monitor patients during/after oral chemolysis of uric acid stones.	Strong
Combine oral chemolysis with tamsulosin in case of (larger) ureteral stones (if active intervention is not indicated).	Weak

Shock Wave lithotripsy (SWL)

The success rate for SWL will depend on the efficacy of the lithotripter and on:

- size, location (ureteral, pelvic or calyceal), and composition (hardness) of the stones;
- patient's habitus;
- performance of SWL.

Contraindications of SWL

Contraindications are few, but include:

- pregnancy;
- bleeding diatheses; which should be compensated for at least 24 hours before and 48 hours after treatment;
- untreated urinary tract infections (UTIs);
- severe skeletal malformations and severe obesity, which prevent targeting of the stone;
- arterial aneurysm in the vicinity of the stone;
- anatomical obstruction distal to the stone.

Best clinical practice (best performance) in SWL

Stenting prior to SWL

Routine use of internal stents before SWL does not improve stone-free rates (SFRs), nor lowers the number of auxiliary treatments. It may, however, reduce formation of steinstrasse.

Pacemaker

Patients with a pacemaker can be treated with SWL. Patients with implanted cardioverter defibrillators must be managed with special care (firing mode temporarily reprogrammed during SWL treatment). However, this might not be necessary with new-generation lithotripters.

Shock waves, energy setting and repeat treatment sessions

- The number of shock waves that can be delivered at each session depends on the type of lithotripter and shock wave power.
- Starting SWL on a lower energy setting with step-wise power ramping prevents renal injury.
- Optimal shock wave frequency is 1.0 to 1.5 Hz.
- Clinical experience has shown that repeat sessions are feasible (within one day for ureteral stones).

Procedural control

Recommendations - Procedural control	Strength rating
Ensure correct use of the coupling agent because this is crucial for effective shock wave transportation.	Strong
Maintain careful fluoroscopic and/or ultrasonographic monitoring during shock wave lithotripsy.	Strong
Use proper analgesia because it improves treatment results by limiting pain-induced movements and excessive respiratory excursions.	Strong

Antibiotic prophylaxis

No standard prophylaxis prior to SWL is recommended.

Recommendation	Strength rating
Prescribe antibiotics prior to shock wave lithotripsy in the case of infected stones or bacteriuria.	Strong

Ureteroscopy (URS) (retrograde and antegrade, RIRS)

Apart from general problems, for example, with general anaesthesia or untreated UTIs, URS can be performed in all patients without any specific contraindications.

If ureteral access is not possible, insertion of a JJ stent followed by URS after several days is an alternative. During URS, placement of a safety wire is recommended, even though some groups have demonstrated that URS can be performed without it.

Ureteral access sheaths allow easy, multiple, access to the upper urinary tract; however, its insertion may lead to ureteral trauma.

Recommendations	Strength rating
Use holmium:yttrium-aluminium-garnet (Ho:YAG) laser lithotripsy for (flexible) ureteroscopy (URS).	Strong
Perform stone extraction only under direct endoscopic visualisation of the stone.	Strong
Do not insert a stent in uncomplicated cases.	Strong
Pre-stenting facilitates URS and improves outcomes of URS (in particular for renal stones).	Strong
Offer medical expulsive therapy for patients suffering from stent-related symptoms and after Ho:YAG laser lithotripsy to facilitate the passage of fragments.	Strong

Percutaneous nephrolithotomy (PNL)

Patients with bleeding diathesis or receiving anticoagulant therapy must be monitored carefully pre- and post-operatively. Anticoagulant therapy must be discontinued before PNL.

Contraindications to PNL include:

- untreated UTI;
- tumour in the presumptive access tract area;
- potential malignant kidney tumour;
- pregnancy.

Best clinical practice

Both prone and supine positions are equally safe. Percutaneous nephrolithotomy performed with small instruments tends to be associated with significantly lower blood loss, but the duration of procedure tends to be significantly longer.

Recommendations	Strength rating
Perform pre-procedural imaging, including contrast medium where possible or retrograde study when starting the procedure, to assess stone comprehensiveness and anatomy of the collecting system to ensure safe access to the renal stone.	Strong
Perform a tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and ureteral stent) percutaneous nephrolithotomy procedure, in uncomplicated cases.	Strong

Stone Removal

Recommendations	Strength rating
Obtain a urine culture or perform urinary microscopy before any treatment is planned.	Strong
Exclude or treat urinary tract infections prior to stone removal.	Strong
Offer peri-operative antibiotic prophylaxis to all patients undergoing endourological treatment.	Strong
Offer active surveillance to patients at high risk of thrombotic complications in the presence of an asymptomatic calyceal stone.	Weak
Decide on temporary discontinuation, or bridging of antithrombotic therapy in high-risk patients, in consultation with the internist.	Strong

Retrograde (flexible) ureteroscopy is the preferred intervention if stone removal is essential and antithrombotic therapy cannot be discontinued, since it is associated with less morbidity.	Strong

Radiolucent uric acid stones can be dissolved by oral chemolysis.

Ureteral stones

Observation of ureteral stones is feasible in informed patients who develop no complications (infection, refractory pain, deterioration of kidney function).

Recommendations	Strength rating
In patients with newly diagnosed small* ureteral stones, if active removal is not indicated, observe patient initially with periodic evaluation.	Strong
Offer α-blockers as medical expulsive therapy as one of the treatment options for (distal) ureteral stones > 5 mm.	Strong
Inform patients that ureteroscopy (URS) has a better chance of achieving stone-free status with a single procedure.	Strong
Inform patients that URS has higher complication rates when compared to shock wave lithotripsy.	Strong
In cases of severe obesity use URS as first-line therapy for ureteral (and renal) stones.	Strong

**See stratification data (J Urol, 2007. 178: 2418).*

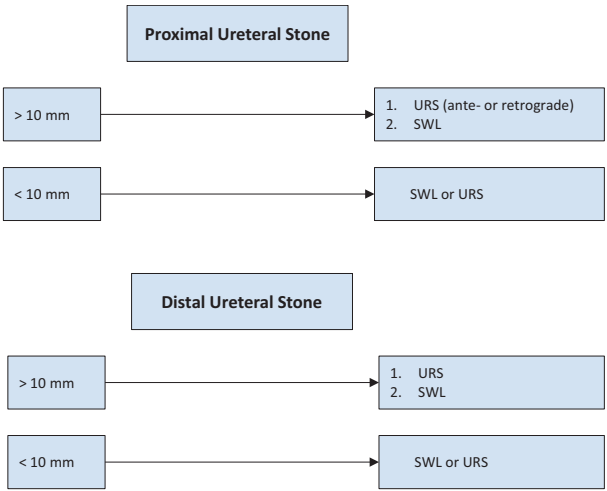
Indication for active stone removal and selection of procedure

Ureter:

- stones with a low likelihood of spontaneous passage;
- persistent pain despite adequate pain medication;
- persistent obstruction;
- renal insufficiency (renal failure, bilateral obstruction, single kidney).

The suspected stone composition might influence the choice of treatment modality.

Figure 1: Treatment algorithm for ureteral stones (If active stone removal is indicated) (Strength rating: Strong)



SWL = shock wave lithotripsy; URS = ureteroscopy.

Recommendation	Strength rating
Use percutaneous antegrade removal of ureteral stones as an alternative when shock wave lithotripsy is not indicated or has failed, and when the upper urinary tract is not amenable to retrograde ureteroscopy.	Strong

Renal stones

It is still debatable whether all stones should be treated, or whether annual follow-up is sufficient for asymptomatic calyceal stones that have remained stable for six months.

Recommendations	Strength rating
Follow-up periodically in cases where renal stones are not treated (initially after six months then yearly, evaluating symptoms and stone status [either by ultrasound, kidney-ureter bladder radiography or computed tomography]).	Strong
Offer active treatment for renal stones in case of stone growth, *de novo* obstruction, associated infection, and acute and/or chronic pain.	Weak
Evaluate stone composition before deciding on the method of removal, based on patient history, former stone analysis of the patient or Hounsfield unit (HU) on unenhanced computed tomography (CT). Stones with density > 1,000 HU on non-contrast-enhanced CT are less likely to be disintegrated by shock wave lithotripsy.	Strong
Perform PNL as first-line treatment of larger stones > 2 cm.	Weak

Treat larger stones (> 2 cm) with flexible ureteroscopy or SWL, in cases where PNL is not an option. However, in such instances there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	Strong
Perform PNL or RIRS for the lower pole, even for stones > 1 cm, as the efficacy of SWL is limited (depending on favourable and unfavourable factors for SWL).	Strong

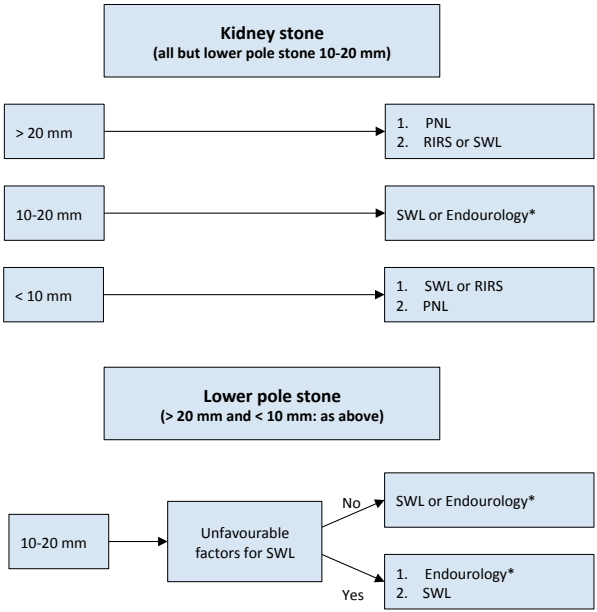
Indication for active stone removal and selection of procedure

Kidney:

- stone growth;
- stones in high-risk patients for stone formation;
- obstruction caused by stones;
- infection;
- symptomatic stones (e.g. pain, haematuria);
- stones > 15 mm;
- stones < 15 mm if observation is not the option of choice;
- patient preference;
- comorbidity;
- social situation of the patient (e.g., profession or travelling).

The suspected stone composition might influence the choice of treatment modality.

Figure 2: Treatment algorithm for renal stones (if active treatment is indicated) (Strength rating: Strong)



** The term 'endourology' encompasses all PNL and URS interventions.*

PNL = percutaneous nephrolithotomy; RIRS = retrograde renal surgery; SWL = shock wave lithotripsy; URS = ureteroscopy.

Recommendation	Strength rating
Use flexible ureteroscopy in cases where percutaneous nephrolithotomy or shock wave lithotripsy are not an option (even for stones > 2 cm). However, in this case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed.	Strong

Open and laparoscopic surgery

Recommendation	Strength rating
Offer laparoscopic or open surgical stone removal in rare cases in which shock wave lithotripsy, retrograde or antegrade ureteroscopy and percutaneous nephrolithotomy fail, or are unlikely to be successful.	Strong

Steinstrasse

The major factor in steinstrasse formation is stone size. Medical expulsion therapy increases the stone expulsion rate of steinstrasse. When spontaneous passage is unlikely, further treatment of steinstrasse is indicated.

Recommendations	Strength rating
Treat steinstrasse associated with urinary tract infection (UTI)/fever preferably with percutaneous nephrostomy.	Weak
Treat steinstrasse when large stone fragments are present with shock wave lithotripsy or ureteroscopy (in absence of signs of UTI).	Weak

Management of patients with residual stones

Following initial treatment with SWL, URS or PNL residual fragments may remain and require additional intervention. The indications for active removal of residual stones and selection of the procedure are based on the same criteria as for primary stone treatment. For well-disintegrated stone material in the lower calyx, inversion therapy with simultaneous mechanical percussion manoeuvre under enforced diuresis may facilitate stone clearance.

Recommendation in case of residual fragments	Strength rating
Perform imaging after shock wave lithotripsy, ureteroscopy or percutaneous antegrade ureteroscopy to determine presence of residual fragments.	Strong

Management of urinary stones and related problems during pregnancy

Recommendation	Strength rating
Treat all uncomplicated cases of urolithiasis in pregnancy conservatively (except where there are clinical indications for intervention).	Strong

If intervention becomes necessary, placement of a ureteral stent or a percutaneous nephrostomy tube are readily available primary options. Ureteroscopy is a reasonable alternative to avoid long-term stenting/drainage. There is a higher tendency for stent encrustation during pregnancy.

Management of stones in patients with urinary diversion

Patients with urinary diversion are at high risk for stone formation in the renal collecting system and ureter, or in the conduit or continent reservoir.

Recommendation	Strength rating
Perform percutaneous lithotomy to remove large renal stones in patients with urinary diversion, as well as for ureteral stones that cannot be accessed via a retrograde approach, or that are not amenable to shock wave lithotripsy.	Strong

Management of stones in patients with neurogenic bladder

Patients with neurogenic bladder are more prone to development of urinary calculi.

In myelomeningocele patients, latex allergy is common so appropriate measures need to be taken regardless of the treatment.

Management of stones in transplanted kidneys

Transplanted patients are at additional risk due to their dependency on a solitary kidney, immunosuppression therapy and possible metabolic impairments. Conservative treatment for small asymptomatic stones is only possible under close surveillance and in absolutely compliant patients.

Stones causing urinary stasis/obstruction require immediate intervention or drainage of the transplanted kidney.

Recommendation	Strength rating
Offer patients with transplanted kidneys, any of the contemporary management options, including shock wave lithotripsy, flexible ureteroscopy and percutaneous nephrolithotomy.	Weak

Special problems in stone removal

Calyceal diverticulum stones	• Shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PNL) (if possible) or retrograde renal surgery (RIRS). • Laparoscopic retroperitoneal surgery. • Patients may become asymptomatic due to stone disintegration (SWL), whilst well-disintegrated stone material remains in the original position due to narrow calyceal neck.
Horseshoe kidneys	• Can be treated in line with the options described above. • Passage of fragments after SWL might be poor. • Acceptable stone-free rates (SFRs) can be achieved with flexible ureteroscopy.
Stones in pelvic kidneys	• SWL, RIRS, PNL or laparoscopic surgery. • In obese patients, the options are RIRS, PNL or open surgery.
Stones formed in a continent reservoir	• Each stone must be considered and treated individually.

Patients with obstruction of the uretero-pelvic junction (UPJ)	• When outflow abnormality requires correction, stones can be removed by PNL together with percutaneous endopyelotomy or open/laparoscopic reconstructive surgery. • Ureteroscopy together with endopyelotomy with holmium:yttrium-aluminium-garnet laser. • Incision with an Acucise® balloon catheter might be considered, provided the stones can be prevented from falling into the pelvic-ureteral incision. • Open surgery with correction of the UPJ obstruction (pyeloplasty) and stone removal is a feasible option.

Management of urolithiasis in children

In children, the indication for SWL and for PNL is similar to those in adults. Compared to adults, children pass fragments more rapidly after SWL. For endourological procedures, the smaller organs in children must be considered when selecting instruments for PNL or URS.

Children with renal stones of a diameter up to 20 mm (~300 mm^2) are ideal candidates for SWL.

Recommendations	Strength rating
Offer children with single ureteral stones less than 10 mm shock wave lithotripsy (SWL) if localisation is possible as first-line option.	Strong
Ureteroscopy is a feasible alternative for ureteral stones not amenable to SWL.	Strong
Offer children with renal stones with a diameter of up to 20 mm (~300 mm^2) SWL.	Strong
Offer children with renal pelvic or calyceal stones with a diameter > 20 mm (~300 mm^2) percutaneous nephrolithotomy.	Strong
Retrograde renal surgery is a feasible alternative for renal stones smaller than 20 mm in all locations.	Weak

Metabolic evaluation and recurrence prevention

After stone passage, every patient should be assigned to a low- or high-risk group for stone formation. For correct classification, two analyses are mandatory:

- reliable stone analysis by infrared spectroscopy or X-ray diffraction;
- basic analysis.

Only high-risk stone formers require specific metabolic evaluation. Stone type is the deciding factor for further diagnostic tests. For both groups, general preventive measures apply (see below).

General preventive measures	
Fluid intake (drinking advice)	• Fluid amount: 2.5-3.0 L/day • Circadian drinking • Neutral pH beverages • Diuresis: 2.0-2.5 L/day • Specific weight of urine: < 1,010 L/day
Nutritional advice for a balanced diet	• Rich in vegetables and fibre • Normal calcium content: 1-1.2 g/day • Limited NaCl content: 4-5 g/day • Limited animal protein content: 0.8-1.0 g/kg/day • Avoid excessive consumption of vitamin supplements
Lifestyle advice to normalise general risk factors	• Body mass index (BMI): Retain a normal BMI level • Adequate physical activity • Balancing of excessive fluid loss

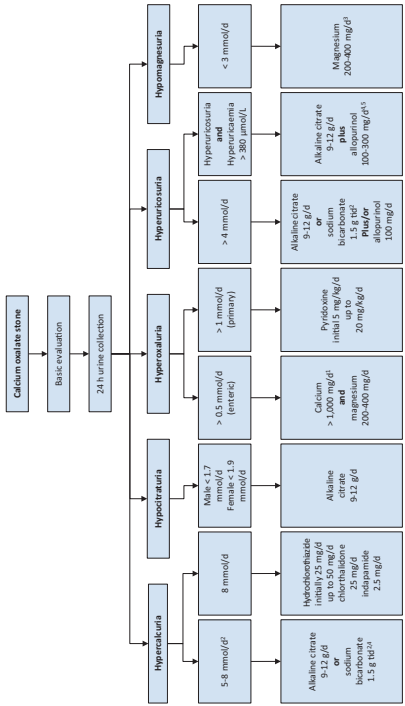
Caution: Protein need is age-group dependent; therefore, protein restriction in childhood should be handled carefully.

Calcium oxalate stones

Hyperparathyroidism is excluded by blood analysis.

Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition (based on 24-hour urine samples)		
Urinary risk factor	**Suggested treatment**	**Strength rating**
Hypercalcuria	Thiazide + alkaline citrate	Strong
Hyperoxaluria	Oxalate restriction	Weak
Enteric hyperoxaluria	Potassium citrate	Weak
	Calcium supplement	Weak
	Diet reduced in fat and oxalate	Weak
Hypocitraturia	Alkaline citrate	Strong
Hypocitraturia	Sodium bicarbonate if intolerant to alkaline citrate	Strong
Hyperuricosuria	Allopurinol	Strong
	Febuxostat	Strong
High sodium excretion	Restricted intake of salt	Strong
Small urine volume	Increased fluid intake	Strong
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein	Strong

Figure 3: Diagnostic and therapeutic algorithm for calcium oxalate stones



[1] *Be aware of excess calcium excretion*

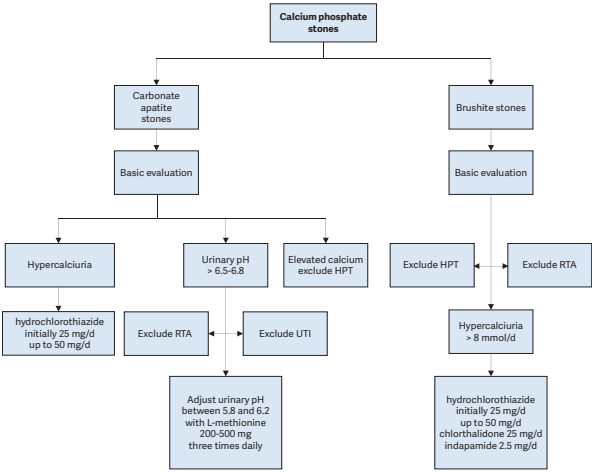
[2] *tid = three times/day (24h).*

[3] *No magnesium therapy for patients with renal insufficiency*

[4] *There is no evidence that combination therapy (thiazide + citrate) or (thiazide + allopurinol) is superior to thiazide therapy alone.*

[5] *Febuxostat 80 mg/day.*

Figure 4: Diagnostic and therapeutic algorithm for calcium phosphate stones



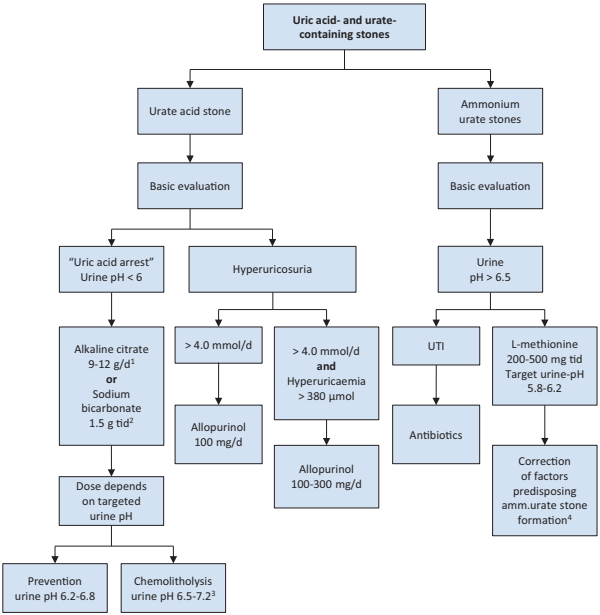
HPT = hyperparathyroidism; RTA = renal tubular acidosis; UTI = urinary tract infection.

Recommendations	Strength rating
Prescribe thiazide in case of hypercalciuria.	Strong
Advise patients to acidify their urine in case of high urine pH.	Weak

Hyperparathyroidism

Elevated levels of ionised calcium in serum (or total calcium and albumin) require assessment of intact parathyroid hormone to confirm or exclude suspected hyperparathyroidism (HPT). Primary HPT can only be cured by surgery.

Figure 5: Diagnostic and therapeutic algorithm for uric acid and urate-containing stones



UTI = urinary tract infection.

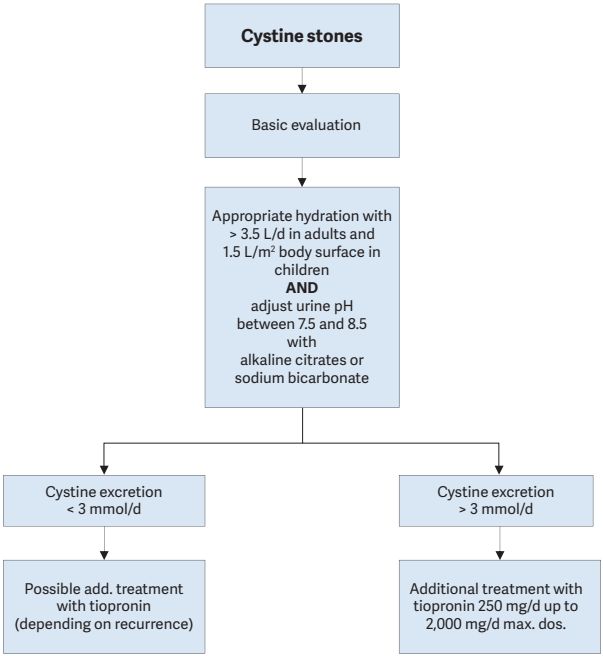
[1] d: day

[2] tid: three times a day

[3] A higher pH may lead to calcium phosphate stone formation.

[4] In patients with high uric acid excretion, allopurinol may be helpful.

Figure 6: Metabolic management of cystine stones



Struvite/infection stones

Recommendations for therapeutic measures of infection stones	Strength rating
Surgically remove the stone material as completely as possible.	Strong
Prescribe antibiotics in case of persistent bacteriuria.	Strong
Prescribe ammonium chloride, 1 g, two or three times daily, to ensure urinary acidification.	Weak
Prescribe methionine, 200-500 mg, one to three times daily, as an alternative, to ensure urinary acidification.	Weak

2,8-Dihydroyadenine stones and xanthine stones

Both stone types are rare. In principle, diagnosis and specific prevention is similar to that of uric acid stones.

Drug stones

Drug stones are induced by pharmacological treatment. Two types exist:

- stones formed by crystallised compounds of the drug;
- stones formed due to unfavourable changes in urine composition under drug therapy.

Treatment includes general preventive measures and the avoidance of the respective drugs.

Investigation	Rationale for investigation
Medical history	• Stone history (former stone events, family history) • Dietary habits • Medication chart
Diagnostic imaging	• Ultrasound in the case of a suspected stone • Unenhanced helical computed tomography • Determination of Hounsfield units provides information about the possible stone composition
Blood analysis	• Creatinine • Calcium (ionised calcium or total calcium + albumin) • Uric acid
Perform a urinalysis	• Urine pH profile (measurement after each voiding, minimum four times daily) • Dipstick test: leukocytes, erythrocytes, nitrites, protein, urine pH, specific weight • Urine cultures • Microscopy of urinary sediment (morning urine) • Cyanide nitroprusside test (cystine exclusion). Further examinations depend on the results of the investigations listed above.

Further examinations depend on the results of the investigations listed above.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-03) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON BLADDER STONES

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Prevalence and stratification

The prevalence of bladder stones is higher in males (male:female ratio between 10:1 and 4:1). The age distribution is bimodal: incidence peaks at three years in children in developing countries and 60 years in adulthood.

Primary or endemic bladder stones occur in the absence of other urinary tract pathology, typically seen in children in areas with a diet deficient in animal protein, poor hydration and recurrent diarrhoea.

Secondary bladder stones occur in the presence of other urinary tract abnormalities, which include bladder outlet obstruction (BOO), neurogenic bladder dysfunction, chronic bacteriuria, foreign bodies including catheters, bladder diverticula, and bladder augmentation or urinary diversion.

Migratory bladder stones are those which have passed from the upper urinary tract where they formed and may then serve as a nidus for bladder stone growth.

Diagnostic imaging

There is a paucity of evidence for the investigation of bladder stones, particularly in children. Ultrasound (US) of the (filled) bladder has a reported sensitivity and specificity for detecting

bladder stones between 20-83% and 98-100%, respectively. Plain X-ray of kidney ureter bladder (KUB) has a sensitivity of 21-78% in adults and this increases for stones ≥ 2.0 cm. In adults, besides US, computed tomography and/or cystoscopy are the benchmark diagnostic investigations.

Disease management

Asymptomatic migratory bladder stones in adults may be left untreated. Primary and secondary bladder stones are usually symptomatic and are unlikely to pass spontaneously; active treatment is usually indicated.

Uric acid stones can be dissolved by oral urinary alkalinisation when a pH > 6.5 is consistently achieved. Irrigation chemolysis is possible for struvite or uric acid stones. For further details see chapter 3.4.4 in the full EAU Guidelines on Urolithiasis.

Bladder stones can be removed with open, laparoscopic or robotic assisted laparoscopic or endoscopic (transurethral or percutaneous) surgery, or extracorporeal shock wave lithotripsy (SWL).

Summary of evidence	LE
The incidence of bladder stones peaks at three years in children (endemic/primary stones in developing countries) and 60 years in adults.	2c
The aetiology of bladder stones is typically multi-factorial. Bladder stones can be classified as primary (endemic), secondary (associated with lower urinary tract abnormalities e.g. BPO, neuropathic bladder, foreign body, chronic bactiuria) or migratory (having formed in the upper tract).	4
In adults, BOO is the most common predisposing factor for bladder stone formation.	2c

Metabolic abnormalities are also likely to contribute to bladder stone formation in patients with secondary bladder stones.	2b
In adults, US has a sensitivity of 20-83% for diagnosing bladder stones.	2b
In adults, X-Ray kidney ureter bladder (XR-KUB) has a sensitivity of 21-78%; sensitivity increases with stone size.	2b
Computed tomography has a higher sensitivity than US for the detection of bladder stones.	2b
Cystoscopy has a higher sensitivity than XR-KUB or US for the detection of bladder stones.	2b
Endoscopic bladder stone treatments are associated with comparable stone-free rates (SFRs) but a shorter length of hospital stay, duration of procedure and duration of catheterisation, compared to open cystolithotomy in adults.	1a
Stone-free rates are lower in patients treated with SWL than those treated with open or endoscopic procedures in both adults and children.	2a
Transurethral cystolithotripsy is associated with a shorter length of hospital stay, less pain and a shorter convalescence period than percutaneous cystolithotripsy in adults.	1b
Transurethral cystolithotripsy with a nephroscope is quicker than when using a cystoscope, with no difference in SFR in adults.	1a
Transurethral cystolithotripsy with a resectoscope is quicker than when using a cystoscope, with no difference in SFR in adults.	2a
Mechanical, pneumatic and laser appear equivalent lithotripsy modalities for use in endoscopic bladder stone treatments in adults and children.	2a

Open cystolithotomy without a retropubic drain or urethral catheter ("tubeless") is associated with a shorter length of hospital stay than traditional cystolithotomy and can be performed safely in children with primary stones and no prior bladder surgery or infections.	2b
Bladder stone removal with concomitant treatment for BOO is associated with no significant difference in major post-operative complications when compared to BOO treatment alone in adults. However, concomitant bladder stone treatment does increase the rates of short-term post-operative incontinence and urinary infection.	2b
The absolute annual risk of stone formation in spinal cord injury patients is significantly higher with an indwelling catheter compared to those voiding with clean intermittent self-catheterisation (CISC). Suprapubic and urethral catheters have equal rates of bladder stone formation in spinal cord injury patients.	2b
The incidence of bladder stone formation after bladder augmentation or vesico-entero-cystostomy is between 2-53% in adults and children.	2b
Urinary diversion including orthotopic ileal neobladders, ileocaecal continent cutaneous urinary diversion and rectosigmoid reservoirs is associated with stone formation in 0-43% of cases.	2b
Primary (endemic) bladder stones typically occur in children in areas with poor hydration, recurrent diarrhoea and a diet deficient in animal protein. The following measures are proposed to reduce their incidence: maintenance of hydration, avoidance of diarrhoea, and a mixed cereal diet with milk and Vitamins A and B supplements; with the addition of eggs, meat and boiled cows' milk after one year of age.	5

Recommendations	Strength rating
Use ultrasound (US) as first-line imaging in adults with symptoms suggestive of a bladder stone.	Strong
Use cystoscopy or computed tomography (CT) kidney ureter bladder (KUB) to investigate adults with persistent symptoms suggestive of a bladder stone if US is negative.	Strong
Use US as first-line imaging in children with symptoms suggestive of a bladder stone.	Strong
Use X-Ray KUB for adults with confirmed bladder stones to guide treatment options and follow-up.	Weak
All patients with bladder stones should be examined and investigated for the cause of bladder stone formation, including: • uroflowmetry and post-void residual; • urine dipstick, pH, ± culture; • metabolic assessment and stone analysis (see sections 3.3.2.3 and 4.1 of the Urolithiasis guideline for further details). In selected patients, consider: • upper tract imaging (in patients with a history of urolithiasis or loin pain); • cysto-urethroscopy or urethrogram.	Weak
Offer oral chemolitholysis for radiolucent or known uric acid bladder stones in adults.	Weak
Offer adults with bladder stones trans-urethral cystolithotripsy where possible.	Strong
Perform transurethral cystolithotripsy with a continuous flow instrument in adults (e.g. nephroscope or resectoscope) where possible.	Weak

Offer adults percutaneous cystolithotripsy where transurethral cystolithotripsy is not possible or advisable.	Strong
Suggest open cystolithotomy as an option for very large bladder stones in adults and children.	Weak
Offer children with bladder stones transurethral cystolithotripsy where possible.	Weak
Offer children percutaneous cystolithotripsy where transurethral cystolithotripsy is not possible or is associated with a high risk of urethral stricture (e.g. young children, previous urethral reconstruction and spinal cord injury).	Weak
Open, laparoscopic and extracorporeal shock wave lithotripsies are alternative treatments where endoscopic treatment is not possible in adults and children.	Weak
Prefer "tubeless" procedure (without placing a catheter or drain) for children with primary bladder stones and no prior infection, surgery or bladder dysfunction, where open cystolithotomy is indicated in children.	Weak
Perform procedures for the stone and underlying bladder outlet obstruction (BOO) simultaneously in adults with bladder stones secondary to BOO, where possible.	Strong

Individualise imaging follow up for each patient as there is a paucity of evidence. Factors affecting follow up will include : • whether the underlying functional predisposition to stone formation can be treated (e.g. TURP); • metabolic risk.	Weak
Recommend regular irrigation therapy with saline solution to adults and children with bladder augmentation, continent cutaneous urinary reservoir or neuropathic bladder dysfunction, and no history of autonomic dysreflexia to reduce the risk of recurrence.	Weak

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON PAEDIATRIC UROLOGY

(Limited text update March 2020)

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Introduction

Due to the scope of the extended Guidelines on Paediatric Urology, no attempt has been made to include all topics, but rather to provide a selection based on practical considerations.

PHIMOSIS

Background

At the end of the first year of life, retraction of the foreskin behind the glandular sulcus is possible in 50% of boys. The phimosis is either primary (physiological), with no sign of scarring, or secondary (pathological), resulting from scarring due to conditions such as balanitis xeroticaobliterans.

Phimosis must be distinguished from normal agglutination of the foreskin to the glans, which is a physiological phenomenon. If the tip remains narrow and glandular adhesions are separated, then the space is filled with urine during voiding, causing the foreskin to balloon outward.

Treatment

Conservative treatment

Administration of a corticoid ointment or cream is an option for primary phimosis with a success rate of > 90%, but with a

recurrence rate of 17%. Agglutination of the foreskin does not respond to steroid treatment.

Circumcision: indication and contraindication

Childhood circumcision should not be recommended without a medical reason. An absolute indication for circumcision is secondary phimosis. Contraindications for circumcision are acute local infection and congenital anomalies of the penis, particularly hypospadias or buried penis, as the foreskin may be required for a reconstructive procedure.

Plastic circumcision (dorsal incision, partial circumcision) carries the potential for recurrence of phimosis. Associated frenulum breve is corrected by frenulotomy. Meatoplasty is added if necessary.

Paraphimosis

It is characterised by retracted foreskin with the constrictive ring localised at the level of the sulcus. A dorsal incision of the constrictive ring may be required, or circumcision is carried out immediately or in a second session.

UNDESCENDED TESTES

Background

Cryptorchidism or undescended testis is one of the most common congenital malformations of male neonates. In newborn cases with non-palpable or undescended testes on both sides and any sign of disorders of sex development (DSD) like concomitant hypospadias, urgent endocrinological and genetic evaluation is required.

Classification

The term cryptorchidism is most often used synonymously for undescended testes. The most useful classification of undescended testes is into palpable and non-palpable testes, and clinical management is decided by the location and

presence of the testes. Approximately 80% of all undescended testes are palpable.

Palpable testes include true undescended testes and ectopic testes. Non-palpable testes include intra-abdominal, inguinal, absent, and sometimes also some ectopic testes.

Most importantly, the diagnosis of a palpable or non-palpable testis needs to be confirmed once the child is under general anaesthesia, as the first step of any surgical procedure for undescended testes. See Figure 1.

Diagnostic Evaluation

History taking and physical examination are key points in evaluating boys with undescended testes. Localisation studies using different imaging modalities are usually without any additional benefit.

Management

Treatment should be started at the age of six months. After that age, undescended testes rarely descend. Any kind of treatment leading to a scrotally positioned testis should be finished by twelve months, or eighteen months at the latest, because histological examination of undescended testes at that age has already revealed a progressive loss of germ and Leydig cells. The early timing of treatment is also driven by the final adult results on spermatogenesis and hormone production, as well as on the risk of tumour development. See Figure 2.

Medical therapy for testicular descent

Unfortunately, most of the studies on hormonal treatment have been of poor quality, with heterogeneous and mixed patient populations, testis location, schedules and dosages of hormonal administration. Additionally, long-term data are almost completely lacking.

Hormonal therapy using human chorionic gonadotropin

or gonadotrophin-releasing hormone (GnRH) is based on the hormonal dependence of testicular descent, but has a maximum success rate of only 20%. In general, success rates depend on testicular location. The higher the testis is located prior to therapy, the lower the success rate. The Panel consensus is that endocrine treatment to achieve testicular descent is not recommended.

Medical therapy for fertility potential

Hormonal treatment may improve fertility indices and therefore serve as an additional tool to orchidopexy. It is still unknown whether this effect on testicular histology persists into adulthood but it has been shown that men who were treated in childhood with buserelin had better semen analyses compared with men who had childhood orchidopexy alone or placebo treatment.

Identification of specific subgroups of boys with undescended testes who would benefit from such an approach using hormones is difficult. The Panel consensus recommends endocrine treatment with GnRH analogues for boys with bilateral undescended testes to preserve fertility potential.

Surgical Treatment

If a testis has not concluded its descent at the age of six months (corrected for gestational age), and since spontaneous testicular descent is unlikely to occur after that age, surgery should be performed within the subsequent year, at age eighteen months, at the latest.

Palpable testes

Surgery for palpable testes includes orchidofunicolysis and orchidopexy, either via an inguinal or scrotal approach.

Non-palpable testes

For non-palpable testes, surgery must clearly determine whether a testis is present or not. If a testis is found, the decision has to be made to remove it or bring it down to the scrotum.

An important step in surgery is a thorough re-examination once the boy is under general anaesthesia, since a previously non-palpable testis might be identifiable and subsequently change the surgical approach to standard inguinal orchidopexy, as described above. Otherwise, the easiest and most accurate way to locate an intra-abdominal testis is diagnostic laparoscopy. Subsequent removal or orchidolysis and orchidopexy can be carried out using the same approach to achieve the therapeutic aims.

In case of a vanishing testis, the procedure is finished once blind-ending spermatic vessels are clearly identified. If the vessels enter the inguinal canal, one may find an atrophic testis upon inguinal exploration or a healthy testis that needs to undergo standard orchidopexy. A peeping testis can be placed down in the scrotum laparoscopically or via an inguinal incision. Placement of an intra-abdominal testis can sometimes be a surgical challenge. Usually, testes lying > 2 cm above the internal inguinal ring may not reach the scrotum without division of the testicular vessels. Under such circumstances, a Fowler–Stephens orchidopexy might be an option.

Undescended testes and fertility

The association of undescended testes with compromised fertility is extensively discussed in the literature and seems to be a result of multiple factors, including germ cell loss, impaired germ cell maturation, Leydig cell diminution, and testicular fibrosis.

Although boys with one undescended testis have a lower fertility rate, they have the same paternity rate as those with bilateral descended testes. Boys with bilateral undescended testes suffer both lower fertility and paternity rates.

Regarding preservation of fertility potential, early surgical correction of undescended testes is highly recommended before twelve months of age, and by eighteen months at the latest.

Undescended testes and malignancy

Boys who are treated for an undescended testis have an increased risk of developing testicular malignancy. Screening and self-examination during and after puberty is therefore recommended.

Pre-pubertal orchidopexy may reduce the risk of testicular cancer and early surgical intervention is indicated in boys with undescended testes.

Recommendations	Strength rating
The Panel do not recommend medical or surgical treatment for retractile testes but recommend close follow-up on a yearly basis until puberty.	Strong
Perform surgical orchidolysis and orchidopexy before the age of twelve months, and by eighteen months at the latest.	Strong
Evaluate male neonates with bilateral non-palpable testes for possible disorders of sex development.	Strong
Perform a diagnostic laparoscopy to locate an intra-abdominal testicle.	Strong

Hormonal therapy in unilateral undescended testes is of no benefit for future paternity.	Weak
Offer endocrine treatment in case of bilateral undescended testes.	Weak
Inform the patient/caregivers about the increased risk of a later malignancy with an undescended testis in a post-pubertal boy or older and discuss removal in case of a contralateral normal testis in a scrotal position.	Weak

Figure 1: Classification of undescended testes

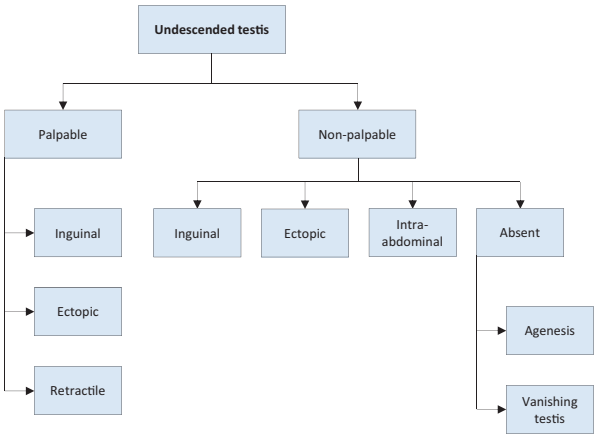
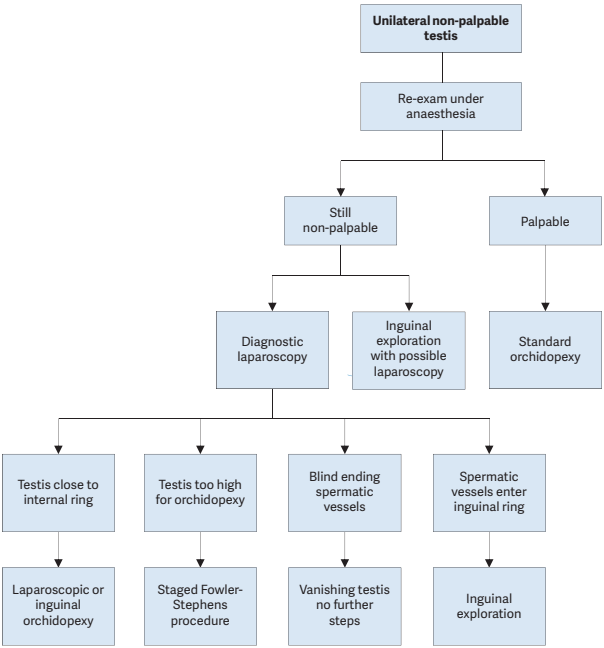


Figure 2: Algorithm for the management of unilateral non-palpable undescended testis



HYDROCELE

Background

Non-communicating hydroceles are found secondary to minor trauma, testicular torsion, epididymitis, or varicocele operation, or may appear as a recurrence after primary repair of a communicating hydrocele.

A communicating hydrocele vacillates in size, usually relative to activity. It is diagnosed by medical history and

physical investigation, the swelling is translucent, and transillumination of the scrotum confirms the diagnosis. If there are any doubts about intra-scrotal mass, ultrasound (US) should be performed. Contralateral disease should be excluded.

Surgical Treatment

Surgical treatment of hydrocele is not indicated within the first 12-24 months because of the tendency for spontaneous resolution.

However, early surgery is indicated if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology. There is no evidence that this type of hydrocele risks testicular damage.

The surgical procedure consists of ligation of the patent processus vaginalis via an inguinal incision, leaving the distal stump open, whereas in hydrocele of the cord, the cystic mass is excised or unroofed. Sclerosing agents should not be used because of the risk of chemical peritonitis in the communicating processus vaginalis peritonei.

The scrotal approach (Lord or Jaboulay technique) is used in the treatment of a secondary non-communicating hydrocele.

Recommendations	Strength rating
Observe hydrocele for twelve months prior to considering surgical treatment in the majority of infants.	Strong
Perform early surgery if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology.	Strong
Perform a scrotal ultrasound in case of doubt about the character of an intra-scrotal mass.	Strong

Do not use sclerosing agents because of the risk for chemical peritonitis.	Strong

HYPOSPADIAS

Background

Hypospadias are usually classified according to the anatomical location of the proximally displaced urethral orifice:

- distal - anterior hypospadias (glanular, coronal or distal penile);
- intermediate - middle (penile);
- proximal - posterior (penoscrotal, scrotal, perineal).

The pathology may be much more severe after skin release.

Diagnostic Evaluation

Patients with hypospadias should be diagnosed at birth. The diagnostic evaluation also includes an assessment of associated anomalies, which include cryptorchidism and open processus vaginalis or inguinal hernia. Severe hypospadias with unilaterally or bilaterally impalpable testis, or with ambiguous genitalia, require a complete genetic and endocrine work-up immediately after birth to exclude disorders of sex development, especially congenital adrenal hyperplasia.

Trickling urine and ballooning of the urethra require exclusion of meatal stenosis.

The length of the hypospadiac penis may be distorted by penile curvature, penoscrotal transposition, or may be smaller due to hypogonadism.

Differentiation between functionally necessary and aesthetically feasible operative procedures is important for therapeutic decision-making. As all surgical procedures carry the risk of complications; thorough pre-operative counselling of the caregivers is crucial. The therapeutic objectives are to

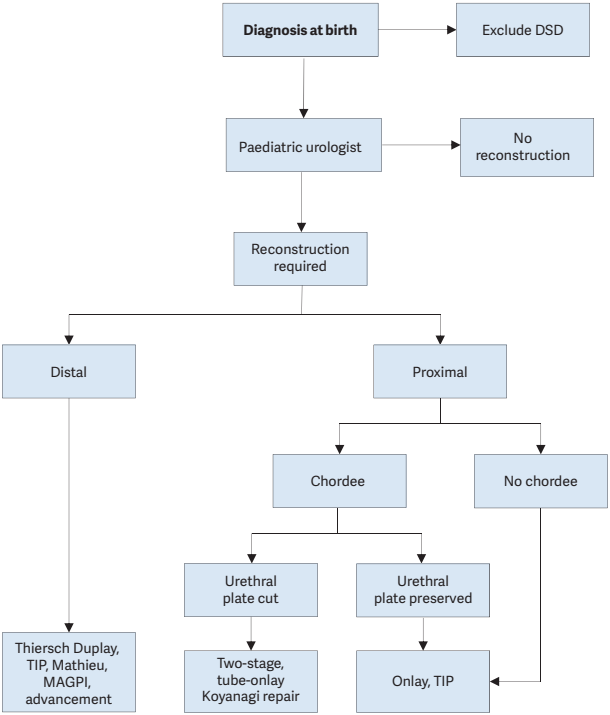
correct the penile curvature, to form a neourethra of an adequate size, to bring the neomeatus to the tip of the glans, if possible, and to achieve an overall acceptable cosmetic appearance. This goal is achieved by using different surgical techniques according to the individual findings.

Surgical Treatment

For repeat hypospadias repairs, no definitive guidelines can be given.

Excellent long-term functional and cosmetic results can be achieved after repair of anterior penile hypospadias. The complication rate in proximal hypospadias repair is higher. Figure 3 provides an algorithm for the management of hypospadias.

Figure 3: Algorithm for the management of hypospadias



DSD = disorders of sex development; GAP = glans approximation procedure; TIP = tubularised incised plate urethroplasty; MAGPI = meatal advancement and glanuloplasty incorporated.

MICROPENIS

Micropenis is defined as a small but otherwise normally formed penis with a stretched length of less than 2.5 cm ± standard deviation (SD) below the mean (Table 1).

Table 1: Length of the penis in boys
(according to Feldmann and Smith)

Age	Mean ± SD (cm)
Newborns	3.5 ± 0.4
0-5 months	3.9 ± 0.8
6-12 months	4.3 ± 0.8
1-2 years	4.7 ± 0.8
2-3 years	5.1 ± 0.9
3-4 years	5.5 ± 0.9
4-5 years	5.7 ± 0.9
5-6 years	6.0 ± 0.9
6-7 years	6.1 ± 0.9
7-8 years	6.2 ± 1.0
8-9 years	6.3 ± 1.0
9-10 years	6.3 ± 1.0
10-11 years	6.4 ± 1.1
Adults	13.3 ± 1.6

VARICOCELE IN CHILDREN AND ADOLESCENTS

Background

Varicocele is unusual in boys under ten years of age, but becomes more frequent at the beginning of puberty. Fertility problems will arise in about 20% of adolescents with varicocele. The adverse influence of varicocele increases with time.

Testicular catch-up growth and improvement in sperm parameters after varicocelectomy has been reported in adolescents. Varicocele is mostly asymptomatic, rarely

causing pain at this age. It may be noticed by the patient or caregivers, or discovered by the paediatrician at a routine visit. Diagnosis and classification depends upon the clinical finding and US investigation.

Surgical Treatment

Surgical intervention is based on ligation or occlusion of the internal spermatic veins. Microsurgical lymphatic-sparing repairs (microscopic or laparoscopic) are associated with the lowest recurrence and complication rates. There is no evidence that treatment of varicocele at paediatric age will offer a better andrological outcome than an operation performed later.

Conservative treatment and follow-up

During adolescence, testicular size should be checked annually. After adolescence, repeated sperm analysis is recommended. Figure 4 shows an algorithm for the diagnosis of varicocele in children and adolescents, and Figure 5 shows an algorithm for its treatment.

Figure 4: Algorithm for the diagnosis of varicocele in children and adolescents

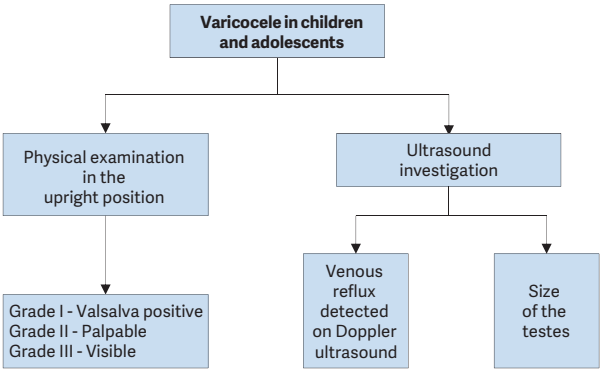
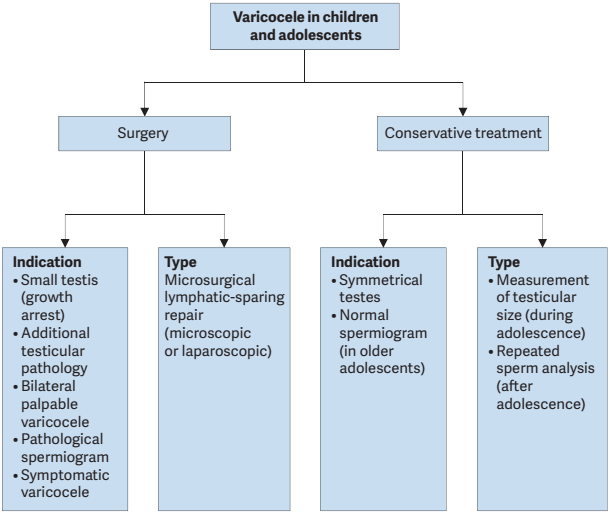


Figure 5: Algorithm for the management of varicocele in children and adolescents



URINARY TRACT INFECTIONS IN CHILDREN

Background

Urinary tract infections (UTIs) represent the most common bacterial infection in children. In neonates, the symptoms differ in many aspects from those in infants and children. The prevalence is higher; there is a male predominance; infections not caused by *Escherichia co*li are more frequent, and there is a higher risk of urosepsis.

- *Site:* Lower urinary tract (cystitis) versus upper urinary tract (pyelonephritis);
- *Episode:* first UTI versus unresolved infection, persistent infection and re-infection;

- *Severity:* simple UTI versus severe UTI;
- *Symptoms:* asymptomatic bacteriuria versus symptomatic UTI;
- *Complicating factors:* uncomplicated versus complicated UTI.

Diagnostic Evaluation

Diagnosis includes a medical history, searching for clinical signs and symptoms and a complete physical examination.

Urine sampling, analysis and culture

Urine sampling has to be performed before any antimicrobial agent is administered. The technique for obtaining urine is important to confirm or exclude UTI. Sampling in neonates, infants and non-toilet-trained children:

- **Plastic bag:** (high incidence of false positive results [85-99%]). Only helpful to exclude a UTI if the dipstick is negative for leukocyte esterase and the culture results are negative, otherwise the UTI has to be confirmed by a more specific method.
- **Clean-catch urine collection:** has a false-positive rate of 5% and false-negative rate of 12% and the contamination rate is higher compared to supra-pubic bladder aspiration (SPA).
- **Bladder catheterisation:** in female infants and in neonates, this technique may be an alternative to SPA, however with a higher contamination rate.
- **Supra-pubic bladder aspiration:** this is the most sensitive method to obtain an uncontaminated urine sample in non-toilet trained children.
- **Midstream urine:** in toilet-trained children who can void on command, could be an acceptable technique for obtaining urine after cleaning the urethral meatus and perineum.

Urinalysis:

- **Dipsticks:** are ready to use and helpful when the result is positive, because it is highly specific.
- **Microscopy:** can be used after centrifugation as well as in uncentrifuged urine and has been demonstrated to be sensitive for UTI. This is rarely done in an outpatient setting.
- **Flow imaging analysis technology:** is being increasingly used to classify particles in uncentrifuged urine specimens and correlates well with manual methods.
- **Urine culture:** is generally not necessary after negative results for dipstick, microscopic or automated urinalysis. If the dipstick result is positive, confirmation by urine culture is strongly recommended.

Pyuria without bacteriuria (sterile pyuria) may be due to incomplete antibiotic treatment, urolithiasis, or foreign bodies in the urinary tract, and infections caused by *Mycobacterium tuberculosis* or *Chlamydia trachomatis.*

Table 2: Criteria for UTI in children

Urine specimen from suprapubic bladder puncture	Urine specimen from bladder catheterisation	Urine specimen from midstream void
Any number of cfu/mL (at least 10 identical colonies	≥ 10^3 - 10^5 cfu/mL	≥ 10^4 cfu/mL with symptoms ≥ 10^5 cfu/mL without symptoms

Imaging

Ultrasound (US): of the kidneys and bladder as soon as possible is advised in infants with febrile UTI to exclude obstruction of the upper and lower urinary tract and post-void residual urine should be measured in toilet-trained children to exclude voiding abnormalities as a cause of UTI.

Radionuclide scanning: changes in dimercaptosuccinic acid (DMSA) clearance during acute UTI (up to four to six weeks) indicating pyelonephritis and renal scars can be detected after three to six months. This correlates well with the presence of dilating reflux and the risk of further pyelonephritis episodes, breakthrough infections and future renal scarring.
Voiding cystourethrography (VCUG): is best practice to exclude or confirm vesicoureteral reflux, due to the risk of renal scarring, VCUG is recommended after the first episode of febrile UTI in boys and girls depending on sex, age and clinical presentation (see Figure 6). Another option is doing DMSA first, followed by VCUG if there is renal cortical uptake deficiency after UTI.
Bladder and bowel dysfunction (BBD): are risk factors for which each child with UTI should be screened for upon presentation. If there are signs of BBD at infection-free intervals, further diagnosis and effective treatment are strongly recommended.

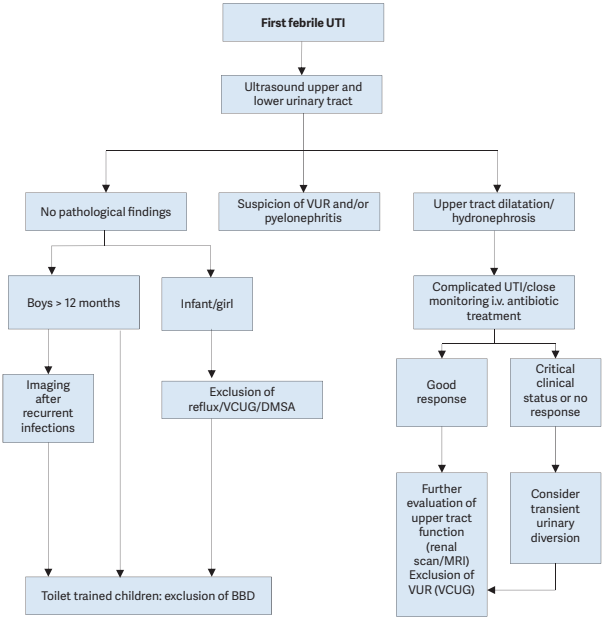
Status of circumcision should be checked in boys and treatment of the phimosis considered in those with pyelonephritis.

Management

Administration route: the choice between oral and parenteral therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; non-compliance; and complicated pyelonephritis (e.g. urinary obstruction). Febrile UTI in early infancy should be treated by i.v. fluids and antibiotics and under close monitoring within the hospital.
Duration of therapy: outcomes of short courses (one to three days) are inferior to those of seven to fourteen days. In late infancy, oral therapy with a third-generation cephalosporin (e.g. cefixime or ceftibuten) is equivalent to the usual two to four days intravenous therapy followed by oral treatment in

uncomplicated UTI's. In complicated UTI parenteral treatment with broad-spectrum antibiotics is preferred.

Figure 6: Algorithm for the management of a first febrile UTI



BBD = Bladder Bowel Dysfunction; DMSA = technetium^{99}-labelled dimercaptosuccinic acid; MRI = magnetic resonance imaging; UTI = urinary tract infection; VCUG = voiding cystourethrography; VUR = vesicoureteral reflux; i.v. = intravenous.

Monitoring of UTI

Urine usually becomes sterile after 24 hours, and leukocyturia disappears within three to four days. Normalisation of body temperature can be expected within 24-48 hours after the start of therapy in 90% of cases. In patients with prolonged fever and failing recovery, treatment-resistant uropathogens or the presence of congenital uropathy or acute urinary obstruction should be considered. Immediate US examination is recommended.

Procalcitonin (among other laboratory inflammatory parameters such as C-reactive protein and leukocyte count) is a reliable serum marker for early prediction of renal parenchymal inflammation. In patients with febrile UTI, serum electrolytes and blood cell counts should be obtained.

Recommendations	Strength rating
Take a medical history, assess clinical signs and symptoms and perform a physical examination to diagnose children suspected of having a urinary tract infection (UTI).	Strong
Exclude bladder and bowel dysfunction (BBD) in any child with febrile and/or recurrent UTI and do not delay diagnosis and treatment of BBD.	Strong
The most effective way to collect an uncontaminated urine sample in an infant is through suprapubic bladder aspiration, bladder catheterisation is an alternative with a higher contamination rate.	Strong

Do not use plastic bags for urine sampling in non-toilet-trained children since it has a high risk of false-positive results. Clean catch urine is an acceptable technique for toilet-trained children.	Strong
Urinalysis by dipstick yields rapid results, but it should be used with caution. Microscopic investigation is the standard method of assessing pyuria after centrifugation. Using flow imaging analysis, the numbers of white blood cells, squamous epithelial cells and red cells correlate well with manual methods.	Weak
The choice between oral and parenteral therapy should be based on patient age; clinical suspicion of urosepsis; illness severity; refusal of fluids, food and/or oral medication; vomiting; diarrhoea; noncompliance; complicated pyelonephritis.	Strong
Treat UTIs with four to seven day courses of oral or parenteral therapy.	Strong
Offer long-term antibacterial prophylaxis in case of high susceptibility to UTI and risk of acquired renal damage and lower urinary tract symptoms.	Weak
Treat complicated UTI, with broad-spectrum antibiotics (parenteral).	Weak
In infants with febrile UTI, use renal and bladder ultrasound to exclude obstruction of the upper and lower urinary tract.	Strong

In all infants, exclude vesicoureteral reflux (VUR) after the first episode of febrile UTI, using voiding cystourethography (VCUG) or a dimercaptosuccinic acid (DMSA) scan first (in case of a positive DMSA-scan, follow-up with VCUG). In boys more than one year of age, exclude VUR after the second febrile UTI.	Strong

MONOSYMPTOMATIC NOCTURNAL ENURESIS - BEDWETTING

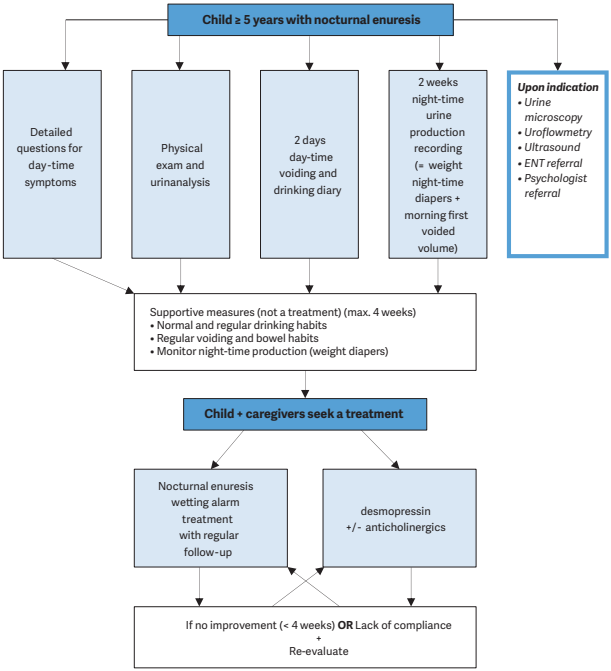
Background

Monosymptomatic nocturnal enuresis is incontinence during the night. Any wetting during sleep above the age of five years is considered nocturnal enuresis. It is important to note that there is a single symptom only. Due to an imbalance between night-time urine output and night-time bladder capacity, the bladder can easily become full at night, and the child will either wake-up to empty the bladder or will void during sleep.

Diagnostic Evaluation

A voiding diary, registering the day-time bladder function and the night-time urine output will help guide the treatment. Measuring the day-time bladder capacity gives an estimate of bladder capacity to compare with normal values for age. Figure 7 presents an algorithm for the diagnosis and treatment of monosymptomatic nocturnal enuresis.

Figure 7: Algorithm for the assessment and management of nocturnal enuresis



ENT = ear, nose, throat

VESICOURETERIC REFLUX IN CHILDREN

Background

Vesicoureteric reflux presents with a wide range of severities, and the majority of reflux (VUR) patients will not develop renal scars and probably will not need any intervention. The main goal in management is the preservation of kidney function.

Diagnostic evaluation

The diagnostic work-up should evaluate the overall health and development of the child. A basic diagnostic work-up includes a detailed medical history (including family history, and screening for lower urinary tract dysfunction [LUTD]), physical examination including blood pressure measurement, urinalysis (assessing proteinuria), urine culture, and serum creatinine in patients with bilateral renal parenchymal abnormalities.

Prenatally diagnosed hydronephrosis

Ultrasound of the kidney and bladder is the first standard evaluation tool for children with prenatally diagnosed hydronephrosis.

It should be delayed until the end of first week after birth because of early oliguria in the neonate. It is essential to evaluate the bladder, as well as the kidneys.

Recommendations	Strength rating
Inform parents of children with vesicoureteric reflux (VUR) that siblings and offspring have a high prevalence of VUR.	Strong
Use renal ultrasound (US) for screening of sibling(s).	Strong
Use voiding cystourethrography if there is evidence of renal scarring on US or a history of urinary tract infection.	Weak
Do not screen older toilet-trained children since there is no added value in screening for VUR.	Weak

Conservative therapy

The objective of conservative therapy is prevention of febrile UTI. It is based on the understanding that:

- VUR resolves spontaneously, mostly in young patients with low-grade reflux. However, spontaneous resolution is low in bilateral high-grade reflux.
- VUR does not damage the kidney when patients are free of infection and have a normal lower urinary tract function.
- There is no evidence that small scars can cause hypertension, renal insufficiency or problems during pregnancy and in the long-term.
- The conservative approach includes watchful waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in those with LUTD.
- Circumcision in early infancy may be considered as part of the conservative approach, because it is effective in reducing the risk of infection in normal children.

Surgical Treatment

Surgical treatment comprises endoscopic injection of bulking agents or ureteral re-implantation.

Subureteric injection of bulking agents: Due to the availability of biodegradable substances, endoscopic subureteric injection of bulking agents has become an alternative to long-term antibiotic prophylaxis and surgical intervention.

Open surgical techniques: Overall, all surgical procedures offer similar very high success rates for correcting VUR.

Laparoscopy: A laparoscopic approach cannot be recommended as a routine procedure. It can be offered as an alternative to the caregivers in centres where there is enough experience.

Recommendations	Strength rating
Initially treat all patients diagnosed within the first year of life with continuous antibiotic prophylaxis, regardless of the grade of reflux or presence of renal scars.	Weak
Offer immediate, parenteral antibiotic treatment for febrile breakthrough infections.	Strong
Offer definitive surgical or endoscopic correction to patients with frequent breakthrough infections.	Weak
Offer open surgical correction to patients with persistent high-grade reflux and endoscopic correction for lower grades of reflux.	Strong
Initially manage all children presenting at age one to five years conservatively.	Strong
Offer surgical repair to children above the age of one presenting with high-grade reflux and abnormal renal parenchyma.	Weak
Offer close surveillance without antibiotic prophylaxis to children presenting with lower grades of reflux and without symptoms.	Strong
Ensure that a detailed investigation for the presence of lower urinary tract dysfunction (LUTD) is done in all and especially in children after toilet-training. If LUTD is found, the initial treatment should always be for LUTD.	Strong
Offer surgical correction, if parents prefer definitive therapy to conservative management.	Strong

Select the most appropriate management option based on: • the presence of renal scars; • clinical course; • the grade of reflux; • ipsilateral renal function; • bilaterality; • bladder function; • associated anomalies of the urinary tract; • age and gender; • compliance; • parental preference. Refer to Table 3 for risk factors and follow-up.	Weak
In high-risk patients who already have renal impairment, a more aggressive, multidisciplinary approach is needed.	Strong

BASIC PRINCIPLES OF LAPAROSCOPIC SURGERY IN CHILDREN

The use of laparoscopy and robot-assisted laparoscopic surgery is rapidly increasing and has gained widespread acceptance for many urological surgeries in children. Diagnostic laparoscopy for undescended testis, nephrectomy, heminephrectomy, varicocelectomy, pyeloplasty, ureteral reimplantation are some of the indications which are commonly being performed. This expanding scope related to technological advancements allows surgeons to perform more complex procedures in a minimally invasive fashion even in infants and younger children. Generally, well-established benefits of minimally invasive surgery are decreased pain, shorter convalescence and better cosmetics compared to traditional open surgery. Additional advantages of robotic surgery over conventional laparoscopy include ergonomics, 3D vision, better manoeuvrability, decreased tremor and easy learning curve. Limitations to be considered are increased

operative time, smaller working space at young age, cost and experience of the surgeon and anesthesiologist.

As worldwide experience increases, there is an accumulating awareness about the physiological consequences related to intra- and retroperitoneal CO_2 insufflation in children. In contrast to traditional open surgery pneumoperitoneum may have physiological responses which require close monitoring during surgery and should be taken seriously.

Laparoscopy in children requires specific anesthetic precautions. Physiological effects of CO_2 pneumoperitoneum, positioning of the patient and in potentially increased operative time need to be considered by the anesthesiology team. Therefore, a detailed medical examination and risk assessment is mandatory preoperatively. Especially cardiac and pulmonary system should be assessed since increased intra-abdominal pressure may lead to decreased ventricular preload.

Pneumoperitoneal pressure (PnP in mmHg) is one of the critical points that needs to be carefully considered by laparoscopic surgeons. A recent RCT compared two different pneumoperitoneal pressure groups (6-8 mmHg vs. 9-10 mmHg) in infants less than 10 kg. It demonstrated that higher pressures were associated with more pronounced respiratory and hemodynamic changes as well as increased post-operative pain scores and prolonged time to resume feeding.

Recommendations	Strength rating
Use lower intra-abdominal pressure (6-8 mmHg) during laparoscopic surgery in infants and smaller children.	Strong
Use open access for laparoscopy in infants and smaller children.	Strong
Monitor for laparoscopy-related cardiac, pulmonary and diuretic responses.	Strong

This short booklet text is based on the more comprehensive EAU/ESPU Paediatric Urology Guidelines (ISBN 978-94-92671-07-3), available at their website, http://www.uroweb.org/guidelines.

Table 3: Management and follow-up according to different risk groups

Risk Groups	Presentation	Initial treatment
High	Symptomatic male or female patients after toilet-training with high-grade reflux (grades IV-V), abnormal kidneys and LUTD	Initial treatment is always for LUTD with CAP; intervention may be considered in cases of BT infections or persistent reflux
High	Symptomatic male or female patients after toilet-training with high-grade reflux (grade IV-V), abnormal kidneys and no LUTD	Intervention should be considered
Moderate	Symptomatic male or female patients before toilet-training, with high-grade reflux and abnormal kidneys	CAP is the initial treatment. Intervention may be considered in cases of BT infections or persistent reflux
Moderate	Asymptomatic patients (PNH or sibling) with high-grade reflux and abnormal kidneys	CAP is the initial treatment. Intervention may be considered in cases of BT, infections or persistent reflux
Moderate	Symptomatic male or female patients after toilet-training, with high-grade reflux and normal kidneys with LUTD	Initial treatment is always for LUTD with CAP. Intervention may be considered in cases of BT infections or persistent reflux

Comment	Follow-up
Greater possibility of earlier intervention	More aggressive follow-up for UTI and LUTD; full re-evaluation after 6 months
Open surgery has better results than endoscopic surgery	Post-operative VCUG on indication only; follow-up of kidney status until after puberty
Spontaneous resolution is higher in males	Follow-up for UTI/ hydronephrosis; full re-evaluation after 12-24 months
	Follow-up for UTI/ hydronephrosis; full re-evaluation after 12-24 months
In case of persistent LUTD, despite urotherapy, intervention should be considered. The choice of intervention is controversial	Follow-up for UTI and LUTD, kidney status; full re-evaluation after successful urotherapy

Moderate	Symptomatic male or female patients after toilet-training with low-grade reflux, abnormal kidneys with or without LUTD	Choice of treatment is controversial. Endoscopic treatment may be an option. LUTD treatment should be given if needed
Moderate	All symptomatic patients with normal kidneys, with low-grade reflux, with LUTD	Initial treatment is always for LUTD with or without CAP
Low	All symptomatic patients with normal kidneys, with low-grade reflux, with no LUTD	No treatment or CAP
Low	All asymptomatic patients with normal kidneys with low-grade reflux	No treatment or CAP in infants

BT = breakthrough; CAP = continuous antibiotic prophylaxis;
LUTD = lower urinary tract dysfunction;
PNH = prenatal diagnosed hydronephrosis;
UTI = urinary tract infection;
VCUG = voiding cystourethrography.

	Follow-up for UTI, LUTD, and kidney status until after puberty
	Follow-up for UTI and LUTD
If no treatment is given, parents should be informed about risk of infection	Follow-up for UTI
If no treatment is given, parents should be informed about risk of infection	Follow-up for UTI

EAU GUIDELINES ON UROLOGICAL TRAUMA

(Limited text update March 2020)

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Introduction

Traumatic injuries are classified according to the basic mechanism of the injury into **penetrating** and **blunt** injuries. Penetrating trauma is further classified according to the velocity of the projectile into high- and medium-velocity projectiles (e.g. rifle and handgun bullets, respectively), and low-velocity items (e.g. knife stab). High-velocity weapons inflict greater damage due to a temporary expansive cavitation that causes destruction in a much larger area than the projectile tract itself. In lower velocity injuries, the damage is usually confined to the projectile tract. **Blast injury** is a complex cause of trauma which includes blunt and penetrating trauma and burns.

Urological trauma is often associated with significant injuries in the polytraumatised patient. Advances in trauma care include the widespread acceptance of damage control principles and trauma centralisation to major trauma centres staffed by dedicated trauma teams. Urologists increasingly understand their role in the context of polytrauma with the ultimate aims of improving survivability and decreasing morbidity in these patients.

Renal Trauma

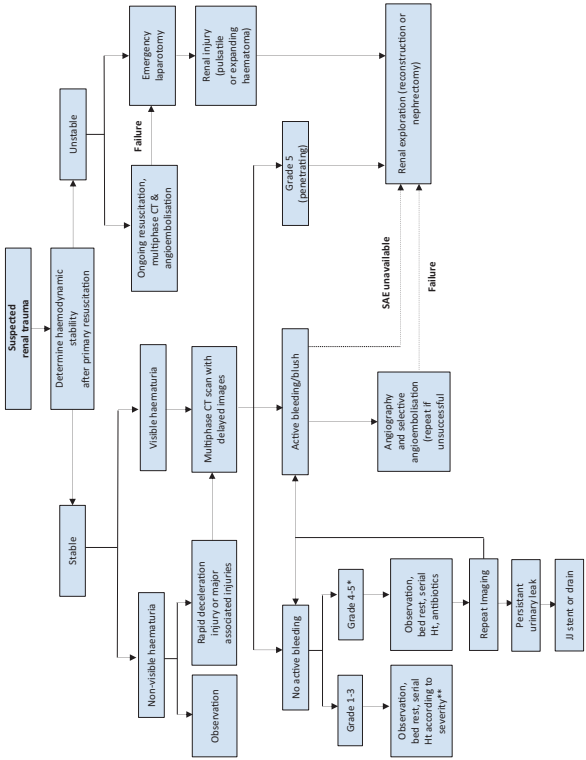
Renal trauma is present in to up 5% of all trauma cases. It is most common in young males and has an overall population incidence of 4.9 per 100,000. Most injuries can be managed non-operatively with successful organ preservation. The most commonly used classification system is that of the American Association for the Surgery of Trauma. It is validated and predicts morbidity and the need for intervention.

Recommendations for evaluation and management of renal trauma

Recommendations	Strength rating
Evaluation	
Assess haemodynamic stability upon admission.	Strong
Record past renal surgery, and known pre-existing renal abnormalities (ureteropelvic junction obstruction, solitary kidney, lithiasis).	Strong
Test for haematuria in a patient with suspected renal injury.	Strong
Perform a multiphase computed tomography scan in trauma patients with: • visible haematuria; • non-visible haematuria and one episode of hypotension; • a history of rapid deceleration injury and/or significant associated injuries; • penetrating trauma; • clinical signs suggesting renal trauma e.g. flank pain, abrasions, fractured ribs, abdominal distension and/or a mass and tenderness.	Strong

Management	
Manage stable patients with blunt renal trauma non-operatively with close monitoring and re-imaging as required.	Strong
Manage isolated Grade 1-4 stab and low-velocity gunshot wounds in stable patients non-operatively.	Strong
Use selective angioembolisation for active renal bleeding if there are no other indications for immediate surgical exploration.	Strong
Proceed with renal exploration in the presence of: • persistent haemodynamic instability; • Grade 5 vascular or penetrating injury; • expanding or pulsatile peri-renal haematoma.	Strong
Attempt renal reconstruction if haemorrhage is controlled and there is sufficient viable renal parenchyma.	Weak
Repeat imaging in high-grade injuries and in cases of fever, worsening flank pain, or falling haematocrit.	Strong
Follow-up approximately three months after major renal injury with: • physical examination; • urinalysis; • individualised radiological investigation including nuclear scintigraphy; • blood pressure measurement; • renal function tests.	Weak
Measure blood pressure annually to diagnose renovascular hypertension.	Strong

Figure 1: Evaluation of blunt renal trauma in adults



* *Excluding Grade 5 penetrating injuries.*

** *Antibiotics should be administered for all penetrating injuries.*

--- *If haemodynamically unstable.*

CT = computed tomography; Ht = haematocrit; SAE = selective angioembolisation.

Ureteral Trauma

Ureteral injuries are quite rare - most are iatrogenic. They are often missed intra-operatively, usually involve the lower ureter, and may result in severe sequelae. Overall, ureteral trauma accounts for 1-2.5% of urinary tract trauma. Ureteral injury should be suspected in all cases of penetrating abdominal injury, especially gunshot wounds, as it occurs in 2-3% of cases. It should also be suspected in blunt trauma with a deceleration mechanism, as the renal pelvis can be torn away from the ureter.

Diagnostic evaluation

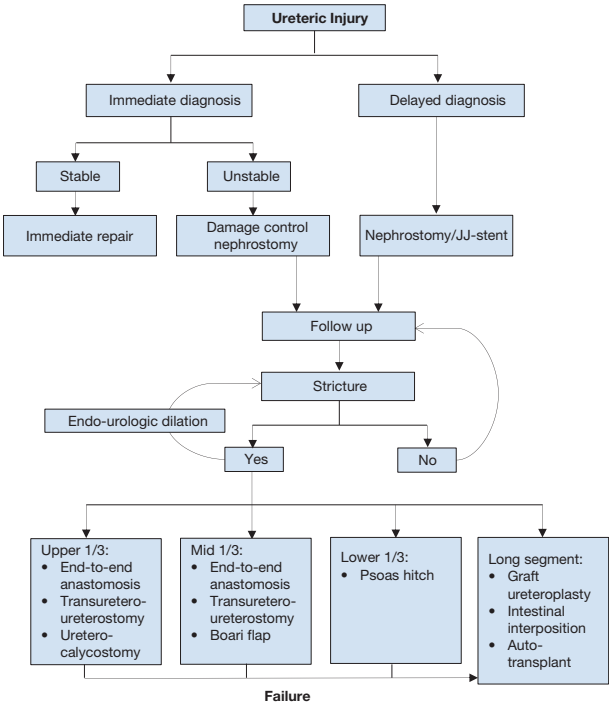
- A high index of suspicion of ureteral injury should be maintained as the majority of cases are diagnosed late, predisposing the patient to pain, infection, and renal function impairment.
- Haematuria is an unreliable indicator.
- Extravasation of contrast material in computed tomography (CT) is the hallmark sign of ureteral trauma.
- In unclear cases, a retrograde or antegrade urography is required for confirmation.

Management of ueteral trauma

Recommendations	Strength rating
Visually identify the ureters to prevent ureteral trauma during abdominal and pelvic surgery.	Strong
Beware of concomitant ureteral injury in all abdominal penetrating trauma, and in deceleration-type blunt trauma.	Strong
Use pre-operative prophylactic stents in high-risk cases.	Strong

Repair iatrogenic ureteral injuries recognised during surgery immediately.	Strong
Treat iatrogenic ureteral injuries with delayed diagnosis by nephrostomy tube/JJ stent urinary diversion.	Strong
Manage ureteral strictures by ureteral reconstruction according to the location and length of the affected segment.	Strong

Figure 2: Management of ureteric injuries



Bladder Trauma

Bladder trauma is primarily classified according to the location of the injury: **intraperitoneal, extraperitoneal,** and **combined** intra-extraperitoneal as it guides further management. Bladder trauma is categorised by aetiology: **non-iatrogenic** (blunt and penetrating) and **iatrogenic** (external and internal). Extraperitoneal injury is almost always associated with pelvic fractures. Intraperitoneal injury is caused by a sudden rise in intravesical pressure of a distended bladder, secondary to a blow to the pelvis or lower abdomen.

Diagnostic evaluation

The principal sign of bladder injury is visible haematuria. Absolute indications for bladder imaging include: visible haematuria and a pelvic fracture or non-visible haematuria combined with high-risk pelvic fracture or posterior urethral injury. In the absence of these absolute indications, further imaging is based on clinical signs and symptoms including:

- inability to void or inadequate urine output;
- abdominal tenderness or distension due to urinary ascites, or signs of urinary ascites in abdominal imaging;
- uraemia and elevated creatinine level due to intra-peritoneal re-absorption;
- entry/exit wounds at lower abdomen, perineum or buttocks in penetrating injuries.

Intra-operative signs of external iatrogenic bladder injury include: extravasation of urine, visible laceration, visible bladder catheter, and blood and/or gas in the urine bag during laparoscopy. Internal bladder injury is recognised by cysto-scopic identification of fatty tissue, dark space, or bowel.

Imaging – Cystography and Cystoscopy

Cystography is the preferred diagnostic modality for non-iatrogenic bladder injury and for a suspected iatrogenic

bladder trauma in the post-operative setting. Intraperitoneal extravasation is visualised by free contrast medium in the abdomen outlining bowel loops or abdominal viscera. Extraperitoneal bladder injury is typically diagnosed by flame-shaped areas of contrast extravasation in the peri-vesical soft tissues. Cystoscopy is the preferred method for detection of intra-operative bladder injuries as it may directly visualise the laceration and can localise the lesion in relation to the position of the trigone and ureteral orifices.

Management of bladder trauma

Recommendations	Strength rating
Perform cystography in the presence of visible haematuria and pelvic fracture.	Strong
Perform cystography in case of suspected iatrogenic bladder injury in the post-operative setting.	Strong
Perform cystography with active retrograde filling of the bladder with dilute contrast (300-350 mL).	Strong
Perform cystoscopy to rule out bladder injury during retropubic sub-urethral sling procedures.	Strong
Manage uncomplicated blunt extra-peritoneal bladder injuries conservatively.	Weak
Manage blunt extraperitoneal bladder injuries operatively in cases of bladder neck involvement and/or associated injuries that require surgical Intervention.	Strong
Manage blunt intraperitoneal injuries by surgical exploration and repair.	Strong

Manage small uncomplicated intra-peritoneal bladder injuries during endoscopic procedures conservatively.	Weak
Perform cystography to assess bladder wall healing after repair of a complex injury or in case of risk factors for wound healing.	Strong

Urethral Trauma

- Injuries to the anterior urethra (AU) are caused by straddle injuries, trauma during sexual intercourse (associated with penile fracture), penetrating trauma and from iatrogenic trauma e.g. endoscopic instruments, catheterisation.
- Pelvic fractures are the predominant cause of male posterior and female urethral injury.
- Pelvic fracture and penetrating urethral injuries have a high likelihood of life-threatening concomitant injuries.
- Female urethral injuries are often associated with vaginal injuries.
- Insertion of a synthetic sub-urethral sling for the treatment of stress urinary incontinence is an important cause of iatrogenic female urethral injury.

Diagnostic evaluation

- Blood at the external urethral meatus is the most common clinical sign, and indicates the need for further diagnostic work up.
- Inability to void is usually a sign of a complete injury.
- Incomplete injuries are associated with pain on urination and haematuria in the majority of cases.
- Blood at the vaginal introitus is present in the majority of female patients with pelvic fractures and co-existing urethral injuries.
- Rectal examination may reveal a "high-riding" prostate. However, this is an unreliable finding. Blood on the examination finger is suggestive of a rectal injury

associated with pelvic fracture.
- Urethral bleeding or urinary extravasation can cause penile and scrotal swelling and haematoma, but these findings are usually delayed (> 1 hr).
- Retrograde urethrography is the standard in the early evaluation of a male urethral injury, except for penile fracture related injuries for which cysto-urethroscopy is preferred.
- Cysto-urethroscopy combined with vaginoscopy is the preferred diagnostic modality in case of suspected female urethral injury.

Management

Male urethral injuries
- The management of male anterior and posterior urethral injuries are summarised in Figure 3 and 4, respectively.

Female urethal injuries
- In case of haemodynamic instability, provide urinary diversion by suprapubic catherisation or a single attempt of urethral catheterisation.
- Early repair within seven days has the highest succes rate and the lowest complication rate in comparison with delayed repair or early endoscopic re-aligment.

Management of urethral trauma

Recommendations	Strength rating
Provide appropriate training to reduce the risk of traumatic catheterisation.	Strong
Evaluate male urethral injuries with flexible cysto-urethroscopy and/or retrograde urethrography.	Strong

Evaluate female urethral injuries with cysto-urethroscopy and vaginoscopy.	Strong
Treat iatrogenic anterior urethral injuries by transurethral or suprapubic urinary diversion.	Strong
Treat partial blunt anterior urethral injuries by suprapubic or urethral catheterisation.	Strong
Treat complete blunt anterior urethral injuries in males by immediate urethroplasty.	Weak
Treat pelvic fracture urethral injuries (PFUIs) in hemodynamically unstable patients by transurethral or suprapubic catheterisation initially.	Strong
Perform early endoscopic re-alignment in male PFUIs when feasible.	Weak
Do not repeat endoscopic treatments after failed re-alignment for male PFUI.	Strong
Treat partial posterior urethral injuries by suprapubic or transurethral catheter.	Strong
Do not perform immediate urethroplasty (< 48 hours) in male PFUIs.	Strong
Perform early urethroplasty (two days to six weeks) for male PFUIs with complete disruption in selected patients (stable, short gap, soft perineum, lithotomy position possible).	Weak
Manage complete posterior urethral disruption in male PFUIs with suprapubic diversion and deferred (at least three months) urethroplasty.	Strong
Perform early repair (within seven days) for female PFUIs (not delayed repair or early re-alignment).	Strong

Figure 3: Management of anterior urethral injuries in men

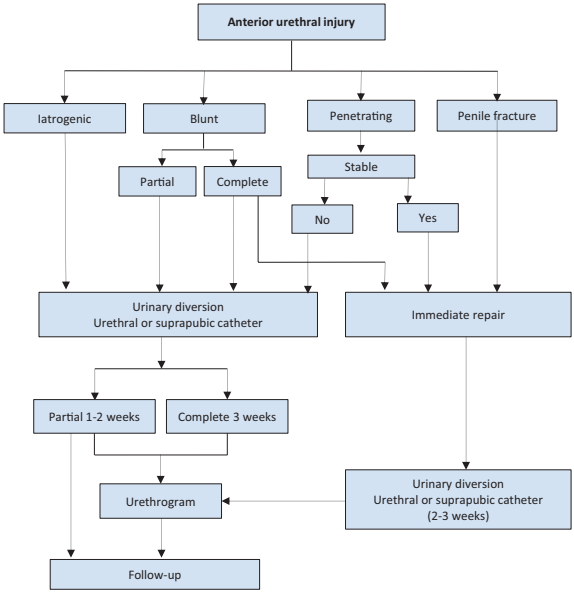
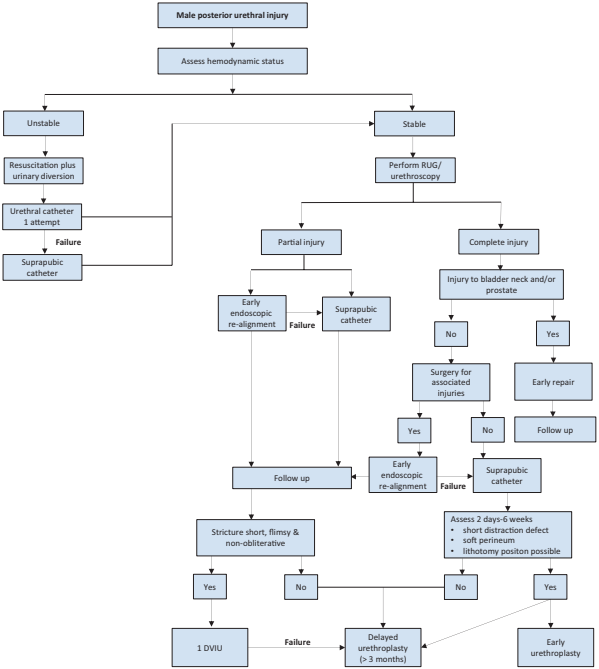


Figure 4: Management of posterior urethral injuries in men



RUG = retrograde urethrography; DVIU = direct visual internal urethrotomy.

Genital Trauma

Of all urological injuries, 33-66% involve the external genitalia. Genital trauma is much more common in males than in females due to anatomical differences, increased frequency of road traffic accidents and increased participation in physical sports, war and crime. The majority of genital trauma is caused by blunt injuries (80%).

Diagnostic evaluation

A summary of key points for penile fracture and testicular trauma are provided in Table 1. Blunt vulvar or perineal trauma in women may be associated with bleeding, pain and voiding problems. In genital trauma:

- Urinalysis should be performed.
- Visible haematuria requires a retrograde urethrogram in males, whilst flexible or rigid cystoscopy is recommended to exclude urethral and bladder injury in females.
- In females with genital injuries and blood at the vaginal introitus, further gynaecologic investigation to exclude vaginal injury is required.

Management

Penetrating penile trauma

- Non-operative management is recommended for small superficial injuries with intact Buck's fascia.
- More significant injuries require surgical exploration and debridement of necrotic tissue.
- Surgical approach depends upon the site and extent of the injury, but a subcoronal incision with penile degloving usually gives good exposure. Initially, a defect in the tunica albuginea should be closed after copious irrigation.
- In penile avulsion injuries acute management involves resuscitation of the patient, and preparation for surgical re-implantation of the penis if it has been recovered and is not too badly damaged.

Blunt scrotal trauma

- May result in testicular dislocation, haematocoele, testicular rupture and/or scrotal haematoma.
- Traumatic dislocation of the testis is treated by manual replacement and secondary orchidopexy. If primary manual reposition cannot be performed, immediate orchidopexy is indicated.
- If haematocele is smaller than three times the size of the contralateral testis – conservative management.
- If large haematocele – explore.
- If testicular rupture suspected, explore, evacuate clot and any necrotic testicular tubules and close the tunica albuginea.

Penetrating scrotal trauma

- Surgical exploration with conservative debridement of non-viable tissue.
- Primary reconstruction of testis and scrotum can be performed in most cases.
- In complete disruption of the spermatic cord, re-alignment without vaso-vasostomy may be considered.
- In extensive destruction of the tunica albuginea, mobilisation of a free tunica vaginalis flap can be performed for testicular closure.
- If reconstruction cannot be achieved, orchiectomy is indicated.
- In improvised explosive device blast injury, the extensive loss of genital tissue often requires complex and staged reconstructive surgical procedures.

Table 1. Summary of key points for penile fracture and testicular trauma

Penile fracture
The most common causes of penile fracture are sexual intercourse, forced flexion, masturbation and rolling over.
Penile fracture is associated with a sudden cracking or popping sound, pain, immediate detumescence and local swelling.
Magnetic resonance imaging (MRI) is superior to all other imaging techniques in diagnosing penile fracture.
Management of penile fracture is surgical intervention with closure of the tunica albuginea.
Testicular trauma
Blunt testicular injury may occur under intense compression of the testis against the inferior pubic ramus or symphysis, resulting in a rupture of the tunica albuginea.
Testicular rupture is associated with immediate pain, nausea, vomiting, and sometimes fainting.
Scrotal ultrasound is the preferred imaging modality for the diagnosis of testicular trauma.
Surgical exploration in patients with testicular trauma ensures preservation of viable tissue, when possible.

Recommendations for the management of genital trauma

Recommendations	Strength rating
Exclude urethral injury in the case of penile fracture.	Strong
Perform ultrasound (US) for the diagnosis of testis trauma.	Strong
Treat penile fractures surgically, with closure of tunica albuginea.	Strong
Explore the injured testis in all cases of testicular rupture and in those with inconclusive US findings.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON CHRONIC PELVIC PAIN

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Introduction

The EAU Guideline for Chronic Pelvic Pain plays an important role in the process of consolidation and improvement of care for patients with abdominal and pelvic pain. From both literature and daily practice it has become clear that abdominal and pelvic pain are areas still under development. The EAU Guideline aims to expand the awareness of caregivers in the field of abdominal and pelvic pain and to assist those who treat patients with abdominal and pelvic pain in their daily practice. The guideline is a useful instrument not only for urologists, but also for gynaecologists, surgeons, physiotherapists, psychologists and pain doctors.

This pocket version aims to synthesise the important clinical messages described in the full text and is presented as a series of 'strength rated recommendations', which follow the standard for levels of evidence used by the EAU (see Introduction chapter of the EAU Guidelines book and online at the EAU website http://www.uroweb.org/guideline/).

Chronic pelvic pain syndromes

Classification

Much debate over the classification of chronic pelvic pain (CPP) has occurred, is ongoing and will continue in the future. Classification involves three aspects of defining a condition: phenotyping, terminology and taxonomy.

Definition of CPP

Chronic pelvic pain is chronic or persistent pain perceived* in structures related to the pelvis of either men or women. It is often associated with negative cognitive, behavioural, sexual and emotional consequences as well as with symptoms suggestive of lower urinary tract, sexual, bowel, pelvic floor or gynaecological dysfunction.
*(*Perceived indicates that the patient and clinician, to the best of their ability from the history, examination and investigations (where appropriate) have localised the pain as being perceived in the specified anatomical pelvic area).*

Definition of CPPS

Chronic pelvic pain syndrome (CPPS) is the occurrence of CPP when there is no proven infection or other obvious local pathology that may account for the pain. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. CPPS is a subdivision of CPP.

Table 1: Classification of chronic pelvic pain syndromes

Axis I Region		Axis II System	Axis III End-organ as pain syndrome as identified from Hx, Ex and Ix	
Chronic pelvic pain	Specific disease associated pelvic pain OR Pelvic pain syndrome	Urological	Prostate	
			Bladder	
			Scrotal Testicular Epididymal	
			Penile Urethral	
			Post-vasectomy	
		Gynaecological	Vulvar Vestibular Clitoral	
			Endometriosis associated	
			CPPS with cyclical exacerbations	
			Dysmenorrhoea	
		Gastrointestinal	Irritable bowel	
			Chronic anal	
			Intermittent chronic anal	
		Peripheral nerves	Pudendal pain syndrome	
		Sexological	Dyspareunia	
			Pelvic pain with sexual dysfunction	
		Psychological	Any pelvic organ	
		Musculo-skeletal	Pelvic floor muscle Abdominal muscle Spinal	
			Coccyx	

	Axis IV Referral character-istics	AAxis V Temporal characteristics	Axis VI Character	Axis VII Associated symptoms	Axis VIII Psychological symptoms
	Suprapubic Inguinal Urethral Penile/clitoral Perineal Rectal Back Buttocks Thighs	ONSET Acute Chronic ONGOING Sporadic Cyclical Continuous TIME Filling Emptying Immediate post Late post TRIGGER Provoked Spontaneous	Aching Burning Stabbing Electric	UROLOGICAL Frequency Nocturia Hesitance Dysfunctional flow Urgency Incontinence GYNAECOLOGICAL Menstrual Menopause GASTROINTESTINAL Constipation Diarrhoea Bloatedness Urgency Incontinence NEUROLOGICAL Dysaesthesia Hyperaesthesia Allodynia Hyperalegesie SEXUOLOGICAL Satisfaction Female dyspareunia Sexual avoidance Erectile dysfunction Medication MUSCLE Function impairment Fasciculation CUTANEOUS Trophic changes Sensory changes	ANXIETY About pain or putative cause of pain Catastrophic thinking about Pain DEPRESSION Attributed to pain or impact of pain Attributed to other causes Unattributed PTSD SYMPTOMS Re-experiencing Avoidance

Table 2: Chronic Pelvic Pain Syndromes

Urological Pain Syndromes	
Prostate pain syndrome	Prostate pain syndrome (PPS) is the occurrence of persistent or recurrent episodic pain (which is convincingly reproduced by prostate palpation). There is no proven infection or other obvious local pathology. PPS is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. The term "chronic prostatitis" continues to be equated with that of PPS. In the authors' and others' opinion, this is an inappropriate term, although it is recognised that it has a long history of use. The National Institutes of Health (NIH) consensus includes infection (types I and II), which the authors feel should not be considered under PPS, but as specific disease-associated pelvic pain. The term prostadynia has also been used in the past but is no longer recommended by the expert panel. Please note that some of the authors of the IASP document disagree with this term and suggest that CPPS of the male is used instead of PPS, which has been agreed by the majority.

Bladder pain syndrome	Bladder pain syndrome (BPS) is the occurrence of persistent or recurrent pain perceived in the urinary bladder region, accompanied by at least one other symptom, such as pain worsening with bladder filling and day-time and/or night-time urinary frequency. There is no proven infection or other obvious local pathology. BPS is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. BPS is believed to represent a heterogeneous spectrum of disorders. There may be specific types of inflammation as a feature in subsets of patients. Localisation of the pain can be difficult by examination, and consequently, another localising symptom is required. Cystoscopy with hydrodistension and biopsy may be indicated to define phenotypes. Recently, ESSIC has suggested a standardised scheme of sub-classifications to acknowledge differences and make it easier to compare various studies. Other terms that have been used include "interstitial cystitis", "painful bladder syndrome", and "PBS/IC" or "BPS/IC". These terms are no longer recommended.
Scrotal pain syndrome	Scrotal pain syndrome is the occurrence of persistent or recurrent episodic pain localised within the organs of the scrotum, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Scrotal pain syndrome is a generic term and is used when the site of the pain is not clearly testicular or epididymal. The pain is not in the skin of the scrotum as such, but perceived within its contents, in a similar way to idiopathic chest pain.

Testicular pain syndrome	Testicular pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the testes, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Testicular pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Previous terms have included orchitis, orchialgia and orchiodynia. These terms are no longer recommended.
Epididymal pain syndrome	Epididymal pain syndrome is the occurrence of persistent or recurrent episodic pain perceived in the epididymis, and may be associated with symptoms suggestive of lower urinary tract or sexual dysfunction. There is no proven infection or other obvious local pathology. Epididymal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences.
Penile pain syndrome	Penile pain syndrome is the occurrence of pain within the penis that is not primarily in the urethra, in the absence of proven infection or other obvious local pathology. Penile pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.
Urethral pain syndrome	Urethral pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the urethra, in the absence of proven infection or other obvious local pathology. Urethral pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Urethral pain syndrome may occur in men and women.

Post-vasectomy scrotal pain syndrome	Post-vasectomy scrotal pain syndrome is a scrotal pain syndrome that follows vasectomy. Post-vasectomy scrotal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. Post-vasectomy pain may be as frequent as 1% following vasectomy, possibly more frequent. The mechanisms are poorly understood and for that reason it is considered a special form of scrotal pain syndrome.
Gynaecological Pain Syndromes: External Genitalia	
Vulvar pain syndrome	Vulvar pain syndrome is the occurrence of persistent or recurrent episodic vulvar pain. There is no proven infection or other local obvious pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Although pain perceived in the vulva was included under sexual disorders in the DSM-IV-R manual for classifying psychiatric disorders, there is no scientific basis for this classification, and pain perceived in the vulva is best understood as a pain problem that usually has psychological consequences. There is no evidence for its classification as a psychiatric disorder. The International Society for the Study of Vulvovaginal Disease (ISSVD) has used the term vulvodynia, where we use the term vulvar pain syndrome. According to the ISSVD, vulvodynia is vulvar pain that is not accounted for by any physical findings. The ISSVD has defined vulvodynia as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder". If physical findings are present, the patient is said to have vulvar pain due to a specified cause. The ISSVD has sub-divided vulvodynia based on pain location and temporal characteristics of the pain (e.g. provoked or unprovoked). The following definitions are based on that approach.

Generalised vulvar pain syndrome	Generalised vulvar pain syndrome refers to a vulvar pain syndrome in which the pain/burning cannot be consistently and precisely localised by point-pressure mapping via probing with a cotton-tipped applicator or similar instrument. Rather, the pain is diffuse and affects all parts of the vulva. The vulvar vestibule (the part that lies between the labia minora into which the urethral meatus and vaginal introitus open) may be involved but the discomfort is not limited to the vestibule. This pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences. Previous terms have included "dysesthetic vulvodynia" and "essential vulvodynia", but are no longer recommended.
Localised vulvar pain syndrome	Localised vulvar pain syndrome refers to pain that can be consistently and precisely localised by point-pressure mapping to one or more portions of the vulva. Clinically, the pain usually occurs as a result of provocation (touch, pressure or friction). Localised vulvar pain syndrome can be sub-divided into vestibular pain syndrome and clitoral pain syndrome.
Vestibular pain syndrome	Vestibular pain syndrome refers to pain that can be localised by point-pressure mapping to the vestibule or is well perceived in the area of the vestibule.
Clitoral pain syndrome	Clitoral pain syndrome refers to pain that can be localised by point-pressure mapping to the clitoris or is well-perceived in the area of the clitoris.

Gynaecological System: Internal Pelvic Pain Syndromes	
Endometriosis associated pain syndrome	Endometriosis-associated pain syndrome is chronic or recurrent pelvic pain in patients with laparoscopically confirmed endometriosis, and the term is used when the symptoms persist despite adequate endometriosis treatment. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. Many patients have pain above and beyond the endometriotic lesions; this term is used to cover that group of patients. Endometriosis may be an incidental finding, is not always painful, and the degree of disease seen laparoscopically does not correlate with severity of symptoms. As with other patients, they often have more than one end-organ involved. It has been suggested that this phenotype should be removed from the classification because the endometriosis may be irrelevant.
Chronic pelvic pain syndrome with cyclical exacerbations	Chronic pelvic pain syndrome with cyclical exacerbations covers the non-gynaecological organ pain that frequently shows cyclical exacerbations (e.g., IBS or BPS) as well as pain similar to that associated with endometriosis/adenomyosis but where no pathology is identified. This condition is different from dysmenorrhoea, in which pain is only present with menstruation.
Dysmenorrhoea	Dysmenorrhoea is pain with menstruation that is not associated with well-defined pathology. Dysmenorrhoea needs to be considered as a chronic pain syndrome if it is persistent and associated with negative cognitive, behavioural, sexual or emotional consequences.

Gastrointestinal Pelvic Pain Syndromes	
Irritable bowel syndrome (IBS)	IBS is the occurrence of chronic or recurrent episodic pain perceived in the bowel, in the absence of proven infection or other obvious local pathology. Bowel dysfunction is frequent. IBS is often associated with worry and pre-occupation about bowel function, and negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract or gynaecological dysfunction. The above classification is based upon the Rome III Criteria: three months of continuous or recurring symptoms of abdominal pain or irritation that may be relieved with a bowel movement, may be coupled with a change in frequency, or may be related to a change in stool consistency. Two or more of the following are present at least 25% of the time: change in stool frequency (> three bowel movements per day or < three per week); noticeable difference in stool form (hard, loose, watery or poorly formed stools); passage of mucus in stools; bloating or feeling of abdominal distension; or altered stool passage (e.g., sensation of incomplete evacuation, straining, or urgency). Extra-intestinal symptoms include: nausea, fatigue, full sensation after even a small meal, and vomiting.
Chronic anal pain syndrome	Chronic anal pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the anus, in the absence of proven infection or other obvious local pathology. Chronic anal pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction.

Intermittent chronic anal pain syndrome	Intermittent chronic anal pain syndrome refers to severe, brief, episodic pain that seems to, arise in the rectum or anal canal and occurs at irregular intervals. This is unrelated to the need to, or the process of defecation. It may be considered a sub-group of the chronic anal pain syndromes. It was previously known as "proctalgia fugax" but this term is no longer recommended.
Musculoskeletal System	
Pelvic floor muscle pain syndrome	Pelvic floor muscle pain syndrome is the occurrence of persistent or recurrent episodic pelvic floor pain. There is no proven well-defined local pathology. It is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. This syndrome may be associated with over-activity of, or trigger points within the pelvic floor muscles. Trigger points may also be found in several muscles, such as the abdominal, thigh and paraspinal muscles and even those not directly related to the pelvis.
Coccyx pain syndrome	Coccyx pain syndrome is the occurrence of chronic or recurrent episodic pain perceived in the region of the coccyx, in the absence of proven infection or other obvious local pathology. Coccyx pain syndrome is often associated with negative cognitive, behavioural, sexual or emotional consequences, as well as with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction. The term "coccydynia" was used but is no longer recommended.

Epidemiology, Aetiology and Pathophysiology
Chronic visceral pain, pelvic pain and abdominal aspects of pelvic pain

Recommendations	Strength rating
All of those involved in the management of Chronic Pelvic Pain (CPP) should have knowledge of peripheral and central pain mechanisms.	Strong
The early assessment of patients with CPP should involve investigations aimed at specific disease-associated pelvic pain.	Strong
The early assessment of patients with CPP should involve assessment of functional, emotional, behavioural, sexual and other quality of life issues, such as effect on work and socialisation.	Strong
Manage Chronic Pelvic Pain Syndrome patients in a multispecialty and multidisciplinary environment with consideration of all their symptoms.	Strong

Diagnostic Evaluation
History and physical examination
History is very important for the evaluation of patients with CPP. Pain syndromes are symptomatic diagnoses which are derived from a history of pain perceived in the region of the pelvis, and absence of other pathology, for a minimum of three out of the past six months. This implies that specific disease-associated pelvic pain caused by bacterial infection, cancer, primary anatomical or functional disease of the pelvic organs, and neurogenic disease must be ruled out. The history should be comprehensive covering functional as well as pain related symptoms. The clinical examination often serves to confirm

or refute the initial impressions gained from a good history. The examination should be aimed at specific questions where the outcome of the examination may change management. As well as a local examination, a general musculoskeletal and neurological examination should be considered an integral part of the assessment and be undertaken, if appropriate.

Figure 1: Diagnosing chronic pelvic pain

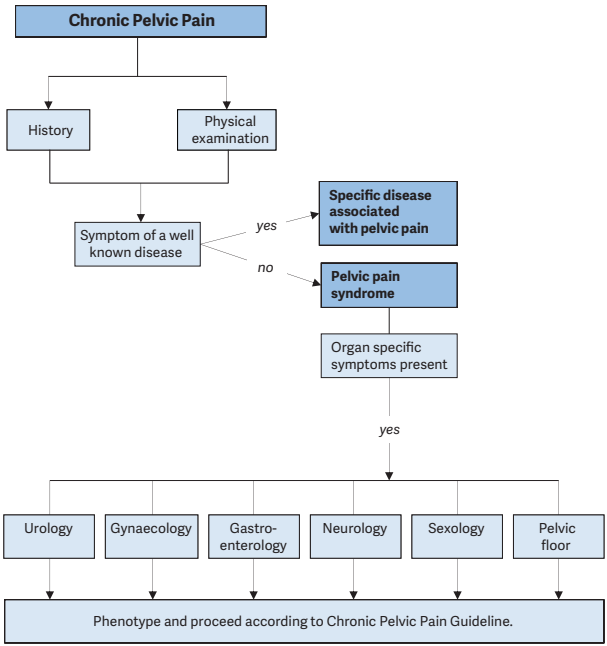

Figure 2: Phenotyping of pelvic pain

Phenotyping	Assessment
Urology	Urinary flow, micturition diary, cystoscopy, ultrasound, uroflowmetry
Psychology	Anxiety about pain, depression and loss of function, history of negative sexual experiences
Organ specific	Ask for gynaecological, gastro-intestinal, ano-rectal, sexological complaints Gynaecological examination, rectal examination
Infection	Semen culture and urine culture, vaginal swab, stool culture
Neurological	Ask for neurological complaints (sensory loss, dysaesthesia) Neurological testing during physical examination: sensory problems, sacral reflexes and muscular function
Tender muscle	Palpation of the pelvic floor muscles, the abdominal muscles and the gluteal muscles
Sexological	Erectile function, ejaculatory function, post-orgasmic pain

Recommendations for diagnostic evaluation

Recommendations for the diagnostic evaluation of Prostate Pain Syndrome	Strength rating
Adapt diagnostic procedures to the patient. Exclude specific diseases with similar symptoms.	Strong
Use a validated symptom and quality of life scoring instrument, such as the National Institutes of Health Chronic Prostatitis Symptom Index, for initial assessment and follow-up.	Strong
Assess prostate pain syndrome associated negative cognitive, behavioural, sexual, or emotional consequences, as well as symptoms of lower urinary tract and sexual dysfunctions.	Strong

Recommendations for management

Recommendations for the diagnostic evaluation of Bladder Pain Syndrome	Strength rating
Perform general anaesthetic rigid cystoscopy in patients with bladder pain to subtype and rule out confusable disease.	Strong
Diagnose patients with symptoms according to the EAU definition, after primary exclusion of specific diseases, with bladder pain syndrome (BPS) by subtype and phenotype.	Strong
Assess BPS associated non-bladder diseases systematically.	Strong
Assess BPS associated negative cognitive, behavioural, sexual, or emotional consequences.	Strong
Use a validated symptom and quality of life scoring instrument for initial assessment and follow-up.	Strong

Recommendations for the diagnostic evaluation of gynaecological aspects of CPP	Strength rating
Take a full gynaecological history and evaluate to rule out a treatable cause (e.g. endometriosis) in all women with chronic pelvic pain.	Strong
Refer to a gynaecologist if clinical suspicion of a gynaecological cause for pain following complete urological evaluation. Laparoscopy should be undertaken in accordance with gynaecological guidelines.	Strong

Recommendation for the diagnostic evaluation of Anorectal Pain Syndrome	Strength rating
Anorectal function tests are recommended in patients with anorectal pain.	Strong

Recommendations for the diagnostic evaluation of Pudendal Neuralgia	Strength rating
Rule out confusable diseases, such as neoplastic disease, infection, trauma and spinal pathology.	Strong
If a peripheral nerve pain syndrome is suspected, refer early to an expert in the field, working within a multidisciplinary team environment.	Weak
Imaging and neurophysiology help diagnosis but image and nerve locator guided local anaesthetic injection is preferable.	Weak

Recommendation for the diagnostic evaluation of sexological aspects in CPP	Strength rating
Screen patients presenting with symptoms suggestive for chronic pelvic pain syndrome for abuse, without suggesting a causal relation with the pain.	Weak

Recommendations for the diagnostic evaluation of psychological aspects of CPP	Strength rating
Assess patient psychological distress in relation to their pain.	Strong
Ask patients what they think is the cause of their pain to allow the opportunity to inform and reassure.	Strong

Recommendations for the diagnostic evaluation of pelvic floor function	Strength rating
Use ICS classification for pelvic floor muscle function and dysfunction.	Strong
Actively look for the presence of myofascial trigger points in patients with chronic pelvic pain syndrome.	Weak

Management

The philosophy for the management of CPP is based on a bio-psychosocial model. This is a holistic approach with the patients' active involvement. Single interventions rarely work in isolation and need to be considered within a broader personalised management strategy. The management strategy may well have elements of self-management. Pharmacological and non-pharmacological interventions should be considered with a clear understanding of the potential outcomes and end points. These may include: psychology, physiotherapy, drugs and more invasive interventions. Providing information that is personalised and responsive to the patient's problems, conveying belief and concern, is a powerful way to allay anxiety. Additional written information or direction to reliable sources is useful; practitioners tend to rely on locally produced material or pharmaceutical products of variable quality while endorsing the need for independent materials for patients.

Recommendations for management

Recommendations for the management of Prostate Pain Syndrome	Strength rating
Offer multimodal and phenotypically directed treatment options for Prostate Pain Syndrome (PPS).	Weak
Use antimicrobial therapy (quinolones or tetracyclines) over a minimum of six weeks in treatment-naïve patients with a duration of PPS less than one year.	Strong
Use α-blockers for patients with a duration of PPS less than one year.	Strong
Offer high-dose oral pentosane polysulphate in PPS.	Weak
Offer acupuncture for use in PPS.	Strong
Offer non-steroidal anti-inflammatory drugs in PPS, but long-term side-effects have to be considered.	Weak

Recommendations for the management of Bladder Pain Syndrome	Strength rating
Offer subtype and phenotype-oriented therapy for the treatment of Bladder Pain Syndrome (BPS).	Strong
Always consider offering multimodal behavioural, physical and psychological techniques alongside oral or invasive treatments of BPS.	Strong

Offer dietary advice.	Weak
Administer amitriptyline for treatment of BPS.	Strong
Offer oral pentosane polysulphate for the treatment of BPS.	Strong
Offer oral pentosane polysulphate plus subcutaneous heparin in low responders to pentosane polysulphate alone.	Weak
Do not recommend oral corticosteroids for long-term treatment.	Strong
Offer intravesical hyaluronic acid or chondroitin sulphate before more invasive measures.	Weak
Offer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	Weak
Offer intravesical heparin before more invasive measures alone or in combination treatment.	Weak
Do not use bladder distension alone as a treatment of BPS.	Weak
Offer submucosal bladder wall and trigonal injection of botulinum toxin type A (BTX-A) plus hydrodistension if intravesical instillation therapies have failed.	Strong
Offer neuromodulation before more invasive interventions.	Weak
Only undertake ablative organ surgery as the last resort and only by experienced and BPS-knowledgeable surgeons.	Strong
Offer transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	Strong

Recommendations for the management of Scrotal Pain Syndrome	Strength rating
Inform about the risk of post-vasectomy pain when counselling patients planned for vasectomy.	Strong
Do open instead of laparoscopic inguinal hernia repair, to reduce the risk of scrotal pain.	Strong
In patients with testicular pain improving after spermatic block, offer microsurgical denervation of the spermatic cord.	Weak

Recommendations for the management of gynaecological aspects of CPP	Strength rating
Involve a gynaecologist to provide therapeutic options such as hormonal therapy or surgery in well-defined disease states.	Strong
Provide a multidisciplinary approach to pain management in persistent disease states.	Strong

Recommendations for functional anorectal pain	Strength rating
Undertake biofeedback treatment in patients with chronic anal pain.	Strong
Offer Botulinum toxin type A and electrogalvanic stimulation in chronic anal pain syndrome.	Strong
Offer percutaneous tibial nerve stimulation in chronic anal pain syndrome.	Weak

Offer sacral neuromodulation in chronic anal pain syndrome.	Weak
Offer inhaled salbutamol in intermittent chronic anal pain syndrome.	Weak

Recommendation for the management of pudendal neuralgia	**Strength rating**
Neuropathic pain guidelines are well-established. Use standard approaches to management of neuropathic pain.	Strong

Recommendations for the management of sexological aspects in CPP	**Strength rating**
Offer behavioural strategies to the patient and his/her partner to reduce sexual dysfunctions.	Weak
Offer pelvic floor muscle therapy as part of the treatment plan to improve quality of life and sexual function.	Weak

Recommendation for the management of psychological aspects in CPP	**Strength rating**
For CPP with significant psychological distress, refer patient for CPP-focused psychological treatment.	Strong

Recommendations for the management of pelvic floor dysfunction	**Strength rating**
Apply myofascial treatment as first-line treatment.	Weak
Offer biofeedback as therapy adjuvant to muscle exercises, in patients with anal pain due to an overactive pelvic floor.	Strong

Recommendations for the management of chronic/non-acute urogenital pain by opioids	Strength rating
Prescribe opioid treatment, following multidisciplinary assessment and only after other reasonable treatments have been tried and failed.	Strong
The decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with the patient and their family doctor.	Strong
Where there is a history or suspicion of drug abuse, involve a psychiatrist or psychologist with an interest in pain management and drug addiction.	Strong

This short booklet is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU GUIDELINES ON RENAL TRANSPLANTATION

(Text update March 2019)

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Introduction

The European Association of Urology (EAU) Renal Transplantation Guidelines aim to provide a comprehensive overview of the medical and technical aspects relating to renal transplantation.

Organ retrieval and transplantation surgery

Living-donor nephrectomy

Recommendations	Strength rating
Offer pure or hand-assisted laparoscopic/ retroperitoneoscopic surgery as the preferential technique for living-donor nephrectomy.	Strong
Perform open living-donor nephrectomy in centres where endoscopic techniques are not implemented.	Strong
Perform laparo-endoscopic single site surgery, robotic and natural orifice trans-luminal endoscopic surgery-assisted living-donor nephrectomy in highly-specialised centres only.	Strong

Organ preservation

Recommendations for kidney storage solutions	Strength rating
Use either University of Wisconsin or histidine tryptophane ketoglutarate preservation solutions for cold storage.	Strong
Use Celsior or Marshall's solution for cold storage if University of Wisconsin or histidine tryptophane ketoglutarate solutions are not available.	Strong

Recommendations for kidney preservation: static and dynamic preservation	Strength rating
Minimise ischemia times.	Strong
Use hypothermic machine-perfusion (where available) in deceased donor kidneys to reduce delayed graft function.	Strong
Hypothermic machine-perfusion may be used in standard criteria deceased donor kidneys.	Strong
Use low pressure values in hypothermic machine perfusion preservation.	Strong
Hypothermic machine-perfusion must be continuous and controlled by pressure and not flow.	Strong
Do not discard grafts due to only increased vascular resistance and high perfusate injury marker concentrations during hypo-thermic machine perfusion preservation.	Weak

Donor kidney biopsies

Recommendations	Strength rating
Do not base decisions on the acceptance of a donor organ on histological findings alone, since this might lead to an unnecessary high rate of discarded grafts. Interpret histology in context with clinical parameters of donor and recipient including perfusion parameters where available.	Strong
Use paraffin histology for histomorphology as it is superior to frozen sections; however, its diagnostic value has to be balanced against a potential delay of transplantation.	Strong
Procurement biopsies should be read by a renal pathologist or a general pathologist with specific training in kidney pathology.	Strong

Living and deceased donor implantation surgery

Recommendations	Strength rating
Immediate pre-op haemodialysis	
Use dialysis or conservative measures to manage fluid and electrolyte imbalance prior to transplant surgery taking into consideration the likelihood of immediate graft function.	Weak
Operating on patients taking anti-platelet and anticoagulation agents	
Consider continuing anti-platelet therapy in patients on the transplant waiting list.	Weak

Discuss patients who take anti-platelet and anti-coagulation agents prior to transplant surgery with relevant cardiologist/ haematologist/nephrologist.	Weak
Prevention of venous thrombosis including deep vein thrombosis during and after renal transplant	
Do not routinely give post-operative prophylactic unfractionated or low-molecular-weight heparin to low-risk living donor transplant recipients.	Weak
Peri-operative antibiotics in renal transplant	
Use single-dose, rather than multi-dose, peri-operative prophylactic antibiotics in routine renal transplant recipients.	Strong
Specific fluid regimes during renal transplantation	
Optimise pre-, peri- and post-operative hydration to improve renal graft function.	Strong
Use balanced crystalloid solutions for intra-operative intravenous fluid therapy.	Weak
Use target directed intra-operative hydration to decrease delayed graft function rates and optimise early graft function.	Strong
Dopaminergic drugs in renal transplantation	
Do not routinely use low-dose dopaminergic agents in the early post-operative period.	Weak

Surgical approaches for first, second, third and further transplants

Single kidney transplant – living and deceased donors

Recommendations	Strength rating
Assess the utility (including inspection) of the kidney for transplantation before commencement of immunosuppression and induction of anaesthesia for deceased donor kidney transplantation.	Strong
Choose either iliac fossa for placement of a first or second single kidney transplant.	Weak
Ligate peri-iliac vessel lymphatics (lymphostasis) to reduce post-operative lymphocele.	Weak
Assess the length of the donor renal vein and if it is short consider one of a variety of surgical techniques to optimise the venous anastomosis.	Weak
Use the external or common iliac arteries for an end-to-side arterial anastomosis to donor renal artery.	Weak
Use an end-to-end anastomosis to the internal iliac artery as an alternative to external or common iliac arteries.	Weak
Check the intima of the donor and recipient arteries prior to commencing the arterial anastomosis to ensure that there is no intimal rupture/flap. If this is found it must be repaired prior to/as part of the arterial anastomosis.	Strong

Pre-operatively plan the surgical approach in third or further transplants, to ensure that appropriate arterial inflow and venous outflow exists with adequate space to implant the new kidney.	Strong

Emerging surgical technologies

Robot-assisted kidney transplant (RAKT) surgery using living donor kidneys has been evaluated in prospective non-randomised trials (using IDEAL consortium principles). Whilst potential advantages may exist (decreased post-operative pain, length of hospital stay, incision length and lymphocele rate), evidence is too premature to recommend RAKT outside of appropriately monitored prospective studies.

Dual kidney transplants

Dual kidney transplant is performed when the quality of a single deceased donor kidney is thought to be insufficient for appropriate long-term graft function and that the outcome with both kidneys would be better. A variety of surgical techniques have been described to implant a pair of donor kidneys these include: unilateral extra-peritoneal or intra-peritoneal and bilateral extra-peritoneal or intra-peritoneal that can be via a midline or two lateral incisions. No randomised controlled trials exist to recommend one technique for all patients or situations.

Ureteric implantation in normal urinary tract

Ureteric anastomotic techniques described for renal transplant recipients with no underlying urological abnormality include: extra (Lich-Gregoir) or intra (Ledbetter-Politano) vesical uretero-neo-cystotomy and uretero-ureterostomy using native ureter.

Recommendations	Strength rating
Perform Lich-Gregoir-like extra-vesical ureteric anastomosis technique to minimise urinary tract complications in renal transplant recipients with normal urological anatomy.	Strong
Pyelo/uretero-ureteral anastomosis is an alternative especially for a very short or poorly vascularised transplant ureter.	Strong
Use transplant ureteric stents prophylactically to prevent major urinary complications.	Strong
Use the same surgical principals for single ureters to manage duplex ureters and anastomose them either separately or combined.	Strong

Transplantation/ureteric implantation in abnormal urogenital tract

The following points should be considered when performing kidney transplantation in the abnormal urogenital tract:

- In patients with an ileal conduit, a kidney transplant may be placed upside down to align the ureter to the conduit and avoid a redundant ureter.
- The technique used to implant transplant ureter(s) into an ileal conduit is the same as the method used with native ureter(s) (Bricker; Wallace).
- In bladder augmentation or continent pouches, ureters should be implanted with a tunnel technique or extra-vesically (Lich-Gregoir). The latter is favoured in most patients.
- In patients with a Mitrofanoff catheterisable stoma or continent ileo-caecal pouch with catheterisable stoma, consideration should be given to the positioning of the

catheterisable stoma (umbilical or iliac fossa - usually right-side) with clear communication with the transplant surgeons so that the position of any future transplant kidney is not compromised. If an intraperitoneal placement of a future kidney transplant is likely, then placement of a Mitrofanoff exiting in the iliac fossa is preferable at the umbilicus. If a future kidney transplant is likely in the right iliac fossa then placement of a Mitrofanoff exiting at the umbilicus or left iliac fossa may be preferable.

Donor complications

Living-donor nephrectomy, like any other intervention, is potentially associated with complications and mortality. However, the fact that the operation is performed on a healthy individual amplifies the relevance of any complications. Intra-operative complications occur in 2.2% (the most common being bleeding in 1.5% and injury to other organs in 0.8%) and post-operative complications occur in 7% (infectious complications in 2.6% and bleeding in 1%). Potential complications should be included in the process of informed consent. Long term complications are mostly related to the single-kidney condition. Health related quality of life, including mental condition, remains on average better than the general population after donation.

Recommendations	Strength rating
Restrict living-donor nephrectomy to specialised centres.	Strong
Offer long-term follow-up to all living kidney donors.	Strong

Recipient complications

Surgical complications during and after kidney transplantation may expose the recipient to an increased risk of morbidity and mortality. The incidence and management of such

complications is therefore of primary importance. The most common surgical complications in renal transplantation are summarised below.

Haemorrhage

The incidence of haematomas is reported to be between 0.2-25%. Small and asymptomatic haematomas do not usually require any intervention. In case of larger haematomas, clinical signs and symptoms due to external pressure with graft dysfunction and/or thrombotic graft vessels complications can be present. These cases may be treated by percutaneous drainage under computed tomography or ultrasound guidance or may require surgical treatment.

Arterial thrombosis

Transplant renal artery thrombosis is a rare complication (prevalence 0.5-3.5%).

Recommendations	Strength rating
Perform ultrasound-colour-Doppler in case of suspected graft thrombosis.	Strong
Perform surgical exploration in case of ultrasound finding of poor graft perfusion.	Strong
Perform a surgical thrombectomy in case of a salvageable graft if arterial thrombosis is confirmed intra-operatively.	Weak
Perform an allograft nephrectomy in case of a non-viable graft.	Strong

Venous thrombosis

Transplant renal vein thrombosis is an early complication (prevalence 0.5-4%) and one of the most important causes of graft loss during the first post-operative month.

Recommendations	Strength rating
Perform ultrasound-colour-Doppler in case of suspected graft thrombosis.	Strong
Perform surgical exploration in case of ultrasound finding of poor graft perfusion.	Weak
If venous thrombosis is confirmed intra-operatively, perform a surgical thrombectomy in case of a salvageable graft or an allograft nephrectomy in case of a non-viable graft.	Weak
Do not routinely use pharmacologic prophylaxis to prevent transplant renal vein thrombosis.	Strong

Transplant renal artery stenosis

The incidence of transplant renal artery stenosis is 1-25%. Risk factors include small calibre and atherosclerosis of the donor artery, trauma to donor artery at procurement, absence of arterial patch, suturing technique (interrupted vs. continuous), and damage to the iliac artery during transplantation.

Recommendations	Strength rating
Perform ultrasound-colour-Doppler to diagnose an arterial stenosis, in case of undetermined results on ultrasound consider a magnetic resonance or computed tomography angiogram.	Strong
Perform percutaneous transluminal angioplasty/stent, if feasible, as first-line treatment for an arterial stenosis.	Strong
Offer surgical treatment in case of recent transplant, multiple, long and narrow stenosis, or after failure of angioplasty.	Strong

Arteriovenous fistulae and pseudo-aneurysms after renal biopsy

Percutaneous biopsy may result in arteriovenous fistulae and/or intrarenal pseudo-aneurysms in 1-18% of cases.

Recommendations	Strength rating
Perform a ultrasound-colour-Doppler if a arteriovenous fistulae or pseudo-aneurysm is suspected.	Strong
Perform angiographic embolisation as first-line treatment in symptomatic cases of arteriovenous fistulae or pseudo-aneurysm.	Strong

Lymphocele

Lymphocele is a relatively common complication (prevalence 1-26%). There is a significant aetiological association with diabetes, m-TOR inhibitors (i.e sirolimus) therapy, and acute rejection.

Recommendations	Strength rating
Perform percutaneous drainage placement as the first treatment for large and symptomatic lymphocele.	Strong
Perform fenestration when percutaneous treatments fail.	Strong

Urinary leak

Urinary leakage occurs in 0-9.3% of cases.

Recommendations	Strength rating
Manage urine leak by JJ-stent and bladder catheter and/or percutaneous nephrostomy tube.	Strong
Perform surgical repair in cases of failure of conservative management.	Strong

Ureteral stenosis

Ureteral stenosis is a common complication in recipients, with an incidence of 0.6-10.5%. Early stenosis (within three months of surgery) is usually caused by surgical technique or compromised ureteral blood supply during surgery. Late stenosis (after six months) is provoked by infection, fibrosis, progressive vascular disease and/or rejection.

Recommendations	Strength rating
In case of a ureteral stricture, place a nephrostomy tube for both kidney decompression and stricture diagnosis via an antegrade pyelogram.	Strong
Manage strictures < 3 cm in length either with surgical reconstruction or endoscopically (percutaneous balloon dilation or antegrade flexible ureteroscopy and holmium laser incision).	Strong
Treat late stricture recurrence and/or stricture > 3 cm in length with surgical reconstruction in appropriate recipients.	Strong

Haematuria

The incidence of haematuria ranges from 1-34%. The Lich-Gregoir technique provides the lowest incidence of haematuria. Bladder irrigation is the first-line treatment. Some cases require cystoscopy with evacuation of clots and/or fulguration of bleeding sites.

Reflux and acute pyelonephritis

The frequency of vesicoureteral reflux is between 1-86%. Acute graft pyelonephritis occurs in 13% of graft recipients. Patients with lower tract urinary infections and cytomegalovirus infection present a higher risk of acute graft pyelonephritis.

Recommendation	Strength rating
Use an endoscopic approach as first-line treatment for symptomatic reflux.	Weak

Kidney stones

Urolithiasis occurs in 0.2-1.7% of recipients.

Recommendations	Strength rating
Evaluate the causes of urolithiasis in the recipient.	Strong
Treat ureteral obstruction due to a stone with a percutaneous nephrostomy tube or JJ-stent placement.	Strong
Perform shockwave lithotripsy or antegrade/retrograde ureteroscopy for stones < 15 mm.	Strong
Perform percutaneous nephrolithotomy for stones > 20 mm.	Weak

Wound infection

Wound infections occur in about 4% of cases. Subcutaneous sutures, pre-dialysis transplantation, sealing or ligation of lymphatic trunks, prophylactic fenestration, reducing corticosteroid load, and avoiding sirolimus/everolimus therapy can decrease wound complication rates.

Incisional hernia

Incisional hernia occurs in approximately 4% of open kidney transplantations. Mesh infection is a risk factor for incisional hernia recurrence. Open and laparoscopic repair approaches are safe and effective.

Malignancy prior to renal transplantation*

Recommendations	Strength rating
In the recipient	
List for renal transplantation patients with a history of appropriately treated low stage/grade renal cell carcinoma or prostate cancer without additional delay.	Weak
In the potential donor kidney	
Do not discard a kidney for potential transplantation on the basis of a small renal mass alone.	Weak
Malignancy after renal transplantation	
Be aware of the presence of a kidney transplant in the pelvis and the possibility of subsequent transplants when planning treatment for prostate cancer.	Strong
Refer kidney transplant patients with prostate cancer to an integrated transplant urology centre.	Strong

Note: These recommendations are limited to a synopsis of three systematic reviews conducted by the EAU Renal Transplantation Panel.

Matching of donors and recipients

Histocompatibility antigens show remarkable polymorphism and human leukocyte antigen (HLA) matching is still very important in kidney transplantation as transplant outcome correlates with the number of HLA mismatches.

Recommendations	Strength rating
Determine the ABO blood group and the human leukocyte antigen A, B, C and DR phenotypes for all candidates awaiting kidney transplantation.	Strong
Test both the donor and recipient for human leukocyte antigen DQ. Human leukocyte antigen DP testing may be performed for sensitised patients.	Strong
Perform thorough testing for HLA anti-bodies before transplantation.	Strong
Perform adequate cross-match tests to avoid hyper-acute rejection, before each kidney and combined kidney/pancreas transplantation.	Strong

Immunosuppression after kidney transplantation

The principle underlying successful immunosuppression is 'the balance of survival'. Practitioners must prescribe a dosage of drug high enough to suppress rejection without endangering the recipient's health.

The currently recommended standard initial immuno-suppression regime provides excellent efficacy with good tolerability.
It is given to most patients and consists of:

- calcineurin inhibitors (preferably tacrolimus, alternatively cyclosporine);
- mycophenolate (MMF or enteric-coated mycophenolate sodium);
- steroids (prednisolone or methylprednisolon);
- induction therapy (preferably basiliximab in low- and standard-risk patients and anti-thymocyte globulin (ATG) in high-risk patients).

Recommendations	Strength rating
General immunosuppression after kidney transplantation	
Perform initial rejection prophylaxis with a combination therapy of a calcineurin inhibitor (preferably tacrolimus), mycophenolate, steroids and an induction agent (either basiliximab or anti-thymocyte globulin).	Strong
Calcineurin inhibitors	
Use calcineurin inhibitors for rejection prophylaxis as they represent current best practice pending publication of long-term results using newer agents.	Strong
Use tacrolimus as first-line calcineurin inhibitor due to its higher efficacy.	Strong
Monitor blood-levels of both cyclosporine and tacrolimus to allow appropriate dose adjustment of calcineurin inhibitors.	Strong
Mycophenolates	
Administer mycophenolate as part of the initial immunosuppressive regimen.	Strong
Azathioprine	
Azathioprine may be used in a low-risk population as an immunosuppressive drug, especially for those intolerant to mycophenolate formulations.	Weak
Steroids	
Initial steroid therapy should be part of immunosuppression in the peri-operative and early post-transplant period.	Strong

Consider steroid withdrawal in standard immunological risk patients on combination therapy with calcineurin inhibitors and mycophenolic acid after the early post-transplant period.	Weak
Inhibitors of the mammalian target of rapamycin (m-TOR)	
The m-TOR inhibitors may be used to prevent rejection in patients who are intolerant to standard therapy.	Weak
Significantly reduce calcineurin inhibitor dosage in a combination regimen with m-TOR inhibitors to prevent aggravated nephrotoxicity.	Strong
Do not convert patients with proteinuria and poor renal function to m-TOR inhibitors.	Strong
Monitor blood-levels of both sirolimus and everolimus to allow for appropriate dose adjustment.	Strong
Induction with Interleukin-2 receptor antibodies	
Use interleukin-2 receptor antibodies for induction in patients with normal immunological risk in order to reduce incidence of acute rejection.	Weak
T-cell depleting induction therapy	
T-cell depleting antibodies may be used for induction therapy in immunologically high-risk patients.	Weak
Belatacept	
Belatacept may be used for immunosuppressive therapy in immunologically low-risk patients, who have a positive Epstein-Barr virus serology.	Weak

Immunological complications

Immunological rejection is a common cause of early and late transplant dysfunction. There is great variation in the timing and severity of rejection episodes and how they respond to treatment. Two main types of immunological reactions are distinguished: T-cell mediated rejections (TCMR) and antibody-mediated rejections (ABMR). Antibody-mediated rejection and TCMR may be diagnosed together, called mixed acute rejection. Antibody-mediated rejection may occur as hyperacute rejection, acute rejection or chronic rejection. Chronic ABMR is considered as one of the leading causes of late graft loss.

Recommendations	Strength rating
Monitor transplant recipients for signs of acute rejection, particularly during the first six months post-transplant.	Strong
Take regular blood samples in addition to regular monitoring of urine output and ultrasound examinations in order to detect graft dysfunction during hospitalisation.	Strong
Immediately rule out other potential causes of graft dysfunction in cases of suspected acute rejection. An ultrasound of the kidney transplant should be performed.	Strong
Perform a renal biopsy, graded according to the most recent Banff criteria, in patients with suspected acute rejection episodes.	Strong
Only if contraindications to renal biopsy are present, can 'blind' steroid bolus therapy be given.	Strong
Test patients who suffer acute rejection as soon as possible for anti-HLA antibodies against the graft.	Strong

Reassess the immunosuppressive therapy of all patients with rejection, including patient adherence to the medication, which is of particular importance in late rejections.	Strong

Hyper-acute rejection

Hyper-acute rejection is the most dramatic and destructive immunological attack on the graft. It results from circulating, complement-fixing IgG antibodies, specifically reactive against incompatible donor antigen, which engages with and destroys the vascular endothelium within minutes or hours after vascularisation.

Recommendation	Strength rating
Prevent hyper-acute rejection by adequate ABO blood group and HLA matching of donor and recipients.	Strong

Treatment of T-cell mediated acute rejection

Recommendations	Strength rating
Use steroid bolus therapy as first-line treatment for T-cell mediated rejection in addition to ensuring adequate baseline immunosuppression.	Strong
In severe or steroid-resistant rejection, use intensified immunosuppression, high-dose steroid treatment, and eventually T-cell depleting agents.	Strong

Treatment of antibody mediated rejection

Recommendation	Strength rating
Treatment of antibody mediated rejection should include antibody elimination.	Strong

Follow-up after transplantation

Long-term graft function is of critical importance for the success of a transplant. Therefore, regular long-term follow-up by experienced transplant physicians is essential in order to detect complications or graft dysfunction early and reassure adherence to the immunosuppressive regimen.

Recommendations	Strength rating
Provide lifelong regular post-transplant follow-up by an experienced and trained transplant specialist at least every six to twelve months.	Strong
Advise patients on appropriate lifestyle changes, potential complications, and the importance of adherence to their immuno-suppressive regimen.	Strong
Regularly monitor (approximately every four to eight weeks) serum creatinine, estimated glomerular filtration rate, blood pressure, urinary protein excretion, immuno-suppression and complications after renal transplantation. Changes in these para-meters over time should trigger further diagnostic work-up including renal biopsy, a search for infectious causes and anti-HLA antibodies.	Strong

Perform an ultrasound of the graft, in case of graft dysfunction, to rule out obstruction and renal artery stenosis.	Strong
In patients with interstitial fibrosis and tubular atrophy undergoing calcineurin inhibitor therapy and/or with histological signs suggestive for calcineurin inhibitor toxicity (e.g. arteriolar hyalinosis, striped fibrosis) consider calcineurin inhibitor reduction or withdrawal.	Strong
Initiate appropriate medical treatment, e.g. tight control of hypertension, diabetes, proteinuria, cardiac risk factors, infections, and other complications according to current guidelines.	Strong

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3) available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines.

EAU GUIDELINES ON THROMBOPROPHYLAXIS IN UROLOGICAL SURGERY

(March 2017)

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Introduction

Utilising recent studies and newly summarised evidence, the EAU Guidelines on Thromboprophylaxis provide practical evidence-based guidance regarding post-surgery thromboprophylaxis and peri-operative management of antithrombotic agents in urology.

The Thromboprophylaxis Panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessment of quality of evidence and grading of recommendations. GRADE offers four levels of evidence quality, reflecting the degree of certainty or confidence in the evidence: high, moderate, low, and very low. The strength of a recommendation reflects the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects. GRADE classifies recommendations as strong or weak.

Thromboprophylaxis post-surgery

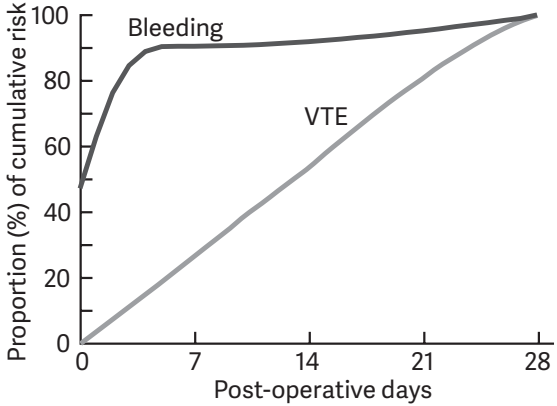
This guideline provides procedure and patient risk-specific guidance weighing the benefit of reduced venous thromboembolism (VTE) against the harm of increased bleeding. The Panel provides recommendations for numerous urologic procedures, with variation across patient risk

strata (Table 1). When creating recommendations, the Panel first calculated the net benefit (absolute reduction in VTE risk – absolute increase in bleeding risk) and then considered quality of evidence for both pharmacological and mechanical prophylaxis (Figure 1).

Table 1: Venous thromboembolism (VTE) according to patient risk factors

	Risk factors
Low risk	No risk factors
Medium risk	Any one of the following: age 75 years or more; body mass index 35 or more; VTE in 1st degree relative (parent, full sibling, or child).
High risk	Prior VTE Patients with any combination of two or more risk factors

Figure 1: Proportion of cumulative risk (%) of venous thromboembolism (VTE) and major bleeding by week since surgery during the first four post-operative weeks



	Proportion of 28-day cumulative bleeding risk
Operation day	47.4%
Post-operative day 1	63.3%
Post-operative day 2	76.6%
Post-operative day 3	84.9%
Post-operative day 4	89.2%
Post-operative day 28	100.0%

The bleeding pattern depicted applies to most bleeds for most surgeries. However, some urological surgeries, such as transurethral resection of the the prostate (TURP), are associated with later bleeding. This is typically minor and occurs around ten days post-surgery.

General statements for all procedure-specific recommendations

The following apply to all recommendations for pharmacological prophylaxis:

- All recommendations are based on a starting time of the morning after surgery.
- The optimal duration of pharmacological prophylaxis for all recommendations is approximately four weeks post-surgery.
- There are number of acceptable alternatives for pharmacologic prophylaxis (Table 2).
- All recommendations for mechanical prophylaxis are until ambulation.

Table 2: Alternative regimens for pharmacological prophylaxis

Pharmacological agent	Dosage*
Low molecular weight heparins:	
Dalteparin	5,000 IU injection once a day
Enoxaparin	40 mg injection once a day
Tinzaparin	3,500/4,500 IU injection once a day
Unfractionated heparin	5,000 IU injection two or three times a day
Fondaparinux†	2.5 mg injection once a day
Direct acting oral anticoagulants†:	
Dabigatran	220 mg tablet once a day
Apixaban	2.5 mg tablet once a day
Edoxaban	30 mg tablet once a day
Rivaroxaban	10 mg tablet once a day

** Dosages may not apply in renal impairment.*

† Fondaparinux and direct acting oral anticoagulants have not been sufficiently studied in urology to warrant on-label use for post-surgery thromboprophylaxis.

Recommendations for prophylaxis in specific procedures according to patient risk

Ambulatory day surgery
R1. In all patients undergoing minor ambulatory day surgery (for example, circumcision, hydrocelectomy and vasectomy), the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)***, and against use of mechanical prophylaxis ***(strong, moderate-quality evidence)***.

Open radical cystectomy
R2. In all patients undergoing open radical cystectomy, the Panel recommends use of pharmacological prophylaxis ***(strong, moderate or high-quality evidence depending on risk stratum)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Robotic radical cystectomy
R3. In all patients undergoing robotic radical cystectomy, the Panel suggests use of pharmacological prophylaxis ***(weak, low-quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Laparoscopic radical prostatectomy
R4. For patients undergoing laparoscopic radical prostatectomy without pelvic lymph node dissection (PLND), for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)*** and suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; for those at moderate and high risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate- or high-quality evidence)*** and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R5. For patients undergoing laparoscopic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)***; for those at medium risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacological prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R6. For patients undergoing laparoscopic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacological prophylaxis ***(weak, high-quality evidence)***; for those at high risk, the Panel recommends use of pharmacological prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Open radical prostatectomy
R7. For patients undergoing open radical prostatectomy without PLND or with standard PLND, for those at low risk of VTE, the use of pharmacological prophylaxis is suggested ***(weak, moderate-quality evidence)***; for those at medium and high risk, use of pharmacological prophylaxis is recommended ***(strong, moderate- or high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R8. For all patients undergoing open radical prostatectomy with extended PLND, the Panel recommends use of pharmacological prophylaxis ***(strong, moderate or high-quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Robotic radical prostatectomy

R9. For patients undergoing robotic radical prostatectomy without PLND, for those at low risk of VTE, the Panel recommends against use of pharmacological prophylaxis ***(strong, moderate-quality evidence)*** and suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; for those at medium and high risk, the Panel suggests against use of pharmacological prophylaxis ***(weak, moderate-quality evidence)*** and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R10. For patients undergoing robotic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; for those at medium risk, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R11. For patients undergoing robotic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

Nephrectomy

R12. For patients undergoing laparoscopic partial nephrectomy, for those at low and medium risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, low-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, moderate-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R13. For all patients undergoing open partial nephrectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R14. For patients undergoing robotic partial nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at medium risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, moderate-quality evidence)***; for those at high risk, the Panel recommends use of pharmacologic prophylaxis ***(strong, high-quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R15. For patients undergoing laparoscopic radical nephrectomy, for those at low or medium risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at high risk, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; and for all patients, the Panel suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R16. For patients undergoing open radical nephrectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R17. For all patients undergoing radical nephrectomy with thrombectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R18. For all patients undergoing open nephroureterectomy, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

R19. For all patients undergoing primary nerve sparing retroperitoneal lymph node dissection, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

Non-cancer urological procedures

R20. For all patients undergoing transurethral resection of the prostate (TURP) or equivalent procedures, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, low-quality evidence)***; and for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, low-quality evidence)***.

R21. For patients undergoing laparoscopic donor nephrectomy or open donor nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests against use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; for medium-risk patients, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; and for high-risk patients, the Panel suggests use of pharmacologic prophylaxis ***(weak, very low or low -quality evidence)***, and suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***.

R22. For all patients undergoing open prolapse surgery or reconstructive pelvic surgery, the Panel suggests against the use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***; while for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, very low or low -quality evidence)***.

R23. For all patients undergoing percutaneous nephrolithotomy, the Panel suggests against use of pharmacologic prophylaxis ***(weak, very low quality evidence)***; for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis ***(weak, very low quality evidence)***; while for those at high risk, the Panel suggests use of mechanical prophylaxis ***(weak, very low quality evidence)***.

Peri-operative management of antithrombotic agents in urology

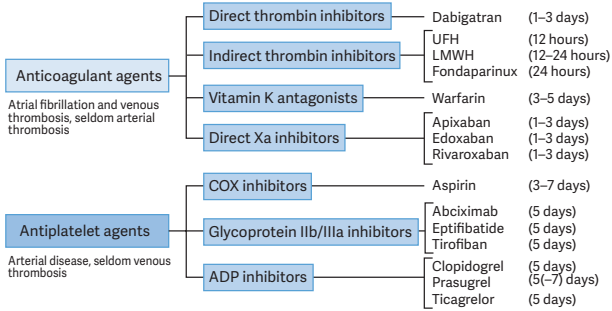
In principle, there are four options to manage use of antithrombotic agents (Figure 2) during the peri-operative period:

1) to defer surgery until antithrombotic agents are not needed;
2) stop antithrombotic agents prior to surgery and restart sometime after surgery;
3) continue through the surgical procedure;
4) administer alternative antithrombotic agents that may still reduce the risk of thrombosis but with less risk of bleeding than agents patients are currently using ("bridging").

Recent evidence has demonstrated that bridging increases bleeding without preventing thrombosis. The Panel therefore makes one of two recommendations for patients receiving antithrombotic agents regularly and contemplating surgery:

1) discontinue antithrombotic therapy for the period around surgery;
2) in those with a temporary very high risk of thrombosis, delay surgery until that risk decreases. If it is not possible to delay, continuing antithrombotic therapy or bridging through surgery may be advisable.

Figure 2: The most widely used antithrombotic agents in patients undergoing urologic surgery
Required period of stopping drug before surgery (if desired) provided in parentheses.



Recommendations for peri-operative management

Five days is an appropriate time to stop antiplatelet agents before surgery, while the optimal time to stop varies across anticoagulants (for details, see Figure 2).

R24. In all patients receiving antiplatelet agents (aspirin, clopidogrel, prasugrel, ticagrelor), except those with very high risk of thrombosis (see recommendations 26 and 27), the Panel recommends stopping antiplatelet agents before surgery and not initiating any alternative antithrombotic therapy ***(strong, high-quality evidence)***.

R25. In patients in whom antiplatelet agents have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk - typically four days post-surgery - rather than withholding for longer periods ***(strong, moderate-quality evidence)***.

R26. In patients with very high risk of thrombosis receiving antiplatelet agents (those with drug-eluting stent placement within six months, those with bare metal stent placement within six weeks, those with transient ischemic attack (TIA) or stroke within 30 days) in whom surgery can be delayed, the Panel recommends delaying surgery ***(strong, high-quality evidence)***.

R27. In patients with very high risk of thrombosis receiving antiplatelet agents (those with drug-eluting stent placement within six months, those with bare metal stent placement within six weeks, those with TIA or stroke within 30 days) in whom surgery cannot be delayed, the Panel suggests continuing the drugs through surgery ***(weak, low-quality evidence)***.

R28. In all patients receiving anticoagulant agents (unfractionated heparin, low molecular weight heparin [LMWH], warfarin, fondaparinux, dabigatran, apixaban, rivaroxaban, edoxaban), except those with very high risk of thrombosis (see recommendation 26), the Panel recommends stopping drugs before surgery (see Figure 2) and not initiating any alternative antithrombotic therapy ***(strong, high-quality evidence)***.
Note: Patients with creatinine clearance <30 ml/min should not receive dabigatran, apixaban, rivaroxaban or edoxaban.

R29. In patients in whom anticoagulants have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk - typically four days post-surgery - rather than withholding for longer periods ***(strong, moderate-quality evidence)***.

R30. In patients with a new VTE, it is recommended that surgery is delayed for at least one month, and if possible three months, to permit discontinuation of anticoagulation pre-operatively, rather than operating within one month of thrombosis ***(strong, high-quality evidence)***.

R31. In patients receiving any anticoagulant with a severe thrombophilia, such as antithrombin deficiency and antiphospholipid antibody syndrome, the Panel suggests anticoagulation with either heparin or LMWH through surgery, rather than stopping anticoagulation before and after surgery ***(weak, low-quality evidence)***.

R32. In patients with high-risk mechanical prosthetic heart valves, such as cage-ball valves, receiving warfarin, the Panel recommends bridging with LMWH prior and subsequent to surgery, rather than discontinuing anticoagulation peri-operatively ***(strong, high-quality evidence)***. Anticoagulation in these patients involves stopping the warfarin five days prior, commencing LMWH four days prior, omitting LMWH on the day of surgery, and recommencing LMWH and warfarin after surgery.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-07-3), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

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