European Association of Urology

Pocket Guidelines

2016 edition

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Introduction

We are honoured to present the 2016 edition of the EAU Pocket Guidelines. The EAU Guidelines Office has introduced Cochrane review methodology across all 20 Guidelines Panels, ensuring that high quality systematic reviews underpin key recommendations. This process would not be possible without the continued work of our exceptional team of young Guidelines Associates, under the leadership of our expert Panel Members who represent some of the most respected, talented and dedicated urologists from across Europe and beyond.

Development of Guidelines, whilst important, must be supported by an effective dissemination strategy. The EAU Guidelines Social Media (SoMe) group has been promoting discussion and triggering feedback from guidelines users via Facebook and Twitter. Since January 2015, the hashtag #eauguidelines has disseminated over 3,000 tweets resulting in upwards of three million impressions and leading to a 40% increase in the number of followers of the EAU Twitter account @uroweb. A considerable proportion of the success of the EAU Guidelines can be attributed to the support of the 41 National Urological Societies worldwide who actively endorse the EAU Guidelines. National Society endorsement drives dissemination of the EAU Guidelines amongst all members of each individual society.

Effective dissemination of the EAU Guidelines must be followed-up by assessment of their impact on clinical practice. In order to achieve this, the EAU Guidelines Office

has launched the IMpact Assessment of Guidelines Implementation aNd Education (IMAGINE) group. It is the goal of the group to establish a knowledge translation setting which will allow the gap between evidence and practice to be bridged, making the EAU Guidelines recommendations more relevant and actionable whilst enhancing their influence on patient care.

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

We hope you enjoy using the 2016 update of the EAU Guidelines!

Prof.Dr. James N'Dow
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Level of evidence and grading system

Recommendations in this text are assessed according to their level of evidence (LE) and Guidelines are given a grade of recommendation (GR), according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence.

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 randomisation.
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.

Table 2: Grade of recommendation*

Grade	Nature of recommendations
A	Based on clinical studies of good quality and consistency addressing the specific recommendations and including at least one randomised trial.
B	Based on well-conducted clinical studies, but without randomised clinical trials.
C	Made despite the absence of directly applicable clinical studies of good quality.

** Modified from [1]*

References

1. Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2009). Produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998. Updated by Jeremy Howick March 2009. http://www.cebm.net/index.aspx?o=1025

EAU GUIDELINES ON NON-MUSCLE INVASIVE (Ta, T1, CIS) BLADDER CANCER

(Limited text update March 2016)

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Introduction

The EAU Working Group has published guidelines on Non-muscle-invasive bladder cancer (NMIBC). It comprises Ta and T1 tumours as well as carcinoma *in situ* (CIS).

Staging and classification systems

The TNM Classification of Malignant Tumours, 7th Edn., 2009 will apply (Table 1).

Table 1: TNM Classification 2009	
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, uterus, vagina, pelvic wall, abdominal wall
T4a	Tumour invades prostate, uterus or vagina
T4b	Tumour invades pelvic wall or abdominal wall
N - 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 common iliac lymph node(s)
M - Distant metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1	Distant metastasis

Carcinoma *in situ* classification

CIS is 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.

Currently, two grading systems for NMIBC are available, WHO 1973 and WHO 2004 (the WHO 2004 was updated recently) (Table 2). The prognostic value of both WHO 1973 and 2004 grading systems has been confirmed. The WHO 2004 system has not yet been fully incorporated into prognostic models.

Table 2: WHO grading in 1973 and in 2004
1973 WHO grading Urothelial papilloma Grade 1: well differentiated Grade 2: moderately differentiated Grade 3: poorly differentiated **2004 WHO grading system** *Papillary lesions:* • *Urothelial papilloma (completely benign lesion)* • Papillary urothelial neoplasm of low malignant potential (PUNLMP) • Low-grade (LG) papillary urothelial carcinoma • High-grade (HG) papillary urothelial carcinoma *Flat lesions:* • Urothelial proliferation of uncertain malignant potential (flat lesion without atypia or papillary aspects) • Reactive atypia (flat lesion with atypia) • Atypia of unknown significance • Urothelial dysplasia • Urothelial CIS is always high grade

Recommendations for bladder cancer classification	GR
For classification of the depth of tumour invasion (staging) use the 2009 TNM system.	A
For histological classification, use the 1973 and 2004/2016 WHO grading systems.	A
Do not use the term "superficial bladder cancer".	A
Whenever you use the terminology NMIBC in individual cases, mention the tumour stage and grade.	A

Diagnosis

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

Recommendations for primary assessment of NMIBC	GR
Patient history should be taken.	A
Renal and bladder US may be used during the initial work-up in patients with haematuria.	C
At the time of the initial diagnosis of NMIBC, CT urography (or IVU) should be performed in selected cases (e.g., tumours located in the trigone, multiple- or high-risk tumours).	B
Cystoscopy is recommended in all patients with symptoms suggestive of bladder cancer. It cannot be replaced by cytology or by any other non-invasive test.	A
Cystoscopy should describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities. A bladder diagram is recommended.	C
Voided urine cytology is advocated as an adjunct to cystoscopy to detect high-grade tumour.	C
Cytology should be performed on fresh urine with adequate fixation. Morning urine is not suitable because of the frequent presence of cytolysis.	C

BC = bladder cancer; CT = computed tomography; IVU = intravenous urography; NMIBC = non-muscle invasive bladder cancer; US = ultrasound.

Papillary (Ta, T1) tumours

The diagnosis of papillary bladder cancer ultimately depends on cystoscopic examination of the bladder and histological evaluation of the resected tissue.

Transurethral resection (TURB) of Ta, T1 tumours

TURB is a crucial procedure in the diagnosis and treatment of BC. It should be performed systematically in individual steps (see recommendations below). The strategy of resection depends on the size of the lesion.

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* (CIS)

CIS is diagnosed by a combination of cystoscopy, urine cytology, and histological evaluation of multiple bladder biopsies. Carcinoma *in situ* cannot be eradicated by TURB and further treatment is mandatory.

Recommendations for TURB and/or biopsies and pathology report	**GR**
In patients suspected of harbouring bladder cancer, TURB followed by pathology investigation of the obtained specimen(s) is recommended as a diagnostic procedure and initial treatment step.	A
Perform TURB systematically in individual steps: • bimanual palpation under anaesthesia; • insertion of the resectoscope, under visual control with inspection of the whole urethra; • inspection of the whole urothelial lining of the bladder; • biopsy from prostatic urethra (if indicated); • cold-cup bladder biopsies (if indicated); • resection of the tumour; • surgical report formulation; • precise description of the specimen for pathological evaluation.	C

Performance of individual steps:	
Perform resection in one piece for small papillary tumours (< 1 cm), including part from the underlying bladder wall.	B
Perform resection in fractions including the exophytic part of the tumour, the underlying bladder wall with the detrusor muscle, and the edges of the resection area for tumours > 1 cm in diameter.	B
Avoid cauterization as much as possible during TURB to avoid tissue deterioration.	C
Take biopsies from abnormal-looking urothelium. Biopsies from normal-looking mucosa (trigone, bladder dome, and right, left, anterior and posterior bladder walls) are recommended when cytology is positive or when high-risk exophytic tumour is expected (non-papillary appearance). If equipment is available, use PDD-guided biopsies.	B
Take a biopsy of the prostatic urethra in cases of bladder neck tumour, when bladder CIS 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. If biopsy is not performed during the initial procedure, it should be completed at the time of the second resection.	C
Take the biopsy from abnormal areas in the prostatic urethra and from the precollicular area (between 5 and 7 o'clock position) using a resection loop. In primary non-muscle-invasive tumours when stromal invasion is not suspected, the cold-cup biopsy with forceps can be used.	C
Refer the specimens from different biopsies and resection fractions to the pathologist in separate containers and label them separately.	C

TURB protocol must describe tumour appearance, all steps of the procedure, as well as the extent and completeness of resection.	C
In patients with positive cytology, but negative cystoscopy, exclude a UTUC, CIS in the bladder (random biopsies or PDD-guided biopsies) and tumour in the prostatic urethra (prostatic urethra biopsy).	C
Perform a second TURB in the following situations: • after incomplete initial TURB; • if there is no muscle in the specimen after initial resection, with the exception of TaG1 tumours and primary CIS; • in all T1 tumours; • in all HG/G3 tumours, except primary CIS.	A
If indicated, perform a second TURB within 2-6 weeks after initial resection. It should include resection of the primary tumour site.	C
Pathological report:	
The pathological report should specify tumour location, tumour grade, depth of tumour invasion, presence of CIS, and whether the detrusor muscle is present in the specimen.	A
The pathological report should specify the presence of LVI or unusual (variant) histology.	C
In difficult cases, consider an additional review by an experienced genitourinary pathologist.	B

CIS = carcinoma in situ; LVI = lymphovascular invasion; PDD = photodynamic diagnosis; TURB = transurethral resection of the bladder; UTUC = upper tract urothelial carcinoma.

Predicting disease recurrence and progression

After TURB, patients should be stratified, according to prognostic factors, into risk groups which will facilitate treatment

recommendations. Their definition, which takes into account the EORTC risk tables probabilities of recurrence and especially progression, can be found in 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 (http://www.eortc.be/tools/bladdercalculator/) is strongly recommended.

For bacillus Calmette-Guérin-treated patients, a scoring model was created by the CUETO. The CUETO risk calculator is available at: http://www.aeu.es/Cueto.html. Recently, new EORTC risk tables for patients treated with 1 to 3 years of maintenance BCG have been published.

Table 3: Risk stratification in Ta, T1 tumours and CIS and risk-adjusted treatment recommendations		
Risk category	**Definition**	**Treatment recommendation**
Low-risk tumours	Primary, solitary, Ta, G1/PUNLMP, LG, < 3 cm, no CIS	One immediate instillation of chemotherapy.
Intermediate-risk tumours	All cases between categories of low and high risk	In patients with previous low recurrence rate (less than or equal to one recurrence per year) and expected EORTC recurrence score < 5, one immediate instillation of intravesical chemotherapy 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 chemotherapy (the optimal schedule is not known) for a maximum of 1 year.

High-risk tumours	Any of the following • T1 tumours; • HG/G3 tumours; • CIS; • Multiple and recurrent and large (> 3 cm) Ta, G1G2 tumours (all these conditions must be presented).	Intravesical full-dose BCG instillations for 1-3 years or cystectomy (in highest-risk tumours - see below).
	Subgroup of highest-risk tumours	
	T1G3/HG associated with concurrent bladder CIS, multiple and/or largeT1G3/HG and/or recurrent T1G3/HG, T1G3/HG with CIS in prostatic urethra, unusual histology of urothelial carcinoma, LVI.	Radical cystectomy (RC) should be considered in those who refuse intravesical full-dose BCG instillations for 1-3 years.
	BCG failures	Radical cystectomy is recommended.

BCG = bacillus Calmette-Guérin; CIS = carcinoma in situ; HG = high-grade: LG = low-grade; LVI = lymphovascular invasion; PUNLMP = Papillary urothelial neoplasm of low malignant potential; TURB = transurethral resection of the bladder.

Recommendations for stratification of NMIBC	GR
Stratify patients into three risk groups.	B
Apply the EORTC risk tables and calculator for individual prediction of the risk of tumour recurrence and progression in different intervals after TURB.	B
For individual prediction of the risk of tumour recurrence and progression in patients treated with BCG, use the CUETO risk tables and the new EORTC risk tables.	B

BCG = bacillus Calmette-Guérin; CUETO = Club Urológico Español de Tratamiento Oncológico; EORTC = European Organization for Research and Treatment of Cancer; TURB = transurethral resection of the bladder.

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 (Ta, T1, and CIS).

- **Immediate single post-operative instillation of chemotherapy** within 6 hours after TURB is recommended in patients with tumours presumed to be at low risk, and in those presumed to be at intermediate risk with previous low recurrence rate (less than or equal to one recurrence per year) and expected EORTC recurrence score < 5. Excluded are cases with bladder perforation or severe bleeding. The choice of drug (mitomycin C, epirubicin, or doxorubicin) is optional.
- **Further chemotherapy instillations** can improve RFS 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. However, intravesical BCG is more toxic.

The individual choice of further intravesical adjuvant therapy depends on the patient's risk (Table 3).

In patients at highest risk of progression, radical cystectomy (RC) should be considered. Patients with BCG failure are unlikely to respond to further BCG therapy; RC is therefore the preferred option.

Recommendations for adjuvant therapy in Ta, T1 tumours and for therapy of CIS	**GR**
Smokers with confirmed NMIBC should be counseled to stop smoking.	B
The type of intravesical therapy after TURB should be based on risk groups.	A
In patients with tumours presumed to be at low risk and in those presumed to be at intermediate risk with previous low recurrence rate (less than or equal to one recurrence per year) and expected EORTC recurrence score < 5, one immediate chemotherapy instillation is recommended.	A
In patients with intermediate-risk tumours (with or without immediate instillation), 1-year full-dose 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 1 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	A

In patients with high-risk tumours, full-dose intravesical BCG for 1-3 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 and inconvenience.	A
In patients with CIS in the epithelial lining of the prostatic urethra, TUR of the prostate followed by intravesical instillation of BCG can be offered.	C
In patients at highest risk of tumour progression, immediate radical cystectomy should be considered.	C
In patients with BCG failure, radical cystectomy is indicated.	B
Intravesical chemotherapy	
One immediate instillation should be administered within 24 hours after TURB.	C
One immediate instillation of chemotherapy should be omitted in any case of overt or suspected intra- or extra-peritoneal perforation (after extensive TURB, or bleeding requiring bladder irrigation).	C
Give clear instructions to the nursing staff to control the free flow of the bladder catheter at the end of the immediate instillation.	C
The optimal schedule of further intravesical chemotherapy instillation and its duration is not defined, it should not exceed 1 year.	C
If intravesical chemotherapy is given, it is advised to use the drug at its optimal pH and to maintain the concentration of the drug by reducing fluid intake before and during instillation.	B
The length of an individual instillation should be 1-2 hours.	C

BCG intravesical immunotherapy	
Absolute contraindications of BCG intravesical instillation are: • during the first 2 weeks after TURB; • in patients with visible haematuria; • after traumatic catheterisation; • in patients with symptomatic urinary tract infection.	C
The management of side effects after BCG intravesical instillation should reflect their type and grade (see recommendations in long text)	C

BCG = bacillus Calmette-Guérin; CIS = carcinoma in situ; TUR = transurethral resection; TURB = transurethral resection of the bladder.

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.

When planning the follow-up schedule and methods, the following aspects should be considered:

- The prompt detection of muscle-invasive and HG/G3 non-muscle-invasive recurrence is crucial because a delay in diagnosis and therapy can be life-threatening.
- Tumour recurrence in the low-risk group is nearly always low stage and LG/G1. Small, Ta LG/G1 papillary recurrence does not present an immediate danger to the patient and early detection is not essential for successful therapy. Fulguration of small papillary recurrences on an outpatient basis could be a safe option that reduces the therapeutic burden. Some authors have even defended temporary surveillance in selected cases.

- The first cystoscopy after TURB at 3 months is a very important prognostic indicator for recurrence and progression. Therefore, the first cystoscopy should always be performed 3 months after TURB in all patients with Ta, T1 tumours and CIS.
- In low-risk tumours, the risk of recurrence after 5 recurrence-free years is low.
- Discontinuation of cystoscopy or its replacement with less invasive methods can be considered.
- In tumours originally intermediate- or high-risk, recurrences after 10 years tumour-free are not unusual. Therefore, life-long follow-up is recommended.
- The follow-up strategy must reflect the risk of extravesical recurrence (prostatic urethra in men and upper urinary tract [UUT]).
- The risk of UUT recurrence increases in patients with multiple and high-risk tumours.
- Positive urine test results have a positive impact on the quality of performed follow-up cystoscopy. It supports the adjunctive role of urine tests during follow-up.

Recommendations for follow-up in patients after TURB	**GR**
The follow-up of Ta, T1 tumours and CIS is based on regular cystoscopy.	A
Patients with low-risk tumours should undergo cystoscopy at 3 months. If negative, subsequent cystoscopy is advised 9 months later, and then yearly for 5 years.	C
Patients with high-risk tumours should undergo cystoscopy and urinary cytology at 3 months. If negative, subsequent cystoscopy and cytology should be repeated every 3 months for a period of 2 years, and every 6 months thereafter until 5 years, and then yearly.	C

Patients with intermediate-risk tumours should have an in-between follow-up scheme using cystoscopy and cytology, which is adapted according to personal and subjective factors.	C
Regular (yearly) upper tract imaging (CT-IVU or IVU) is recommended for high-risk tumours.	C
Endoscopy under anaesthesia and bladder biopsies should be performed when office cystoscopy shows suspicious findings or if urinary cytology is positive.	B
Consider R-biopsies or PDD-guided biopsies after intravesical treatment (at 3 or 6 months) in patients with CIS.	C
During follow-up in patients with positive cytology and no visible tumour in the bladder, R-biopsies or PDD-guided biopsies (if equipment is available) and investigation of extravesical locations (CT urography, prostatic urethra biopsy) are recommended.	B

CIS = carcinoma in situ; CT-IVU = computed tomography intravenous urography; IVU = intravenous urography; PDD = photodynamic diagnosis; R-biopsies = random biopsies.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website: http://www.uroweb.org.

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

(Limited text update March 2016)

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Epidemiology

UTUCs are uncommon and account for only 5-10% of urothelial cell carcinomas. They have a similar morphology to bladder carcinomas and nearly all UTUCs are urothelial in origin.

Staging and grading systems

The UICC 2009 TNM (Tumour, Node, Metastasis Classification) for renal pelvis and ureter is used for staging (Table 1).

Tumour grade

There are currently two main classifications used for UTUCs; the 1973 WHO classification, which classifies tumours into three grades, G1, G2 and G3, and the 2004 WHO classification, which classifies tumours into three groups:

- Papillary urothelial neoplasia of low malignant potential;
- Low-grade carcinomas;
- High-grade carcinomas.

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

Table 1: TNM Classification 2009	
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 muscle
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 the greatest dimension
N2	Metastasis in a single lymph node more than 2 cm but not more than 5 cm in the greatest dimension or multiple lymph nodes, none more than 5 cm in greatest dimension
N3	Metastasis in a lymph node more than 5 cm in greatest dimension
M - Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis

Diagnosis

UTUCs are diagnosed using imaging, cystoscopy, urinary cytology and diagnostic ureteroscopy. The benefits of ureteroscopy for pre-operative assessment should also be discussed with the patient.

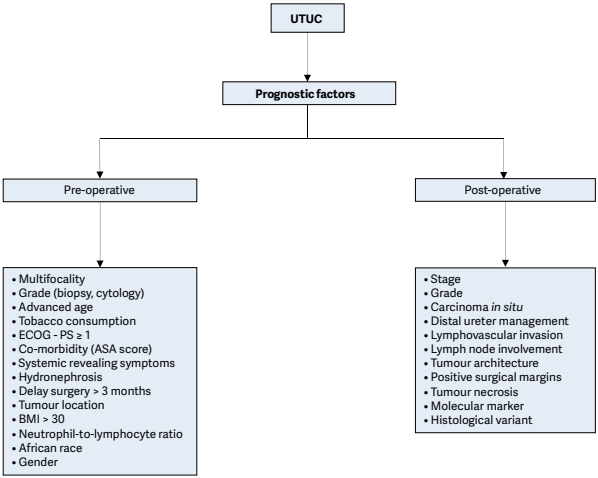
Recommendations for the diagnosis of UTUCs	GR
Perform urinary cytology as part of a standard diagnostic work-up.	A
Perform a cystoscopy to rule out concomitant bladder tumour.	A
Perform a CT-urography for the diagnostic work-up.	A
Use diagnostic ureteroscopy and biopsy in cases where additional information will impact treatment decisions.	C
Perform retrograde ureteropyelography in case CT-urography or ureteroscopy do no reliably reveal the presence or extent of the tumour.	C

CT-urography = computed tomography urography.

Prognosis

UTUCs invading the muscle wall usually have a very poor prognosis. Recognised prognostic facts, as listed in Figure 1.

Figure 1: UTUCs - Prognostic factors

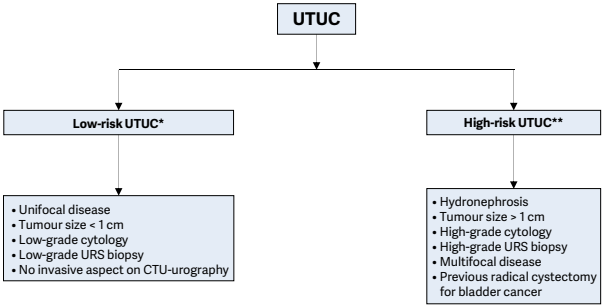


ASA = American Society of Anesthesiologists; BMI = body mass index: ECOG = Eastern Cooperative Oncology Group; PS = performance score.

Risk stratification

It is necessary to 'risk-stratify' UTUC cases before treatment to identify those patients (and tumours) who are more suitable for kidney-sparing management rather than radical extirpative surgery (Figure 2).

Figure 2: Pre-intervention risk stratification of UTUCs



**All of these factors need to be present.*
*** Any of these factors need to be present.*
CTU = computed tomography urography;
URS = ureterorenoscopy.

Disease management (see also Figs. 3 & 4)

Localised disease

Kidney-sparing surgery

Kidney-sparing surgery for low-risk UTUCs consists of surgery preserving the upper urinary renal unit. It is used in imperative cases (renal insufficiency, solitary functional kidney). It can also be discussed in low-risk patients in case of a functional contralateral kidney. Kidney-sparing surgery in low-risk UTUCs potentially allows avoiding the morbidity associated with open radical surgery without compromising oncological outcomes and kidney function.

Recommendations for the kidney-sparing management of UTUCs	GR
Offer kidney-sparing management as primary treatment option to patients with low-risk tumour and two functional kidneys.	C
In patients with solitary kidney and/or impaired renal function, offer kidney-sparing management, providing it will not compromise the oncological outcome. This decision will have to be made on a case-by-case basis, engaging the patient in a shared decision-making process.	C
In high-risk cancers, offer a kidney-sparing approach for distal ureteral tumours and in imperative cases (solitary kidney and/or impaired renal function).	C
Offer kidney-sparing management in case of:	
• Unifocal tumour; • Tumour < 1 cm; • Low-grade tumour; • No evidence of infiltrative lesion on CTU; • Understanding of close follow-up.	B
If treatment is done endoscopically, use a laser.	C

CTU = computed tomography urography.

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 conservative treatment of UTUCs. However, the benefits have not been confirmed.

Radical nephroureteretcomy

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

Recommendations for radical nephroureterectomy	GR
RNU is the standard in high-risk UTUC, regardless of tumour location.	B
Use RNU in the following situations:	
• Suspicion of infiltrating UTUC on imaging;	B
• High-grade tumour (urinary cytology);	B
• Multifocality (with two functional kidneys);	B
• Non-invasive but large (> 1 cm) UTUC.	B
RNU techniques:	
• Remove the bladder cuff;	A
• Perform a lymphadenectomy in invasive UTUC;	C
• Offer a postoperative bladder instillation to lower the bladder recurrence rate.	B
Open and laparoscopic approaches have equivalent efficacy and safety in T1–T2/N0 UTUCs.	B

RNU = radical nephroureterectomy.

Advanced disease

RNU has no benefit in metastatic (M+) disease, but may be used in palliative care. As UTUCs are urothelial tumours, platinum-based chemotherapy should give similar results to those in bladder cancer. Currently, insufficient data are available to provide any recommendations.

Radiotherapy is scarcely relevant nowadays, both as a unique therapy and associated with chemotherapy as a tumour adjuvant.

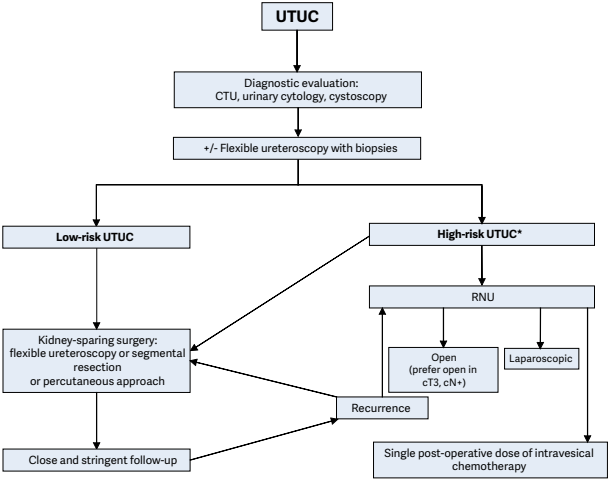
Follow-up after initial treatment

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. In conservative management, the ipsilateral upper urinary tract requires careful follow-up due to the high risk of recurrence.

Recommendations for follow-up of UTUC after initial treatment	GR
After RNU, ≥ five years	
Non-invasive tumour	
• Perform cystoscopy/urinary cytology at three months, and then annually.	C
• Perform CT-urography every year.	C
Invasive tumour	
• Perform cystoscopy/urinary cytology at three months, and then annually.	C
• Perform CT-urography every six months for two years, and then annually.	C
After kidney-sparing management, ≥ five years	
• Perform urinary cytology and CTU at three and six months, and then annually.	C
• Perform cystoscopy, ureteroscopy and cytology *in situ* at three and six months, and then every six months for two years, and then annually.	C

CT-urography = computed tomography urography; RNU = radical nephroureterectomy.

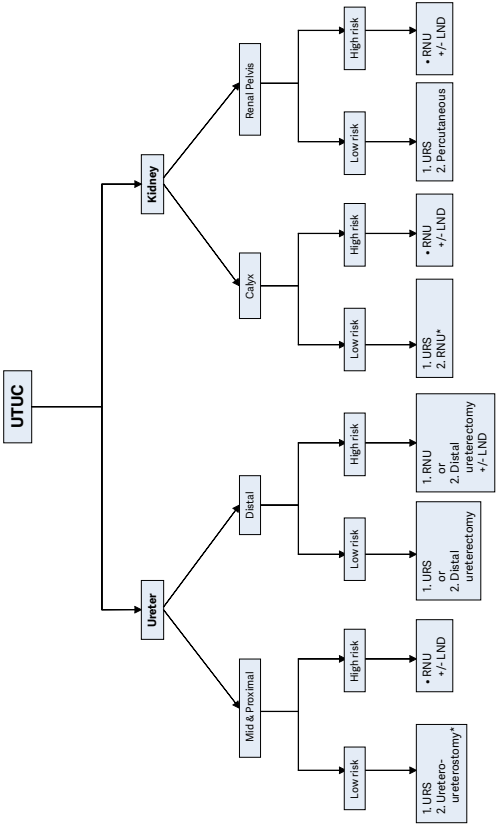
Figure 3: Proposed flowchart for the management of UTUC



**In patients with a solitary kidney, consider a more conservative approach.*
CTU = computed tomography urography;
RNU = nephroureterectomy.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-90-79754-98-4), available to all members of the European Association of Urology at their website: http://www.uroweb.org/guidelines/.

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.*

EAU MUSCLE-INVASIVE AND METASTATIC BLADDER CANCER

(Limited text update March 2016)

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Introduction

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

Staging and grading systems

The 2009 TNM (Tumour, Node, Metastasis Classification) is used for staging. For grading, the 1973 and 2016 WHO grading classifications are used.

Table 1: 2009 TNM classification of urinary bladder cancer	
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, ureterus, 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
M1	Distant metastasis

Table 2: WHO grading in 1973 and in 2016
1973 WHO grading Urothelial papilloma Grade 1: well differentiated Grade 2: moderately differentiated Grade 3: poorly differentiated **2016 WHO grading system** *Papillary lesions:* • Urothelial papilloma (completely benign lesion) • Papillary urothelial neoplasm of low malignant potential (PUNLMP) • Low-grade (LG) papillary urothelial carcinoma • High-grade (HG) papillary urothelial carcinoma *Flat lesions:* • Urothelial proliferation of uncertain malignant potential (flat lesion without atypia or papillary aspects) • Reactive atypia (flat lesion with atypia) • Atypia of unknown significance • Urothelial dysplasia • Urothelial CIS is always high-grade

Pathology of MIBC

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

1. urothelial carcinoma (more than 90% of all cases);
2. urothelial carcinomas with partial squamous and/or glandular differentiation;
3. micropapillary and microcystic urothelial carcinoma;
4. nested variant (including large nested variety); lympho-epithelioma, plasmocytoid, giant cell, undifferentiated;
5. some urothelial carcinomas with trophoblastic differentiation;

6. small-cell carcinomas;
7. sarcomatoid carcinomas.

Recommendations for the assessment of tumour specimens	GR
Record the depth of invasion (categories pT2a & pT2b, pT3a, pT3b or pT4).	A*
Margins with special attention paid to the radial margin, prostate, ureter, urethra and peritoneal fat and uterus and vaginal top.	
Record the number of lymph nodes and number of positive lymph nodes.	
Record lymphatic or blood vessel invasion.	
Record the presence of CIS.	

**Upgraded following panel consensus.*
CIS = carcinoma in situ.

Specific recommendations for the primary assessment of presumably invasive bladder tumours*	GR
Cystoscopy should describe all macroscopic features of the tumour (site, size, number and appearance) and mucosal abnormalities. A bladder diagram is recommended.	C
Take a biopsy of the prostatic urethra for cases of bladder neck tumour, when bladder CIS 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.	
Take a biopsy at the time of the second resection, if no biopsy was taken during the initial procedure.	C

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.	C
Specify the grade, depth of tumour invasion, and whether the lamina propria and muscle tissue are present in the specimen in the pathological report.	C

CIS = carcinoma in situ.

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

Recommendations for staging of MIBC	**GR**
In patients with confirmed MIBC, use CT of the chest, abdomen and pelvis as the optimal form of staging.	
Include excretory-phase CT urography for complete examination of the upper urinary tract.	B
Diagnose UTUC using excretory-phase CT urography rather than MR urography as excretory-phase CT urography has greater diagnostic accuracy and is associated with less cost, and greater patient acceptability.	C
Use MR urography when CT urography is contraindicated for reasons related to contrast administration or radiation dose.	C
Perform endoscopically-guided biopsy for histopathological confirmation of preoperative diagnosis of UTUC.	C
Use CT or MRI for staging locally advanced or metastatic disease in patients in whom radical treatment is being considered.	B

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

CT = computed tomography; DWI = diffusion-weighted imaging; FDG-PET/CT = fluorodeoxyglucose-positron emission tomography; MIBC = muscle-invasive bladder cancer; MR = magnetic resonance; MRI = magnetic resonance imaging; UTUC = upper urinary tract urothelial carcinoma.

Prognosis

Recommendations for the assessment of elderly patients	**GR**
Base the decision on bladder-sparing or radical cystectomy in elderly/geriatric patients with invasive bladder cancer on tumour stage and comorbidity.	B
Assess comorbidity by a validated score, such as the Charlson Comorbidity Index, the ASA score should not be used in this setting.	

ASA = American Society of Anesthesiologists.

Disease Management

Recommendations for treatment failure of non-MIBC	**GR**
Consider immediate radical treatment in all T1 tumours at high risk of progression (i.e., high grade, multifocality, CIS, and tumour size, as outlined in the EAU guidelines for non-muscle-invasive bladder cancer).	C
Offer radical treatment to all T1 patients failing intravesical therapy.	B

CIS = carcinoma in situ.

Neoadjuvant chemotherapy (NAC)

Neoadjuvant cisplatin-containing combination chemotherapy

improves overall survival (5-8% at 5 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.

However, NAC has its limitations regarding patient selection, current development of surgical techniques, and current chemotherapy combinations.

Recommendations for neoadjuvant chemotherapy	**GR**
Offer neoadjuvant chemotherapy for T2-T4a, cN0M0 bladder cancer. In this case, always use cisplatin-based combination therapy.	A
Do not offer neoadjuvant chemotherapy to patients who are ineligible for cisplatin-based combination chemotherapy.	A

Recommendations for pre- and post-operative radiotherapy in MIBC	**GR**
Do not offer pre-operative radiotherapy to improve survival.	A
Offer pre-operative radiotherapy for operable MIBC since it can result in tumour downstaging after 4-6 weeks.	C

MIBC = muscle-invasive bladder cancer.

Radical cystectomy and urinary diversion

Summary of evidence	LE
For MIBC, offer radical cystectomy as the curative treatment of choice.	3
A higher case load reduces morbidity and mortality of cystectomy.	3
Radical cystectomy includes removal of regional lymph nodes.	3
There are data to support that extended lymph node dissection (vs. standard or limited LND) improves survival after radical cystectomy.	3
Radical cystectomy in both sexes must not include removal of the entire urethra in all cases, which may then serve as the outlet for an orthotopic bladder substitution. The terminal ileum and colon are the intestinal segments of choice for urinary diversion.	3
The type of urinary diversion does not affect oncological outcome.	3
Laparoscopic cystectomy and robotic-assisted laparoscopic cystectomy are feasible but still investigational. Current best practice is open radical cystectomy.	3
In patients aged > 80 years with MIBC, cystectomy is an option.	3
Surgical outcome is influenced by comorbidity, age, previous treatment for bladder cancer or other pelvic diseases, surgeon and hospital volumes of cystectomy, and type of urinary diversion.	2
Surgical complications of cystectomy and urinary diversion should be reported using a uniform grading system. Currently, the best-adapted, graded system for cystectomy is the Clavien grading system.	2
No conclusive evidence exists as to the optimal extent of LND.	2a

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	**GR**
Do not delay cystectomy for > 3 months because it increases the risk of progression and cancer-specific mortality.	B
Before cystectomy, fully inform the patient about the benefits and potential risks of all possible alternatives, and the final decision should be based on a balanced discussion between patient and surgeon.	B
Offer an orthotopic bladder substitute or ileal conduit diversion to male and female patients lacking any contraindications and who have no tumour in the urethra or at the level of urethral dissection.	B
Do not offer pre-operative radiotherapy when subsequent cystectomy with urinary diversion is planned.	A
Do not offer sexual preserving cystectomy as standard therapy for MIBC.	C
Offer sexual-preserving techniques to men motivated to preserve their sexual function since the majority will benefit.	B
Select patients based on: • Organ-confined disease; • Absence of any kind of tumour at the level of the prostate, prostatic urethra or bladder neck.	A
Do not offer pelvic organ preserving radical cystectomy to female patients as standard therapy for MIBC.	C

Offer sexual-preserving techniques to female patients motivated to preserve their sexual function since the majority will benefit.	C
Select patients based on: • Organ-confined disease; • Absence of tumour in bladder neck or urethra.	C
Pre-operative bowel preparation is not mandatory. "Fast track" measurements may reduce the time of bowel recovery.	C
Offer radical cystectomy in T2-T4a, N0M0, and high-risk non-MIBC.	A*
Lymph node dissection must be an integral part of cystectomy.	A
Preserve the urethra if margins are negative. Check the urethra regularly if no bladder substitution is attached.	B

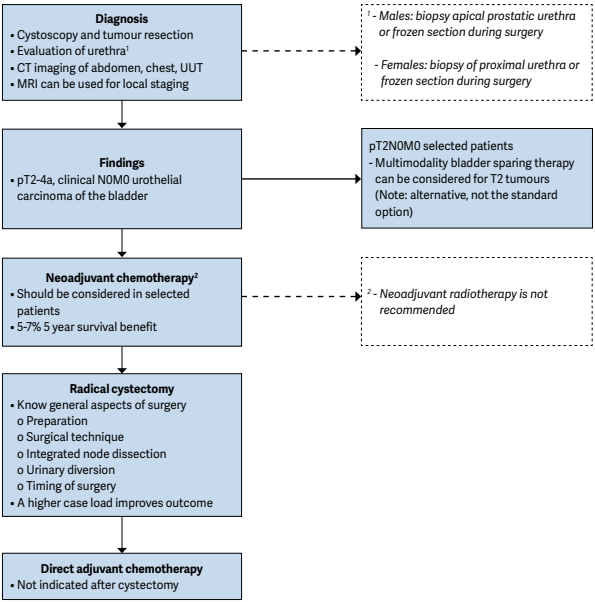
**Upgraded following EAU Working Panel consensus.*
MIBC = muscle-invasive bladder cancer.

Summary of evidence and recommendations for laparoscopic/robotic-assisted laparoscopic cystectomy	LE
RARC has a longer operative time (1-1.5 hours), major costs; but shorter LOS (1-1.5 days) and less blood loss compared to ORC.	1
RARC series suffer from a significant stage selection bias when compared to ORC.	1
Grade 3, 90-day complication rate is lower with RARC.	2
Most endpoints, if reported, including intermediate term oncological endpoint and QoL are not different between RARC and ORC.	2
Surgeons experience and institutional volume are considered the key factors for outcome of both RARC and ORC, not the technique.	2
Recommendations on how to define challenging patients and an experienced RARC surgeon are still under discussion.	3
The use of neobladder after RARC still seems under-utilised, and functional results of intracorporeally constructed neobladders should be studied.	4

Recommendations	GR
Inform the patient of the advantages and disadvantages of ORC and RARC to select the proper procedure.	C
Select experienced centres, not specific techniques, both for RARC and ORC.	B
Beware of neobladder under-utilisation and outcome after RARC.	C

LOS = length of hospital stay; ORC = open radical cystectomy; QoL = quality of life; RARC = robot-assisted radical cystectomy.

Fig. 1: Flowchart 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 (TURB)

TURB 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 (EBRT)

EBRT 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

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

Multimodality treatment

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

Recommendations for bladder-sparing treatments for localised disease	**GR**
Do not offer transurethral resection of bladder tumour alone as a curative treatment option. Most patients will not benefit.	
Do not offer pre-operative radiotherapy to improve survival.	A
Do not offer radiotherapy alone as primary therapy for localised bladder cancer.	B
Offer pre-operative radiotherapy for operable MIBC since it can result in tumour down-staging after 4-6 weeks.	C
Do not offer chemotherapy alone as primary therapy for localised bladder cancer.	A

Offer surgical intervention or multimodality treatments as primary curative therapeutic approaches since they are more effective than radiotherapy alone.	B
Offer multimodality treatment as an alternative in selected, well-informed and compliant patients, especially for whom cystectomy is not an option.	B

MIBC = muscle-invasive bladder cancer.

Surgically non-curable tumours

Palliative cystectomy for metastatic disease

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

Recommendations	GR
Offer radical cystectomy as a palliative treatment to patients with inoperable locally advanced tumours (T4b).	B
In patients with symptoms, palliative cystectomy may be offered.	B

Adjuvant Chemotherapy

Recommendation	GR
Offer adjuvant cisplatin-based combination chemotherapy to patients with pT3/4 and/or pN+ disease if no neoadjuvant chemotherapy has been given.	C

Metastatic disease

Summary of evidence	LE
In a first-line setting, performance status and the presence or absence of visceral metastases are independent prognostic factors for survival.	1b
In a second-line setting, negative prognostic factors are: liver metastasis, PS ≥ 1 and low haemoglobin (< 10 g/dL).	1b
Cisplatin-containing combination chemotherapy can achieve median survival of up to 14 months, with long-term disease-free survival reported in ~15% of patients with nodal disease and good PS.	1b
Single-agent chemotherapy provides low response rates of usually short duration.	2a
Carboplatin combination chemotherapy is less effective than cisplatin-based chemotherapy in terms of complete response and survival.	2a
Non-platinum combination chemotherapy produces substantial responses in first- and second-line settings.	2a
Non-platinum combination chemotherapy has not been tested against standard chemotherapy in patients who are fit or unfit for cisplatin combination chemotherapy.	4
There is no defined standard chemotherapy for unfit patients with advanced or metastatic urothelial cancer.	2b
Vinflunine reaches the highest level of evidence ever reported for second-line use.	1b
Post-chemotherapy surgery after partial or complete response may contribute to long-term disease-free survival.	3

Zoledronic acid and denosumab have been approved for all cancer types including urothelial cancer, because they reduce and delay skeletal related events in metastatic bone disease.	1b

Recommendations	**GR**
First-line treatment for fit patients:	
Use cisplatin-containing combination chemotherapy with GC, PCG, MVAC, preferably with G-CSF, or HD-MVAC with G-CSF.	A
Do not use carboplatin and non-platinum combination chemotherapy.	B
First-line treatment in patients ineligible (unfit) for cisplatin:	
Use carboplatin combination chemotherapy or single agents.	C
For cisplatin-ineligible (unfit) patients, with PS2 or impaired renal function, as well as those with 0 or 1 poor Bajorin prognostic factors and impaired renal function, offer carboplatin-containing combination chemotherapy, preferably with gemcitabine/carboplatin.	B
Second-line treatment:	
Offer vinflunine to patients progressing after platinum-based combination chemotherapy for metastatic disease. Alternatively, offer treatment within a clinical trial setting.	A*
Offer zoledronic acid or denosumab to treat bone metastases.	B

** Grade A recommendation is weakened by a problem of statistical significance.*

GC = gemcitabine plus cisplatin; G-CSF = granulocyte colony-stimulating factor; MVAC = methotrexate, vinblastine, adriamycin plus cisplatin; HD MVAC = high-dose methotrex-

ate, vinblastine, adriamycin plus cisplatin; PS = performance status; PCG = paclitaxel, cisplatin, gemcitabine.

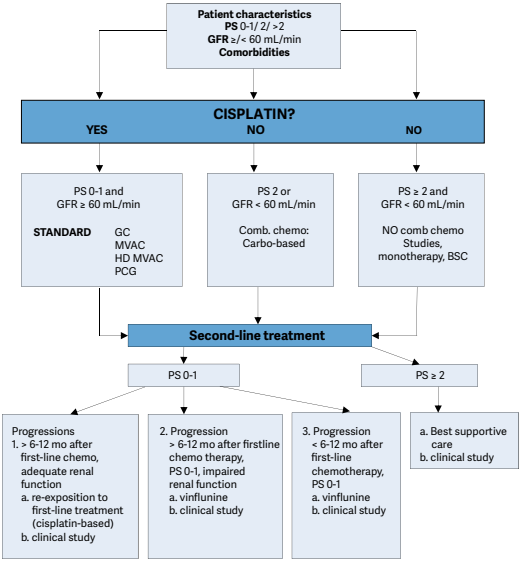
Health-related quality-of-life (HRQoL)

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

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

HRQoL = health-related quality of life; MIBC = muscle-invasive bladder cancer.

Figure 2: Flowchart for the management of metastatic urothelial bladder 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.

This short booklet text is based on the more comprehensive EAU Guidelines (978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org/guidelines/.

EAU-ESTRO-SIOG GUIDELINES ON PROSTATE CANCER

(Text update March 2016)

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Introduction

Please note that this text presents an abridged version of the full text Prostate Cancer (PCa) Guidelines and consultation of the more detailed, underlying document, is strongly advised. Prostate cancer is a complex disease, and, aside from 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 most common cancer in males in Europe. 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 2009 Tumour Node Metastasis (TNM) classification is used for staging (Table 1).

Table 1: 2009 TNM classification	
T - Primary tumour	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T1	Clinically inapparent tumour not palpable or visible by imaging
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 prostate-specific antigen (PSA) level)
T2	Tumour confined within the prostate[1]
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[2]
T3a	Extracapsular extension (unilateral or bilateral) including microscopic bladder neck involvement
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 lymph nodes[3]	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis[4]

M - Distant metastasis[5]	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis
M1a	Non-regional lymph node(s)
M1b	Bone(s)
M1c	Other site(s)

[1] *Tumour found in one or both lobes by needle biopsy, but not palpable or visible by imaging, is classified as T1c.*

[2] *Invasion into the prostatic apex, or into (but not beyond) the prostate capsule, is not classified as pT3, but as pT2.*

[3] *The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries.*

[4] *Laterality does not affect the N-classification.*

[5] *When more than one site of metastasis is present, the most advanced category should be used.*

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

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

GS = Gleason score; PSA = prostate-specific antigen.

Guidelines for screening and early detection	LE	GR
Do not subject men to PSA testing without counselling on the potential risks and benefits.	3	B
Offer an individualised risk-adapted strategy for early detection to a well-informed man with a good performance status and a life expectancy of at least 10-15 years.	3	B
Offer early PSA testing in men at elevated risk of having PCa: • men > 50 years of age; • men > 45 years of age and a family history of PCa; • African-Americans > 45 years of age; • 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.	2b	A
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.	3	C
Decide on the age at which early diagnosis of PCa should be stopped based on life expectancy and performance status; men who have a life expectancy of < 15-years are unlikely to benefit.	3	A

PSA = prostate-specific antigen.

Diagnostic Evaluation

Clinical diagnosis

Prostate cancer is usually suspected on the basis of digital rectal examination (DRE) and/or PSA levels. Definitive diagnosis depends on histopathological verification of adenocarcinoma in prostate biopsy cores or unexpected discovery in specimens from transurethral resection of the prostate 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 age and comorbidity into consideration. Procedures that will not affect the treatment decision can usually be avoided.

A biopsy pathology report includes the type of carcinoma and parameters describing its extent (e.g. proportion of positive cores, percentage or mm carcinoma involvement per core) as well as Gleason score per biopsy site and global Gleason score. Reporting of a radical prostatectomy specimen includes type of carcinoma, global Gleason score, pathological stage and surgical margin status. Recently, the ISUP-WHO 2014 grade groups were adopted which allow patients to better understand the behaviour of their diagnosed prostate carcinoma, while separating Gleason score 7 adenocarcinoma into two prognostically very distinct categories; grade group 2 for Gleason score 7 (3 + 4) and grade group 3 for Gleason score 7 (4 + 3) (see Table 3). This ISUP-WHO 2014 grade grouping will gradually be introduced into the standard pathology reporting.

Table 3: ISUP 2014 grade groups	
Gleason score	**Grade group**
2-6	1
7 (3 + 4)	2
7 (4 + 3)	3
8 (4 + 4) or (3 + 5) or (5 + 3)	4
9-10	5

ISUP = International Society of Urological Pathology.

Guidelines for the clinical diagnosis of PCa	LE	GR
Base the decision to perform a biopsy on PSA testing and DRE.	2b	A
Use a local anaesthetic by periprostatic infiltration for prostate needle biopsies.	1a	A
For initial diagnosis, perform a core biopsy of 10–12 systematic transrectal or transperineal peripheral zone biopsies under ultrasound guidance.	2a	B
Perform transrectal prostate needle biopsies under antibiotic protection.	1b	A
Do not initially offer transition zone biopsies due to low detection rates.	2b	B
Use the additional diagnostic options in asymptomatic men with a normal DRE and a PSA between 2.0 and 10 ng/mL (risk calculator, or an additional serum or urine-based test [e.g. PHI, 4Kscore or PCA3] or imaging).	3	C
Do not use transurethral resection of the prostate as a tool for cancer detection.	2a	A
Perform one set of repeat biopsies for persistent indications for PCa (abnormal DRE, elevated PSA or histopathological findings suggestive of malignancy at initial biopsy).	2a	B

Ensure that prostate core biopsies from different sites are submitted separately for processing and pathology reporting.	3	A
Use the ISUP 2005 modified Gleason grading system for grading of PCa.	2a	A
Adhere to the 2010 ISUP consensus meeting Guidelines for processing and reporting of prostatectomy specimens.	3	A

DRE = digital rectal examination; ISUP = International Society of Urological Pathology; PCA3 = prostate cancer gene 3; PHI = Prostate Health Index; PSA = prostate-specific antigen.

Guidelines for processing prostatectomy specimens	**LE**	**GR**
Ensure total embedding, by conventional (quadrant) or whole-mount sectioning.	3	C
Ink the entire surface before cutting, to evaluate the surgical margin.	3	A
Examine the apex and base separately, using the cone method with sagittal or radial sectioning.	3	A

Recommendations for imaging - repeat biopsy	**LE**	**GR**
Before repeat biopsy, perform mpMRI when clinical suspicion of PCa persists in spite of negative biopsies.	1a	A
During repeat biopsy include systematic biopsies and targeting of any mpMRI lesions seen.	2a	B

mpMRI = multiparametric magnetic resonance imaging.

Guidelines for staging of PCa

Any risk group staging	LE	GR
Do not use CT and TRUS for local staging.	2a	A

Low-risk localised PCa	LE	GR
Do not use additional imaging for staging purposes.	2a	A

Intermediate-risk PCa	LE	GR
In predominantly Gleason pattern 4, metastatic screening, include at least cross-sectional abdominopelvic imaging and a CT/MRI and bone-scan for staging purposes.	2a	A*
In predominantly Gleason pattern 4, use prostate mpMRI for local staging and metastatic screening.	2b	A

High-risk localised PCa/ High-risk locally advanced PCa	LE	GR
Use prostate mpMRI for local staging.	2b	A
Perform metastatic screening including at least cross-sectional abdominopelvic imaging and a bone-scan.	2a	A

**Upgraded following panel consensus.*
CT = computed tomography; mpMRI = multiparametric magnetic resonance imaging; TRUS = transrectal ultrasound.

Disease Management

Deferred treatment

Many men with localised PCa will not benefit from definitive treatment, and 45% of men with PSA-detected PCa would be

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

Guidelines overview - Primary treatment of PCa

Primary treatment of PCa			GR
General comments	Discuss several treatment modalities (active surveillance, surgery and radiotherapy) with patients suitable for such treatments.		A*
	In patients who are surgical candidates for radical prostatectomy, discuss all approaches (i.e. open, laparoscopic or robotic) as acceptable treatment options since none have clearly shown superiority in terms of functional or oncological results.		A
	Offer EBRT to all risk groups of non-metastatic PCa.		A
	Offer IMRT for definitive treatment of PCa by EBRT.		A
	Treatment	**Comment**	
Low risk PCa	**Watchful waiting**	Offer WW to patients not eligible for local curative treatment and those with a short life expectancy.	A
		While on WW, base the decision to start non-curative treatment on symptoms and disease progression.	B

	Active surveillance	Offer AS to patients with the lowest risk of cancer progression: > 10 years life expectancy, cT1/2, PSA ≤ 10 ng/mL, biopsy Gleason score ≤ 6, ≤ 2 positive biopsies, minimal biopsy core involvement (≤ 50% cancer per biopsy).	A
		Base follow-up on DRE, PSA and repeat biopsies. The optimal follow-up interval is still unclear.	A
	Radical prostatectomy	Offer RP to patients with a life expectancy > 10 years.	A
		Offer a nerve-sparing surgery in pre-operatively potent patients with low risk of extracapsular disease (T1c, GS < 7 and PSA < 10 ng/mL, or refer to Partin tables/nomograms).	B
		Do not perform LND in low-risk PCa	A
	Radiotherapy	In low-risk PCa, the total dose should be 74 to 78 Gy.	A
		In patients with low-risk PCa, without a previous TURP and with a good IPSS and a prostate volume < 50 mL, offer LDR brachytherapy.	A

	Cryotherapy, HIFU	Only offer cryotherapy and HIFU within a clinical trial setting. The lack of long-term efficacy compared to standard modality has to be discussed with patients.	C
	Focal treatment	Do not offer focal therapy of PCa as a therapeutic alternative outside clinical trials.	A
	Androgen suppression	Unsuitable.	A
Intermediate risk PCa	**Watchful waiting**	Offer WW to patients not eligible for local curative treatment and those with a short life expectancy.	A
	Active surveillance	Not an option.	A
	Radical prostatectomy	Offer RP to patients with a life expectancy > 10 years.	A
		Offer a nerve-sparing surgery in pre-operatively potent patients with low risk of extracapsular disease (T1c, GS < 7 and PSA < 10 ng/mL, or refer to Partin tables/nomograms).	B
		In intermediate-risk, extracapsular disease, use mpMRI as a decision tool to select patients for nerve-sparing procedures.	B
		Perform an eLND if the estimated risk for positive LNs exceeds 5%.	B
		Do not perform a limited LND.	A

		In patients with pT3,N0M0 PCa and an undetectable PSA following RP, discuss adjuvant EBRT because it at least improves BFS.	A
		Inform patients with pT3,N0M0 PCa and an undetectable PSA following RP about salvage irradiation as an alternative to adjuvant irradiation when PSA increases.	A
		Do not offer adjuvant HT for pN0.	
	Radiotherapy	In intermediate-risk PCa use a total dose of 76-78 Gy, in combination with short-term ADT (4-6 mo).	A
	Androgen suppression monotherapy	No place in asymptomatic patients.	A
High risk PCa	**Watchful waiting**	**High risk localised**: Offer WW to patients not eligible for local curative treatment and those with a short life expectancy.	
		High risk locally advanced: In locally advanced M0 patients unwilling or unable to receive any form of local treatment, offer a deferred treatment policy using ADT as mono-therapy to asymptomatic patients with a PSA-DT > 12 months and a PSA < 50 ng/mL and non-poorly differentiated tumour.	A

	Active surveillance	Not appropriate.	A
	Radical prostatectomy	Do not offer NHT before RP.	A
		Perform an eLND in high-risk PCa.	A
		Do not perform a limited LND.	A
		High risk localised: Offer RP in a multimodality setting to patients with high-risk localised PCa and a life expectancy of > 10 years.	B
		Offer nerve-sparing surgery in pre-operatively potent patients with low risk for extracapsular disease (refer to Partin tables/ nomograms).	B
		In high-risk disease, use mpMRI as a decision-making tool to select patients for nerve-sparing procedures.	B
		High risk locally advanced: Offer RP in a multimodality setting to highly selected patients with locally advanced PCa (cT3b-T4 N0 or any T N1). Do not consider nerve sparing surgery.	C
		In patients with pT3,N0M0 PCa and an undetectable PSA following RP, discuss adjuvant EBRT because it at least improves BFS.	A

		Inform patients with pT3,N0M0 PCa and an undetectable PSA following RP about salvage irradiation as an alternative to adjuvant irradiation when PSA increases.	A
	Radiotherapy	In patients with high-risk localised PCa, use a total dose of 76-78 Gy in combination with long-term ADT (2-3 years is recommended).	A
		In patients with locally advanced cN0 PCa, offer RT in combination with long-term ADT (2-3 years is recommended).	A
	Androgen suppression monotherapy	Reserved for those patients unwilling or unable to receive any form of local treatment and that are either symptomatic or asymptomatic with a PSA-DT < 12 months and a PSA > 50 ng/mL and a poorly differentiated tumour.	A
N1 patients			
cN1	In patients with cN+ PCa, offer pelvic EBRT in combination with immediate long-term ADT.		B
pN1 after eLND	Offer adjuvant ADT for node-positive (pN+).		A
	Offer adjuvant ADT with additional radiotherapy.		B
	Offer observation (expectant management) to a patient after eLND and ≤ 2 nodes showing microscopic involvement, with a PSA < 0.1 ng/mL and absence of extranodal extension.		B

Metastatic PCa	**Watchful waiting**	In M1 asymptomatic patients, deferred castration should be discussed with a well-informed patient.	B
	Active surveillance	Unsuitable.	A
	Radical prostatectomy	Unsuitable outside clinical trial.	A
	Radiotherapy to the prostate	Unsuitable outside clinical trial.	A
	Androgen suppression	Offer surgical or medical castration (LHRH agonist or antagonist).	A
		Offer castration combined with chemotherapy to all patients whose first presentation is M1 disease and who are fit enough for chemotherapy.	A
		Offer castration alone with or without an antiandrogen to patients unfit for, or unwilling to consider castration combined with chemotherapy.	A
		Do not offer castration combined with local treatment/ other new hormonal treatments (abiraterone acetate or enzalutamide) outside clinical trials.	A
		In M1 asymptomatic patients, offer immediate castration to defer progression to a symptomatic stage and prevent serious disease progression-related complications.	A

		In M1 symptomatic patients, offer immediate castration to palliate symptoms and reduce the risk for potentially catastrophic sequelae of advanced disease (spinal cord compression, pathological fractures, urethral obstruction, extra-skeletal metastases).	A
		In M1 patients treated with an LHRH agonist, offer short-term administration of anti-androgens to reduce the risk of the 'flare-up' phenomenon.	A
		Start anti-androgens used for 'flare-up' prevention on the same day as an LHRH analogue is started or for up to 7 days before the first LHRH analogue injection if the patient has symptoms). Treat for four weeks.	A
		Do not offer anti-androgen monotherapy in M1 patients.	A
		Offer LHRH antagonists, especially in patients with an impending spinal cord compression or bladder outlet obstruction.	B
		In asymptomatic M1 patients, offer intermittent treatment to highly motivated patients, with a major PSA response after the induction period.	B

		In M1 patients follow the schedules used in published clinical trials on timing of intermittent treatment. Stop treatment when the PSA level is < 4 ng/mL after 6-7 months of treatment. Resume treatment when the PSA level is > 10-20 ng/mL (or back to the original level, if < 20 ng/mL).	C
		In M1 patients, offer combined treatment with LHRH agonists and NSAA when an intermittent modality is used.	A

**Upgraded following panel consensus.*
ADT = androgen deprivation therapy; AS = active surveillance; BFS = biochemical progression-free survival; DRE = digital rectal examination; EBRT = external beam radiation therapy; HIFU = high-intensity focused ultrasound; HT = hormonal therapy; IMRT = intensity-modulated radiotherapy; IPSS = International Prostate Symptom Score; LDR = low-dose-rate; LHRH = luteinising-hormone-releasing hormone; eLND = (extended) lymph node dissection; LN = lymph node; mpMRI = multiparametric magnetic resonance imaging; NHT = neoadjuvant hormonal therapy; NSAA = non-steroidal anti-androgen; PSA = prostate-specific antigen; PSA-DT = PSA doubling time; RP = radical prostatectomy; RT = radiation therapy; TURP = transurethral resection of the prostate; WW = watchful waiting.

Guidelines for the treatment of senior adults (> 70 years of age)

Assessment	GR
Perform systematic health status screening in senior adults with localised PCa.	A
Use the G8 screening tool for health status screening.	A
Perform a full specialist geriatric evaluation in patients with G8 score ≤ 14.	A
Treatment options for senior adults according to their health status: 1. Offer standard treatment to fit or healthy older men; 2. Offer standard treatment to vulnerable patients (reversible impairment) after resolution of geriatric problems; 3. Offer adapted treatment to frail patients (irreversible impairment); 4. Offer only symptomatic palliative treatment to patients who are too sick with terminal illness.	B

Treatment	LE	GR
Localised disease		
Offer standard treatment to fit and vulnerable senior adults (after status optimisation) with a life expectancy > 10 years.	2b	A
Offer individualised treatment based on life expectancy, symptoms and risk factors to senior adults with a life expectancy < 10 years.	2b	A
In frail or 'too–sick' senior adults, offer immediate ADT only for symptom palliation.	1b	A
Offer minimally invasive energy-ablative therapies only to selected fit and vulnerable senior adults with intermediate-risk disease.	3	B

Advanced disease (locally advanced / metastatic disease)		
Evaluate bone mineral status and prevent osteoporosis-related fractures in senior adults.	2b	A
Offer new chemotherapeutic and hormonal agents to fit and vulnerable adults.	1b	B

ADT = androgen deprivation therapy.

Castrate resistant PCa

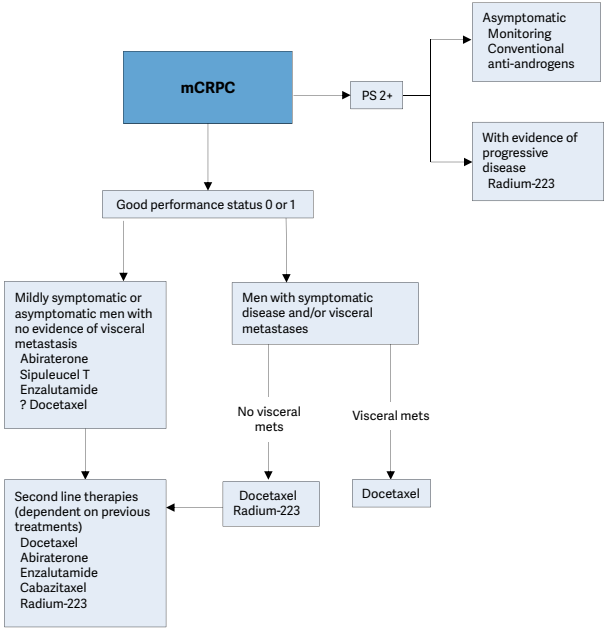
No definitive strategy regarding treatment choices (which drug/drug family first) can be devised.

Castrate resistant status	**GR**
Ensure that testosterone levels are confirmed as < 50 ng/mL, before diagnosing CRPC.	A
Do not treat patients for non-metastatic CRPC outside of a clinical trial.	A
Counsel, manage and treat patients with mCRPC in a multidisciplinary team.	A
In men treated with maximal androgen blockade, stop anti-androgen therapy once PSA progression is documented. *Comment: Four to six weeks after discontinuation of flutamide or bicalutamide, an eventual anti-androgen withdrawal effect will be apparent.*	A
Treat patients with mCRPC with life prolonging agents. Base the choice of first line treatment on the performance status, symptoms, comorbidities and extent of disease (alphabetical order: abiraterone, docetaxel, enzalutamide, radium-223, sipuleucel-T).	A
Offer patients with mCRPC who are candidates for cytotoxic therapy docetaxel with 75 mg/m^2 every 3 weeks.	A

In patients with mCRPC and progression following docetaxel chemotherapy, offer further life-prolonging treatment options, which include cabazitaxel, abiraterone, enzalutamide and radium-223.	A
Offer bone protective agents to patients with skeletal metastases to prevent osseous complications. However, the benefits must be balanced against the toxicity of these agents, and jaw necrosis, in particular, must be avoided.	A
Offer calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonates.	A
Treat painful bone metastases early on with palliative measures such as EBRT, radionuclides, and adequate use of analgesics.	B
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.	A

EBRT = external beam radiation therapy; mCRPC = metastatic castrate-resistant prostate cancer; PSA = prostate-specific antigen.

Figure 1: Flowchart of the potential therapeutic options after PSA progression following hormonal therapy in metastatic patients.



PS = performance status; mCRPC = metastatic castrate resistant prostate cancer; mets = metastases.

Guidelines for supportive care of mCRPC

These recommendations are in addition to appropriate systemic therapy.

Recommendations	LE	GR
Offer bone protective agents to patients with skeletal metastases to prevent osseous complications. However, the benefits must be balanced against the toxicity of these agents, and jaw necrosis in particular must be avoided.	1a	B
Prescribe calcium and vitamin D supplementation when prescribing either denosumab or bisphosphonates.	1b	A
Treat painful bone metastases early on with palliative measures such as external beam radiotherapy, radionuclides, and adequate use of analgesics.	1a	B
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	1b	A

Follow-up

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 tissue. After an undetectable PSA is obtained following RP, a PSA > 0.2 ng/mL, and rising, is associated with recurrent disease.
- After radiotherapy, an increase in PSA > 2 ng/mL above the nadir, rather than a specific threshold value, is the most reliable sign of recurrence.
- Palpable nodules and increasing serum PSA are often signs of local recurrence.

Guidelines for follow up after treatment with curative intent	**GR**
Routinely follow-up asymptomatic patients, by obtaining a disease-specific history and serum PSA measurement supplemented by DRE. These should be performed at 3, 6 and 12 months after treatment, then every 6 months until 3 years, and then annually.	B
Imaging to detect local recurrence is only recommended if it affects treatment planning. Biopsy is usually not necessary before second-line therapy.	B
Do not routinely offer bone scans and other imaging modalities to asymptomatic patients if there are no signs of biochemical relapse. In case patients have bone pain or other symptoms of progression, re-staging should be considered irrespective of serum PSA level.	B

DRE = digital rectal examination; PSA = prostate-specific antigen.

Guidelines for follow-up during hormonal treatment	GR
Evaluate patients at 3 - 6 months after the initiation of treatment.	A
As a minimum, tests should include serum PSA measurement, DRE, serum testosterone, and careful evaluation of symptoms in order to assess the treatment response and side effects.	A
In patients undergoing intermittent androgen deprivation, monitor PSA and testosterone at fixed intervals during the treatment pause (monthly or at three month intervals).	A
Adapt follow-up to the individual patient, according to stage of disease, prior symptoms, prognostic factors and the treatment given.	A
In patients with stage M0 disease with a good treatment response, schedule follow-up every 6 months. As a minimum requirement, include a disease-specific history, DRE and serum PSA determination in the diagnostic work-up.	A
In patients with stage M1 disease with a good treatment response, schedule follow-up every 3 to 6 months. As a minimum requirement, include a disease-specific history, 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.	A
Counsel patients (especially with M1b status) about the clinical signs suggestive of spinal cord compression.	A
When disease progression occurs, or if the patient does not respond to treatment, adapt/individualise follow up.	A

In patients with suspected progression, assess the testosterone level. By definition, CRPC definition requires a testosterone level < 50 ng/mL (< 1 mL/L).	B
Do not offer routine imaging to otherwise stable patients.	B

CRPC = castrate-resistant prostate cancer; DRE = digital rectal examination; PSA = prostate-specific antigen.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON RENAL CELL CARCINOMA

(Limited text update March 2016)

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Introduction

The use of imaging techniques such as ultrasound (US) and computerised tomography (CT) have increased the detection of asymptomatic renal cell cancer (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. The most effective prophylaxis is to avoid cigarette smoking and obesity.

Histological diagnosis

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

Summary of evidence	LE
Except for AML, most other renal tumours cannot be differentiated from RCC by radiology and should be treated in the same way as RCC.	3
In biopsy-proven oncocytomas, watchful waiting is an option.	3
In advanced uncommon renal tumours, a standardised oncological treatment approach does not exist.	3

Recommendations	GR
Bosniak cysts ≥ type III should be regarded as RCC and treated accordingly. Treat Bosniak type III or IV cysts the same as RCC.	C
Treat most AMLs with active surveillance. Treat with selective arterial embolisation or NSS for: • large tumours (recommended threshold of intervention does not exist, the formerly recommended size of > 4 cm wide is disputed); • females of childbearing age; • patients in whom follow-up or access to emergency care may be inadequate.	C
In AML > 3 cm not requiring surgical intervention, medical treatment with everolimus can be considered.	C
Treat all tumours with the radiologic appearance of RCC in the same way.	C
Offer watchful waiting to patients with biopsy-proven oncocytomas.	C
For advanced uncommon renal tumours, develop individualised oncological treatment plans for each patient.	C

AML = angiomyolipoma; NSS = nephron-sparing surgery.

Staging system

The current UICC 2009 TNM (Tumour Node Metastasis) classification is recommended for the staging of RCC (Table 1).

Table 1: The 2009 TNM staging classification system

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

M - Distant metastasis	
M0	No distant metastasis
M1	Distant metastasis

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

Diagnostic evaluation

Many renal masses remain asymptomatic until the late disease stages. More than 50% of RCCs are detected incidentally by non-invasive imaging used to investigate various non-specific symptoms and other abdominal diseases. The classic triad of flank pain, visible haematuria, and palpable abdominal mass is rare (6-10%) 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.

Radiological investigations of RCC

Computed tomography (CT) 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 extrarenal spread, venous involvement, and enlargement of lymph nodes (LNs) and adrenals.

Abdominal US and magnetic resonance (MR) imaging 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 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 chest staging and is recommended in the primary work–up of patients with suspected RCC.

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 estimation should always be undertaken to optimise the treatment decision.

Recommendations for the diagnostic assessment of renal cell carcinoma	**GR**
Contrast-enhanced multi-phasic abdominal CT and MRI are recommended for the work-up of patients with RCC and are considered equal both for staging and diagnosis.	B
Contrast-enhanced multi-phasic abdominal CT and MRI are the most appropriate imaging modalities for renal tumour characterisation and staging prior to surgery.	C
A chest CT is recommended for staging assessment of the lungs and mediastinum.	C
Bone scan is not routinely recommended.	C

Renal tumour biopsy is recommended before ablative therapy and systemic therapy without previous pathology.	C
Percutaneous biopsy is recommended in patients in whom active surveillance is pursued.	C
Obtain percutaneous renal tumour biopsy with a coaxial technique.	C

CT = computed tomography; MRI = magnetic resonance imaging.

Histopathological classification

Fuhrman nuclear grade is the most commonly used grading system. The most aggressive pattern observed defines the Fuhrman grade. RCC comprises different subtypes with genetic and histological differences. The three most common RCC types are: clear cell RCC (80-90%), papillary RCC (10-15%), and chromophobe RCC (4-5%). Generally, the various RCC types have different clinical courses and responses to therapy.

Recommendations	**GR**
Use the current TNM classification system.	B
Use grading systems and classify RCC type.	B

TNM = tumour node metastasis (classification); WHO = World Health Organization.

Prognostic factors

In all RCC types, prognosis worsens with stage and histopathological grade. The 5-year overall survival (OS) for all types of RCC is 49%. Clinical factors include performance status, localised symptoms, cachexia, anaemia, and platelet count.

Summary of evidence	LE
In RCC patients, TNM stage, Fuhrman nuclear grade, and RCC subtype (WHO, 2004), provide important prognostic information.	2

TNM = tumour node metastasis (classification); WHO = World Health Organization.

Disease Management

Treatment of localised RCC

Localised renal cancers 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 deterioration in patient health.

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 lymph node dissection (eLND) 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 renal cancers are best managed by NSS rather than RN, irrespective of the surgical approach. Before routine nephrectomy, tumour embolisation has no benefit.

Summary of evidence	LE
PN achieves similar oncological outcomes to RN for clinically localised tumours (cT1).	1b
Ipsilateral adrenalectomy during RN or PN has no survival advantage.	3
In patients with localised disease without evidence of LN metastases, there is no survival advantage of LND in conjunction with RN.	1b
In patients unfit for surgery with massive haematuria or flank pain, embolisation can be a beneficial palliative approach.	3

Recommendations	GR
Surgery is recommended to achieve cure in localised RCC.	B
PN is recommended in patients with T1a tumours.	A
Favour PN over RN in patients with T1b tumour, whenever feasible.	B
Ipsilateral adrenalectomy is not recommended when there is no clinical evidence of invasion of the adrenal gland.	B
LND is not recommended in localised tumour without clinical evidence of lymph node invasion.	A

LND = lymph node dissection; PN = partial nephrectomy; RN = radical nephrectomy.

Radical- and partial nephrectomy techniques

Summary of evidence	LE
Laparoscopic RN has lower morbidity than open surgery.	1b
Oncological outcomes for T1-T2a tumours are equivalent between laparoscopic and open RN.	2a
PN can be performed, either with an open, pure laparoscopic- or robot-assisted approach, based on surgeon's expertise and skills.	2b

Recommendations	GR
Laparoscopic RN is recommended for patients with T2 tumours and localised masses not treatable by PN.	B
RN should not be performed in patients with T1 tumours for whom PN is indicated.	B

PN = partial nephrectomy; RN = radical nephrectomy.

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 is appropriate to initially monitor small renal masses, followed, if required, by treatment for progression.

Cryoablation and radiofrequency ablation

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

Summary of evidence	LE
Population-based analyses show a significantly lower cancer-specific mortality for patients treated with surgery compared to non-surgical management. However, the same benefit in cancer-specific mortality is not confirmed in analyses focusing on older patients (> 75 years).	3
In active surveillance cohorts, the growth of small renal masses is low in most cases and progression to metastatic disease is rare (1-2%).	3
Quality of the available data does not allow definitive conclusions regarding morbidity and oncological outcomes of cryoablation and RFA.	3
Low quality studies suggest a higher local recurrence rate for minimally invasive therapies compared to PN.	3

Recommendations	GR
Due to the low quality of available data no recommendation can be made on radiofrequency ablation and cryoablation.	C
In the elderly and/or comorbid patients with small renal masses and limited life expectancy, active surveillance, radiofrequency ablation and cryoablation may be offered.	C

PN = partial nephrectomy; RFA = radiofrequency.

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 controversial.

In patients unfit for surgery, or with non-resectable disease, embolisation can control symptoms, including visible haematuria or flank pain.

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.

At present there is no evidence for the use of adjuvant therapy following surgery.

Treatment of advanced / metastatic RCC

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 oligo-metastatic resectable disease. For most patients with metastatic disease, cytoreductive nephrectomy is palliative and systemic treatments are necessary.

Summary of evidence	LE
Cytoreductive nephrectomy combined with IFN-α improves survival in patients with mRCC and good PFS.	1a
Cytoreductive nephrectomy for patients with simultaneous complete resection of a single metastasis or oligometastases may improve survival and delay systemic therapy.	3

Recommendation	GR
Cytoreductive nephrectomy is recommended in appropriately selected patients with mRCC.	C

IFN-α = interferon-alpha; PFS = progression-free survival; mRCC = metastatic renal cell cancer.

Local therapy of metastases in mRCC

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 included studies 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 overall survival, cancer-specific survival 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	GR
No general recommendations can be made. The decision to resect metastases has to be taken for each site, and on a case-by-case basis; performance status, risk profiles, profiles and patient preference. Alternative techniques to achieve local control such as stereotactic radiotherapy and radiofrequency ablation must be considered.	C
Stereotactic radiotherapy for bone metastases and stereotactic radiosurgery for brain metastases may be offered for local control and symptom relief.	C

Systemic therapy for advanced / metastatic RCC

Summary of evidence	LE
In mRCC, 5-fluorouracil combined with immunotherapy has equivalent efficacy to IFN-α.	1b
In mRCC, chemotherapy is otherwise not effective.	3

Recommendation	GR
In patients with clear-cell mRCC, chemotherapy should not be offered.	B

IFN-α = interferon alpha; mRCC = metastatic renal cell cancer.

Immunotherapy

Interferon-alpha may only be effective in some patient subgroups, including patients with ccRCC, favourable-risk criteria, as defined by the Memorial Sloan-Kettering Cancer Center and lung metastases only. Interleukin-2, vaccines and targeted immunotherapy have no place in the standard treatment of advanced/ mRCC.

Summary of evidence	LE
IFN-α monotherapy is inferior to VEGF-targeted therapy or mTOR inhibition in mRCC.	1b
IL-2 monotherapy may have an effect in selected cases (good PS, ccRCC, lung metastases only).	2
IL-2 has more side-effects than IFN-α.	2-3
High-dose IL-2 is associated with durable complete responses in a limited number of patients. However, no clinical factors or biomarkers exist to accurately predict a durable response in patients treated with HD-IL2.	1b
Bevacizumab plus IFN-α is more effective than IFN-α treatment-naïve, low-risk and intermediate-risk tumours.	1b

Vaccination therapy with tumour antigen 5T4 showed no survival benefit over first-line standard therapy.	1b
Cytokine combinations, with or without additional chemotherapy, do not improve OS compared with monotherapy.	1b
Nivolumab leads to superior OS compared to everolimus in patients failing one or two lines of VEGF-targeted therapy.	1b

Recommendations	GR
Nivolumab is strongly recommended after one or two lines of VEGF-targeted therapy in mRCC.	A
Monotherapy with IFN-α or HD bolus IL-2 is not routinely recommended as first-line therapy in mRCC.	A

ccRCC = clear cell RCC; HD = high-dose; IFN-α = interferon alpha; IL-2 = interleukin-2; mRCC = metastatic renal cell cancer; OS = overall survival; PS = performance status.

Targeted therapies

Novel agents for the treatment of mRCC include drugs targeting VEGF, other receptor kinases and mammalian target of rapamycin (mTOR). At present, several targeting drugs have been approved both in the USA and in Europe for the treatment of mRCC.

Summary of evidence	LE
VEGF TKIs increase PFS and/or OS as both first-line and second-line treatments for clear-cell mRCC.	1b
Axitinib has proven efficacy and superiority in PFS as a second-line treatment after failure of cytokines and VEGF-targeted therapy in comparison with sorafenib.	1b

Sunitinib is more effective than IFN-α in treatment-naïve patients.	1b
Bevacizumab plus IFN-α is more effective than IFN-α in treatment-naïve low-risk and intermediate-risk patients.	1b
Pazopanib is superior to placebo in both naïve mRCC patients and post-cytokine patients.	1b
Pazopanib is not inferior to sunitinib in clear-cell mRCC patients.	1b
Temsirolimus monotherapy prolongs OS compared to IFN-α in poor-risk mRCC.	1b
Nivolumab is superior to everolimus in terms of OS and adverse events in patients failing one or two lines of VEGF-targeted therapy.	1b
Cabozantinib is superior to everolimus in terms of PFS in patients failing one or more lines of VEGF-targeted therapy.	1b
Everolimus prolongs PFS in patients who have previously failed or are intolerant of VEGF-targeted therapy.	1b
Sorafenib has broad activity in a spectrum of settings in clear-cell renal cancer patients previously treated with cytokine or targeted therapies. It is inferior to axitinib in both sunitinib or cytokine pre-treated patients.	4
Both mTOR inhibitors (everolimus and temsirolimus) and VEFG-targeted therapies (sunitinib or sorafenib) can be used in non-clear cell RCC.	3
No combination has proven to be better than single-agent therapy.	1a

EAU 2016 evidence-based recommendations for systemic therapy in pati				
RCC type	**MSKCC risk group**	**First-line**	**LE^**	
Clear cell*	favourable, intermediate and poor	sunitinib pazopanib bevacizumab + IFN-α (favourable-inter- mediate only)	1b 1b 1b	
Clear cell*	poor¶	temsirolimus	1b	
Non-clear cell §	any	sunitinib everolimus temsirolimus	2a 2b 2b	

IFN-α = interferon alpha; MSKCC = Memorial Sloan-Kettering Cancer Center; mTOR = mammalian target of rapamycin inhibitor; RCC = renal cell carcinoma; TKI= tyrosine kinase inhibitor.

* Doses: IFN-α - 9 MU three times per week subcutaneously, bevacizumab 10 mg/kg biweekly intravenously; sunitinib 50 mg daily orally for 4 weeks, followed by 2 weeks of rest (37.5 mg continuous dosing did not show significant differences); temsirolimus 25 mg weekly intravenously; pazopanib 800 mg daily orally. Axitinib 5 mg twice daily, to be increased to 7 mg twice daily, unless greater than grade 2 toxicity, blood pressure higher than 150/90 mmHg, or the patient is receiving antihypertensive medication. Everolimus, 10 mg daily orally.

ents with mRCC						
	Second-Line after VEGF therapy*	**LE^**	**Third-line***	**LE^**	**Later lines**	**LE**
	<u>based on OS:</u> nivolumab <u>based on PFS:</u> cabozantinib axitinib sorafenib# everolimus&	 2a 2a 2a 2a 2a	**after VEGF therapy:** nivolumab cabozantinib everolimus& **after VEGF and mTOR therapy:** sorafenib **after VEGF and nivolumab:** cabozantinib axitinib everolimus	 2a 2a 2a 1b 4 4 4	any targeted agent	4
	any targeted agent	4				
	Any targeted agent	4				

§ No standard treatment available. Patients should be treated in the framework of clinical trials or a decision can be made in consultation with the patient to perform treatment in line with ccRCC.

¶ Poor risk criteria in the NCT00065468 trial consisted of MSKCC risk plus metastases in multiple organs. Evidence for subsequent therapies unclear, making this option less appealing.

Sorafenib was inferior to axitinib in a RCT in terms of PFS but not OS.

^ Level of evidence was downgraded in instances when data were obtained from subgroup analysis within an RCT.

& Everolimus was inferior in terms of OS to nivolumab and in terms of PFS to cabozantinib and should not routinely be given where other superior agents are available.

Recommendations - Systemic therapy in mRCC	GR
Systemic therapy for mRCC should be based on targeted and immune agents.	A
Sunitinib and pazopanib are recommended as first-line therapy for advanced/metastatic clear-cell RCC.	A
Bevacizumab + IFN-α are recommended as first-line therapy for advanced/metastatic RCC in favourable-risk and intermediate-risk cRCC.	A
Temsirolimus is recommended as first-line treatment in poor-risk RCC patients. Data on subsequent therapies is lacking in this setting.	A
Cabozantinib should be given for cRCC patients who failed one or two lines of VEGF-targeted therapy based on a PFS advantage over everolimus.	A
Nivolumab is strongly recommended for cRCC patients who failed one or two lines of VEGF-targeted therapy based on and OS advantage over everolimus.	A
Axitinib can be given as second-line treatment for mRCC after cytokines or first-line VEGF where other drugs are not safe, tolerable or available.	A
Everolimus can be given for cRCC patients who failed VEGF-targeted therapy where other drugs are not safe, tolerable or available.	A
Sequencing of targeted agents is strongly recommended.	A
Sunitinib or everolimus can be given as first-line therapy for non-clear cell mRCC.	B

ccRCC = clear cell RCC; HD = high-dose; IFN-α = interferon alpha; IL-2 = interleukin-2; mRCC = metastatic renal cell cancer; OS = overall survival; PS = performance status; VEFG = vascular endothelial growth factor.

Recurrent RCC

Locally recurrent disease can occur either after nephrectomy, partial nephrectomy, or after ablative therapy. After nephron-sparing treatment approaches the recurrence may be intrarenal or in addition regional, e.g. venous tumour thrombi or retroperitoneal lymph node metastases. Isolated local recurrence is rare. In cases where complete surgical removal is not feasible due to advanced tumour growth and pain, palliative treatments including radiation treatment can be considered.

Summary of evidence	LE
Isolated recurrence in the local renal fossa is rare.	3
Patients who undergo resection of local recurrences in the absence of sarcomatoid features may benefit from durable local control and improved survival.	3

Recommendation	GR
Surgical resection of local recurrent disease may be offered.	C

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. There is no evidence whether early versus later diagnosis of recurrence improves survival. Surveillance also allows the urologist to identify:

- 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 and treatment efficacy

		Surveillance						
Risk profile	**Treatment**	**6 mo**	**1 y**	**2 y**	**3 y**	**4 y**	**5 y**	**> 5 y**
Low	RN/PN only	US	CT	US	CT	US	CT	Discharge
Intermediate	RN/PN/ cryo/RFA	CT	CT	CT	US	CT	CT	CT once every 2 y
High	RN/PN/ cryo/RFA	CT	CT	CT	CT	CT	CT	CT once every 2 y

Cryo = cryotherapy; CT = computed tomography of chest and abdomen, or MRI = magnetic resonance imaging; PN = partial nephrectomy; RFA = radiofrequency ablation; RN = radical nephrectomy; US = ultrasound of abdomen, kidneys and renal bed.

Summary of evidence and recommendations for surveillance following RN or PN or ablative 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 in larger (> 7 cm) tumours, or when there is a positive surgical margin.	3

Recommendations	GR
Follow-up after RCC should be based on the risk of recurrence.	C
For low-risk disease, CT/MRI can be used infrequently.	C
In intermediate-risk patients, intensified follow-up should be performed, including CT/MRI scans at regular intervals in accordance with a risk-stratified nomogram.	C
In high-risk patients, the follow-up examinations should include routine CT/MRI scans.	C
Follow-up should be intensified in patients after NSS for tumours > 7 cm or with a positive surgical margin.	C
Risk stratification can be based on pre-existing classification systems such as the UISS integrated risk assessment score: http://urology.ucla.edu/body.cfm?id=443.	C

CT = computed tomography; MRI = magnetic resonance imaging; NSS = nephron-sparing surgery; PN = partial nephrectomy; RN = radical nephrectomy.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN: 978-90-79754-98-4), 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 2015)

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Introduction

Compared with other types of cancer, testicular cancer is relatively rare accounting for approximately 1-1.5% of all cancers in men. Nowadays, testicular tumours show excellent cure rates, mainly due to early diagnosis and their extreme chemo- and radiosensitivity.

Staging and Classification

Staging

For an accurate staging the following steps are necessary:
Postorchiectomy half-life kinetics of serum tumour markers. The persistence of elevated serum tumour markers after orchiectomy may indicate the presence of disease, while their normalisation does not necessarily mean absence of tumour.
Tumour markers should be assessed until they are normal, as long as they follow their half-life kinetics and no metastases are revealed.

A chest computed tomography (CT) scan should be routinely performed in patients diagnosed with non-seminomatous germ cell tumours (NSGCT), because in up to 10% of cases, small subpleural nodes may be present that are not visible radiologically.

For staging purposes. recommendations are:		
Test	**Recommendation**	**GR**
Serum tumour markers	AFP hCG LDH	A
Abdominopelvic CT	All patients	A
Chest CT	All patients	A
Testis ultrasound (bilateral)	All patients	A
Bone scan or MRI columna	In case of symptoms	
Brain scan (CT/MRI)	In case of symptoms and patients with metastatic disease with multiple lung metastases and/or high beta-hCG values.	
Further investigations		
Fertility investigations: Total testosterone LH FSH Semen analysis		B
Discuss sperm banking with all men prior to starting treatment for testicular cancer.		A

hCG = human chorionic gonadotrophin; LDH = lactate dehydrogenase; CT = computed tomography; AFP = alpha-fetoprotein; LH = luteinising hormone; FSH = follicle-stimulating hormone.

Staging system

The Tumour, Node, Metastasis (TNM 2009) staging system is endorsed (Table 1).

Table 1: TNM classification for testicular cancer	
pT	**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 (testicular intraepithelial neoplasia)
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion: tumour may invade unica albuginea but not tunica vaginalis
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea 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 multiple lymph nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
N3	Metastasis with a lymph node mass more than 5 cm in greatest dimension

Pn	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 M1b Other sites		
S	**Serum tumour markers**		
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	S1 < 1.5 x N and	< 5,000 and	< 1,000
S2	S2 1.5-10 x N or	5,000-50,000 or	1,000-10,000
S3	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.

[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.

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 NSGCT (Table 2).

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/retroperitoneal 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%	*All of the following criteria:* • Testis/retroperitoneal 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 testicular cancer is based on:
Clinical examination of the testis and general examination to rule out enlarged nodes or abdominal masses. Ultrasound (US) of both testes should be performed whenever a testicular tumour is suspected. An additional US of the retroperitoneum is recommended to screen for extensive retroperitoneal metastasis. Ultrasound of both testes should also be performed in patients with a retroperitoneal mass and/or elevated tumour serum markers without a palpable scrotal mass.

Serum tumour markers, both before, and 5-7 days after orchiectomy (AFP and hCG) and LDH. The latter is mandatory in advanced tumours.

Inguinal exploration and orchiectomy with en bloc removal of testis, tunica albuginea, and spermatic cord. If the diagnosis is not clear, a testicular biopsy (tumour enucleation) is to be taken for histopathological frozen section.

Organ-sparing surgery can be attempted in special cases (bilateral tumour or solitary testes). Routine contralateral biopsy for diagnosis of carcinoma in situ 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).

Pathological examination of the testis

Following orchiectomy, 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 epididymis, spermatic cord and tunica vaginalis.
2. Sampling: 1 cm^2 section for every centimetre of maximum tumour diameter, including normal macroscopic parenchyma (if present), albuginea and epididymis with selection of suspected areas. At least one proximal and one distal section of the spermatic cord plus any suspected area.
3. Microscopic features and diagnosis:
    - histological type (specify individual components and estimate amount as a percentage);
    - 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, and;
- presence or absence of (TIN/IGCNU) in non-tumour parenchyma.

4. pT category according to the TNM 2009.
5. Immunohistochemical studies: in seminoma and mixed germ cell tumour, AFP and hCG.

Diagnosis and treatment of testicular intraepithelial neoplasia (TIN)

Biopsy should be offered to patients at high risk for contralateral TIN (testicular volume < 12 mL, history of cryptorchidism or poor spermatogenesis). If performed, a double biopsy is preferred. In the case of TIN, local radiotherapy is indicated following counselling on impaired testosterone production and infertility.

Guidelines for the diagnosis and staging of testicular cancer	GR
Perform testicular US in all patients with suspicion of testicular cancer.	A
Offer biopsy of the contralateral testis and discuss its consequences with patients at high risk for contralateral TIN.	A
Perform orchiectomy 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 orchiectomy.	A
Perform serum determination of tumour markers (AFP, hCG, and LDH), both before and 5-7 days after orchiectomy for staging and prognostic reasons.	A
Assess the state of the retroperitoneal, mediastinal and supraclavicular nodes and viscera in testicular cancer.	A

AFP = alpha-fetoprotein; GR = grade of recommendation; hCG = human chorionic gonadotrophin; LDH = lactate dehydrogenase; TIN = testicular intraepithelial neoplasia; US = ultrasound.

Prognosis

Risk factors for occult metastatic disease in stage I testicular cancer		
Pathological (for stage I)	**For seminoma**	**For non-seminoma**
Histopathological type	• Tumour size (> 4 cm) • Invasion of the rete testis	• Vascular/lymphatic or peri-tumoural invasion • Proliferation rate > 70% • Percentage of embryonal carcinoma > 50%

Disease management

Guidelines for the treatment of stage I seminoma	GR
Offer surveillance as a management option if facilities are available and the patient compliant.	A*
Offer one course at AUC 7, if carboplatin-based chemotherapy is considered.	A
Do not perform adjuvant treatment in patients at very low risk.	A
Do not perform radiotherapy as adjuvant treatment.	A

**Upgraded following panel consensus.*
AUC = area under the curve.

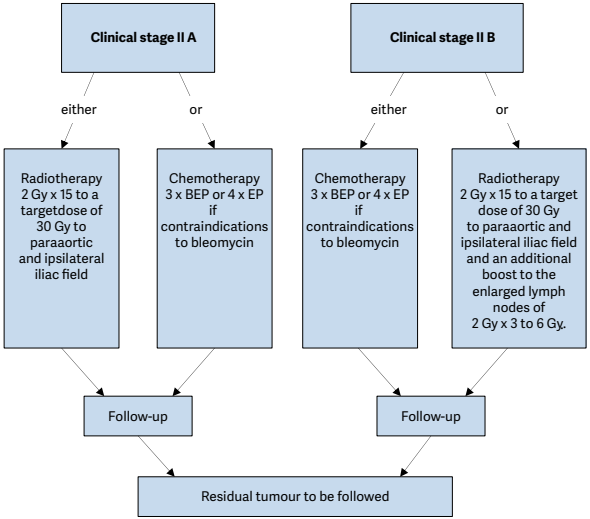
Guidelines for the treatment of stage I NSGCT	LE	GR
Inform patients with stage 1 NSGCT about all adjuvant treatment options after orchiectomy (surveillance, adjuvant chemotherapy, and RPLND) including treatment-specific recurrence rates as well as acute and long-term side effects.	2a	A*
In patients with stage 1 NSGCT, offer surveillance or risk-adapted treatment based on vascular invasion (see below).	2a	A*
If patients are not willing to undergo surveillance, offer one course of BEP as an adjuvant treatment alternative since it has proven to be superior to RPLND in terms of recurrence rates.	1b	A*
In patients with marker-positive recurrent and/or progressing lesion during surveillance, perform salvage treatment consisting of three or four courses of BEP chemotherapy according to the IGCCCG classification, followed by postchemotherapy RPLND.	2a	A

** Upgraded following panel consensus.*
BEP = cisplatin, eposide, bleomycin; RPLND = retroperitoneal lymph node dissection; IGCCCG = International Germ Cell Cancer Collaborative Group.

Risk-adapted treatment for clinical stage I based on vascular invasion	LE	GR
Stage 1A (pT1, no vascular invasion): low risk		
Offer surveillance if the patient is willing and able to comply.	2a	A
In low-risk patients not willing (or suitable) to undergo surveillance, offer adjuvant chemotherapy with one course of BEP.	2a	A*
Stage 1B (pT2-pT4): high risk		
Offer primary chemotherapy with one course of BEP.	2a	A*
Inform patients having adjuvant chemotherapy about the advantages and disadvantages of one versus two cycles of BEP?	2a	A*
Offer surveillance or nerve-sparing RPLND in high-risk patients not willing to undergo adjuvant chemotherapy. If pathological stage II is revealed at RPLND, discuss further chemotherapy as well as observation with the patient.		A*

** Upgraded following panel consensus.*
BEP = cisplatin, eposide, bleomycin; RPLND = retroperitoneal lymph node dissection.

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



Guidelines for the treatment of metastatic germ cell tumours	LE	GR
Treat low volume NSGCT stage IIA/B with elevated markers like 'good or intermediate prognosis' advanced NSGCT, with three or four cycles of BEP.	2	A
In stage IIA/B NSGCT without marker elevation, exclude marker negative embryonal carcinoma by obtaining histology by either RPLND or biopsy. If not possible, repeat staging after 6 weeks of surveillance before making a final decision on further treatment.	3	B

In metastatic NSGCT (≥ stage IIC) with good prognosis, treat with three courses of BEP.	1	A
In metastatic NSGCT with an intermediate prognosis, treat with four courses of standard BEP.	1	A
In metastatic NSGCT with a poor prognosis, treat with one cycle of BEP, followed by tumour marker assessment after 3 weeks: in the case of an unfavourable decline, initiate chemotherapy intensification; in the case of a favourable decline, continue BEP up to a total of four cycles.	1	A
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.	2	A
Treat seminoma CSII A/B initially with radiotherapy. When necessary, use chemotherapy as a salvage treatment with the same schedule as for the corresponding prognostic groups of NSGCT.	2	B
In seminoma stage CS IIA/B, offer chemotherapy (3 x BEP or 4 x EP, in good prognosis) as an alternative to radiotherapy.	1	A
Treat seminoma stage IIC and higher with primary chemotherapy according to the same principles used for NSGCT.	1	A

EP = etoposide, cisplatin; NSGCT = non-seminomatous germ cell tumour; BEP = cisplatin, etoposide, bleomycin; RPLND = retroperitoneal lymph node dissection.

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 CR/

PRM- and gonadal primary tumour) 4 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 (> first) relapse, high-dose chemotherapy with autologous stem cell support is recommended.

Follow-up

The aim of follow-up is to detect relapse as early as possible and to monitor the contralateral testis. In the presence of a curative- or life prolongation therapy, the following principles should apply;

a) Interval between examinations and duration of follow-up should be consistent with the time of maximal risk of recurrence;
b) Tests should be directed at the most likely sites of recurrence and have a good accuracy;
c) 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;
d) Non-malignant complications of therapy must also be considered.

Table 3: Recommended minimum follow-up schedule in a surveillance policy: stage I non-seminoma

Procedure	Year			
	1	2	3	4-5
Physical examination	4 times	4 times	4 times	Once/yr.
Tumour markers	4 times	4 times	4 times	Once/yr.
Plain radiography chest	Twice	Twice	Twice	Twice
Abdominopelvic CT	Twice at 3 and 12 months	Once in year 2 at 24 months	Once in year 3 at 36 months	

CT = computed tomography.

Table 4: Recommended minimum follow-up schedule after RPLND or adjuvant chemotherapy: stage I non-seminoma

Procedure	Year				
	1	2	3	4-5	6-10
Physical examination	4 times	4 times	4 times	Once/yr.	Once/yr.
Tumour markers	4 times	4 times	4 times	Once/yr.	Once/yr.
Plain radiography chest	Twice	Twice	Twice		
Abdominopelvic CT	Once	Once	Once	Once/yr.	

CT = computed tomography.

Table 5: Recommended minimum follow-up schedule for post-orchidectomy surveillance, radiotherapy or chemotherapy: stage I seminoma

Procedure	Year		
	1	2	3-5
Physical examination	3 times	3 times	Once/yr.
Tumour markers	3 times	3 times	Once/yr.
Plain radiography chest	Twice	Twice	
Abdominopelvic CT	Twice	Twice	At 36 and 60 months

CT = computed tomography.

Table 6: Recommended minimum follow-up schedule in metastatic NSGCT and seminoma

Procedure	Year			
	1	2	3-5	Thereafter
Physical examination	4 times	4 times	Twice/yr.	Once/yr.
Tumour markers	4 times	4 times	Twice/yr.	Once/yr.
Plain radiography chest	4 times	4 times	Twice/yr.	Once/yr.
Abdominopelvic CT*†	Twice	Twice	Once/yr.	As indicated
Chest CT†‡	Once/yr.	Once/yr.	Once/yr.	As indicated
Brain CT§	Once/yr.	Once/yr.	Once/yr.	As indicated

CT = computed tomography.

** An abdominal CT must be performed at least annually if teratoma is found in the retroperitoneum.*

† If the post-chemotherapy evaluation in a seminoma patient shows any mass > 3 cm, the appropriate CT should be repeated 2 and 4 months later to ensure that the mass is continuing to regress. If available, FDG-PET/CT can be performed.

‡ A chest CT is indicated if abnormality is detected on a plain radiography chest and after pulmonary resection.

§ In patients with headaches, focal neurological findings, or any central nervous system symptoms.

Quality of life and long-term toxicities after cure

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

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);
- Cytologic atypia and DNA aneuploidy;
- Increased mitotic activity 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 orchiectomy because they are misinterpreted as germ cell tumours. In patients with symptoms of gynaecomastia or hormonal disorders or typical imaging on US, until final histology is available, a partial orchiectomy (+ frozen section) should be considered. In the case of histological signs of malignancy, orchiectomy and RPLND are the treatment of choice.

Sertoli cell tumours

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

- Large size (> 5 cm);
- Pleomorphic nuclei with nucleoli;
- Increased mitotic activity;
- Necrosis and vascular invasion.

They 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 orchiectomy is performed.

Organ-sparing surgery should be considered (with caution) but, in the case of histological signs of malignancy, orchiectomy and RPLND are the treatment of choice.

Conclusions

Most testis tumours are diagnosed at an early stage. Staging is the cornerstone. The 2009 TNM system is recommended for classification and staging purposes.

The IGCCCG staging system is recommended for metastatic disease. Following orchiectomy, 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 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON PENILE CANCER

(Text update April 2014)

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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	OR 11-16 vs. no phimosis
Chronic penile inflammation (balanoposthitis related to phimosis) Balanitis xerotica obliterans (lichen sclerosus)	Risk
Sporalene and UVA phototherapy for various dermatological conditions such as psoriasis	Incidence rate ratio 9.51 with > 250 treatments
Smoking	5-fold increased risk (95% CI: 2.0-10.1) vs. non-smokers
HPV infection condylomata acuminata	22.4% in verrucous SCC 36-66.3% in basaloid-warty
Rural areas, low socioeconomic status, unmarried	
Multiple sexual partners, early age of first intercourse	3-5-fold increased risk of penile cancer

HPV = human papilloma virus; OR = odds ratio; SCC = squamous cell carcinoma; UVA = ultraviolet A.

Pathology

Squamous cell carcinoma (SCC) in different variants 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 SCC of the penis • Cutaneous horn of the penis • Bowenoid papulosis of the penis • Lichen sclerosus (balanitis xerotica obliterans)
Premalignant lesions (up to one-third transform to invasive SCC) • Intraepithelial neoplasia grade III • Giant condylomata (Buschke-Löwenstein) • Erythroplasia of Queyrat • 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 SCC	48-65	Depends on location, stage and grade
Basaloid carcinoma	4-10	Poor prognosis, frequently early inguinal nodal metastasis [40]
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 sclerosus, 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 [41] (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 HPV, aggressive, early metastasis, poor prognosis, outcome is lesion-dependent, frequent lymphatic metastasis

Biopsy

In the management of penile cancer there is need for histological confirmation if:

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

Staging and classification systems

The 2009, Tumour Node Metastasis (TNM) classification should be used (Table 3). A subclassification of the T2 category regarding invasion of the corpus spongiosum only, or the corpora cavernosa as well, would be desirable as it has been shown that the prognosis for corpus spongiosum invasion alone is much better than for corpora cavernosa invasion.

Table 3: 2009 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 carcinoma	
T1	Tumour invades subepithelial connective tissue	
	T1a	Tumour invades subepithelial connective tissue without lymphovascular invasion and is not poorly differentiated or undifferentiated (T1G1-2)
	T1b	Tumour invades subepithelial connective tissue with lymphovascular invasion or is poorly differentiated or undifferentiated (T1G3-4)

T2	Tumour invades corpus spongiosum and/or corpora cavernosa
T3	Tumour invades 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 node
N1	Palpable mobile unilateral inguinal lymph node
N2	Palpable mobile multiple unilateral 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	Intranodal metastasis in a single inguinal lymph node
pN2	Metastasis in multiple or bilateral inguinal lymph nodes
pN3	Metastasis in pelvic lymph node(s), unilateral or bilateral or extranodal extension of any regional lymph node metastasis
pM - Distant Metastasis	
pM0	No distant metastasis
pM1	Distant metastasis

G - Histopathological Grading	
GX	Grade of differentiation cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3-4	Poorly differentiated/undifferentiated

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 nodes.
- In 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	GR
Primary tumour	
Perform a physical examination, record morphology, extent and invasion of penile structures.	C
Obtain MRI with artificial erection in cases for which organ-preserving surgery is intended.	
Inguinal lymph nodes	
For physical examination of both groins, record number, laterality and characteristics of inguinal nodes and: • If nodes are not palpable, offer invasive lymph node staging in high-risk patients. • If nodes are palpable, stage with a pelvic CT or PET/CT.	C
Distant metastases	
In N+ patients, obtain an abdominopelvic CT scan and chest X-ray for systemic staging. Alternatively, stage with a PET/CT scan.	C
In patients with systemic disease or with relevant symptoms, obtain a bone scan.	

CT = computed tomography; PET = positron emission tomography; MRI = magnetic resonance imaging.

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**	**LE**	**GR**
Tis	Topical treatment with 5-fluorouracil or imiquimod for superficial lesions with or without photodynamic control.	3	C
	Laser ablation with CO2 or Nd:YAG laser.		
	Glans resurfacing.		
Ta, T1a (G1, G2)	Wide local excision with circumcision CO2 or Nd:YAG laser surgery with circumcision.	3	C
	Laser ablation with CO2 or Nd:YAG laser.		
	Glans resurfacing.		
	Glansectomy with reconstructive surgery, with or without skin grafting.		
	Radiotherapy by external beam or as brachytherapy for lesions < 4 cm.		

T1b (G3) and T2 confined to the glans	Wide local excision plus reconstructive surgery, with or without skin grafting.	3	C
	Laser ablation with circumcision.		
	Glansectomy with circumcision, with reconstruction.		
	Radiotherapy by external beam or brachytherapy for lesions < 4 cm in diameter.		
T2 with invasion of the corpora cavernosa	Partial amputation and reconstruction or radiotherapy by external beam or brachytherapy for lesions <4 cm in diameter.	3	C
T3 with invasion of the urethra	Partial penectomy or total penectomy with perineal urethrostomy.	3	C
T4 with invasion of other adjacent structures	Neoadjuvant chemotherapy followed by surgery in responders. Alternative: palliative external beam radiation.	3	C
Local recurrence after conservative treatment	Salvage surgery with penis-sparing treatment in small recurrences or partial amputation.	3	C
	Large or high-stage recurrence: partial or total amputation.		

CO2 = carbon dioxide; Nd:YAG = neodymium:yttrium-aluminum-garnet.

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**	**LE**	**GR**
No palpable inguinal nodes (cN0)	Tis, Ta G1, T1G1: surveillance.	2a	B
	> T1G2: invasive lymph node staging by bilateral modified inguinal lymphadenectomy or DSNB.	2a	B
Palpable inguinal nodes (cN1/cN2)	Radical inguinal lymphadenectomy.		
Fixed inguinal lymph nodes (cN3)	Neoadjuvant chemotherapy followed by radical inguinal lymphadenectomy in responders.		

Pelvic lymphadenopathy	Ipsilateral pelvic lymphadenectomy if two or more inguinal nodes are involved on one side (pN2) and if extracapsular nodal metastasis (pN3) is confirmed.	2a	B
Adjuvant chemotherapy	In pN2/pN3 patients after radical lymphadenectomy.	2b	B
Radiotherapy	Do not use for the treatment of nodal disease in penile cancer.		

DSNB = dynamic sentinel node biopsy.

Recommendations for chemotherapy in penile cancer patients	**LE**	**GR**
Treat with adjuvant chemotherapy (3-4 cycles of TPF) in patients with pN2-3 tumours.	2b	C
Treat with neoadjuvant chemotherapy (four cycles of a cisplatin and taxane-based regimen) followed by radical surgery in patients with non-resectable or recurrent lymph node metastases.	2a	B
In patients with systemic disease and a limited metastatic load, treat with chemotherapy.	3	C

TPF = cisplatin, 5-fluorouracil paclitaxel.

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.

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.

Recommendations for follow-up in penile cancer					
	Interval of follow-up		Examinations and investigations	Minimum duration of follow-up	GR
	Years 1-2	Years 3-5			
Recommendations for follow-up of the primary tumour					
Penile-preserving treatment	3 months	6 months	Regular physician or self-examination. Repeat biopsy after topical or laser treatment for CIS.	5 years	C
Amputation	3 months	1 year	Regular physician or self-examination.	5 years	C
Recommendations for follow-up of the inguinal lymph nodes					
Surveillance	3 months	6 months	Regular physician or self-examination.	5 years	C
pN0 at initial treatment	3 months	1 year	Regular physician or self-examination. Ultrasound with FNAB optional.	5 years	C
pN+ at initial treatment	3 months	6 months	Regular physician or self-examination Ultrasound with FNAC optional, CT/ MRI optional.	5 years	C

CIS = carcinoma in situ; CT = computed tomography; FNAB = fine-needle aspiration biopsy; FNAC = fine-needle aspiration cytology; MRI = magnetic resonance imaging.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

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

(Limited text update March 2016)

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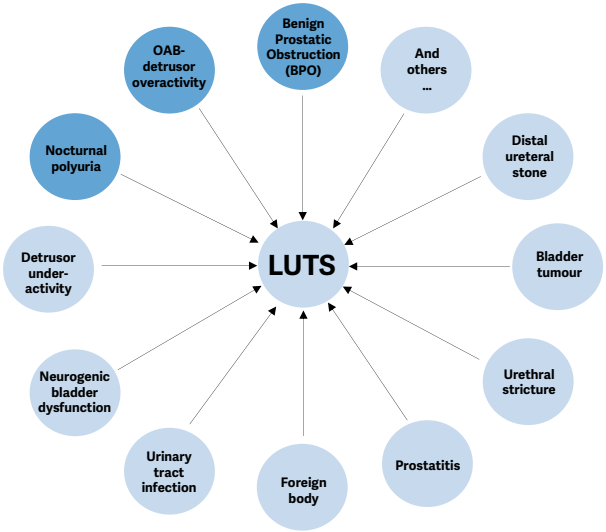
Introduction

The EAU Guidelines on Male Lower Urinary Tract Symptoms (LUTS) is a symptom-orientated guideline that mainly reviews LUTS secondary to benign prostatic enlargement (BPE) or benign prostatic obstruction (BPO), detrusor overactivity or overactive bladder, and nocturia due to 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 mean 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	LE	GR
A medical history must be taken from men with LUTS.	4	A*
A validated symptom score questionnaire with QoL assessment should be used during the assessment of male LUTS and for re-evaluation during and/or after treatment.	3	B
Micturition frequency volume charts or bladder diaries should be used to assess male LUTS with a prominent storage component or nocturia.	3	B
Frequency volume charts should be performed for the duration of at least three days.	2b	B
Physical examination including DRE should be a routine part of the assessment of male LUTS.	3	B
Urinalysis (by dipstick or urinary sediment) must be used in the assessment of male LUTS.	3	A*
PSA measurement should be performed only if a diagnosis of PCa will change the management or if PSA can assist in decision-making in patients at risk of progression of BPE.	1b	A
Renal function assessment must be performed 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.	3	A*
Measurement of post-void residual in male LUTS should be a routine part of the assessment.	3	B
Uroflowmetry in the initial assessment of male LUTS may be performed and should be performed prior to any treatment.	2b	B

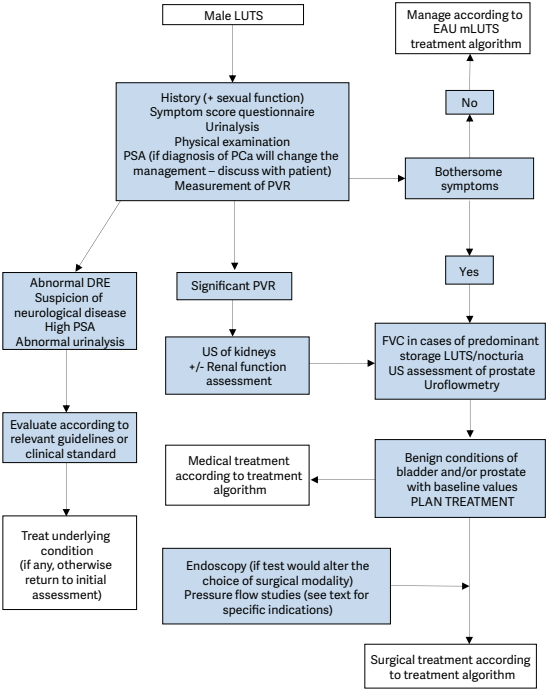
Imaging of the upper urinary tract (with US) in men with LUTS should be performed in patients with a large PVR, haematuria or a history of urolithiasis.	3	B
When considering medical treatment for male LUTS, imaging of the prostate (either by TRUS or transabdominal US) should be performed if it assists the choice of the appropriate drug.	3	B
When considering surgical treatment, imaging of the prostate (either by TRUS or transabdominal US) should be performed.	3	B
Urethrocystoscopy should be performed in men with LUTS to exclude suspected bladder or urethral pathology and/or prior to minimally invasive/surgical therapies if the findings may change treatment.	3	B
PFS should be performed only in individual patients for specific indications prior to invasive treatment or when evaluation of the underlying pathophysiology of LUTS is warranted.	3	B
PFS should be performed in men who have had previous unsuccessful (invasive) treatment for LUTS.	3	B
When considering invasive treatment, PFS may be used for patients who cannot void > 150 mL.	3	C
When considering invasive therapy in men with bothersome, predominantly voiding LUTS, PFS may be performed in men with a PVR > 300 mL.	3	C
When considering invasive treatment in men with bothersome, predominantly voiding LUTS, PFS may be performed in men aged > 80 years.	3	C

When considering invasive treatment in men with bothersome, predominantly voiding LUTS, PFS should be performed in men aged < 50 years.	3	B
None of the non-invasive tests in diagnosing bladder outlet obstruction in men with LUTS can currently be recommended as an alternative for PFS.	1a	B

**Upgraded based on Panel consensus.*
BPE = Benign prostatic enlargement; DRE = digital-rectal examination; LUTS = lower urinary tract symptoms; PCa = prostate cancer; PFS = pressure flow studies; PSA = prostate specific antigen; PVR = post-void residual; QoL = quality of life; TRUS = transrectal ultrasound; US = ultrasound.

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

Readers are strongly recommended to read the full text that highlights the current position of each test in detail.



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.

Treatment

Conservative treatment

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

Pharmacological management

The level of evidence (LE) and the grade of recommendation (GR) for each treatment option are summarised below.

Recommendations for the conservative and pharmacological management of male LUTS.	**LE**	**GR**
Offer men with mild/moderate symptoms, minimally bothered by their symptoms, watchful waiting.	1b	A
Offer men with LUTS lifestyle advice prior to or concurrent with treatment.	1b	A
Offer α1-blockers to men with moderate-to-severe LUTS.	1a	A
Offer 5α-reductase inhibitors to men who have moderate-to-severe LUTS and an enlarged prostate (>40 mL).	1b	A
5α-reductase inhibitors can prevent disease progression with regard to acute urinary retention and the need for surgery.	1b	A
Muscarinic receptor antagonists may be used in men with moderate-to-severe LUTS who mainly have bladder storage symptoms.	1b	B
Caution is advised in men with a post void residual volume greater than 150 mL.	4	C
PDE5Is may be used in men with moderate-to-severe LUTS with or without erectile dysfunction.	1a	A

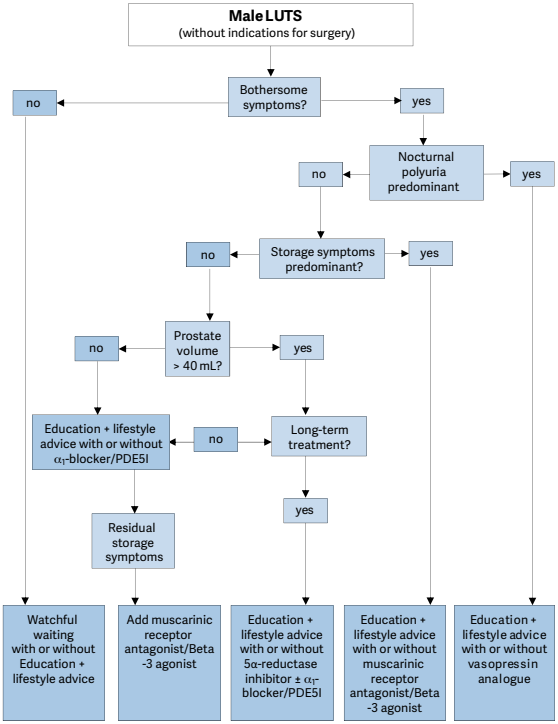
Beta-3 agonists may be used in men with moderate-to-severe LUTS who have predominantly bladder storage symptoms.	1b	B
Offer combination treatment with an α1-blocker and a 5α-reductase inhibitor to men with moderate-to-severe LUTS and risk of disease progression (e.g. prostate volume > 40mL).	1b	A
Use combination treatment of an 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.	1b	B
Prescribe combination treatment with caution in men with a post void residual volume > 150 mL.	2b	B

LUTS = lower urinary tract symptoms; PDE5Is = phosphodiesterase type 5 inhibitors.

Summary conservative and/or medical treatment

First choice of therapy is behavioural modification, with or without medical treatment. A flowchart illustrating conservative and medical 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.



LUTS = lower urinary tract symptoms;
PDE5I = phosphodiesterase type 5 inhibitor.

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 macroscopic 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 from LUTS or PVR after conservative or medical treatments (relative operation indications).

Recommendations for surgical treatment of male LUTS	LE	GR
M-TURP is the current surgical standard procedure for men with prostate sizes of 30-80 mL and bothersome moderate-to-severe LUTS secondary of BPO. M-TURP provides subjective and objective improvement rates superior to medical or minimally invasive treatments.	1a	A
The morbidity of M-TURP is higher than for drugs or other minimally invasive procedures.	1a	A
B-TURP achieves short- and mid-term results comparable with M-TURP.	1a	A
B-TURP has a more favourable peri-operative safety profile compared with M-TURP.	1a	A
TUIP is the surgical therapy of choice for men with prostate sizes < 30 mL, without a middle lobe, and bothersome moderate-to-severe LUTS secondary to BPO.	1a	A

OP or EEP such as holmium laser or bipolar enucleation are the first choice of surgical treatment in men with a substantially enlarged prostate (e.g. > 80 mL) and moderate-to-severe LUTS.	1a	A
OP has a high operative morbidity.	1b	A
TUMT achieves symptom improvement comparable with TURP, but TUMT is associated with decreased morbidity and lower flow improvements.	1a	A
Durability is in favour of TURP which has lower re-treatment rates compared to TUMT.	1a	A
TUNA™ is a minimally invasive alternative with decreased morbidity compared to TURP but with less efficacy.	1a	A
Durability is in favour of TURP with lower re-treatment rates compared to TUNA™.	1a	A
HoLEP and 532-nm laser vaporisation of the prostate are alternatives to TURP in men with moderate-to-severe LUTS leading to immediate, objective, and subjective improvements comparable with TURP.	1a	A
The short-term and mid-term functional results of 532-nm laser vaporisation of the prostate are comparable with TURP.	1b	A
The long-term functional results of HoLEP are comparable with TURP or open prostatectomy.	1b	A
Thulium enucleation may be an alternative to TURP and HoLEP in men with moderate-to-severe LUTS leading to immediate and mid-term objective and subjective improvements.	1b	A
Diode laser operations lead to short-term objective and subjective improvement.	1b	B

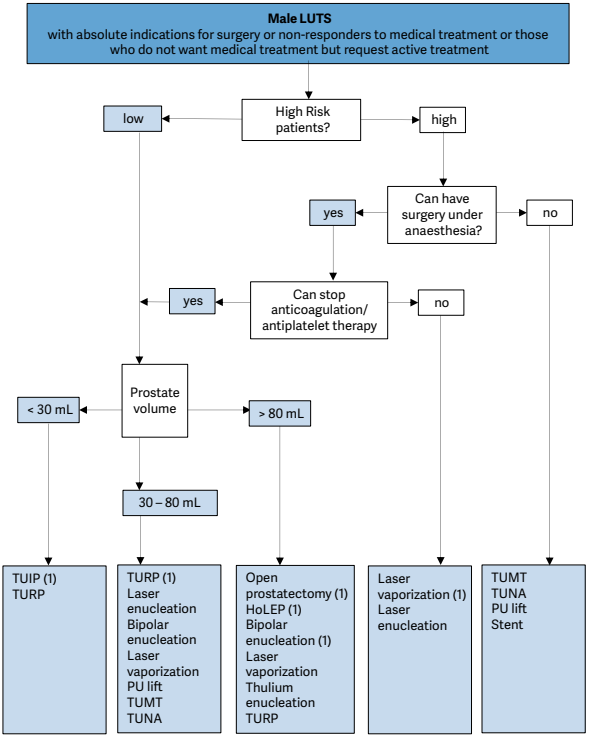
ThuVaRP is an alternative to TURP for small- and medium-size prostates.	1b	A
With regard to intra-operative safety and haemostatic properties, diode and thulium lasers appear to be safe.	3	C
With regard to intra-operative safety, 532-nm laser vaporisation is superior to TURP.	1b	A
532-nm laser vaporisation should be considered in patients receiving anticoagulant medication or with a high cardiovascular risk.	3	B
Offer prostatic stents as an alternative to catheterisation for men unfit for surgery.	3	C
Prostatic urethral lift (UroliftTM) leads to objective and subjective short- and mid-term improvements. RCTs with longer follow-up are required.	1a	B
Recommendations for investigational operations		
MISP seems to be feasible in men with prostate sizes > 80 mL needing surgical treatment. Since more data are required, MISP remains under evaluation.	2	B

TURP = transurethral resection of the prostate ; M-TURP = monopolar TURP; LUTS = lower urinary tract symptoms; BPO = benign prostatic obstruction; B-TURP = bipolar TURP; OP = open prostatectomy; EEP = enucleation of the prostate; TUMT = transurethral microwave therapy; TUNA = transurethral needle ablation; HoLEP = holmium laser enucleation; ThuVaRP = Tm:YAG vaporesection; MISP= minimal invasive simple prostatectomy; TUIP = transurethral incision of the prostate; LUTS = lower urinary tract symptoms; RCTs = randomised controlled trails.

Summary surgical treatment

The choice of the surgical technique depends on prostate size, co-morbidities, ability to undergo anaesthesia, and 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 was stratified by the patient's ability to have anaesthesia, cardiovascular risk, and prostate size.



(1) Current standard/first choice. The alternative treatments are presented in alphabetical order. *Notice*: Readers are strongly recommended to read the full text that highlights the current position of each treatment in detail.

Laser vaporisation includes GreenLight, thulium, and diode lasers vaporisation; Laser enucleation includes holmium and thulium laser enucleation.
HoLEP = holmium laser enucleation; TUIP = transurethral incision of the prostate; TUMT = transurethral microwave therapy; TUNA = transurethral needle ablation; TURP = transurethral resection of the prostate.

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

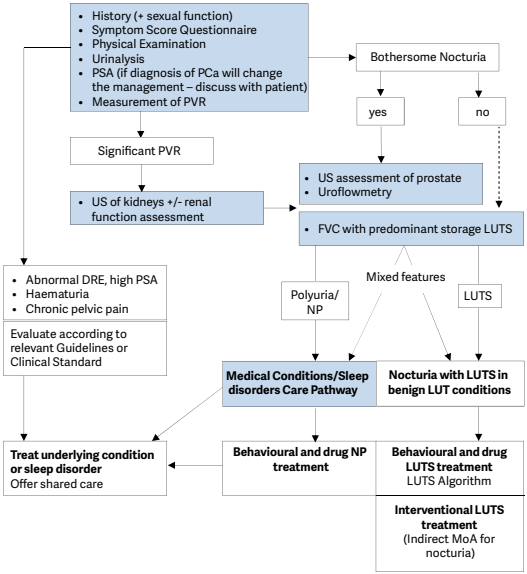


Figure 6. Shared care pathway for nocturia, highlighting the need to manage potentially complex patients using relevant expertise for the causative factors.

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	**Conservative management** • Antidiuretic • Diuretics • Drugs to aid sleep	**Management** • Initiation of therapy for new diagnosis • Optimised therapy of known conditions
Interventional therapy • Therapy of refractory storage LUTS • Therapy of refractory voiding LUTS		

* 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

Treatment for nocturia

Recommendations for treatment of nocturia	LE	GR
Treatment should aim to address underlying causative factors, which may be behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	4	A*
Discuss lifestyle changes to reduce nocturnal urine volume and episodes of nocturia, and improve sleep quality.	3	A*
Desmopressin may be prescribed to decrease nocturia due to nocturnal polyuria in men under the age of 65. Screening for hyponatremia must be undertaken at baseline, during dose titration and during treatment.	1a	A
α1-adrenergic antagonists may be offered to men with nocturia associated with lower urinary tract symptoms.	1b	B
Anti-muscarinic drugs may be offered to men with nocturia associated with overactive bladder.	1b	B
5α-reductase inhibitors may be offered to men with nocturia who have moderate-to-severe LUTS and an enlarged prostate (> 40 mL).	1b	C
Do not offer PDE5Is for the treatment of nocturia.	1b	B
A trial of timed diuretic therapy may be offered to men with nocturia due to nocturnal polyuria. Screening for hyponatremia should be undertaken at baseline and during treatment.	1b	C

Agents to promote sleep may be used to aid return to sleep in men with nocturia.	2	C

**Upgraded based on Panel consensus.*
PDE5Is = Phospodiesterase 5 inhibitors.

Follow-up

Recommended follow-up strategy:

- Patients on watchful waiting should be reviewed at 6 months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving α1-blockers, muscarinic receptor antagonists, PDE5Is, or a combination should be reviewed 4-6 weeks after drug initiation. If patients gain symptomatic relief, without troublesome side-effects, drug therapy may be continued. Patients should be reviewed at 6 months and then annually, provided symptoms do not deteriorate or absolute indications develop for surgical treatment.
- Patients receiving a 5α-reductase inhibitor should be reviewed after 12 weeks and 6 months to determine their response and adverse events.
- Patients receiving desmopressin: serum sodium concentration should be measured at day 3 and 7 and after 1 month and, if serum sodium concentration has remained normal, every 3 months subsequently; the follow-up sequence should be re-started after dose escalation.
- After prostate surgery patients should be reviewed 4-6 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 of male LUTS	LE	GR
Follow-up for all conservative, medical, or operative treatment modalities is based on empirical data or theoretical considerations, but not on evidence-based studies.	3-4	C

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 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON URINARY INCONTINENCE

(Partial text update March 2016)

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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 'graded 'action based recommendations', which follow the standard for levels of evidence used by the EAU (see Introduction chapter of the EAU Guidelines book ISBN 978-90-79754-98-4).

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	GR
Use a validated and appropriate questionnaire when standardised assessment is required	B*

** Recommendation based on expert opinion.*

Voiding Diaries

Recommendations	GR
Ask patients with urinary incontinence to complete a voiding diary	A
Use a diary duration of between 3 and 7 days.	B

Urinalysis and urinary tract infection

Recommendations	GR
Do urinalysis as a part of the initial assessment of a patient with urinary incontinence.	A*
If a symptomatic urinary tract infection is present with urinary incontinence, reassess the patient after treatment.	A*
Do not routinely treat asymptomatic bacteriuria in elderly patients to improve urinary incontinence.	B

** Recommendation based on expert opinion.*

Post-voiding residual volume

Recommendations	GR
When measuring post void residual urine volume, use ultrasound	A
Measure post-voiding residual in patients with urinary incontinence who have voiding symptoms.	B
Measure post-voiding residual when assessing patients with complicated urinary incontinence.	C
Post-voiding residual should be monitored in patients receiving treatments that may cause or worsen voiding dysfunction, including surgery for stress urinary incontinence.	A*

** Recommendation based on expert opinion.*

Urodynamics

Recommendations	GR
(NB: Concerning only neurologically intact adults with urinary incontinence)	
Clinicians carrying out urodynamics in patients with urinary incontinence should: • Ensure that the test replicates the patient's symptoms. • Interpret results in the context of the clinical problem. • Check recordings for quality control. • Remember there may be physiological variability within the same individual.	C

Advise patients that the results of urodynamics may be useful in discussing treatment options, although there is limited evidence that performing urodynamics will predict the outcome of treatment for uncomplicated urinary incontinence.	C
Do not routinely carry out urodynamics when offering treatment for uncomplicated urinary incontinence.	B
Perform urodynamics if the findings may change the choice of invasive treatment.	B
Do not use urethral pressure profilometry or leak point pressure to grade severity of incontinence or predict the outcome of treatment.	C
Urodynamic practitioners should adhere to standards defined by the International Continence Society.	C

Pad testing

Recommendations	GR
Have a standardised duration and activity protocol for pad test.	B
Use a pad test when quantification of urinary incontinence is required.	C
Use repeat pad test after treatment if an objective outcome measure is required.	C

Imaging

Recommendation	GR
Do not routinely carry out imaging of the upper or lower urinary tract as part of the assessment of urinary incontinence.	A

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 resort to those associated with higher risks.

Simple Medical Interventions

Correction of Underlying disease/cognitive impairment

Urinary incontinence, especially in the elderly, can be worsened or caused by underlying diseases, especially conditions that cause polyuria, nocturia, increased abdominal pressure or CNS disturbances. These conditions include:

- 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;
- obesity.

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	GR
Take a drug history from all patients with urinary incontinence.	A
Review any new medication associated with the development or worsening of urinary incontinence.	C

Constipation

There is no evidence to show whether or not treating constipation improves UI, although both constipation and UI appear to be improved by certain behavioural interventions.

Recommendation	GR
Adults with urinary incontinence who also suffer from constipation should be given advice about bowel management in line with good medical practice.	C

Containment (pads etc)

Recommendations	GR
Ensure that adults with urinary incontinence and/or their carers are informed regarding available treatment options before deciding on containment alone.	A*
Suggest use of disposable insert pads for women and men with light urinary incontinence.	A*
In collaboration with other healthcare professionals with expertise in urinary incontinence help adults with moderate/severe urinary incontinence to select the individually best containment regimen considering pads, external devices and catheters, and balancing benefits and harms.	A*
Choice of pad from the wide variety of different absorbent materials and designs available should be made with consideration of the individual patient's circumstance, degree of incontinence and preference.	B

** Recommendation based on expert opinion.*

Lifestyle Changes

Examples of lifestyle factors that may be associated with incontinence include obesity, smoking, level of physical

activity and diet. Modification of these factors may improve UI.

Recommendations	GR
Encourage obese women with urinary incontinence to lose weight and maintain weight loss.	A
Advise adults with urinary incontinence that reducing caffeine intake may improve symptoms of urgency and frequency but not incontinence.	B
Patients with abnormally high or abnormally low fluid intake should be advised to modify their fluid intake appropriately in line with good medical practice.	C
Counsel female athletes experiencing urinary incontinence with intense physical activity that it will not predispose to urinary incontinence in later life.	C
Patients with urinary incontinence who smoke should be given smoking cessation advice in line with good medical practice.	A

Behavioural and physical therapies

Recommendations	GR
Offer bladder training as a first-line therapy to adults with urgency urinary incontinence or mixed urinary incontinence.	A
Offer prompted voiding for adults with incontinence, who are cognitively impaired.	A
Offer supervised intensive PFMT, lasting at least 3 months, as a first-line therapy to women with stress urinary incontinence or mixed urinary incontinence.	A
PFMT programmes should be as intensive as possible.	A
Offer PFMT to elderly women with urinary incontinence.	B

Offer PFMT to post-natal women with urinary incontinence.	A
Consider using biofeedback as an adjunct in women with stress urinary incontinence.	A
Offer PFMT to men undergoing radical prostatectomy to speed recovery of incontinence.	B
Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of stress urinary incontinence.	A
Consider offering electrical stimulation as an adjunct to behavioural therapy in patients with urgency urinary incontinence.	B
Do not offer magnetic stimulation for the treatment of incontinence or overactive bladder in adult women.	B
Offer, if available, P-PTNS as an option for improvement of urgency urinary incontinence in women who have not benefitted from antimuscarinic medication.	B
Support other healthcare professionals in use of rehabilitation programmes including prompted voiding for elderly care-dependent people with urinary incontinence.	A

PFMT = pelvic floor muscle training; P-PTNS = percutaneous posterior tibial nerve stimulation.

Conservative therapy in mixed urinary incontinence

Recommendations	**GR**
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Warn patients with mixed urinary incontinence that the chance of success of pelvic floor muscle training is lower than for stress urinary incontinence alone.	B

Pharmacological management

Antimuscarinics

Recommendations	GR
Offer IR or ER formulations of antimuscarinic drugs for adults with urgency urinary incontinence.	A
If IR formulations of antimuscarinic drugs are unsuccessful for adults with urgency urinary incontinence, offer ER formulations or longer-acting antimuscarinic agents.	A
Consider using transdermal oxybutynin if oral antimuscarinic agents cannot be tolerated due to dry mouth.	B
Offer and encourage early review (of efficacy and side effects) of patients on antimuscarinic medication for urgency urinary incontinence (< 30 days).	A

IR = immediate release; ER = extended release

Antimuscarinic drugs in the elderly

Recommendations	GR
In older people being treated for urinary incontinence, every effort should be made to employ non-pharmacological treatments first.	C
Use antimuscarinic drugs with caution in elderly patients who are at risk of, or have, cognitive dysfunction.	B
Do not use oxybutynin in elderly patients who are at risk of cognitive dysfunction.	A*

In older people who are being prescribed antimuscarinic drugs for control of urinary incontinence, consider modifications to other medications to help reduce anticholinergic load.	C

** Recommendation based on expert opinion*

Mirabegron

Recommendation	GR
Offer mirabegron to people with urgency urinary incontinence, but inform patients receiving mirabegron that the possible long-term side effects remain uncertain.	B

Drugs for stress urinary incontinence

Recommendations	GR
Duloxetine should not be offered to women or men who are seeking a cure for their incontinence.	A
Duloxetine can be offered to women or men who are seeking temporary improvement in incontinence symptoms.	B*
Duloxetine should be initiated using dose titration because of high adverse effect rates.	A

** Downgraded based on expert opinion.*

Oestrogen

Recommendations	GR
Offer post-menopausal women with urinary incontinence vaginal oestrogen therapy particularly if other symptoms of vulvovaginal atrophy are present.	A
Vaginal oestrogen therapy should be long-term and in an appropriate dose	C
For women taking oral conjugated equine oestrogen as hormone replacement therapy who develop or experience worsening urinary incontinence, discuss alternative hormone replacement therapies.	A
Advise women who are taking systemic oestradiol who suffer from urinary incontinence, that stopping the oestradiol is unlikely to improve their incontinence.	A

Desmopressin

Recommendations	GR
Offer desmopressin to patients requiring occasional short-term relief from daytime urinary incontinence and inform them that this drug is not licensed for this indication.	B
Do not use desmopressin for long-term control of urinary incontinence.	A

Drug treatment in mixed urinary incontinence

Recommendations	GR
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Offer antimuscarinic drugs to patients with urgency-predominant mixed urinary incontinence.	A*
Consider duloxetine for patients with mixed urinary incontinence unresponsive to other conservative treatments and who are not seeking cure.	B

** Recommendation based on expert opinion.*

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 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 in men with post-prostatectomy incontinence without neurological disease affecting the lower urinary tract.
- Patients with refractory DO incontinence.

Women with uncomplicated stress urinary incontinence

Recommendations for surgery for uncomplicated stress urinary incontinence in women	GR
Offer the mid-urethral sling to women with uncomplicated stress urinary incontinence as the preferred surgical intervention whenever available.	A
Warn women who are being offered a retropubic insertion of mid-urethral sling about the relatively higher risk of peri-operative complications compared to transobturator insertion.	A
Warn women who are being offered transobturator insertion of mid-urethral sling about the higher risk of pain and dyspareunia in the longer term.	A
Warn women who are being offered a single-incision sling that long-term efficacy remains uncertain.	A
Do a cystourethroscopy as part of the insertion of a mid-urethral sling.	C
Offer colposuspension (open or laparoscopic) or autologous fascial sling for women with stress urinary incontinence if mid-urethral sling cannot be considered.	A
Warn women undergoing autologous fascial sling that there is a high risk of voiding difficulty and the need to perform clean intermittent self-catheterisation; ensure they are willing and able to do so.	C
Inform older women with stress urinary incontinence about the increased risks associated with surgery, including the lower probability of success.	B
Inform women that any vaginal surgery may have an impact on sexual function.	B

Only offer new devices, for which there is no level 1 evidence base, as part of a structured research programme.	A*
Only offer adjustable mid-urethral sling as a primary surgical treatment for stress urinary incontinence as part of a structured research programme.	A*
Do not offer bulking agents to women who are seeking a permanent cure for stress urinary incontinence.	A*

** Recommendation based on expert opinion.*

Complicated stress urinary incontinence in women

Recommendations for surgery for complicated stress urinary incontinence in women	GR
Management of complicated stress urinary incontinence should only be offered in expert** centres.	A*
The choice of surgery for recurrent stress urinary incontinence should be based on careful evaluation of the individual patient including mutichannel urodynamics and imaging as appropriate.	C
Warn women with recurrent stress urinary incontinence, 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.	C
Consider secondary synthetic sling, colposuspension or autologous sling as first options for women with complicated stress urinary incontinence.	C
Warn women receiving AUS or ACT that, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	C

** Recommendation based on expert opinion.*
*** Expert centres refers to the comments on surgeon volume in the introduction to the surgical chapter.*
AUS = artificial urinary sphincter; ACT = adjustable compression therapy

Women with both stress urinary incontinence and pelvic organ prolapse

Recommendations for women requiring surgery for bothersome POP who have symptomatic or unmasked stress urinary incontinence	**GR**
Offer simultaneous surgery for POP and stress urinary incontinence.	A
Warn women of the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	A
Recommendations for women requiring surgery for bothersome POP without symptomatic or unmasked stress urinary incontinence	**GR**
Warn women that there is a risk of developing de novo stress urinary incontinence after prolapse surgery.	A
Inform women that the benefit of prophylactic stress urinary incontinence surgery is uncertain.	C
Warn women that the benefit of surgery for stress urinary incontinence may be outweighed by the increased risk of adverse events with combined surgery compared to prolapse surgery alone.	A

POP = pelvic organ prolapse.
** Recommendation based on expert opinion*

Urethral diverticulum

Recommendation	**GR**
Symptomatic urethral diverticula should be completely surgically removed.	A*

**Recommendation based on expert opinion*

Men with stress urinary incontinence

Recommendations for surgery in men with stress urinary incontinence	GR
Only offer bulking agents to men with mild post-prostatectomy incontinence who desire temporary relief of incontinence symptoms.	C
Do not offer bulking agents to men with severe post-prostatectomy incontinence.	C
Offer fixed slings to men with mild-to-moderate* post-prostatectomy incontinence.	B
Warn men that severe incontinence, prior pelvic radiotherapy or urethral stricture surgery, may worsen the outcome of fixed male sling surgery.	C
Offer AUS to men with moderate-to-severe post-prostatectomy incontinence.	B
Implantation of AUS or ACT for men should only be offered in expert centres.	C
Warn men receiving AUS or ACT that, even in expert centres, there is a high risk of complications, mechanical failure or a need for explantation.	C
Do not offer non-circumferential compression device (ProACT®) to men who have had pelvic radiotherapy.	C

AUS = artificial urinary sphincter; ACT = artificial compression device.

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

Surgical interventions for refractory detrusor overactivity

Intravesical injection of botulinumtoxin A

Recommendations	GR
Offer bladder wall injections of onabotulinum toxin A (100 U) to patients with urgency urinary incontinence refractory to antimuscarinic therapy.	A
Warn patients of the limited duration of response, risk of UTI and the possible prolonged need to self-catheterise (ensure that they are willing and able to do so).	A

UTI = urinary tract infection.

Sacral nerve stimulation (neuromodulation)

Recommendation	GR
Offer sacral nerve modulation to patients who have urgency urinary incontinence refractory to antimuscarinic therapy.	A

Cystoplasty/urinary diversion

Recommendations	GR
Only offer augmentation cystoplasty to patients with detrusor overactivity incontinence who have failed conservative therapy, in whom the possibility of botulinum toxin and sacral nerve stimulation has been discussed.	C
Warn 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.	C
Do not offer detrusor myectomy as a treatment for urinary incontinence.	C
Only offer urinary diversion to patients who have failed less invasive therapies for the treatment of urinary incontinence and who will accept a stoma.	C
Warn patients undergoing augmentation cystoplasty or urinary diversion of the high risk of short-term and long-term complications, and the possible small risk of malignancy.	C
Life-long follow-up is recommended for patients who have undergone augmentation cystoplasty or urinary diversion.	C

Surgery in patients with mixed urinary incontinence

Recommendations	GR
Treat the most bothersome symptom first in patients with mixed urinary incontinence.	C
Warn patients with mixed urinary incontinence that surgery is less likely to be successful than surgery in patients with stress urinary incontinence alone.	A

Warn patients with mixed urinary incontinence 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.	A*

** Upgraded following panel consensus.*

Surgery for urinary incontinence in the elderly

Recommendation	GR
Inform older women with urinary incontinence about the increased risks associated with surgery (including onabotA injection), together with the lower probability of benefit.	B

Non Obstetric Urinary Fistula*

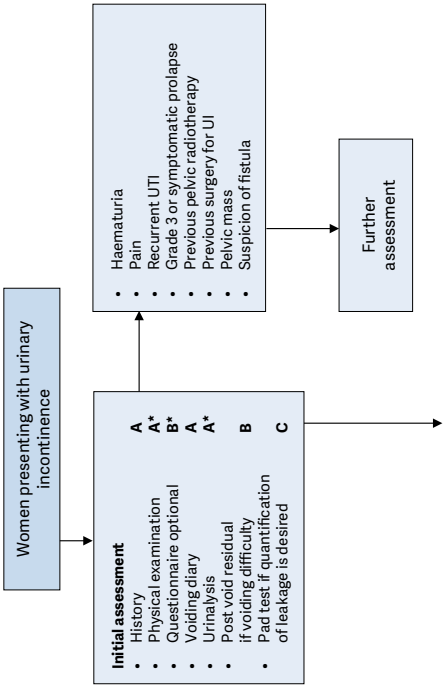
Recommendations	GR
General	
Surgeons undertaking complex pelvic surgery should be competent at identifying, preserving and repairing the ureter.	C
Do not routinely use ureteric stents as prophylaxis against injury during routine gynaecological surgery.	B
Suspect ureteric injury or fistula in patients following pelvic surgery if a fluid leak or pelvicalyceal dilatation occurs post-operatively or if drainage fluid contains high levels of creatinine.	C
Suspect uretero-arterial fistula in patients presenting with haematuria with a history of relevant surgery.	C
Use three dimensional imaging techniques to diagnose and localise urinary fistulae.	C
Manage upper urinary tract fistulae by conservative or endoluminal technique where such expertise and facilities exists.	B
Surgical principles	
Surgeons involved in fistula surgery should have appropriate training, skills, and experience to select an appropriate procedure for each patient.	C
Attention should be given as appropriate to skin care, nutrition, rehabilitation, counselling and support prior to and following fistula repair.	C
If a vesicovaginal fistula is diagnosed within six weeks of surgery, consider indwelling catheterisation for a period of up to 12 weeks after the causative event.	C
Tailor the timing of fistula repair to the individual patient and surgeon requirements once any oedema, inflammation, tissue necrosis, or infection, are resolved.	B

Where concurrent ureteric re-implantation or augmentation cystoplasty are required, the abdominal approach is necessary.	C
Ensure that the bladder is continuously drained following fistula repair until healing is confirmed (expert opinion suggests: 10-14 days for simple and/or postsurgical fistulae; 14-21 days for complex and/or post-radiation fistulae).	C
Where urinary and/or faecal diversions are required, avoid using irradiated tissue for repair.	C
Use interposition grafts when repair of radiation associated fistulae is undertaken.	C
In patients with intractable urinary incontinence from radiation-associated fistula, where life expectancy is very short, consider performing ureteric occlusion.	C
Repair persistent ureterovaginal fistula by an abdominal approach using open, laparoscopic or robotic techniques according to availability and competence.	C
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.	C
Urethrovaginal fistulae should preferably be repaired by a vaginal approach.	C

** These recommendations are derived from summarisation of the ICUD 2013 review and have not been fully validated by the EAU guidelines panel methodology.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

Figure 1: Management and treatment of women presenting with urinary incontinence.



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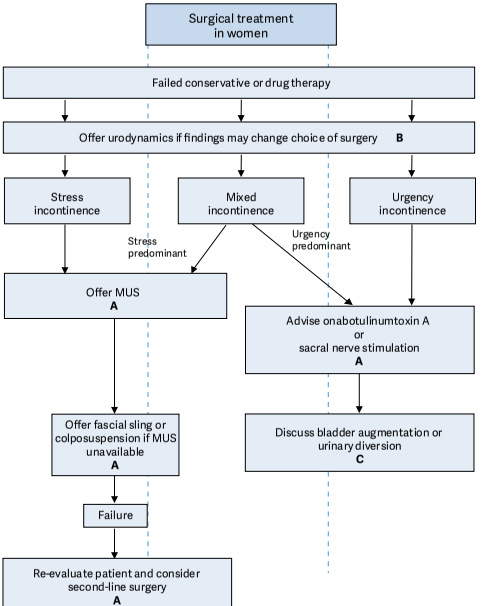
Surgical treatment in women
Failed conservative or drug therapy
Offer urodynamics if findings may change choice of surgery B
Stress incontinence
Mixed incontinence
Urgency incontinence
Stress predominant
Urgency predominant
Offer MUS A
Advise onabotulinumtoxin A or sacral nerve stimulation A
Offer fascial sling or colposuspension if MUS unavailable A
Discuss bladder augmentation or urinary diversion C
Failure
Re-evaluate patient and consider second-line surgery A

Figure 2: Management and treatment of men presenting with urinary incontinence.

** Based on expert opinion.*

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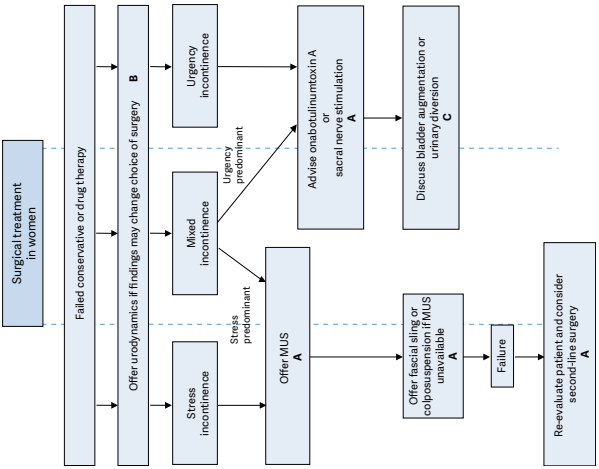
continued on page 179



** Based on expert opinion*

** Available evidence on onabotulinumtoxin A and sacral nerve stimulation refers mainly to women.*

EAU GUIDELINES ON NEURO-UROLOGY

(Limited text update March 2016)

B. Blok (Co-chair), J. Pannek (Co-chair) D. Castro-Diaz, G. del Popolo, J. Groen, R. Hamid, G. Karsenty, T.M. Kessler. Guidelines Associates: R. Boissier, H. Ecclestone, B. Padilla Fernandez, T. Gross, L. 't Hoen, S. Musco, V. Phé, M.P. Schneider

Eur Urol 2009 Jul;56(1):81-8

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 (ICS).

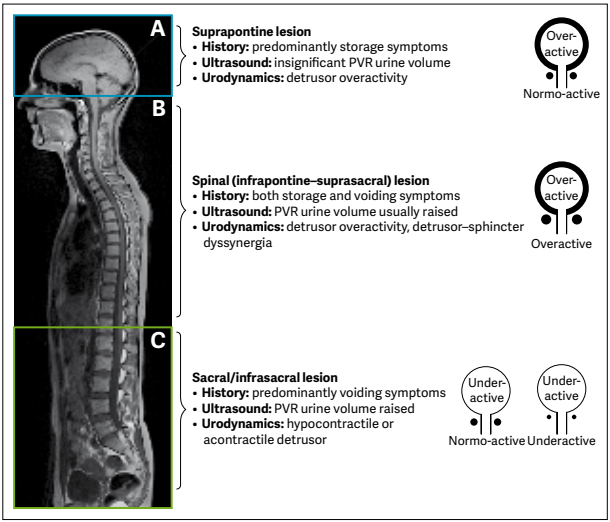
Risk factors and epidemiology

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.

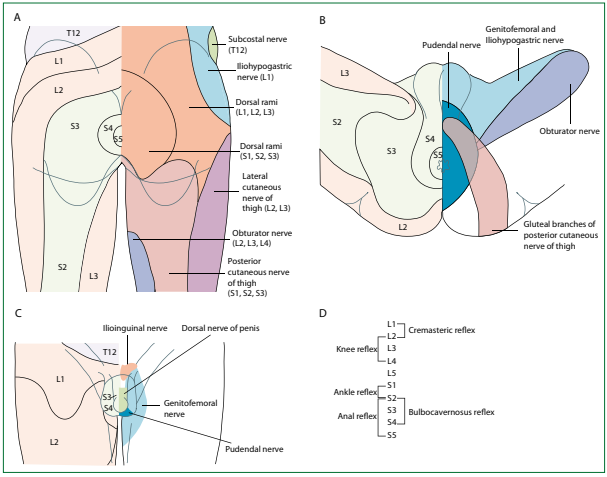
History

An extensive general and specific history is mandatory and should concentrate on past and present symptoms, disorders of the urinary tract and bowel and 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). Parts A–C adapted from Standring, with permission from Elsevier.

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 2-3 days. Uroflowmetry and ultrasound assessment of post-void residual should be repeated at least 2 or 3 times in patients able to void. Invasive urodynamic studies comprise mandatory assessment tools to determine the exact type of neuro-urological disorder.

Recommendations for urodynamics and uro-neurophysiology

Recommendations	LE	GR
The recording of a bladder diary is advisable.	3	A
Non-invasive testing is mandatory before invasive urodynamics is planned.	4	A
Urodynamic investigation is necessary to detect and specify lower urinary tract (dys-)function and same session repeat measurement is crucial in clinical decision making.	1b	A
Video-urodynamics is the gold standard for invasive urodynamics in neuro-urological patients. If this is not available, then a filling cystometry continuing into a pressure flow study should be performed.	4	A
A physiological filling rate and body-warm saline should be used.	4	A
Specific uro-neurophysiological tests are elective procedures.	4	C

Video-urodynamics combines filling cystometry and pressure flow studies with radiological imaging. Currently, videouro-dynamics is considered to provide the most comprehensive information for evaluating neuro-urological disorders.

Recommendations for history taking and physical examination*

History taking	LE	GR
An extensive general history is mandatory, concentrating on past and present symptoms including urinary, sexual, bowel, and neurological functions.	4	A
Special attention should be paid to the possible existence of alarm signs, e.g. pain, infection, haematuria, fever, that warrant further specific diagnosis.	4	A
A specific history should be taken for each of the four mentioned functions.	4	A
Quality of life should be assessed when evaluating and treating the neuro-urological patient.	2a	B
The available validated tools are the Qualiveen and I-QoL for urinary symptoms and the QoL-BM for bowel dysfunction for MS and SCI patients. In addition, generic, (SF-36 or KHQ) questionnaires can be used.	1a	A
Physical examination		
Individual patient disabilities should be acknowledged in planning further investigations.	4	A
The neurological status should be described as completely as possible. Sensations and reflexes in the urogenital area must all be tested.	4	A
The anal sphincter and pelvic floor functions must be tested.	4	A

Urinalysis, blood chemistry, bladder diary, residual and free flowmetry, incontinence quantification and urinary tract imaging should be performed.	4	A

** All grade A recommendations are based on panel consensus. MS = multiple sclerosis; SCI = spinal cord injury.*

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) the LUT function;
4. improvement of the patient's 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 it may 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, and 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 on drug treatment

Recommendations	LE	GR
For NDO, antimuscarinic therapy is the recommended first-line medical treatment.	1a	A
Alternative routes of administration (i.e., transdermal or intravesical) of antimuscarinic agents may be used.	2	A
Outcomes for NDO may be maximised by considering a combination of antimuscarinic agents.	3	B
To decrease bladder outlet resistance, alpha-blockers could be prescribed.	1b	A
For underactive detrusor, parasympathomimetics should not be prescribed.	1a	A
In neurogenic stress urinary incontinence, drug treatment should not be prescribed.	4	A

NDO = neurogenic detrusor overactivity

Recommendations for catheterisation

Recommendations	LE	GR
Intermittent catheterisation - whenever possible aseptic technique - should be used as a standard treatment for patients who are unable to empty their bladder.	3	A
Patients must be well instructed in the technique and risks of IC.	3	A
The catheter size should be 12-16 Fr.	4	B
Whenever possible, indwelling transurethral and suprapubic catheterisation should be avoided.	3	A

IC = intermittent catheterisation

Recommendations for minimal invasive treatment

Recommendations	LE	GR
Botulinum toxin injection in the detrusor is the most effective minimally invasive treatment to reduce neurogenic detrusor overactivity in MS or SCI.	1a	A
Bladder neck incision is effective in a fibrotic bladder neck.	4	B

MS = multiple sclerosis; SCI = spinal cord injury.

Recommendations for surgical treatment

Recommendations	LE	GR
In order to treat refractory neurogenic detrusor overactivity, bladder augmentation is recommended. Detrusor myectomy is an acceptable alternative in highly selected cases.	3	A

In female patients with neurogenic stress urinary incontinence who are able to self-catheterise, placement of an autologous urethral sling should be used.	4	B
In male patients with neurogenic stress urinary incontinence, an artificial urinary sphincter should be used.	3	A

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	LE	GR
Asymptomatic bacteriuria in patients with neuro-urological disorders should neither be screened for nor be treated.	4	A
The use of long-term antibiotics for recurrent UTI should be avoided.	2a	A
In patients with recurrent UTI, treatment of neuro-urological symptoms should be optimised and foreign bodies (e.g. stones, indwelling catheters) should be removed from the urinary tract.	3	A
In patients with neuro-urological disorders, UTI prophylaxis must be individualised since there is no optimal prophylactic measure available.	4	C

UTI = urinary tract infection.

Sexual (dys)function and fertility

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

Recommendations for erectile dysfunction and male fertility

Recommendations	LE	GR
In neurogenic ED, oral PDE5Is are the recommended first-line medical treatment.	1b	A
In neurogenic ED, intracavernous injections of vasoactive drugs (alone or in combination) are the recommended second-line medical treatment.	3	A
In neurogenic ED, mechanical devices such as vacuum devices and rings can be effective and may be offered to patients.	3	B
In neurogenic ED, penile prostheses should be reserved for selected patients.	4	B
In men with SCI, vibrostimulation and transrectal electroejaculation are effective methods of sperm retrieval.	3	B
In men with SCI; MESA, TESE or ICSI may be used after failed vibrostimulation and/or transrectal electroejaculation.	3	B
In men with SCI, especially at or above T6, it is essential to counsel patients at risk and fertility clinics about the potentially life-threatening condition of autonomic dysreflexia.	3	A

ED = erectile dysfunction; ICSI = intracytoplasmic sperm injection; MESA = microsurgical epididymal sperm aspiration; PDE5Is = phosphodiesterase type 5 inhibitors; SCI = spinal cord injury; TESE = testicular sperm extraction.

Recommendations on female sexuality and fertility

Recommendation	LE	GR
There is no effective medical therapy for the treatment of neurogenic sexual dysfunction in women.	4	A
In women with a neurological disease, the management of fertility, pregnancy and delivery requires a multidisciplinary approach tailored to individual patient's needs and preferences.	4	A

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	LE	GR
In high-risk patients, the upper urinary tract should be assessed at regular intervals.	4	A
In high-risk patients, physical examination, and urine laboratory should take place every year.	4	A
Any significant clinical changes should instigate further, specialised, investigation.	4	A
Urodynamic investigation is a mandatory baseline diagnostic and in high-risk patients, should be done at regular intervals.	3	A

Summary

Neuro-urological disorders present a multi-faceted 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 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON MALE SEXUAL DYSFUNCTION: Erectile Dysfunction and Premature Ejaculation

(Partial text update March 2015)

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ERECTILE DYSFUNCTION

Erectile dysfunction (ED) 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 quality of life QoL) of sufferers and their partners. There is increasing evidence that ED can 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 cardiovascular disease (CVD).

Table 1: Pathophysiology of ED

Vasculogenic	
•	Cardiovascular disease (hypertension, coronary artery disease, peripheral vasculopathy, etc)
•	Diabetes mellitus
•	Hyperlipidaemia
•	Smoking

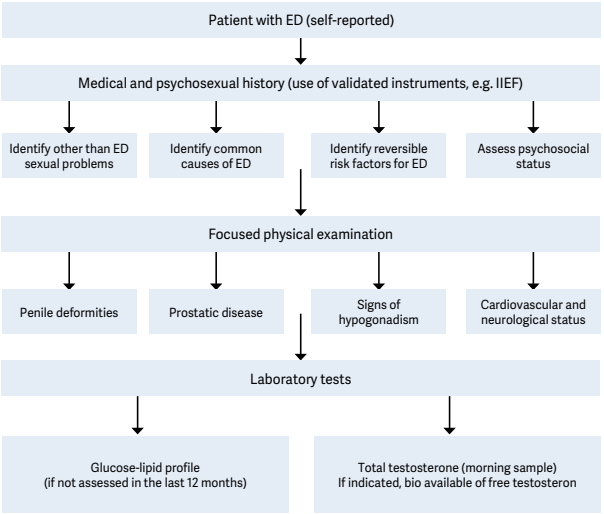
•	Major pelvic surgery (RP) or radiotherapy (pelvis or retroperitoneum)
Neurogenic	
Central causes	
•	Degenerative disorders (multiple sclerosis, Parkinson's disease, multiple atrophy, etc)
•	Spinal cord trauma or diseases
•	Stroke
•	Central nervous system tumours
Peripheral causes	
•	Type 1 and 2 diabetes mellitus
•	Chronic renal failure
•	Polyneuropathy
•	Surgery (major surgery of pelvis/retroperitoneum, RP, colorectal surgery, etc)
•	Surgery of the urethra (urethral stricture urethroplasty etc.)
Anatomical or structural	
•	Hypospadias, epispadias
•	Micropenis
•	Peyronie's disease
Hormonal	
•	Hypogonadism
•	Hyperprolactinaemia
•	Hyper- and hypothyroidism
•	Hyper- and hypocortisolism (Cushing's disease, etc)
•	Panhypopituitarism and multiple endocrine disorders
Drug-induced	
•	Antihypertensives (thiazide diuretics, etc)
•	Antidepressants (selective serotonin reuptake inhibitors, tricyclics)

•	Antipsychotics (neuroleptics, etc)
•	Antiandrogens (GnRH analogues and antagonists)
•	Recreational drugs (alcohol, heroin, cocaine, marijuana, methadone, synthetic drugs, anabolic steroids, etc.)
Psychogenic	
•	Generalised type (e.g., lack of arousability and disorders of sexual intimacy)
•	Situational type (e.g., partner-related, performance-related issues or due to distress)
Trauma	
•	Penile fracture
•	Pelvic fractures

RP = radical prostatectomy.

Diagnostic evaluation

Figure 1: Minimal diagnostic evaluation (basic work-up) in patients with ED



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

Table 2: 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)	LVD/CHF (NYHA class II)	LVD/CHF (NYHA class III/IV)
Post-successful coronary Revascularisation	Non-cardiac sequelae of Atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
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 3: Indications for specific diagnostic tests

Primary ED (not caused by organic disease or psychogenic disorder).
Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative vascular surgery.
Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital 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 his partner.
Medico-legal reasons (e.g., implantation of penile prosthesis, sexual abuse).

Table 4: Specific diagnostic tests

NTPR using Rigiscan
Vascular studies
- Intracavernous vasoactive drug injection
- Penile Dynamic Duplex Doppler study
- Penile Dynamic Infusion Cavernosometry and Cavernosography
- Internal pudendal arteriography
Neurological studies (e.g., bulbocavernosus reflex latency, nerve conduction studies)
Endocrinological studies
Specialised psychodiagnostic evaluation

Recommendations for the diagnostic evaluation of ED	LE	GR
Take a comprehensive medical and sexual history in every patient.	3	B
Use a validated questionnaire related to ED to assess all sexual function domains and the effect of a specific treatment modality.	3	B
Include a physical examination in the initial assessment of men with ED to identify underlying medical conditions that may be associated with ED.	4	B
Assess routine laboratory tests, including glucose-lipid profile and total testosterone, to identify and treat any reversible risk factors and lifestyle factors that can be modified.	4	B
Include specific diagnostic tests in the initial evaluation only in the presence of the conditions presented in table 3.	4	B

ED = erectile dysfunction.

Disease management

Figure 2: Treatment algorithm for ED

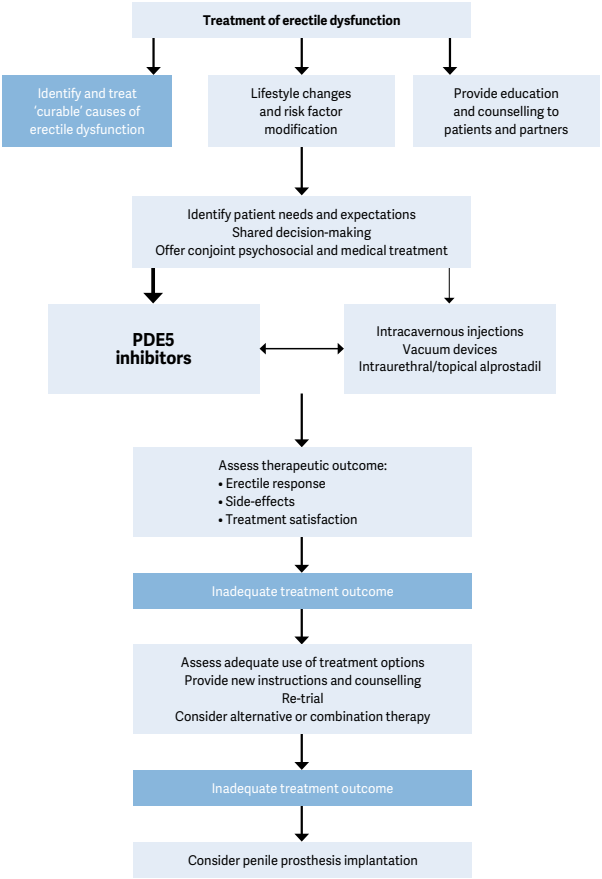


Table 5: Summary of the key pharmacokinetic data for the-four PDE5 inhibitors currently EMA-approved to treat ED*

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 h	2 h	0.9 h	0.5-0.75 h
T1/2	2.6-3.7 h	17.5 h	3.9 h	6 – 17 h
AUC	1685 µg.h/L	8066 µg.h/L	56.8 µg.h/L	11.6 µg.h/L
Protein binding	96%	94%	94%	99%
Bioavailability	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 6: Common adverse events of the four PDE5 inhibitors currently EMA-approved to treat ED*

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.*

Recommendations for the treatment of ED	LE	GR
Enact lifestyle changes and risk factor modification prior to or accompanying ED treatment.	1a	A
Start pro-erectile treatments at the earliest opportunity after RP.	1b	A
Treat a curable cause of ED first, when found.	1b	B
Use PDE5Is as first-line therapy.	1a	A
Assess all patients for inadequate/incorrect prescriptions and poor patient education, since they are the main causes of a lack of response to PDE5Is.	3	B
Use VED as a first-line therapy in well-informed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management of ED.	4	C

Use intracavernous injections as second-line therapy.	1b	B
Use implantation of a penile prosthesis as third-line therapy.	4	C

ED = erectile dysfunction; RP = radical prostatectomy; VED = vacuum erection devices; PDE5I = phosphodiesterase type 5 [inhibitors].

PREMATURE EJACULATION

Although PE is a common male sexual dysfunction, it is poorly understood. Patients are often unwilling to discuss their symptoms and many physicians do not know about effective treatments. As a result, patients may be misdiagnosed or mistreated.

PE (lifelong and acquired) is a male sexual dysfunction characterized by the following:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE).
2. The inability to delay ejaculation on all or nearly all vaginal penetrations.
3. Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

Diagnostic evaluation

Recommendations for the diagnostic evaluation of PE	LE	GR
Perform the diagnosis and classification of PE based on medical and sexual history, which should include assessment of IELT (self-estimated), perceived control, distress and interpersonal difficulty due to the ejaculatory dysfunction.	1a	A
Do not use stopwatch-measured IELT in clinical practice.	2a	B
Do not use patient-reported outcomes (PROs) in clinical practice.	3	C
Include physical examination in the initial assessment of PE to identify anatomical abnormalities that may be associated with PE or other sexual dysfunctions, particularly ED.	3	C
Do not perform routine laboratory or neurophysiological tests. They should only be directed by specific findings from history or physical examination.	3	C

PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; ED = erectile dysfunction.

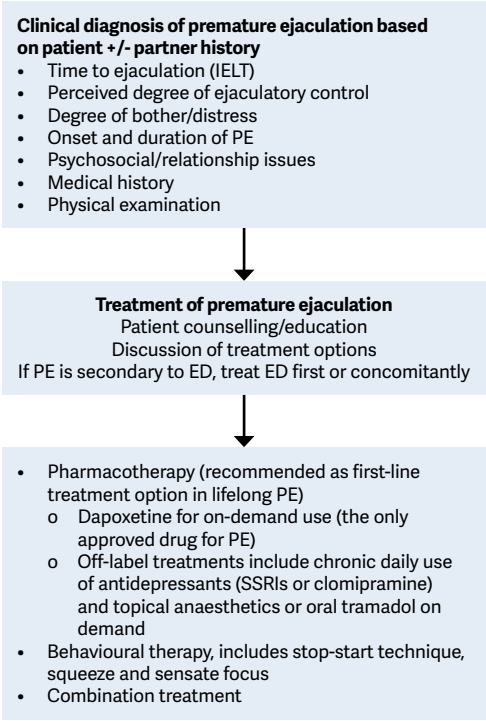
Disease management

Recommendations for the treatment of PE	LE	GR
Treat erectile dysfunction, other sexual dysfunction or genitourinary infection (e.g. prostatitis first.	2a	B
Use pharmacotherapy as first-line treatment of lifelong premature ejaculation.	1a	A

Use off-label topical anaesthetic agents as a viable alternative to oral treatment with SSRIs.	1b	A
Use tramadol on demand as a weak alternative to SSRI's.	2a	B
Do not use PDE5Is in patients with PE without ED.	3	C
Use psychological/behavioural therapies in combination with pharmacological treatment in the management of acquired premature ejaculation.	3	C

ED = erectile dysfunction; PE = premature ejaculation; PDE5Is = phosphodiesterase type 5 inhibitors; SSRI = selective serotonin reuptake inhibitor.

Figure 4: Management of PE*



** Adapted from Lue et al. 2004.*
ED = erectile dysfunction; PE = premature ejaculation; IELT = intravaginal ejaculatory latency time; SSRI = selective serotonin receptor inhibitor.

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EAU GUIDELINES ON PRIAPISM

(Text update March 2015)

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Introduction

Priapism is a pathological condition representing a true disorder of penile erection that persists more than 4 hours and is beyond or unrelated to sexual interest or stimulation. Erections lasting up to 4 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 flow distally. The patient typically complains of penile pain and examination reveals a rigid erection.

Arterial 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 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 self-limited with intervening periods of detumescence. These are analogous

to repeated episodes of low flow (or ischaemic) 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 major ischaemic priapic episode.

Ischaemic (Low-Flow or Veno-Occlusive) Priapism

Diagnostic evaluation

Table 1: Key points in taking the history of priapism

• Duration of erection
• Presence and degree 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 drugs
• Sickle cell disease, haemoglobinopathies, hypercoagulable states
• Trauma to the pelvis, perineum, or penis

Table 2: Key findings in priapism

	Ischaemic priapism	Arterial priapism
Corpora cavernosa fully rigid	Usually	Seldom
Penile pain	Usually	Seldom
Abnormal penile blood gas	Usually	Seldom
Haematological abnormalities	Usually	Seldom
Recent intracorporeal 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	GR
Take a comprehensive history for diagnosis which can help to determine the underlying type of priapism.	B
Include physical examination of the genitalia, the perineum and the abdomen in the diagnostic evaluation which may help to determine the underlying type of priapism.	B
For laboratory testing, include complete blood count, white blood count with blood cell differential, platelet count and coagulation profile. Direct further laboratory testing by the history and clinical and laboratory findings. In children with priapism, perform a complete evaluation of all possible causes.	B
Analyse blood gas of blood aspirated from the penis for the differentiation between ischaemic and arterial priapism.	B

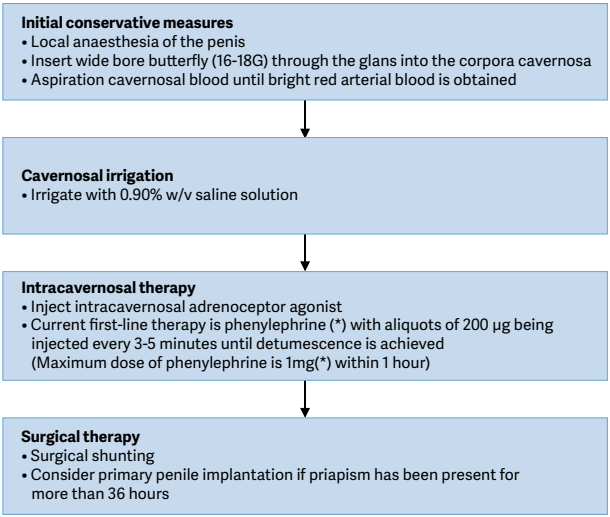
Perform colour duplex ultrasound of the penis and perineum for the differentiation between ischaemic and arterial priapism as an alternative or adjunct to blood gas analysis.	B
In cases of prolonged ischaemic priapism, use magnetic resonance imaging of the penis to predict smooth muscle viability and confirm erectile function restoration.	B
Perform selected pudendal arteriogram when embolisation is planned for the management of arterial priapism.	B

US = ultrasound.

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 and monitoring of pulse, blood pressure and 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 1 hour.
	- The 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 20-minute period.
Terbutaline	- Oral administration of 5 mg for prolonged erections lasting more than 2.5 hours that have arisen following intracavernosal injection of vasoactive agents.

Recommendations for the treatment of ischaemic priapism	GR
Start management of ischaemic priapism as early as possible (within four to six hours) and follow a step-wise approach.	B
First, decompress the corpora cavernosa by penile aspiration until fresh red blood is obtained.	C
In priapism secondary to intracavernous injections of vasoactive agents, replace blood aspiration with intra-cavernous injection of a sympathomimetic drug as the first step.	C
In priapism that persists despite aspiration, proceed to the next step, which is intracavernous injection of a sympathomimetic drug.	B
In cases that persist despite aspiration and intracav-ernous injection of a sympathomimetic drug, repeat these steps several times before considering surgical intervention.	C
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.	B
Proceed to surgical treatment only when blood aspira-tion and intracavernous injection of sympathomimetic drugs have failed or for priapism events lasting $\leq$ 72 hours.	C
Perform distal shunt surgical procedures first followed by proximal procedures in case of failure.	C
Discuss the immediate implantation of a penile pros-thesis with the patient in cases of priapism presenting > 36 hours after onset, or in cases for which all other interventions have failed.	B

Arterial (High-Flow or Non-Ischaemic) Priapism

Diagnostic evaluation

History

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

Recommendations for the diagnosis of arterial priapism

The same recommendations as for ischaemic priapism apply.

Disease management

Recommendations for the treatment of arterial priapism	GR
Because high-flow priapism is not an emergency, perform definitive management at the discretion of the treating physician.	B
Manage conservatively with the use of ice applied to the perineum or site-specific perineal compression as the first step, especially in children. Use androgen deprivation therapy only in adults.	C
Perform selective artery embolisation, using temporary or permanent substances.	B
Repeat the procedure for the recurrence of arterial priapism following selective artery embolisation.	B
Reserve selective surgical ligation of the fistula as a final treatment option when embolisation has failed.	C

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	GR
Manage each acute episode similar to that for ischaemic priapism.	B
Use hormonal therapies (mainly GnRH agonists or antagonists) and/or antiandrogens for the prevention of future episodes in patients with frequent relapses. Do not use them before sexual maturation is reached.	C
Initiate treatment with PDE5Is only when the penis is in its flaccid state.	C
Use digoxin, α-adrenergic agonists, baclofen, gabapentin or terbutaline) only in patients with very frequent and uncontrolled relapses.	C
Use intracavernosal self-injections at home of sympathomimetic drugs for the treatment of acute episodes on an interim basis until ischaemic priapism has been alleviated.	C

GnRH = gonadotropin-receptor hormone
PDE5Is = phosphodiesterase type 5 inhibitors

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EAU GUIDELINES ON PENILE CURVATURE

(February 2012)

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Introduction

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

Diagnostic evaluation

Taking medical and sexual history are usually sufficient to establish the diagnosis of congenital penile curvature. Patients usually present after reaching puberty as the curvature becomes more apparent with erections, and 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 procedure with excision of an ellipse of the tunica albuginea is the gold standard of 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 is required in order to avoid loss of sensation and ischemia to the glans penis.

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. A prolonged inflammatory response will result in the remodelling of connective tissue into a fibrotic plaque. Penile plaque formation can result in curvature which, if severe, may prevent vaginal intromission.

The most commonly associated comorbidities and risk factors are diabetes, hypertension, lipid abnormalities, ischaemic cardiopathy, erectile dysfunction (ED), smoking, and excessive consumption of alcohol.

Two phases of the disease can be distinguished. The first is the acute inflammatory phase, which may be associated with pain in the flaccid state or painful erections and a palpable nodule or plaque in the tunica of the penis; typically a penile curvature begins to develop. The second is the fibrotic phase with the formation of hard palpable plaques that can be calcified, which also results in disease stabilisation.

Diagnostic evaluation

The aim of the initial evaluation is to provide information on the presenting symptoms and their duration (erectile pain, palpable nodules, curvature, length, rigidity, and girth) and erectile function status. It is mandatory to obtain information on the distress provoked by the symptoms and the potential risk factors for erectile dysfunction and Peyronie's disease.

Major attention should be given to whether the disease is still active, as this will influence medical treatment or the timing of surgery. Patients who are still likely to have an active disease are those with short symptom duration, pain during erection, or a recent change in penile curvature.

The examination should start with a routine genitourinary assessment, which is then extended to the hands and feet for detecting possible Dupuytren's contracture or Ledderhose scarring of the plantar fascia. Penile examination consists generally of a palpable node or plaque. Measurement of length during erection is important because it may have impact on treatment decisions.

Erectile dysfunction is common in patients with Peyronie's disease (> 50%) but it is important to define whether it pre- or post-dates the onset of Peyronie's disease.

Recommendations for the evaluation of Peyronie's disease	**LE**	**GR**
In the medical and sexual history in patients with Peyronie's disease, include duration of the disease, penile pain, change of penile deformity, difficulty in vaginal intromission due to deformity, and erectile dysfunction.	2b	B
In the physical examination, include assessment of palpable plaques, penile length, extent of curvature (self-photograph, vacuum-assisted erection test or pharmacological-induced erection) and any other possibly related diseases (Dupuytren's contracture, Ledderhose disease).	2a	B
Do not use PDQ in everyday clinical practice.	2a	B
Do not use ultrasound measurement of plaque size in everyday clinical practice.	3	C

Use Doppler US only in the case of diagnostic evaluation of ED, to ascertain vascular parameters associated with erectile dysfunction.	2a	B

PDQ = Peyronie's disease-specific questionnaire; US = ultrasound.

Disease management

Non-operative treatment

Clostridium collagenase is the only drug approved for the treatment of Peyronie's disease by the FDA. No single drug has been approved by the European Medicines Agency (EMA) for the treatment of Peyronie's disease at this time.

Table 1: Non-operative treatments for Peyronie's disease

Oral treatments
Vitamin E
Potassium para-aminobenzoate (Potaba)
Tamoxifen
Colchicine
Acetyl esters of carnitine
Pentoxifylline
Phosphodiesterase type 5 inhibitors (PDE5i)
Intralesional treatments
Steroids
Verapamil
Clostridium collagenase
Interferon
Topical treatments
Verapamil
Iontophoresis
Extracorporeal shock wave treatment (ESWT)
Traction devices
Vacuum devices

Recommendations for non-operative treatment of Peyronie's disease	LE	GR
Use conservative treatment in patients not fit for surgery or when surgery is not acceptable to the patient.	3	C
Do not use extracorporeal shock-wave treatment to improve penile curvature and plaque size.	1b	C
Use penile traction devices and vacuum devices to reduce penile deformity and increase penile length.	2b	C
Do not use intralesional treatment with steroids to reduce penile curvature, plaque size or pain.	1b	B
Do not use oral treatment with vitamin E and tamoxifen for significant reduction in penile curvature or plaque size.	2b	B
Do not offer other oral treatments (acetyl esters of carnitine, pentoxifylline, colchicine).	3	C

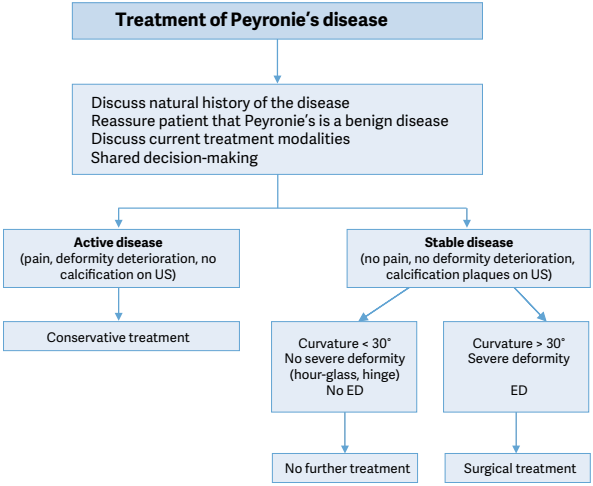
Surgical treatment

Recommendations for the surgical treatment of penile curvature	LE	GR
Perform surgery only when Peyronie's disease has been stable for at least 3 months (without pain or deformity deterioration), which is usually the case after 12 months from the onset of symptoms, and intercourse is compromised due to deformity.	3	C
Prior to surgery, assess penile length, curvature severity, erectile function (including response to pharmacotherapy in case of erectile dysfunction) and patient expectations.	3	C
Use tunical shortening procedures, especially plication techniques as the first treatment option for congenital penile curvature and for Peyronie's disease with adequate penile length, curvature < 60° and absence of special deformities (hour-glass, hinge).	2b	B
Use grafting techniques for patients with Peyronie's disease and normal erectile function, with no adequate penile length, curvature > 60° and presence of special deformities (hour-glass, hinge).	2b	B
Use penile prosthesis implantation, with or without any additional procedure (modelling, plication or grafting), in Peyronie's disease patients with erectile dysfunction not responding to pharmacotherapy.	2b	B

Table 2: Types of grafts used in Peyronie's disease surgery

Autologous grafts
Dermis
Vein grafts
Tunica albuginea
Tunica vaginalis
Temporalis fascia
Buccal mucosa
Allografts
Cadaveric pericardium
Cadaveric fascia lata
Cadaveric dura matter
Cadaveric dermis
Xenografts
Porcine small intestinal submucosa
Bovine pericardium
Porcine dermis
Synthetic grafts
Gore-Tex
Dacron

Figure 1: Treatment algorithm for Peyronie's disease



This short booklet text is based on the more comprehensive EAU Guidelines (978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON MALE INFERTILITY

(Limited text update March 2016)

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Introduction

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

Epidemiology and aetiology

About 15% of couples do not achieve pregnancy within one year and seek medical treatment for infertility.

Male fertility can be reduced as a result of:

- congenital or acquired urogenital abnormalities;
- malignancies;
- urogenital tract infections;
- increased scrotal temperature (e.g. as a consequence of varicocele);
- endocrine disturbances;
- genetic abnormalities;
- immunological factors.

Prognostic factors

The main factors influencing the prognosis in infertility are:

- duration of infertility;

- primary or secondary infertility;
- results of semen analysis;
- age and fertility status of the female partner.

Diagnostic evaluation

The diagnosis of male fertility should focus on a number of prevalent disorders (Table 1). Simultaneous assessment of the female partner is preferable, even if abnormalities are found in the male, since data show that in 1 out of 4 couples both male and female partners have pathological findings.

Semen analysis

A comprehensive andrological examination is indicated if semen analysis shows abnormalities compared with reference values (Table 1).

Table 1: 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.

It is important to differentiate between the following:

- oligozoospermia: spermatozoa < 15 million/mL;
- asthenozoospermia: < 32% progressive motile spermatozoa;
- teratozoospermia: < 4% normal forms.

Recommendations	GR
Perform semen analyses according to the guidelines of the WHO Laboratory Manual for the Examination and Processing of Human Semen (5th edn).	A*
Perform further andrological assessment when semen analysis is abnormal in at least two tests.	A*
Adhere to the 2010 WHO Manual for the standardised investigation, diagnosis and management of the infertile male for diagnosis and evaluation of male subfertility.	C

**Upgraded following panel consensus.*

Primary Spermatogenic Failure

Diagnostic evaluation

Routine investigations include semen analysis and hormonal determinations. Other investigations may be required depending on the individual situation.

Semen analysis

In non-obstructive azoospermia (NOA), semen analysis shows normal ejaculate volume and azoospermia after centrifugation. A recommended method is semen centrifugation at 3000 g for 15 min and a thorough microscopic examination by phase contrast optics at ×200 magnification of the pellet. All samples can be stained and re-examined microscopically.

Hormonal determinations

In men with testicular deficiency, hypergonadotropic hypogonadism is usually present, with elevated levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH), and sometimes low levels of testosterone. Generally, the levels of FSH correlate with the number of spermatogonia and are elevated when spermatogonia are absent or markedly dimin-

ished. Spermatocytic arrest is typically associated with normal FSH.

Testicular biopsy

Testicular biopsy and testicular sperm extraction (TESE) can be part of intracytoplasmic sperm injection (ICSI) treatment in patients with clinical evidence of NOA.

Recommendations	GR
For men who are candidates for sperm retrieval, give appropriate genetic counselling - also when testing for genetic abnormalities was negative.	A
In men with NOA, perform simultaneous testicular biopsy with multiple TESE (or micro TESE) to define spermatogenesis and diagnose ITGCNU.	A

ICSI = intracytoplasmic sperm injection; ITGCNU = intratubular germ cell neoplasma of unclassified type; TESE = testicular sperm extraction; NOA = non-obstructive azoospermia.

Genetic Disorders in Infertility

Current routine clinical practice is based on the screening of genomic DNA from peripheral blood samples, however, screening of chromosomal anomalies in spermatozoa is also feasible and can be performed in selected cases.

Recommendations	GR
Obtain standard karyotype analysis in all men with damaged spermatogenesis (spermatozoa < 10 million/mL) who are seeking fertility treatment by IVF.	B
Provide genetic counselling in all couples with a genetic abnormality found in clinical or genetic investigation and in patients who carry a (potential) inheritable disease.	A

For all men with Klinefelter's syndrome, provide long-term endocrine follow-up and androgen replacement therapy, if necessary.	A
Do not test for microdeletions in men with obstructive azoospermia (OA) when ICSI is used because spermatogenesis should be normal.	A
Inform men with Yq microdeletion and their partners who wish to proceed with ICSI that microdeletions will be passed to sons, but not to daughters.	A
In men with structural abnormalities of the vas deferens (unilateral or bilateral absence), test the man and his partner for CFTR gene mutations.	A

IVF = in vitro fertilisation; OA = obstructive azoospermia; FSH = follicle-stimulating hormone; ICSI = intracytoplasmic sperm injection; TESE = testicular sperm extraction; CFTR = transmembrane conductance regulator; CF = cystic fibrosis.

Obstructive Azoospermia

Obstructive azoospermia (OA) is the absence of spermatozoa and spermatogenetic cells in semen and post-ejaculate urine due to obstruction. Sometimes, the vas deferens is absent (CBAVD or CUAVD). Obstruction in primary infertile men is frequently present at the epididymal level.

Diagnostic evaluation

Clinical examination should follow suggestions for the diagnostic evaluation of infertile men. The following findings indicate OA:

- At least one testis with a volume > 15 mL, although a smaller volume may be found in some patients with OA and concomitant partial testicular failure.
- Enlarged and hardened epididymis.

- Nodules in the epididymis or vas deferens.
- Absence or partial atresia of the vas.

Semen analysis

At least two examinations must be carried out at an interval of one to two months, according to the WHO. When semen volume is low, a search must be made for spermatozoa in urine after ejaculation. Absence of spermatozoa and immature germ cells in semen smears suggest complete seminal duct obstruction.

Hormone levels

Serum FSH levels may be normal, but do not exclude a testicular cause of azoospermia.

Ultrasonography

In addition to physical examination, a scrotal ultrasound may be helpful in finding signs of obstruction (e.g., dilatation of rete testis, enlarged epididymis with cystic lesions, or absent vas deferens) and may demonstrate signs of testicular dysgenesis (e.g., non-homogeneous testicular architecture and microcalcifications) and testis tumours.

Testicular biopsy

In selected cases, testicular biopsy is indicated to exclude spermatogenic failure. Testicular biopsy should be combined with extraction of testicular spermatozoa (i.e. TESE) for cryopreservation.

Recommendations	GR
For azoospermia caused by vasal or epididymal obstruction, perform microsurgical vasovasostomy or tubulovasostomy.	B

Use sperm retrieval techniques, such as MESA, TESE, and PESA only when cryostorage of the material obtained is available.	B

CBAVD = Congenital Bilateral Absence of the Vas Deferens; CUAVD = Congenital Unilateral Absence of the Vas Deferens

Varicocele

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

- Failure of ipsilateral testicular growth and development.
- Symptoms of pain and discomfort.
- Male subfertility.
- Hypogonadism.

Diagnostic evaluation

The diagnosis of varicocele is made by clinical examination and should be confirmed by colour Duplex analysis. In centres where treatment is carried out by antegrade or retrograde sclerotherapy or embolisation, diagnosis is additionally confirmed by X-ray.

Disease management

Several treatments are available for varicocele. Current evidence indicates that microsurgical varicocelectomy is the most effective with the lowest complication rate among the varicocelectomy techniques.

Recommendations	GR
Treat varicoceles in adolescents with progressive failure of testicular development documented by serial clinical examination.	B
Do not treat varicoceles in infertile men who have normal semen analysis and in men with a subclinical varicocele.	A

Treat varicoceles in men with a clinical varicocele, oligospermia and otherwise unexplained infertility in the couple.	A

Hypogonadism

Idiopathic hypogonadotropic hypogonadism

Idiopathic hypogonadotropic hypogonadism is characterised by low levels of gonadotropins and sex steroid in the absence of anatomical or functional abnormalities of the hypothalamicpituitary-gonadal axis.

Hypergonadotropic hypogonadism

Many conditions in men are associated with hypergonadotropic hypogonadism and impaired fertility (e.g. anorchia, maldescended testes, Klinefelter's syndrome, trauma, orchitis, systemic diseases, testicular tumour, varicocele etc).

Recommendations	GR
Provide testosterone replacement therapy for symptomatic patients with primary and secondary hypogonadism who are not considering parenthood.	A
In men with hypogonadotropic hypogonadism, induce spermatogenesis by an effective drug therapy (hCG/hMG/rFSH).	A*
Do not use testosterone replacement for the treatment of male infertility.	A*

**Upgraded following panel consensus.*
FSH = follicle-stimulating hormone; LH = luteinising hormone.

Cryptorchidism

The aetiology of cryptorchidism is multifactorial, involving disrupted endocrine regulation and several gene defects. It

has been postulated that cryptorchidism may be a part of the so-called testicular dysgenesis syndrome (TDS), which is a developmental disorder of the gonads caused by environmental and/or genetic influences early in pregnancy. Besides cryptorchidism, TDS may include hypospadias, reduced fertility, increased risk of malignancy, and Leydig cell dysfunction.

Recommendations	GR
Do not use hormonal treatment of cryptorchidism in adults.	A
If undescended testes are corrected in adulthood, perform simultaneous testicular biopsy for detection of ITGCNU (formerly CIS).	B

CIS = carcinoma in situ; ITGCNU = intratubular germ cell neoplasia of unclassified type.

Idiopathic Male Infertility

Recommendation	GR
Use medical treatment of male infertility only for cases of hypogonadotropic hypogonadism.	A
No recommendation can be made for treatment with gonadotropins, anti-oestrogens and antioxidants even for a subset of patients.	B

Male Contraception

Recommendations	GR
Vasectomy is the gold standard for the male contribution to permanent contraception.	A
Cauterisation and fascial interposition are the most effective techniques for the prevention of early recanalisation.	A
Inform patients seeking vasectomy about the surgical method, risk of failure, potential irreversibility, the need for post-procedure contraception until clearance, and the risk of complications.	A*
To achieve pregnancy, MESA/PESA/TESE - together with ICSI is a second-line option for men who decline a vasectomy reversal and those with failed vasectomy reversal surgery.	B

**Upgraded following panel consensus*
MESA = microsurgical epididymal sperm aspiration;
PESA = percutaneous epididymal sperm aspiration;
TESE = testicular sperm extraction; ICSI = intracytoplasmic sperm injection.

Male Accessory Gland Infections and Infertility

Diagnostic evaluation

Ejaculate analysis

Ejaculate analysis clarifies whether the prostate is involved as part of a generalised male accessory gland infection and provides information about sperm quality.

Microbiological findings

After exclusion of urethritis and bladder infection, $>10^6$ peroxidase-positive white blood cells (WBCs) per millilitre of ejaculate indicate an inflammatory process. In this case, a culture

should be performed for common urinary tract pathogens.

Epididymitis

Inflammation of the epididymis causes unilateral pain and swelling, usually with acute onset.

Diagnostic evaluation

Ejaculate analysis

Ejaculate analysis according to WHO criteria, might indicate persistent inflammatory activity.

Disease management

Antibiotic therapy is indicated before culture results are available.

Recommendation	GR
Instruct patients with epididymitis that is known or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* to refer their sexual partners for evaluation and treatment.	B

Germ Cell Malignancy and Testicular Microcalcification (TM)

Recommendations	GR
As for all men, encourage patients with TM and without special risk factors (see below) to perform self-examination because this might result in early detection of TGCT.	B
Do not perform testicular biopsy, follow-up scrotal ultrasound, routine use of biochemical tumour markers, or abdominal or pelvic CT, in men with isolated TM without associated risk factors (e.g. infertility, cryptorchidism, testicular cancer, and atrophic testis).	B
Perform testicular biopsy for men with TM, who belong to one of the following high-risk groups: infertility and bilateral TM, atrophic testes, undescended testes, a history of TGCT.	B
If there are suspicious findings on physical examination or ultrasound in patients with TM and associated lesions, perform surgical exploration with testicular biopsy or orchidectomy.	B
Follow men with TGCT because they are at increased risk of developing hypogonadism and sexual dysfunction.	B

TM = testicular microlithiasis; TGCT = testicular germ cell tumour; CT = computed tomography.

Disorders of Ejaculation

Disorders of ejaculation are uncommon, but important causes of male infertility.

Diagnostic evaluation

Diagnostic management includes the following recommended procedures.

1. Clinical history
2. Physical examination
3. Post-ejaculatory urinalysis
4. Microbiological examination
5. Optional diagnostic work-up

This diagnostic work-up can include:

- neurophysiological tests (bulbocavernosus evoked response and dorsal nerve somatosensory evoked potentials);
- tests for autonomic neuropathy;
- psychosexual evaluation;
- videocystometry;
- cystoscopy;
- transrectal ultrasonography;
- uroflowmetry;
- vibratory stimulation of the penis.

Disease management

The following aspects must be considered when selecting treatment:

- Age of patient and his partner.
- Psychological problems of the patient and his partner.
- Couple's willingness and acceptance of different fertility procedures.
- Associated pathology.
- Psychosexual counselling.

Recommendations	GR
Offer aetiological treatments for ejaculatory disorders before performing sperm collection and ART.	B
To treat disorders of ejaculation, offer pharmacological treatment of either dapoxetine on demand (a short-acting SSRI that is the only approved pharmacological treatment for premature ejaculation) or other off-label antidepressants, i.e. daily SSRIs and clomipramine, that are not amenable to on-demand dosing.	A
Alternatively offer topical anaesthetics or tramadol.	A

ART = assisted reproduction technique; SSRIs = selective serotonin reuptake inhibitors.

Semen cryopreservation

Recommendations	GR
Offer cryopreservation of semen to all men who are candidates for chemotherapy, radiation or surgical interventions that might interfere with spermatogenesis or cause ejaculatory disorders.	A
Offer simultaneous sperm cryopreservation if testicular biopsies will be performed for fertility diagnosis.	A
If cryopreservation is not available locally, inform patients about the possibility of visiting, or transferring to a cryopreservation unit before therapy starts.	C

Take precautions to prevent transmission of viral, sexually transmitted or any other infection by cryostored materials from donor to recipient, and to prevent contamination of stored samples. These precautions include testing of the patient and the use of rapid testing and quarantine of samples until test results are known. Do not store samples from men who are positive for hepatitis virus or HIV. It must not be stored in the same container as samples from men who have been tested and are free from infection.	C

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON MALE HYPOGONADISM

(Text update March 2015)

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Introduction

Male hypogonadism is a clinical syndrome caused by androgen deficiency which may adversely affect multiple organ functions and quality of life. Androgen deficiency increases slightly with age. In middle-aged men the incidence is 6%. Hypogonadism is more prevalent in older men, in men with obesity, those with co-morbidities, and in men with a poor health status.

Aetiology and classification

Male hypogonadism can be classified in accordance with disturbances at the level of:

- the testes (primary hypogonadism);
- the hypothalamus and pituitary (secondary hypogonadism);
- the hypothalamus/pituitary and gonads (hypogonadism in adult men);
- androgen target organs (androgen insensitivity/resistance).

Table 1: Most common forms of primary hypogonadism

Disease	Pathophysiology
Maldescended or ectopic testes	Failure of testicular descent, maldevelopment of the testis
Testicular cancer	Testicular maldevelopment
Orchitis	Viral or unspecific orchitis
Acquired anorchia	Trauma, tumour, torsion, inflammation, iatrogenic, surgical removal
Secondary testicular dysfunction	Medication, drugs, toxins, systemic diseases
(Idiopathic) testicular atrophy	Male infertility (idiopathic or specific causes)
Congenital anorchia (bilateral in 1 in 20,000 males, unilateral 4 times as often)	Intrauterine torsion is the most probable cause
Klinefelter syndrome 47,XXY	Sex-chromosomal non-disjunction in germ cells

Table 2: Most common forms of secondary hypogonadism

Disease	Pathophysiology
Hyperprolactinemia	Prolactin-secreting pituitary adenomas (prolactinomas) or drug-induced
Isolated hypogonadotropic hypogonadism (IHH) (formerly termed idiopathic hypogonadotropic hypogonadism)	SGnRH deficiency specific (or unknown) mutations affecting GnRH synthesis or action

Kallmann syndrome (hypogonadotropic hypogonadism with anosmia) (prevalence 1 in 10,000)	GnRH deficiency and anosmia, genetically determined
Secondary GnRH deficiency	Medication, drugs, toxins, systemic diseases
Hypopituitarism	Radiotherapy, trauma, infections, haemochromatosis and vascular insufficiency or congenital
Pituitary adenomas	Hormone-secreting adenomas; hormone-inactive pituitary adenomas; metastases to the pituitary or pituitary stalk

Recommendation	**LE**	**GR**
Differentiate the two forms of hypogonadism (primary and secondary) (LH levels), as this has implications for patient evaluation and treatment and makes it possible to identify patients with associated health problems and infertility.	1b	B

LH = luteinising hormone; GnRH = gonadotropin-releasing hormone.

Diagnostic evaluation

Table 3: Signs and symptoms suggesting prepubertal-onset hypogonadism

Small testes
Cryptorchidism
Gynaecomastia
High pitched voice
Unclosed epiphyses
Linear growth into adulthood
Eunuchoid habitus
Sparse body hair/facial hair
Infertility
Low bone mass
Sarcopenia
Reduced sexual desire/activity

Table 4: Signs and symptoms associated with adult-onset hypogonadism

Loss of libido
Erectile dysfunction
Fewer and decreased morning erections
Overweight or obesity
Sarcopenia
Low bone mass
Depressive thoughts
Fatigue
Loss of body hair
Hot flushes
Loss of vigour

Recommendations diagnostic evaluation	LE	GR
Restrict the diagnosis of testosterone deficiency to men with persistent symptoms suggesting hypogonadism (Table 3).	3	C
Measure testosterone in the morning before 11.00 hours in the fasting state.	2	A
Repeat total testosterone assessment on at least two occasions with a reliable method. In addition, measure the free testosterone level in men with: - Total testosterone levels close to the lower normal range (8-12 nmol/L), to strengthen the laboratory assessment. - Suspected or known abnormal sex hormone-binding globulin (SHBG) levels.	1	A
Assess testosterone in men with a disease or treatment in which testosterone deficiency is common and in whom treatment may be indicated. This includes men with: - Type 2 diabetes. - Metabolic syndrome - Obesity. - Pituitary mass, following radiation involving the sellar region and other diseases in the hypothalamic and sellar region. - End-stage renal disease receiving haemodialysis. - Treatment with medications that cause suppression of testosterone levels - e.g. corticosteroids and opiates. - Moderate to severe chronic obstructive lung disease. - Infertility.	2	B

- Osteoporosis or low-trauma fractures. - HIV infection with sarcopenia.		
Analyse LH serum levels to differentiate between primary and secondary forms of hypogonadism.	2	A

Recommendations for screening men with adult-onset hypogonadism	**LE**	**GR**
Screen for testosterone deficiency only in adult men with consistent and multiple signs and symptoms listed in Table 3 and 4.	3	C
In adult men with established hypogonadism, screen for concomitant osteoporosis.	2	B

Disease management

Table 5: Indications for testosterone treatment

Delayed puberty (idiopathic, Kallmann syndrome)
Klinefelter syndrome with hypogonadism
Sexual dysfunction and low testosterone
Low bone mass in hypogonadism
Adult men with low testosterone and consistent and preferably multiple signs and symptoms of hypogonadism (listed in Table 3 and 4) following unsuccessful treatment of obesity and comorbidities
Hypopituitarism
Testicular dysgenesis and hypogonadism
Type 2 diabetes mellitus with hypogonadism

Table 6: Contraindications against testosterone treatment

Prostate cancer
PSA > 4 ng/mL
Male breast cancer
Severe sleep apnoea
Male infertility-active desire to have children
Haematocrit > 0.54%
Severe lower urinary tract symptoms due to benign prostatic hyperplasia
Severe chronic cardiac failure/New York Heart Association Class IV
Uncontrolled cardiovascular disease

Table 7: Testosterone preparations for replacement therapy

Formulation	Administration	Advantages	Disadvantages
Testosterone undecanoate	Oral; 2-6 cps every 6 hours	Absorbed through the lymphatic system, with consequent reduction of liver involvement.	Variable levels of testosterone above and below the mid-range. Need for several doses per day with intake of fatty food.
Testosterone cypionate	Intramuscular; one injection every two to three weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Possible fluctuation of testosterone levels.

Testosterone enanthate	Intramuscular; one injection every two to three weeks	Short-acting preparation that allows drug withdrawal in case of onset of side-effects.	Fluctuation of testosterone levels.
Testosterone undecanoate	Intramuscular; one injection every 10-14 weeks	Steady-state testosterone levels without fluctuation.	Long-acting preparation that cannot allow drug withdrawal in case of onset of side-effects.
Transdermal testosterone	Gel or skin patches; daily application	Steady-state testosterone level without fluctuation.	Skin irritation at the site of application and risk of interpersonal transfer.
Sublingual testosterone	Sublingual; daily doses	Rapid absorption and achievement of physiological serum level of testosterone.	Local irritation.
Buccal testosterone	Buccal tablet; two doses per day	Rapid absorption and achievement of physiological serum level of testosterone.	Irritation and pain at the site of application.
Subdermal depots	Subdermal implant every five to seven months	Long duration and constant serum testosterone level.	Risk of infection and extrusion of the implants.

Recommendations for testosterone replacement therapy	LE	GR
Fully inform the patient about expected benefits and side-effects of the treatment option. Select the preparation with a joint decision by an informed patient and the physician.	3	A
Use short-acting preparations rather than long-acting depot administration when starting the initial treatment, so that therapy can be adjusted or stopped in case of adverse side-effects.	3	B
Do not use testosterone therapy in patients with male infertility and active child wish since it may suppress spermatogenensis.	1b	A
Only use hCG treatment for hypogonadotropic hypogonadal patients with simultaneous fertility treatment.	1b	B
In patients with adult-onset hypogonadism, only attempt testosterone treatment in men with major symptoms and if weight loss, lifestyle modification and good treatment balance of comorbidities have proven unsuccessful.	2	A

hCG = human chorionic gonadotropin.

Recommendations on risk factors in testosterone treatment (TRT)	LE	GR
Perform haematological, cardiovascular, breast and prostatic assessment before the start of treatment.	1a	A
Monitor haematocrit, and haemoglobin and PSA during TRT therapy.	3	A
Offer TRT cautiously in symptomatic hypogonadal men who have been surgically treated for localised prostate cancer and who are currently without evidence of active disease (i.e. measurable PSA, abnormal rectal examination, evidence of bone/visceral metastasis): treatment should be restricted to those patients with a low risk for recurrent prostate cancer (i.e. Gleason score <8; pathological stage pT1-2; pre-operative PSA <10 ng/mL) and should not start before 1 year of follow-up.	3	B
Assess for cardiovascular risk factors before commencing TRT and optimise secondary prevention in men with pre-existing cardiovascular disease.	1a	A
Treat men men with hypogonadism and either pre-existing cardiovascular disease, venous thromboembolism or chronic cardiac failure who require TRT with caution by monitoring carefully with clinical assessment, haematocrit (not exceeding 0.54) and testosterone levels maintained as best possible for age within the mid-normal healthy range.	1b	A

PSA = prostate-specific antigen; TRT = testosterone replacement therapy.

Recommendations for follow-up	LE	GR
Assess the response to treatment at three, six and twelve months after the onset of treatment, and thereafter annually.	4	C
Monitor haematocrit at three, six and twelve months and thereafter annually. Decrease the testosterone dosage or switch testosterone preparation from parenteral to topical or venesection, if haematocrit is above 0.54. If haematocrit remains elevated, stop testosterone and reintroduce at a lower dose once haematocrit has normalised.	4	C
Assess prostate health by digital rectal examination and PSA before the start of TRT. Follow-up by PSA at three, six and twelve months and thereafter annually.	4	C
Assess men with cardiovascular diseases for cardiovascular symptoms before TRT is initiated and continue close clinical assessment during TRT.	1b	A

BMD = bone mineral density; PSA = prostate-specific antigen; TRT = testosterone replacement therapy.

This short booklet text is based on the more comprehensive EAU Guidelines (978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON UROLOGICAL INFECTIONS

(Complete text update March 2016)

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Introduction

This 2016 document consists of the first completed sections of an entirely new Urological Infections Pocket Guideline, formulated following new EAU guideline production methodology. Subsequent sections will be added over the next three years to cover the key clinical questions. In the interim, the previous 2015 full length and pocket guidelines will be available through the EAU website Uroweb for sections not yet contained in the new guideline, http://uroweb.org/guideline/urological-infections/.

Antimicrobial Stewardship

Antimicrobial stewardship programmes aim to optimise the outcome of prevention and treatment of infection whilst curbing overuse and misuse of antimicrobial agents.

The most 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, with audit.

- Treatment outcome evaluation.
- Monitoring and regular feedback to prescribers of their antimicrobial prescribing performance and local pathogen resistance profiles.

Detection of bacteriuria prior to urological procedures

Identifying bacteriuria prior to diagnostic and therapeutic procedures is recommended to reduce the risk of infectious complications by controlling any pre-operative detected bacteriuria and to streamline the antimicrobial coverage in conjunction with the procedure.

Recommendation for the detection of bacteriuria prior to invasive urological procedures

Recommendation	LE	GR
Laboratory urine culture is the recommended method to determine the presence or absence of clinically significant bacteriuria in patients prior to undergoing urological interventions.	3	B

Acute Infective Epididymitis

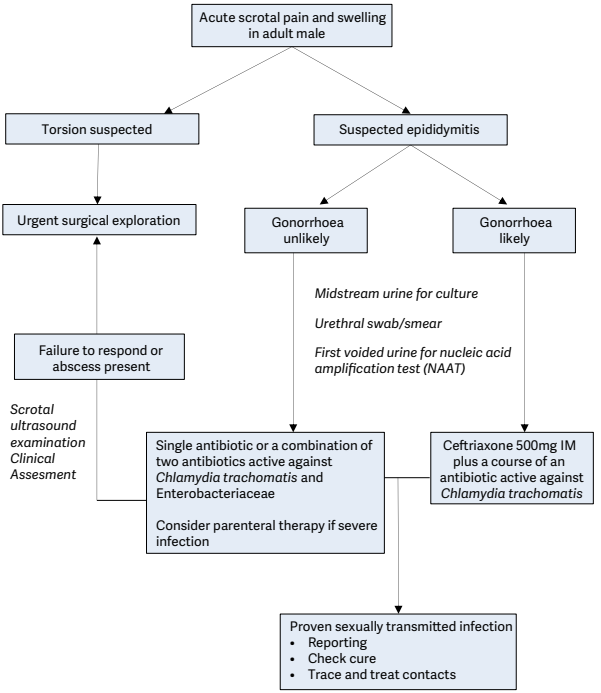
Acute epididymitis is clinically characterised by pain, swelling and increased temperature of the epididymis, which may involve the testis and scrotal skin. It is generally caused by migration of pathogens from the urethra or bladder. The predominant pathogens isolated are *Chlamydia trachomatis*, Enterobacteriaceae (typically *Escherichia coli*) and *Neisseria gonorrhoeae*.

Recommendations for the treatment of acute infective epididymitis

Recommendations	LE	GR
Obtain a mid-stream urine and a first voided urine for pathogen identification.	3	A*
Initially prescribe a single antibiotic or a combination of two antibiotics active against *Chlamydia trachomatis* and Enterobacteriaceae in young sexual active men; in older men without sexual risk factors only Enterobacteriaceae have to be considered.	3	A*
If Gonorrhoeal infection is likely give single dose ceftriaxone 500 mg intramuscularly in addition to a course of an antibiotic active against *Chlamydia trachomatis*.	3	A*
Adjust antibiotic agent when pathogen has been identified and adjust duration according to clinical response.	3	A*
Follow national policies on reporting and tracing/treatment of contacts for STI.	3	A*

** Upgraded based on Panel consensus*
STI = sexually transmitted infections

Figure 1: Diagnostic and treatment algorithm for adult men with acute epididymitis.



IM = intramuscularly

Prostate Biopsy Infection: Non-antibiotic Prevention

Histological examination of needle biopsies of the prostate is the principle method for prostate cancer diagnosis. Infection is the most clinically significant harm experienced by men

following prostate biopsy and includes urinary tract infection, prostatitis, and urosepsis.

Recommendations on non-antibiotic strategies for reducing the risk of infective complications in men undergoing prostate biopsy

Recommendation	LE	GR
Use rectal cleansing with povidone-iodine in men prior to transrectal prostate biopsy in addition to antibiotic prophylaxis if local risk of infectious complication is high.	1a	B*

** Downgraded as highest quality trial in meta-analysis showed no difference.*

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4), available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON UROLITHIASIS

(Limited text update March 2016)

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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 risk of stone formation, but prevention of stone recurrence is of more importance)

Diseases associated with stone formation
Hyperparathyroidism
Metabolic syndrome
Nephrocalcinosis
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
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
Drugs associated with 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

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	LE	GR
With fever or solitary kidney, and when diagnosis is doubtful, immediate imaging is indicated.	4	A*

**Upgraded following panel consensus.*

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

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

Evaluation of patients with acute flank pain

Recommendation for radiologic examinations of patients with acute flank pain/suspected ureteral stones	LE	GR
Following initial US assessment, use NCCT to confirm stone diagnosis in patients with acute flank pain, as it is superior to IVU.	1a	A

IVU = intravenous urography; NCCT = non-contrast enhanced computed tomography; US = ultrasound.

Recommendations for radiologic examination of patients with renal stones	LE	GR
Perform a contrast study if stone removal is planned and the anatomy of the renal collecting system needs to be assessed.	3	A*
Use enhanced CT in complex cases because it enables 3D reconstruction of the collecting system, as well as measurement of stone density and skin-to-stone distance. IVU may also be used.	4	C

**Upgraded following panel consensus.*
CT = computed tomography; IVU = intravenous urography.

Diagnostics - Metabolism-related

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

Recommendations: basic laboratory analysis - emergency stone patient	GR
Urine	
Dipstick test of spot urine sample	A*
• red cells • white cells • nitrite • approximate urine pH	A
Urine microscopy and/or culture	

Blood	
Serum blood sample • creatinine • uric acid • (ionised) calcium • sodium • potassium • blood cell count • CRP	A*
Perform a coagulation test (PTT and INR) if intervention is likely or planned.	A*

**Upgraded following panel consensus.*
CPR = C-reactive protein; INR = international normalised ratio; PTT = partial thromboplastin time.

Examination of sodium, potassium, CRP, and blood coagulation time can be omitted in the non-emergency stone patient. Patients at high risk for stone recurrences should undergo a more specific analytical programme (see Section on Metabolic Evaluation below).

Recommendations related to stone analysis	LE	GR
Perform stone analysis in first-time formers using a validated procedure (XRD or IRS).	2	A
Repeat stone analysis in patients: • presenting with recurrent stones despite drug therapy; • with early recurrence after complete stone clearance; • with late recurrence after a long stone-free period because stone composition may change.	2	B

IRS = infrared spectroscopy; XRD = X-ray diffraction.

Diagnosis for special groups/conditions

Pregnancy

Recommendation	LE	GR
Use ultrasound as the preferred method of imaging in pregnant women.	1a	A*
In pregnant women, use MRI as a second-line imaging modality.	3	C
In pregnant women, use low-dose CT as a last-line option.	3	C

**Upgraded following panel consensus.*
CT = computed tomography; MRI = magnetic resonance imaging.

Children

Recommendations	GR
In children, use ultrasound as first-line imaging modality when a stone is suspected; it should include the kidney, fluid-filled bladder and the ureter next to the kidney and the (filled) bladder.	B
If US does not provide the required information, perform a KUB radiography (or low-dose NCCT).	B
Collect stone material for analysis to classify the stone type.	A*
In all paediatric patients, complete a metabolic evaluation based on stone analysis as they have a high risk of recurrence.	A

KUB = kidney, ureter, bladder; NCCT = non-contrast enhanced computer tomography; US = ultrasound.

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 for pain relief during and prevention of recurrent renal colic	LE	GR
First choice: start with an NSAID as the first drug of choice. e.g. metamizol (dipyrone); alternatively, depending on cardio-vascular risk factors diclofenac*, indomethacin or ibuprofen**.	1b	A
Second choice: hydromorphine, pentazocine and tramadol.	4	C
Use α-blockers to reduce recurrent colic in informed patients.	1a	A

** Caution: Diclofenac sodium affects glomerular filtration rate in patients with reduced renal function, but not in patients with normal renal function (LE: 2a).*

*** Recommended to counteract recurrent pain after renal colic (see extended document).*

NSAID = non-steroidal anti-inflammatory drug.

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

Management of sepsis in the obstructed kidney

The obstructed, infected kidney is a urological emergency.

Recommendations	LE	GR
Urgently decompress the collecting system in case of sepsis with obstructing stones, using percutaneous drainage or ureteral stenting.	1b	A
Delay definitive treatment of the stone until sepsis is resolved.	1b	A

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

Recommendations - Further Measures	GR
Collect (again) urine for antibiogram following decompression.	A*
Start antibiotics immediately (+ intensive care if necessary).	
Re-evaluate antibiotic treatment regimen following antibiogram findings.	

** Upgraded following panel consensus.*

Stone relief

Observation of ureteral stones

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

Recommendations	LE	GR
In patients with newly diagnosed small* ureteral stones, if active stone removal is not indicated, observe patient initially along with periodic evaluation.	1a	A
Offer patients appropriate medication to facilitate stone passage during observation.		

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

Observation of kidney stones

It is still debatable whether kidney stones should be treated, or whether annual follow-up is sufficient for asymptomatic caliceal stones that have remained stable for 6 months.

Recommendations	GR
Assess comorbidity, stone composition if possible and patient preference when making treatment decisions.	C

Medical expulsive therapy (MET)

Medical expulsive therapy (MET) should only be used in informed patients. Treatment should be discontinued if complications develop (infection, refractory pain, deterioration of kidney function). Patients who elect for an attempt at spontaneous passage or MET should have well-controlled pain, no clinical evidence of sepsis, and adequate renal functional reserve.

Recommendations for MET	LE	GR
Offer α-blockers as MET as one of the options.	1a	C
Counsel patients regarding the lack of efficacy in a recent large multicentre trial, attendant risks of MET, including associated drug side effects as well as inform the patients that α-blockers are administered off-label†**.		A*
Follow up patients in short intervals to monitor stone position and assess for hydronephrosis.	4	A*

**Upgraded following panel consensus.*

*** MET using α-blockers in children and during pregnancy cannot be recommended due to the limited data in this specific population.*

† It is not known if tamsulosin harms the human foetus or if it is found in breast milk.

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.

Recommendations - Oral chemolysis	GR
Inform the patient how to monitor and modify the dosage of alkalising medication according to urine pH, which is a direct consequence of such medication.	A
Carefully monitor radiolucent stones during/after therapy.	A*
Inform the patient of the significance of compliance.	A

**Upgraded following panel consensus.*

Percutaneous irrigation chemolysis is rarely used any more.

SWL

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

- Size, location (ureteral, pelvic or caliceal), and composition (hardness) of the stones;
- Patient's habitus;
- Performance of SWL.

Contraindications of SWL

Contraindications to the use of SWL are few, but include:

- Pregnancy;
- Bleeding diatheses; which should be compensated for at least 24 h before, and 48 h 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 of the stone.

Best clinical practice (best performance) in SWL

Stenting prior to SWL

When treating kidney stones, a JJ stent reduces the risk of renal colic and obstruction, but does not reduce formation of steinstrasse or infective complications.

Recommendation	LE	GR
Do no routinely use a stent as part of SWL treatment of ureteral stones.	1b	A

SWL = shock wave lithotripsy.

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 shockwave power.
- Starting SWL on a lower energy setting with step-wise power (and SWL sequence) ramping prevents renal injury.
- Clinical experience has shown that repeat sessions are feasible (within 1 day for ureteral stones).

Recommendation - Shock wave rate	LE	GR
Use a shock wave frequency of 1.0-1.5 Hz.	1a	A

Procedural control

Recommendation - Procedural control	LE	GR
Maintain careful fluoroscopic and/or ultrasonographic monitoring during the procedure.		A*
Ensure correct use of the coupling agent as this is crucial for effective shock wave transportation.	2a	B
Use proper analgesia as it improves treatment results by limiting induced movements and excessive respiratory excursions.	4	C

**Upgraded following panel consensus.*

Antibiotic prophylaxis

No standard prophylaxis prior to SWL is recommended.

Recommendation	LE	GR
In the case of infected stones or bacteriuria, prescribe antibiotics prior to SWL.	4	C

SWL = shock wave lithotripsy.

Percutaneous nephrolithotomy (PNL)

Contraindications:

- Untreated UTI;
- Atypical bowel interposition;
- Tumour in the presumptive access tract area;
- Potential malignant kidney tumour;
- Pregnancy.

Best clinical practice

Recommendation - Preoperative imaging	GR
Perform preprocedural 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.	A*

** Upgraded following panel consensus.*

Colon interposition in the access tract of PNL can lead to colon injuries. Pre-operative CT or intra-operative US allows identification of the tissue between the skin and kidney and lowers the incidence of bowel injury.

Recommendations - Intracorporeal lithotripsy	GR
Use ultrasonic, ballistic and Ho:YAG devices for intracorporeal lithotripsy during PNL.	A*
When using flexible instruments, use the Ho:YAG laser since it is currently the most effective device.	

** Upgraded following panel consensus.*
Ho:YAG = holmium:yttrium-aluminium-garnet (laser);
PNL = percutaneous nephrolithotomy.

Nephrostomy and stents after PNL

Recommendation - Nephrostomy and stents after PNL	LE	GR
In uncomplicated cases, perform a tubeless (without nephrostomy tube) or totally tubeless (without nephrostomy tube and ureteral stent) PNL procedure as it is a safe alternative.	1b	A

PNL = percutaneous nephrolithotomy.

Ureterorenoscopy (URS) (including retrograde access to renal collecting system, RIRS)

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

Recommendations	LE	GR
Place a safety wire.		C
Do not perform stone extraction using a basket without endoscopic visualisation of the stone (blind basketing).	4	A*
Use Ho:YAG laser lithotripsy for (flexible) URS.	3	B
In uncomplicated cases there is no need need to insert a stent.	1a	B

**Upgraded following panel consensus.*
Ho:YAG = holmium:yttrium-aluminium-garnet (laser);
URS = ureterorenoscopy.

An α-blocker can reduce stent-related symptoms.

Open and laparoscopic surgery

Recommendations	LE	GR
Offer laparoscopic or open surgical stone removal in rare cases in which SWL, (flexible) URS and PNL fail, or are unlikely to be successful.	3	C
When expertise is available, perform surgery laparoscopically before proceeding to open surgery, especially when the stone mass is centrally located.	3	C
For ureterolithotomy, perform laparoscopy for large impacted stones when endoscopic lithotripsy or SWL has failed.	2	B

PNL = percutaneous nephrolithotomy; SWL = shockwave lithotripsy; URS = ureterorenoscopy.

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).

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);
- Choice of treatment.

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

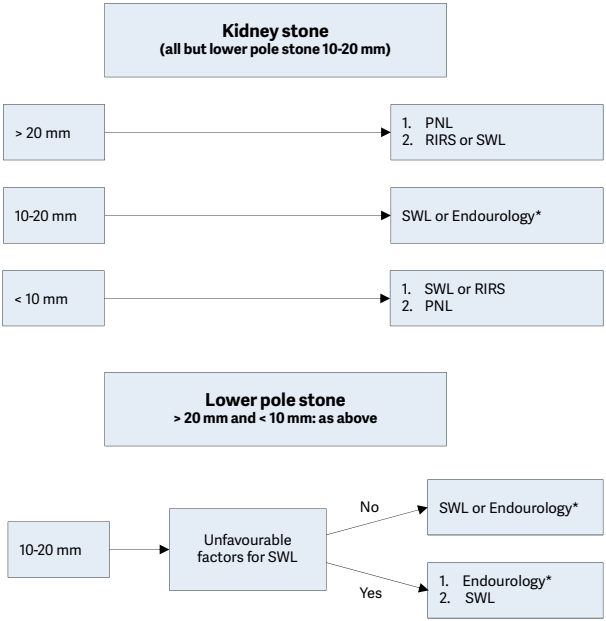
STONE REMOVAL

Recommendations	GR
Obtain a urine culture or perform urinary microscopy before any treatment is planned. Exclude or treat UTIs prior to endourologic stone removal.	A*
Offer perioperative antibiotic prophylaxis to all patients undergoing endourological treatment.	A*
Offer active surveillance to patients at high-risk for thrombotic complications in the presence of an asymptomatic caliceal stone.	C
Decide on temporary discontinuation, or bridging of antithrombotic therapy in high-risk patients, in consultation with the internist.	B
Perform retrograde (flexible) ureterorenoscopy if stone removal is essential and antithrombotic therapy cannot be discontinued, since it is associated with less morbidity.	A*

**Upgraded following panel consensus.*
UTI = urinary tract infection.

Radiolucent uric acid stones, but not sodium urate or ammonium urate stones, can be dissolved by oral chemolysis.

Figure 1: Treatment algorithm for renal calculi



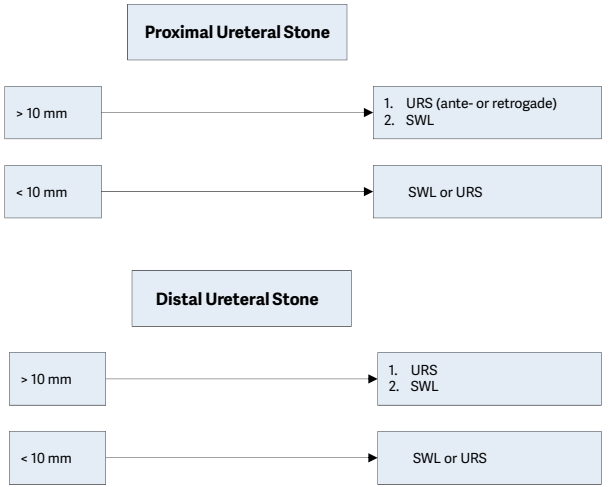
** The term 'Endourology' encompasses all PNL and URS interventions.*

PNL = percutaneous nephrolithotomy; RIRS = retrograde renal surgery; SFR = stone-free rate; SWL = shockwave lithotripsy; URS = ureterorenoscopy.

Recommendation for the treatment of renal calculi	GR
Use flexible URS in case PNL or SWL are not an option (even for stones > 2 cm). However, in that case there is a higher risk that a follow-up procedure and placement of a ureteral stent may be needed. In complex stone cases, use open or laparoscopic approaches as possible alternatives.	B

PNL = percutaneous nephrolithotomy; SWL = shockwave lithotripsy; URS = ureterorenoscopy.

Figure 2: Recommended treatment options (if indicated for active stone removal) (GR: A*)



SWL = shock wave lithotripsy; URS = ureterorenoscopy.

Recommendation	GR
Use percutaneous antegrade removal of ureteral stones as an alternative when SWL is not indicated or has failed, and when the upper urinary tract is not amenable to retrograde URS.	A

SWL = shock wave lithotripsy; URS =ureterorenoscopy.

Steinstrasse

Steinstrasse occurs in 4% to 7% of cases after SWL, the major factor in steinstrasse formation is stone size.

Recommendations	LE	GR
Medical expulsion therapy increases the stone expulsion rate of steinstrasse.	1b	A
Treat steinstrasse associated with urinary tract infection/fever preferably with percutaneous nephrostomy.	4	C
Treat steinstrasse when large stone fragments are present with shockwave lithotripsy or ureterorenoscopy.	4	C

Management of patients with residual stones

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 calix, inversion therapy with simultaneous mechanical percussion manoeuvre under enforced diuresis may facilitate stone clearance

Recommendations in case of residual fragments	LE	GR
Identify biochemical risk factors and appropriate stone prevention in patients with residual fragments or stones.	1b	A
Follow-up patients with residual fragments or stones regularly to monitor disease course.	4	C
After SWL and URS, and in the presence of residual fragments, offer MET using an α-blocker to improve fragment clearance.	1a	A

MET = medical expulsive therapy; SWL = shock wave lithotripsy; URS = ureterorenoscopy.

Management of specific patient groups

Management of urinary stones and related problems during pregnancy

Recommendations	GR
Treat all non-complicated cases of urolithiasis in pregnancy conservatively (except those that have clinical indications for intervention).	A
If intervention becomes necessary, place a ureteral stent or a percutaneous nephrostomy tube as readily available primary options.	A*
Use ureteroscopy as a reasonable alternative to avoid long-term stenting/drainage.	A
In case of stent insertion ensure regular follow-up until final stone removal because of the higher encrustation tendency of stents during pregnancy.	B

**Upgraded following panel consensus.*

Management of stones in patients with urinary diversion

Patients with urinary diversion are at high risk for stone forma-

tion in the renal collecting system and ureter or in the conduit or continent reservoir.

Recommendations	GR
Perform PNL 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 SWL.	A*

PNL = percutaneous nephrolithotomy; SWL = shock wave lithotripsy.

Management of stones in patients with neurogenic bladder

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

In myelomeningocoele patients, latex allergy is common so that 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, immunsuppresion therapy and possible metabolic impairments.

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

Recommendations	LE	GR
Perform US or NCCT to rule out calculi in patients with transplanted kidneys, unexplained fever, or unexplained failure to thrive (particularly in children).	4	B
Offer patients with transplanted kidneys, any of the contemporary treatment modalities, including shockwave therapy, (flexible) ureteroscopy, and percutaneous nephrolithotomy as management options.		B
Complete metabolic evaluation after stone removal.		A*

**Upgraded following panel consensus.*
NCCT = non-contrast enhanced computed tomography; US = ultrasound.

Special problems in stone removal

Caliceal diverticulum stones	• SWL, PNL (if possible) or RIRS. • Can also be removed using 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 caliceal 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 can be achieved with flexible ureteroscopy.

Stones in pelvic kidneys	• SWL, RIRS, PNL or laparoscopic surgery. • For obese patients, the options are RIRS, PNL or open surgery.
Patients with obstruction of the ureteropelvic junction	• When outflow abnormality requires correction, stones can be removed by PNL together with percutaneous endopyelotomy or open/laparoscopic reconstructive surgery. • URS together with endopyelotomy with Ho:YAG. • Incision with an Acucise balloon catheter might be considered, provided the stones can be prevented from falling into the pyeloureteral incision.

Ho:YAG = holmium:yttrium-aluminium-garnet (laser); PNL = percutaneous nephrolithotomy; SWL = shockwave lithotripsy; URS = ureterorenoscopy; RIRS = retrograde renal surgery.

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.

Recommendations	**GR**
In children, perform PNL for the treatment of renal pelvic or caliceal stones with a diameter > 20 mm (~300 mm^2).	C
For intracorporeal lithotripsy, use the same devices as in adults (Ho:YAG laser, pneumatic- and US lithotripters).	C

Ho:YAG holmium:yttrium-aluminium-garnet (laser); PNL = percutaneous nephrolithotomy.

Follow-up

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:

General preventive measures

Fluid intake (drinking advice)	Fluid amount: 2.5-3.0 L/day Circadian drinking Neutral pH beverages Diuresis: ≥ 2.5 L/day Specific weight of urine: < 1010
Nutritional advice for a balanced diet	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
Lifestyle advice to normalize general risk factors	BMI: retain a normal BMI level Adequate physical activity Balancing of excessive fluid loss

Caution: The protein need is age-group dependent, therefore protein restriction in childhood should be handled carefully.
**Avoid excessive consumption of vitamin supplements.*

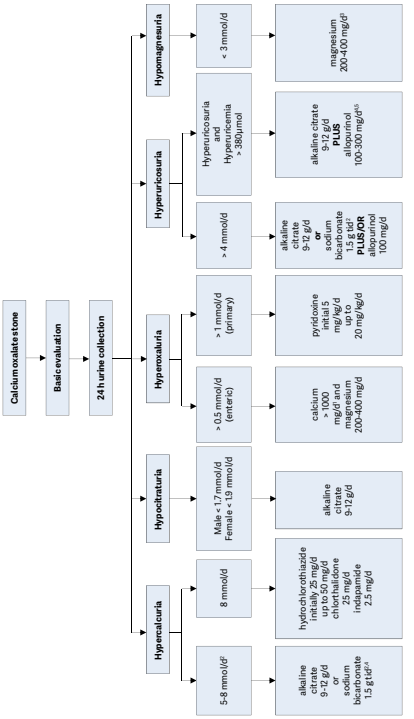
Calcium oxalate stones

(Hyperparathyroidism excluded by blood examination)

Recommendations for pharmacological treatment of patients with specific abnormalities in urine composition

Urinary risk factor	Suggested treatment	LE	GR
Hypercalciuria	Thiazide + potassium citrate	1a	A
Hyperoxaluria	Oxalate restriction	2b	A
Enteric hyperoxaluria	Potassium citrate	3-4	C
	Calcium supplement	2	B
	Diet reduced in fat and oxalate	3	B
Hypocitraturia	Potassium citrate	1b	A
Hypocitraturia	Sodium bicarbonate if intolerant to potassium citrate	1b	A
Hyperuricosuria	Allopurinol	1a	A
	Febuxostat	1b	A
High sodium excretion	Restricted intake of salt	1b	A
Small urine volume	Increased fluid intake	1b	A
Urea level indicating a high intake of animal protein	Avoid excessive intake of animal protein	1b	A
No abnormality identified	High fluid intake	2b	B

Figure 3: Diagnostic and therapeutic algorithm for calcium oxalate stones



[1] *Be aware of excess calcium excretion.*

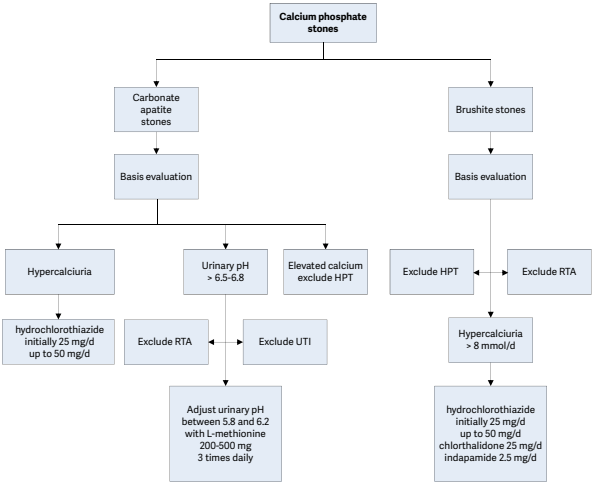
[2] *tid = three times/day (24h).*

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

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

[5] *Febuxostat 80 mg/d.*

Figure 4: Diagnostic and therapeutic algorithm for calcium phosphate stones



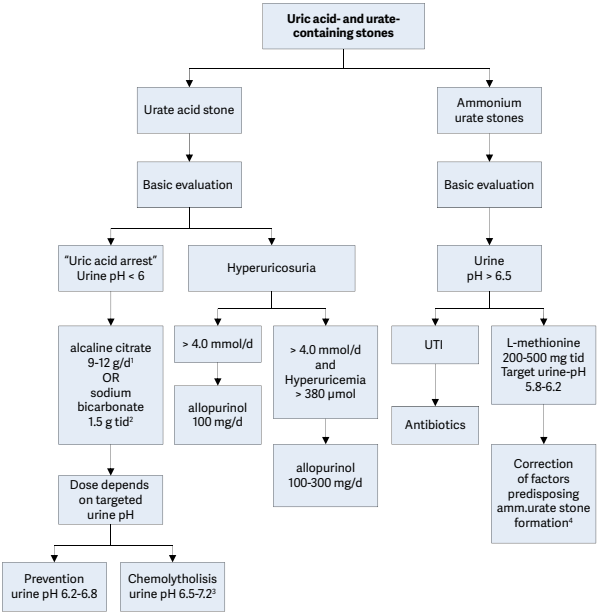
HPT = hyperparathyroidism; RTA = renal tubular acidosis; UTI = urinary tract infection.

Hyperparathyroidism

Elevated levels of ionized calcium in serum (or total calcium and albumin) require assessment of intact parathyroid hormone to confirm or exclude suspected hyperparathyroidism (HPT). Primary HTP can only be cured by surgery.

Uric acid and ammonium urate stones

Figure 5: Diagnostic and therapeutic algorithm for uric acid- and urate-containing stones



UTI = urinary tract infection.

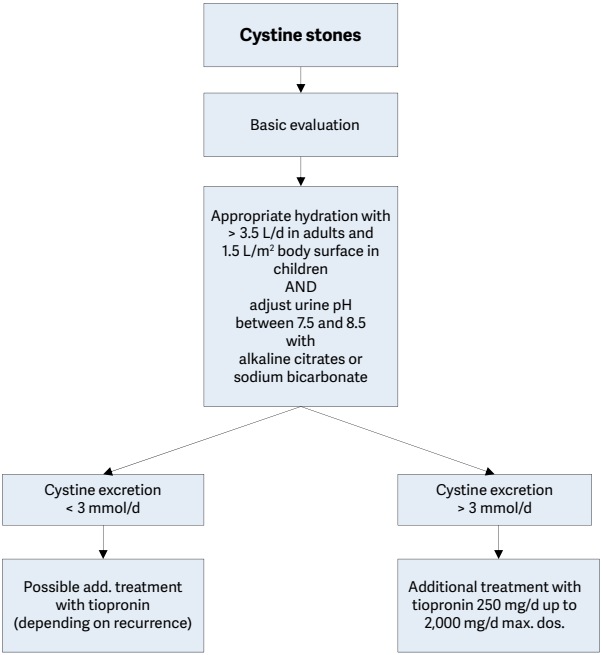
[1] d: day.

[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	LE	GR
Surgically remove the stone material as completely as possible.	3-4	A*
Prescribe a short-term antibiotic course.	3	B
Prescribe a long-term antibiotic course in case of recurrent infections.	3	B
Prescribe ammonium chloride, 1 g, 2 or 3 times daily to ensure urinary acidification.	3	B
Prescribe methionine, 200-500 mg, 1-3 times daily, as an alternative, to ensure urinary acidification.	3	B
Consider prescribing urease inhibitors in case of severe infections (if licensed).	1b	A

**Upgraded following panel consensus*

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

Investigating a patient with stones of unknown composition

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 CT • Determination of Hounsfield units provides information on the possible stone composition
Blood analysis	• Creatinine • Calcium (ionised calcium or total calcium + albumin) • Uric acid
Urinalysis	• Urine pH profile (measurement after each voiding, minimum 4 times daily) • Dipstick test: leukocytes, erythrocytes, nitrite, protein, urine pH, specific weight • Urine culture • Microscopy of urinary sediment (morning urine) • Cyanide nitroprusside test (cysteine exclusion)

Further examinations depend on the results of the investigations listed above.

This short booklet text is based on the more comprehensive EAU Guidelines (978-90-79754-98-4) available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON PAEDIATRIC UROLOGY

(Text update March 2016)

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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 glanular sulcus is possible in only about 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 xerotica obliterans.

Phimosis must be distinguished from normal agglutination of the foreskin to the glans, which is a physiological phenomenon. If the tip remains narrow and glanular 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.

MANAGEMENT OF 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 (DSDs) 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 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 6 months. After that age, undescended testes rarely descend. Any kind of treatment leading to a scrotally positioned testis should be finished by 12 months, or 18 months at the latest, because histological examination of undescended testes at that age has already revealed a progressive loss of germ cells 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 (LE: 4, GR: C).

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 the fertility potential (LE: 4, GR: C).

Surgical therapy

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 18 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 12 months of age, and 18 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 both during and after puberty is therefore recommended.

A systematic review and meta-analysis of the literature concluded that pre-pubertal orchidopexy may reduce the risk of testicular cancer and that early surgical intervention is indicated in boys with undescended testes.

Recommendations	LE	GR
Boys with retractile testes do not need medical or surgical treatment, but close follow-up until puberty is recommended.	2a	A
Surgical orchidolysis and orchidopexy are strongly recommended before the age of 12 months, and by 18 months at the latest.	2b	B
Male neonates with bilateral non-palpable testes should be evaluated for possible DSDs.	1b	A
In case of non-palpable testes and no evidence of DSDs, laparoscopy is recommended because of its excellent sensitivity and specificity in identifying an intra-abdominal testis, as well as the possibility for subsequent treatment in the same session.	1a	A
Hormonal therapy, either in an adjuvant or neo-adjuvant setting, is not routinely recommended. Patients have to be evaluated on an individual basis.	2a	C
In case of bilateral undescended testes, endocrine treatment is recommended.	4	C
For an undescended testis in a post-pubertal boy or older, with a normal contralateral testis, removal should be discussed with the patient/parents because of the theoretical risk of a later malignancy.	3	B

DSD = disorders of sex development.

Figure 1: Classification of undescended testes

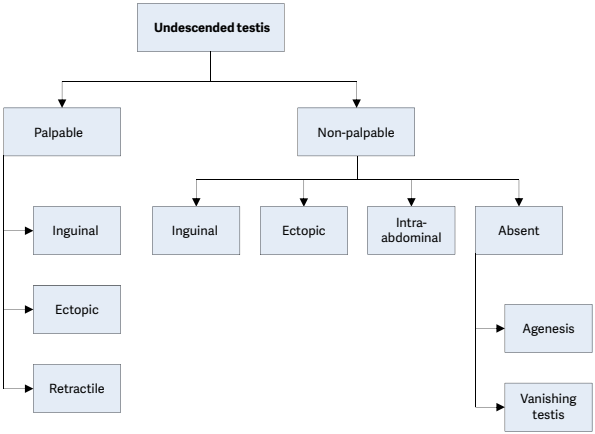
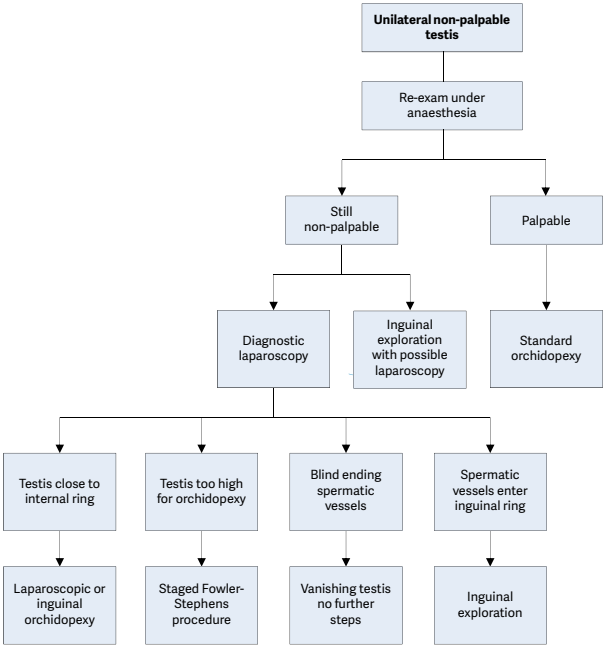


Figure 2: Algorithm for the management of unilateral non-palpable undescended testis



HYDROCELE

Background

Incomplete obliteration of the processus vaginalis peritonei results in formation of various types of communicating hydrocele, alone or connected with other intrascrotal pathology (hernia).

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 the intrascrotal 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.

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.

In the paediatric age group, the operation 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	LE	GR
In the majority of infants, observe hydrocele for 12 months prior to considering surgical treatment.	2a	B
Perform early surgery if there is suspicion of a concomitant inguinal hernia or underlying testicular pathology.	2b	B
Perform a scrotal US in case of doubt about the character of an intrascrotal mass.	4	C
Do not use sclerosing agents because of the risk for chemical peritonitis.	4	C

US = ultrasound.

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.

Assessment

Patients with hypospadias should be diagnosed at birth. The diagnostic evaluation also includes an assessment of associated anomalies, which are 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, by 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 parents is crucial. The therapeutic objectives are to correct the penile curvature, to form a neo-urethra 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.

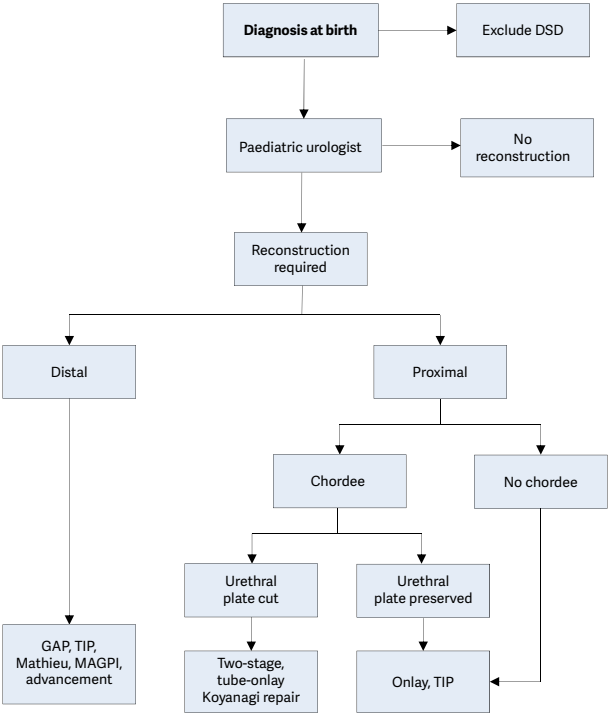
Surgery

For repeat hypospadias repairs, no definitive guidelines can be given.

Outcome

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 ± 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 y	4.7 ± 0.8
2-3 y	5.1 ± 0.9
3-4 y	5.5 ± 0.9
4-5 y	5.7 ± 0.9
5-6 y	6.0 ± 0.9
6-7 y	6.1 ± 0.9
7-8 y	6.2 ± 1.0
8-9 y	6.3 ± 1.0
9-10 y	6.3 ± 1.0
10-11 y	6.4 ± 1.1
Adults	13.3 ± 1.6

VARICOCELE IN CHILDREN AND ADOLESCENTS

Background

Varicocele is unusual in boys under 10 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 parents, 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 - Follow-up

During adolescence, testicular size should be checked annually. After adolescence, repeated sperm analysis is to be 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

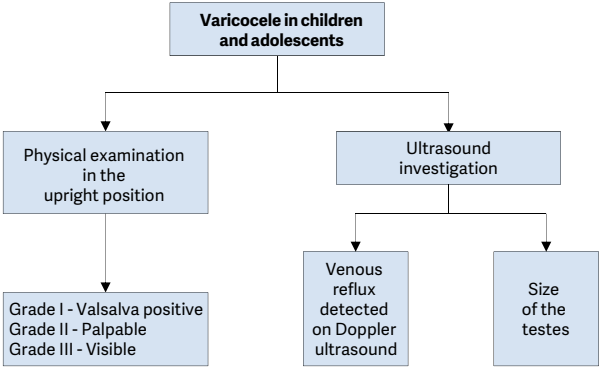
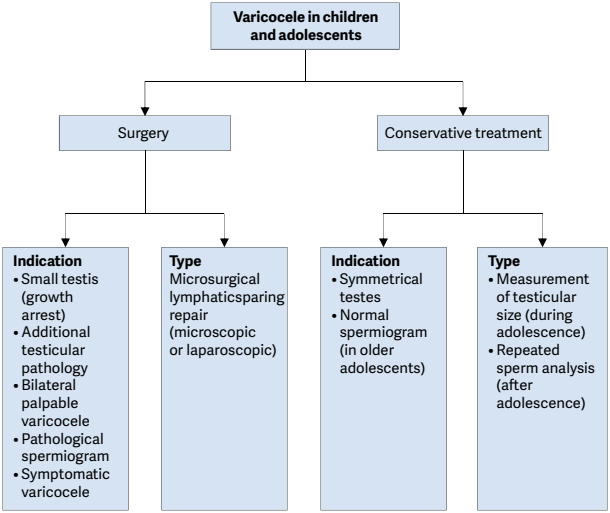


Figure 5: Algorithm for the management of varicocele in children and adolescents



URINARY TRACT INFECTIONS IN CHILDREN

Epidemiology, aetiology and pathophysiology

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 coli* are more frequent, and there is a higher risk of urosepsis.

Classification according to:

- *Site:* Lower urinary tract (cystitis) versus upper urinary tract (pyelonephritis);

- *Episode:* first UTI versus unresolved infection, persistent infection and reinfection;
- *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 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 (SPA):** 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 (adapted from the EAU Guidelines on Urological Infections 2015)

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)	$\geq 10^3$ - 10^5 cfu/mL	$\geq 10^4$ cfu/mL with symptoms $\geq 10^5$ cfu/mL without symptoms

Imaging

Ultrasound of the kidneys and bladder US 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 4-6 weeks) indicating pyelonephritis and renal scars can be detected after 3-6 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: is the gold standard 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 upon presentation. If there are signs of BBD at infection-free intervals, further diagnosis and effective treatment are strongly recommended.

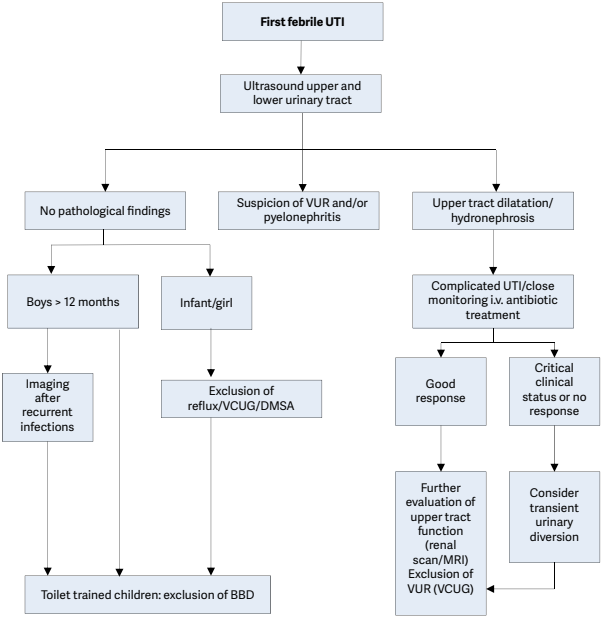
Status of circumcision should be checked in boys and treatment of the phimosis considered in those with pyelonephritis.

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 (1-3 days) are inferior to those of 7-14 day courses. In late infancy, oral therapy with a third-generation cephalosporin (e.g. cefixime

or ceftibuten) is equivalent to the usual 2-4 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.

Monitoring of UTI

Urine usually becomes sterile after 24 h, and leukocyturia normally disappears within 3-4 days. Normalisation of body temperature can be expected within 24-48 h 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	LE	GR
Take a medical history, assess clinical signs and symptoms and perform a physical examination to diagnose children suspected of having a UTI.	3	A
Exclude bladder- and bowel dysfunction and obstruction in any child with febrile and/or recurrent UTI.	3	A
Do not delay diagnosis and treatment of bladder-bowel-dysfunction.	2a	A
Collect an uncontaminated urine sample in an infant through suprapubic bladder aspiration.	2a	B
Bladder catheterisation is an alternative (traumatic especially in boys).	2a	B
Do not use plastic bags to for urine sampling in non-toilet-trained children since it has a high risk of false-positive results.	2a	B
Clean catch urine is an acceptable technique for toilet-trained children.	2a	B
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 WBCs, squamous epithelial cells and red cells correlate well with manual methods.	2a	B
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; complicated pyelonephritis.	2a	B

Treat UTIs with 4-7 day courses of oral or parenteral therapy. Do not use of short courses (1-3 days) since outcomes are inferior.	1b	B
Offer long-term antibacterial prophylaxis in case of high susceptibility to UTI and risk of acquired renal damage and LUTS.	1b	B
Treat complicated UTI, with broad-spectrum antibiotics (parenteral).	1b	B
In infants with febrile UTI, use renal and bladder ultrasonography to exclude obstruction of the upper and lower urinary tract.	3	B
In all infants, exclude VUR after the first episode of febrile UTI, using VCUG or a DMSA-scan first (in case of a positive DMSA-scan, follow-up with VCUG). In boys > 1 year of age, exclude VUR after the second febrile UTI.	2a	B

DMSA = dimercaptasuccinic acid; LUTS = lower urinary tract symptoms; UTI = urinary tract infections; VCUG = voiding cystourethography; VUR = vesicoureteral reflux; WBC = white blood cell.

MONOSYMPTOMATIC NOCTURNAL ENURESIS

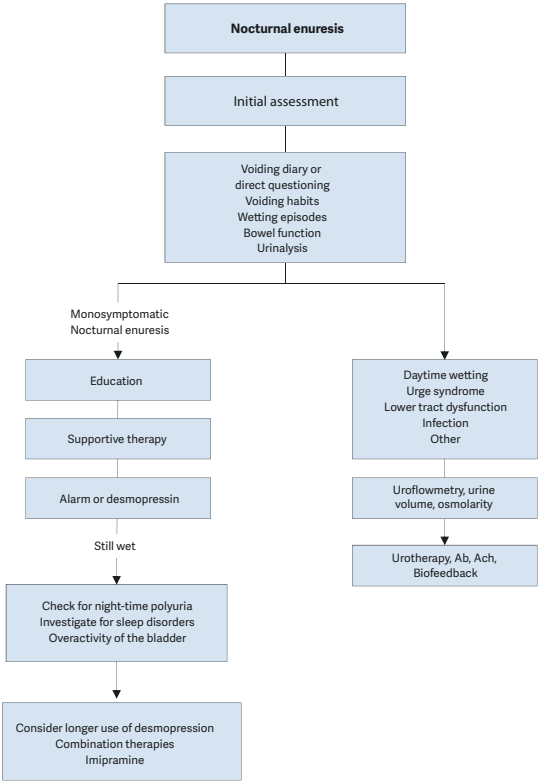
Background

Enuresis is incontinence during the night. Any wetting during sleep above the age of five years is 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.

Assessment

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.

Fig. 7: Algorithm for the diagnosis and management of mono-symptomatic nocturnal enuresis



Ab = antibody; Ach = acetylcholine.

Vesicouretereric reflux (VUR) in children

VUR presents with a wide range of severities, and the majority of reflux patients will not develop renal scars and probably will not need any intervention. The main goal in management is the preservation of kidney function.

Diagnosis

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 for paediatric screening of VUR
Inform parents of children with VUR that siblings and offspring have a high prevalence of VUR.
Use renal US for screening of sibling(s).
Use VCUG if there is evidence of renal scarring on US or a history of UTI.
Do not screen older toilet-trained children since there is no added value in screening for VUR.

US = ultrasound; UTI = urinary tract infection; VCU = voiding cystourethrography; VUR = vesicoureteral reflux.

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 for bilateral high-grade reflux.
- VUR does not damage the kidney when patients are free of infection and have normal LUT function.
- There is no evidence that small scars can cause hypertension, renal insufficiency or problems during pregnancy.
- The conservative approach includes watchful waiting, intermittent or continuous antibiotic prophylaxis, and bladder rehabilitation in those with LUTD.
- Circumcision during 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 reimplantation.

Subureteric infection 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 very high and similar 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 parents in centres where there is enough experience.

Recommendations for the management of vesicoureteric reflux in childhood	GR
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.	C
Offer immediate, parenteral antibiotic treatment for febrile breakthrough infections.	A
Offer definitive surgical or endoscopic correction to patients with frequent breakthrough infections.	A
Offer surgical correction to patients with persistent high-grade reflux (grades IV/V) if intervention is needed; the outcome of open surgical correction is better than endoscopic correction for higher grades of reflux, whereas satisfactory results can be achieved by endoscopic injection for lower grades.	B
Initially manage all children presenting at age 1-5 years conservatively.	B
Offer surgical repair to children presenting with high-grade reflux or abnormal renal parenchyma.	B
Offer close surveillance without antibiotic prophylaxis to children presenting with lower grades of reflux and without symptoms.	B
Ensure that a detailed investigation for the presence of LUTD is done in all children after toilet-training. If LUTD is found, the initial treatment should always be for LUTD.	A
Consider surgical correction, if parents prefer definitive therapy to conservative management. Endoscopic treatment is an option for all children with low grades of reflux.	B

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.	A
In high-risk patients who already have renal impairment, a more aggressive, multidisciplinary approach is needed.	A

LUTD = lower urinary tract dysfunction.

This short booklet text is based on the more comprehensive E AU/ESPU Paediatric Urology Guidelines (ISBN 978-90-79754-98-4), available at their website, http://www.uroweb.org.

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 breakthrough 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 breakthrough 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 breakthrough 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	Postoperative 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

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 breakthrough infections or persistent reflux
Moderate	Symptomatic male or female patients after toilet-training, with high-grade reflux and normal kidneys with 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

CAP = continuous antibiotic prophylaxis; LUTD = lower urinary tract dysfunction; PNH = prenatal diagnosed hydronephrosis; UTI = urinary tract infection; VCUG = voiding cystourethrography.

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
	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 2016)

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Eur Urol 2010 May;57(5):791-803
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Eur Urol 2015 May;67(5):925-9
Eur Urol 2015 May;67(5):930-6

Introduction

Genito-urinary trauma is seen in both sexes and in all age groups, but is more common in males. Traumatic injuries are classified according to the basic mechanism into **penetrating** and **blunt**.

Penetrating trauma is further classified according to the velocity of the projectile:
1. High-velocity projectiles (e.g. rifle bullets - 800-1000m/sec).
2. Medium-velocity (e.g. handgun bullets - 200-300 m/sec).
3. Low-velocity items (e.g. knife stab).

High-velocity weapons inflict greater damage as the bullets transmit large amounts of energy to the tissues, resulting in damage to a much larger area then the projectile tract itself. In lower velocity injuries, the damage is usually confined to the track of the projectile.

Blast injury is a complex cause of trauma as it commonly includes both blunt and penetrating trauma, and may also be accompanied by a burn injury.

Initial evaluation and management

The first priority is stabilisation of the patient and treatment of associated life-threatening injuries. A direct history is obtained from the patient (if conscious) or from witnesses/emergency personnel (if patient unconscious and/or seriously injured).

In penetrating injuries, assess size of the weapon in stabbings, and the type and calibre of the weapon used in gunshot wounds. The medical history should be as detailed as possible. It is important to recognise the high risk of hepatitis B and C infection in trauma patients and take appropriate precautions.

In any penetrating trauma, tetanus vaccination should be considered according to the patient's vaccination history and nature of the wound.

Renal Trauma

Renal injuries are associated with youth and male gender and the incidence is about 4.9 per 100,000 population.

Table 1: Injury severity scale for the kidney*#

Grade	Description
1	Contusion or non-expanding subcapsular haematoma, no laceration
2	Non-expanding perirenal haematoma, cortical laceration < 1 cm deep without extravasation
3	Cortical laceration > 1 cm without urinary extravasation

4	Laceration: through corticomedullary junction into collecting system or vascular: segmental renal artery or vein injury with contained haematoma
5	Laceration: shattered kidney or vascular: renal pedicle injury or avulsion

** Adapted from the American Association for the Surgery of Trauma (AAST).*

 # Advance one grade for multiple injuries up to grade 3.

Diagnostic evaluation

- Haemodynamic stability should be assessed upon admission.
- History: time and setting of incident, past renal surgery, known renal abnormalities.
- Lab: visible haematuria, dipstick urine analysis, serial haematocrit, baseline serum creatinine.
- In blunt trauma with visible- or non-visible haematuria and hypotension, a history of rapid deceleration injury and/or significant associated injuries should undergo radiographic evaluation.
- Any degree of haematuria after penetrating abdominal or thoracic injury requires urgent imaging.
- Imaging: computed tomography (CT) scan, with and without intravenous contrast material, in haemodynamically stable patients.
- Angiography can be used for diagnosis and simultaneous selective embolisation of bleeding vessels if necessary.

Management

- Following blunt renal trauma, stable patients should be managed conservatively with close monitoring of vital signs.
- Isolated grade 1-3 stab and low-velocity gunshot wounds in stable patients, after complete staging, should be managed expectantly.

- Indications for renal exploration include:
  - haemodynamic instability;
  - exploration for associated injuries;
  - expanding or pulsatile peri-renal haematoma identified during laparotomy;
  - grade 5 vascular injury (Figures 1 & 2).
- Radiological embolisation is indicated in patients with active bleeding from renal injury, but without other indications for immediate abdominal operation.
- Intraoperatively, reconstruction should be attempted once haemorrhage is controlled and there is sufficient viable renal parenchyma.

Figure 1: Evaluation of blunt renal trauma in adults

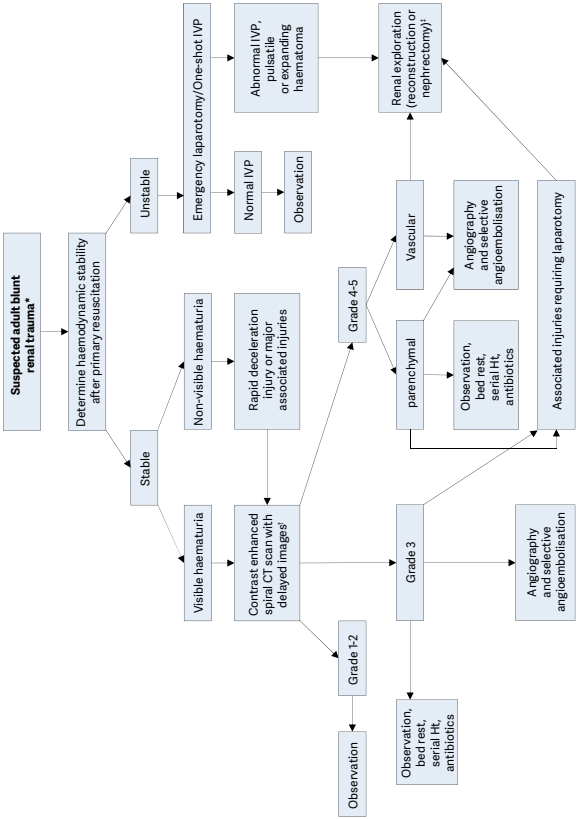
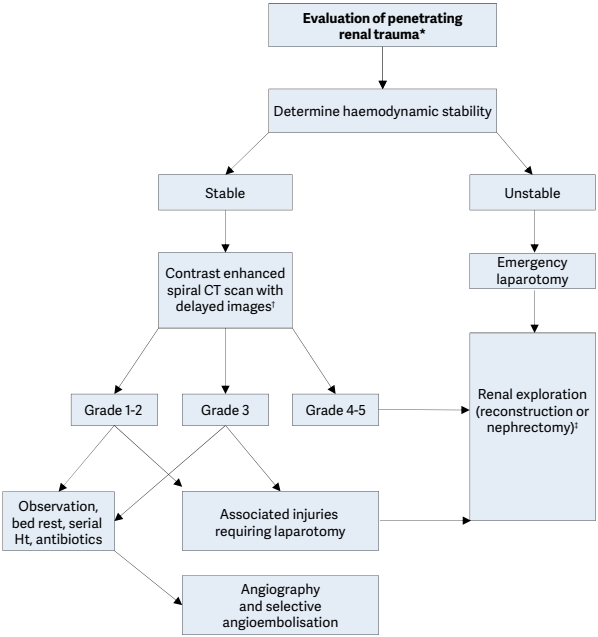


Figure 2: Evaluation of penetrating renal trauma in adults



Post-operative care, follow-up and complications

- Repeat imaging is recommended in cases of suspected complications; fever, flank pain, or falling haematocrit.
- Nuclear scintigraphy is useful for documenting functional recovery.
- First follow up should be at approximately 3 months after major injury and should include: physical examination, urinalysis, individualised radiological investigation, blood pressure measurement and serum determination of renal function.

- Long-term follow-up should be decided on a case-by-case basis.
- Medical management and minimally invasive techniques should be the first choice for the management of complications.

Iatrogenic renal injuries

- Iatrogenic renal injuries are procedure-dependent (1.8-15%).
- Significant injury requiring intervention is rare.
- Most common injuries are vascular.
- Renal allografts are more susceptible.
- Injuries occurring during surgery are rectified immediately.
- Symptoms suggestive of a significant injury require investigation.
- Patients with minor injuries should be treated conservatively.
- Severe or persistent injuries require intervention with embolisation.
- In stable patients, a second embolisation should be considered in case of failure.

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. Risk factors include advanced malignancy, prior surgery or irradiation - i.e. conditions which alter the normal anatomy. Preoperative prophylactic stents do not prevent ureteral injury, but may assist in its detection. External ureteral trauma usually accompanies severe abdominal and pelvic injuries. Gunshot wounds account for the majority of penetrating ureteral trauma, while motor vehicle accidents account for most of blunt injuries.

Diagnostic evaluation

- A high index of suspicion of ureteral injury should be

maintained because the majority of cases are diagnosed late and predispose the patient to pain, infection, and renal function impairment.
- Haematuria is an unreliable indicator.
- Extravasation of contrast material in CT is the hallmark sign of ureteral trauma, and in unclear cases, a retrograde or antegrade urography is required for confirmation.

Management

- Partial injury can be managed with ureteral stenting or urinary diversion by a nephrostomy.
- In complete injuries, ureteral reconstruction following temporary urinary diversion is required.
- The type of repair procedure depends on the site of the injury (Table 2), and it should follow the principles outlined in Table 3.
- Proximal- and mid-ureteral injuries can often be managed by primary uretero-ureterostomy, while a distal injury is often treated with ureteral reimplantation.

Table 2: Ureteral reconstruction options by site of injury

Site of injury	Reconstruction options
Upper ureter	Uretero-ureterostomy Transuretero-ureterostomy Uretero-calycostomy
Mid ureter	Uretero-ureterostomy Transuretero-ureterostomy Ureteral reimplantation and a Boari flap
Lower ureter	Ureteral reimplantation Ureteral reimplantation with a psoas hitch
Complete	Ileal interposition graft Autotransplantation

Table 3: Principles of surgical repair of ureteral injury
Debridement of necrotic tissue
Spatulation of ureteral ends
Watertight mucosa-to-mucosa anastomosis with absorbable sutures
Internal stenting
External drain
Isolation of injury with peritoneum or omentum

Bladder Trauma

Bladder injuries can be due to external (blunt or penetrating) or iatrogenic trauma. Iatrogenic trauma is caused by external laceration or internal perforation (mainly during TURB). Blunt bladder injuries are strongly associated with pelvic fractures. Bladder injuries are classified as extraperitoneal, intraperitoneal or combined.

Diagnostic evaluation

Clinical signs and symptoms

External trauma

- Cardinal sign: visible haematuria.
- Others: abdominal tenderness, inability to void, bruises over the suprapubic region, and abdominal distension (in case of urinary ascites).
- Penetrating bladder injury: entrance- and exit wounds in lower abdomen or perineum.
- Bloody urethrorrhagia: suspect concomitant urethral injury.

Iatrogenic trauma

- External perforation: extravasation of urine, visible laceration, clear fluid in the surgical field, appearance of the bladder catheter, and blood and/or gas (in case of laparoscopy) in the urine bag.
- Internal perforation: fatty tissue or bowel between detrusor

muscle fibres, inability to distend the bladder, low return of irrigation fluid and/or abdominal distension.
- Postoperative symptoms of unrecognised bladder perforation: haematuria, lower abdominal pain, abdominal distension, ileus, peritonitis, sepsis, urine leakage from the wound, decreased urinary output, and increased serum creatinine.

Imaging

Cystography (conventional or CT-cystography)

- Fill the bladder with at least 350 mL of dilute contrast material.
- CT cystography is preferred in case of other possible abdominal injuries or causes of abdominal pain.
- Standard evaluation for external trauma and in case of suspicion of an iatrogenic bladder injury in the postoperative setting.
- Imperative in case of visible haematuria combined with pelvic fracture.

Cystoscopy

- To detect intra-operative bladder injuries.
- Recommended after minimally invasive synthetic suburethral sling operations by retropubic route and major gynaecologic operations.
- Optional after any other type of sling procedure or transvaginal mesh procedure.

Management

Surgical repair (two-layer vesicorraphy)

- Penetrating injury.
- Blunt intraperitoneal injury.
- Blunt extraperitoneal injury with internal osteosynthetic fixation of pelvic fracture.
- (large) Iatrogenic internal intraperitoneal injury.

- Intra-operative recognised injury.
- In case of bladder neck involvement, bony fragment(s) in the bladder, concomitant rectal injury and/or bladder wall entrapment.
- Intraperitoneal bladder ruptures by blunt trauma, and any type of bladder injury by penetrating trauma, must be managed by emergency surgical exploration and repair.

Conservative management (urinary catheter)

- Conservative management is an option for small, uncomplicated, iatrogenic intraperitoneal bladder perforations.
- In the absence of bladder neck involvement and/or associated injuries that require surgical intervention, extraperitoneal bladder ruptures caused by blunt trauma are managed conservatively.
- Postoperative recognised extraperitoneal perforation.
- Blunt extraperitoneal perforation.
- Iatrogenic internal extraperitoneal perforation.
- Small internal intraperitoneal perforation in absence of ileus and peritonitis. Placement of an intraperitoneal drain is optional.

Urethral Trauma

- Injuries to the anterior urethra (AU) are caused by trauma during sexual intercourse (associated with penile fracture), penetrating trauma, placement of penile constriction bands, and from iatrogenic trauma e.g. endoscopic instruments, catheterisation.
- Injuries to the posterior urethra (PU) occur with pelvic fractures, mostly as a result of motor vehicle accidents. The male PU is injured in 4-19% of pelvic fractures, and the female urethra in 0-6% of all pelvic fractures.
- The combination of straddle fractures with diastasis of the sacroiliac joint has the highest risk of urethral injury.
- Injuries can vary from simple stretching to partial rupture

to complete disruptions.
- Urethral injuries in women are rare.

Diagnostic evaluation

- Blood at the external urethral meatus is the most common clinical sign, and indicates the need for further diagnostic work up.
- Although non-specific, haematuria on a first voided specimen may indicate urethral injury. The amount of urethral bleeding correlates poorly with the severity of injury.
- Pain on urination or inability to void may indicate disruption.
- Blood at the vaginal introitus is present in more than 80% 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.
- Retrograde urethrography is the gold standard for evaluating urethral injury and urethral catheterisation should be avoided until the urethra is imaged.
- In an unstable patient, however, an attempt can be made to pass a urethral catheter (gently, by someone with urological experience). If this is not possible, a suprapubic catheter is inserted and a retrograde urethrogram is performed later.
- In females, urethroscopy may be an important adjunct for the identification and staging of urethral injuries.

Management

While intervention should be guided by the clinical circumstances, the following treatment is suggested:

- Retrograde urethrography is the gold standard for evaluating urethral injuries.
- Delayed formal urethroplasty is the procedure of choice for the treatment of posterior urethral distraction defects.
- Partial posterior urethral ruptures should be treated by urethral or suprapubic catheterisation.
- Blunt anterior urethral injuries should be treated by suprapubic diversion.

Iatrogenic urethral trauma

- Most commonly caused by urethral instrumentation, and results in stricture formation.
- Due to their variable location and severity, they often require different management strategies.
- Short and flimsy strictures can be treated by urethrotomy.
- If the stricture is longer or denser, urethroplasty should be considered.

Genital Trauma

Of all genito-urinary injuries, one-third to two-thirds involve the external genitalia and is much more common in males - due to anatomical differences and increased frequency of road traffic accidents, physical sports, violent crime, and war-fighting. 80% is blunt trauma, 20% is due to penetrating injuries.

Diagnostic evaluation

- Urinalysis should be performed.
- Visible- and/or non-visible haematuria require a retrograde urethrogram in males, and consideration of cystoscopy in females.
- In women with genital injuries and blood at the vaginal introitus, further gynaecologic investigation to exclude vaginal injury.
- In cases of suspected sexual abuse gynaecologic and

forensic support and advice is necessary and the emotional situation and privacy of the patient must be respected.

Blunt penile trauma

- Usually results from trauma to the erect penis during sexual intercourse or masturbation.

Penile fracture

- Sudden cracking or popping sound, pain and immediate detumescence.
- Local swelling of the penile shaft is seen and this may extend to the lower abdominal wall.
- The rupture of the tunica may be palpable.
- Thorough history and examination confirms diagnosis
- Imaging (US or magnetic resonance imaging [MRI]) may be useful.

Management

- Subcutaneous haematoma, without associated rupture of the cavernosal tunica albuginea does not require surgical intervention. Nonsteroidal analgesics and ice-packs are recommended.
- In penile fracture, early surgical intervention with closure of the tunica albuginea is recommended.
- Intra-operative flexible cystoscopy is useful to diagnose urethral injury and to further localise tunical damage.
- Conservative management of penile fracture is not recommended.

Penetrating penile trauma

- Rarely seen in isolation.
- Due to gunshot/knife injury, animal or human bites, assault and industrial or self-inflicted mutilation.
- Non-operative management is recommended in small superficial injuries with intact Buck's fascia.

- More significant injuries require surgical exploration and debridement of necrotic tissue.
- In extended injuries of the penis, primary alignment of the disrupted tissues may allow for acceptable healing because of the robust penile blood supply.
- In avulsion of the penis, resuscitate the patient and attempt re-implantation of the penis (if not too badly damaged) - ideally microsurgical.

Blunt scrotal trauma

- May result in testicular dislocation, haematocoele, testicular rupture and/or scrotal haematoma.
- Dislocation of the testicle is rare. Treat by manual replacement and secondary orchidopexy. If 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 nonviable tissue.
- Primary reconstruction of testis and scrotum can be performed in most cases.
- In complete disruption of the spermatic cord, realignment 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 IED blast injury, the extensive loss of genital tissue often requires complex and staged reconstructive surgical procedures.

Genital trauma in females

- In blunt trauma to the external genitalia, imaging studies of the pelvis with US, CT, or MRI should be performed.
- Vulvar haematomas usually do not require surgical intervention, but in massive vulvar haematoma or haemodynamically unstable patients, surgical intervention, lavage and drainage is indicated.
- In vulvar laceration, suturing after conservative debridement is indicated with concomitant primary repair of any associated vaginal injuries.

Polytrauma, Damage Control and Mass Casualty Events

Urological trauma is often associated with significant and higher priority injuries in the polytraumatised patient. Damage control principles govern the management of the severely injured patient and urologists need to understand their role in the context of polytrauma.

Damage control is a three-phase approach - rapid control of haemorrhage and wound contamination, resuscitation in the intensive care unit, and delayed definitive surgery.

Procedures should be directed at the rapid control of bleeding, debridement of dead and devitalised tissue, and minimising urinary extravasation by simple diversionary measures.

A mass casualty event is one in which the number of injured people is significantly higher than the number of healthcare providers available. Examples include the collapse of buildings or bridges, earthquakes, floods, tsunamis, train collisions, aircraft catastrophes, civilian terrorism.

Triage sorts patients into four groups:

1. Patients with life-threatening injuries that require immediate intervention, presenting with **A**irway compromise, **B**reathing failure and/or **C**irculatory compromise from ongoing external haemorrhage.
2. Patients with severe but non-life-threatening injuries, in whom treatment can be acceptably delayed: major fractures, vascular injuries of the limbs and large soft tissue wounds.
3. 'Walking wounded' with minimal injuries.
4. Patients who are so severely injured that treatment would require allocation of resources and time that would deny other, more salvageable patients, timely care. These patients are given minimal or no treatment, and re-evaluated when resources become available. There is no absolute definition for this group because triage is individualised according to the number and severity of casualties related to the available resources.

Principles urological consultations during a mass casualty scenario:

- Rule out under-triage by the surgeon in charge, and perform a rapid primary survey of every patient.
- Avoid unnecessary imaging procedures such as CT scans and retrograde urethrography. These procedures should be performed later, after mass casualty protocols have been suspended.
- Treat unstable patients who are to have surgery using damage control principles.
- Stable patients with suspected renal injuries should be transferred to the surgical ward without imaging procedures. Re-evaluate if there is any change in their haemodynamic status, or when possible as dictated by the constraints of the mass casualty event. Patients managed in this delayed fashion should be treated according to

traditional trauma management protocols.

- 'Minimal acceptable' procedures should be performed in order to transfer patients to the surgical wards, e.g. suprapubic drainage of the bladder when bladder or urethral injuries are suspected, clamping and ligation of bleeding vessels from wounds to the external genitalia, etc.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-90-79754-98-4) available to all members of the European Association of Urology at their website, http://www.uroweb.org.

EAU GUIDELINES ON CHRONIC PELVIC PAIN

(Partial text update March 2016)

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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 'graded action based recommendations', which follow the standard for levels of evidence used by the EAU (see Introduction chapter of the EAU Guidelines book ISBN 978-90-79754-98-4).

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) has localised the pain as being perceived in the specified anatomical pelvic area.)

Definition of CPPS

Chronic pelvic pain syndrome 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	
			Postvasectomy	
		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	

Hx = History; Ex= Examination; Ix = Investigation; PTSD = post-traumatic stress disorder.

	Axis IV Referral character-istics	Axis 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 Urge Incontinence GYNAECOLOGICAL Menstrual Menopause GASTROINTESTINAL Constipation Diarrhoea Bloatedness Urge Incontinence NEUROLOGICAL Dysaesthesia Hyperaesthesia Allodynia Hyperalegesie SEXOLOGICAL 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: Urological pain syndromes

Urological Pain Syndromes	
Abdominal and Pelvic Pain Syndromes	
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.
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.

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 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, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction. 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 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, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.
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 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, as well as with symptoms suggestive of lower urinary tract and sexual dysfunction.
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.
Postvasectomy scrotal pain syndrome	Postvasectomy scrotal pain syndrome is a scrotal pain syndrome that follows vasectomy. Postvasectomy 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. Postvasectomy pain may be as frequent as 1% following vasectomy, possibly more frequent. The mechanisms are poorly understood and it is for that reason 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 subsumed 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 subdivided 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.
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 subdivided 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.
CPPS with cyclical exacerbations	CPPS 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 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 preoccupation 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: 3 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 (> 3 bowel movements per day or < 3 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 subgroup of the chronic anal pain syndromes.
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 overactivity 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.

Epidemiology, Aetiology and Pathophysiology

Chronic visceral pain, pelvic pain and abdominal aspects of pelvic pain

Recommendations: Chronic Pelvic Pain (CPP) and mechanisms	GR
All of those involved in the management of CPP should have knowledge of peripheral and central pain mechanisms.	A
The early assessment of patients with CPP should involve: • investigations aimed at specific disease-associated pelvic pain • assessment of functional, emotional, behavioural, sexual and other quality of life issues, such as effect on work and socialisation.	A
CPPS patients should be managed in a multispecialty and multidisciplinary environment with consideration of all their symptoms.	A

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 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

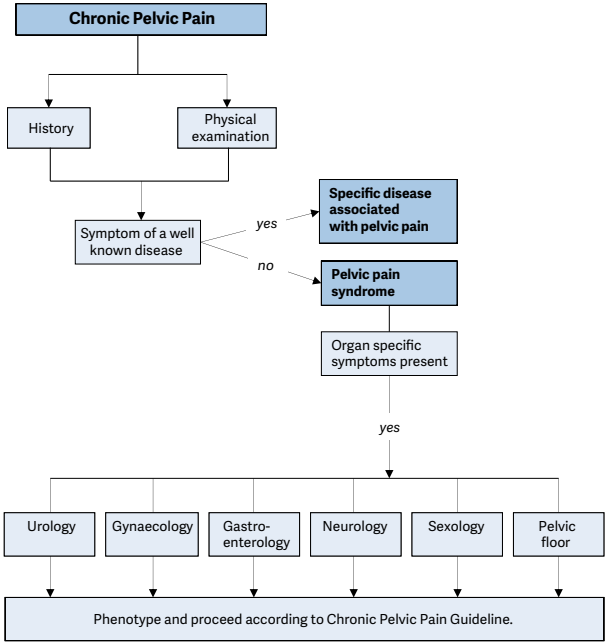

Figure 2: Phenotyping of pelvic pain

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

Recommendations for diagnostic evaluation

Recommendations for the management of prostate pain syndrome (PPS)	GR
Adapt diagnostic procedures to the patient. Specific diseases with similar symptoms must be excluded.	A
Use a validated symptom and quality of life (QoL) scoring instrument, such as the NIH-CPSI, for initial assessment and follow-up.	B
Assess prostate pain syndrome associated negative cognitive, behavioural, sexual, or emotional consequences, as well as symptoms of lower urinary tract and sexual dysfunctions.	B

CPSI = Chronic Prostatitis Symptom Index.

Recommendations for the management of bladder pain syndrome (BPS)	GR
Patients with bladder pain should undergo general anaesthetic rigid cystoscopy in accordance with ESSIC guidelines	A
After primary exclusion of specific diseases, patients with symptoms according to the above definition should be diagnosed with BPS by subtype and phenotype.	A
Assess BPS associated non-bladder diseases systematically.	A
Assess BPS associated negative cognitive, behavioural, sexual, or emotional consequences.	A
Use a validated symptom and quality of life (QoL) scoring instrument for initial assessment and follow-up.	B

ESSIC = International Society for the Study of BPS.

Recommendations for the management of gynaecological aspects of CPP	GR
All women with pelvic pain should have a full gynaecological history and evaluation, including laparoscopy is recommended to rule out a treatable cause (e.g. endometriosis).	A

Recommendations for the management of anorectal pain syndrome	GR
Functional testing is recommended in patients with anorectal pain.	A

Recommendations for the management of pudendal neuralgia	GR
Rule out confusable diseases.	A
If a peripheral nerve pain syndrome is suspected, early referral should occur to an expert in the field, working within a multidisciplinary team environment.	B
Imaging and neurophysiology helps diagnosis but image and nerve locator guided local anaesthetic injection is preferable.	B

Recommendations for the management of sexological aspects in CPP	GR
Patients presenting with symptoms suggestive for chronic pelvic pain syndrome, should be screened for abuse, without suggesting a causal relation with the pain.	B
The biopsychosocial model should be applied in the evaluation of the effect of chronic pelvic pain syndrome on the sexual function of the patient.	B
The biopsychosocial model should be incorporated in research in the role of chronic pelvic pain in sexual dysfunction.	B

Recommendations for the management of psychological aspects of CPP	GR
Psychological distress is common in pelvic pain in women, but should be interpreted in the context of pain.	A
Ask the patient what they think is the cause of their pain to allow the opportunity to inform and reassure as appropriate.	B

Recommendations for the management of pelvic floor function	GR
Use ICS classification on pelvic floor muscle function and dysfunction.	A
In patients with chronic pelvic pain syndrome it is recommended to actively look for the presence of myofascial trigger points.	B

ICS = International Continence Society.

Management

The philosophy for the management of chronic pelvic pain is based on a biopsychosocial 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 well 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 the management of PPS	GR
Offer multimodal and phenotypically directed treatment options for PPS.	A
Single use of antimicrobial therapy (quinolones or tetracyclines) is recommended in treatment-naïve patients over a minimum of 6 weeks with a duration of PPS < 1 year.	A
Alpha-blockers are recommended for patients with a duration of PPS < 1 year.	A
High-dose pentosan polysulphate is recommended in PPS.	A
NSAIDs are recommended for use in PPS, but long-term side-effects have to be considered.	B
For PPS with significant psychological distress, psychological treatment focused on PPS is recommended.	B

NSAIDs = Non-steroidal anti-inflamatory drugs.

Recommendations for the management of BPS	GR
Offer subtype and phenotype-oriented therapy for the treatment of BPS.	A
Multimodal behavioural, physical and psychological techniques should always be considered alongside oral or invasive treatments of BPS.	A
Administer amitriptyline for use in BPS.	A
Offer oral pentosanpolysulphate sodium for the treatment of BPS.	A
Treatment with oral pentosanpolysulphate sodium plus subcutaneous heparin is recommended especially in low responders to pentosanpolysulphate sodium alone.	A
Administer intravesical lidocaine plus sodium bicarbonate prior to more invasive methods.	A
Administer intravesical pentosanpolysulphate sodium before more invasive treatment alone or combined with oral pentosanpolysulphate sodium.	A
Administer submucosal injection of BTX-A plus hydrodistension if intravesical instillation therapies have failed.	A
All ablative organ surgery should be the last resort for experienced and BPS knowledgeable surgeons only.	A
Offer intravesical hyaluronic acid before more invasive measures.	B
Offer intravesical chondroitin sulphate before more invasive measures.	B
Offer transurethral resection (or coagulation or laser) of bladder lesions, but in BPS type 3 C only.	B
Offer neuromodulation before more invasive interventions.	B
Offer dietary advice.	C

Offer intravesical heparin before more invasive measures alone or in combination treatment.	C
Offer intravesical bladder wall and trigonal injection of BTX-A if intravesical instillation therapies have failed.	C
Corticosteroids are not recommended for long-term treatment.	C
Bladder distension is not recommended as a treatment of BPS.	C

BCG = Bacillus Calmette Guérin.

Recommendations for the management of scrotal pain syndrome	**GR**
Start with general treatment options for chronic pelvic pain.	A
Inform about the risk of postvasectomy pain when counselling patients planned for vasectomy.	A
To reduce the risk of scrotal pain, open instead of laparoscopic inguinal hernia repair is recommended.	A
It is recommended that during inguinal hernia repair all the nerves in the spermatic cord are identified.	A
For patients who are treated surgically, microsurgical denervation of the spermatic cord is recommended.	A
We recommend that orchiectomy should not be done, unless all other therapies, including pain management assessment, have failed.	C

Recommendations for the management of urethral pain syndrome	GR
Start with general treatment options for chronic pelvic pain.	A
It is recommended that patients with urethral pain syndrome are treated in a multidisciplinary and multimodal programme.	B
When patients are distressed, it is recommended to refer them for pain-relevant psychological treatment to improve function and quality of life.	B

Recommendations for the management of gynaecological aspects of CPP	GR
Provide therapeutic options such as hormonal therapy or surgery in well-defined disease states.	B
Provide a multidisciplinary approach to pain management in persistent disease states.	B

Recommendations for the management of functional anorectal pain	GR
Biofeedback treatment is recommended in patients with pelvic pain and dyssynergic defecation.	A
Offer botulinum toxin A and electrogalvanic stimulation in the chronic anal pain syndrome.	B
Offer percutaneous tibial nerve stimulation in the chronic anal pain syndrome.	B
Offer sacral neuromodulation in the chronic anal pain syndrome.	C
Offer inhaled salbutamol in the intermittent chronic anal pain syndrome.	C

Recommendations for the management of pudendal neuralgia	GR
Neuropathic pain guidelines are well established. Standard approaches to management of neuropathic pain should be utilised.	A

Recommendations for the management of sexological aspects in CPP	GR
Offer behavioural strategies to the patient and his/her partner to cope with sexual dysfunctions.	B
Training of the pelvic floor muscles is recommended to improve quality of life and sexual function.	B

Recommendations for the management of pelvic floor functions	GR
Apply pelvic floor muscle treatment as first line treatment in patients with chronic pelvic pain syndrome.	A
In patients with an overactive pelvic floor, biofeedback is recommended as therapy adjuvant to muscle exercises.	A
When myofascial trigger points are found, treatment by pressure or needling is recommended.	A

Recommendations for the management of chronic/ non-acute urogenital pain by opioids	GR
All other reasonable treatments must have been tried and failed.	A
The decision to instigate long-term opioid therapy should be made by an appropriately trained specialist in consultation with another physician (including the patient and their family doctor).	A
Where there is a history or suspicion of drug abuse, a psychiatrist or psychologist with an interest in pain management and drug addiction should be involved.	A

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Due to their unique nature – as international guidelines, the EAU Guidelines are not embedded within one distinct healthcare setting - variations in clinical settings, resources, or common patient characteristics, are not accounted for.