EAU Guidelines on Thromboprophylaxis in Urological Surgery

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1. INTRODUCTION

1.1 Aims and objectives

Due to the hypercoagulable state induced by surgery, serious complications of urological surgery include deep vein thrombosis (DVT) and pulmonary embolism (PE) - together referred to as venous thromboembolism (VTE) - and major bleeding [1-4]. Decisions regarding pharmacologic thromboprophylaxis in urologic surgery involve a trade-off between decreased risk of (VTE) and increased risk of bleeding [1-3]. Currently, there exists substantial practice variation in the use of thromboprophylaxis in urology, both within and between countries [5-7]. This variation is unsurprising when one considers that recommendations from national and international guidelines often conflict [2].

To date, existing recommendations for thromboprophylaxis have been limited by a lack of urology-specific evidence [2]. Decisions regarding thromboprophylaxis require both estimates of relative effects on VTE and bleeding, and absolute risks of VTE and bleeding in the absence of prophylaxis (the latter is refered to as baseline risk). Substantial evidence from randomised control trials (RCTs) across a range of surgical procedures is available, and it is reasonable to assume that relative effects of prophylaxis are similar across surgical procedures. Evidence regarding baseline risk across urological procedures is, however, more limited, and systematic summaries of the available evidence have thus far been unavailable [1, 3].

To develop these guidelines, the Panel conducted systematic reviews of the baseline risk of VTE and bleeding in a wide variety of urological procedures [1, 8, 9]. These reviews provide a stronger evidence base for urological thromboprophylaxis guidelines than has been previously available.

Utilising this newly summarised evidence [8, 9], these Guidelines from the European Association of Urology (EAU) Working Panel on Thromboprophylaxis in Urological Surgery provide practical evidence-based guidance regarding post-surgery thromboprophylaxis and peri-operative management of antithrombotic agents in urology.

Clinicians who wish to implement our recommendations should bear in mind that guidelines can never replace clinical expertise when making treatment decisions for individual patients, but rather help to guide decisions that must also take into account patients' values and preferences as well as their individual circumstances. Guidelines are not mandates and do not purport to be a legal standard of care.

1.2 Panel composition

The EAU Guidelines on Thromboprophylaxis in Urological Surgery Panel consists of physicians/methodologists with expertise from urology, internal medicine, haematology, gynaecology and clinical epidemiology. Although the Guidelines are written primarily for urologists, they can also be used by other physicians, patients or other interested parties.

1.3 Available publications

A quick reference document, the Pocket Guidelines, is also available, both in print and as a mobile application, presenting the main findings of the Thromboprophylaxis in Urological Surgery Guidelines. These are abridged versions which may require consultation together with the full text version. All are available through the EAU website: http://www.uroweb.org/guidelines/.

1.4 Publication history

These EAU Guidelines on Thromboprophylaxis in Urological Surgery are the first of their kind.

2. METHODS

2.1 Guideline methodology

The EAU Guidelines on Thromboprophylaxis in Urological Surgery Panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessment of quality of evidence and grading of recommendations [10-12].

GRADE offers four levels of evidence quality, reflecting the degree of certainty or confidence in the evidence: high, moderate, low, and very low [11]. For relative treatment effect, RCTs are high-quality evidence

and observational studies are low-quality evidence. For baseline risk (such as risk of VTE post-surgery), observational studies are high-quality evidence. Quality may be rated down as a result of limitations in study design or implementation (risk of bias), imprecision of estimates (wide confidence intervals), inconsistency (variability in results), indirectness of evidence, or publication bias. Quality may be rated up on the basis of a very large magnitude of effect, a dose-response gradient, and if consideration of all plausible biases would reduce an apparent treatment effect, or create an effect when none is apparent. The lowest quality of any critical outcome represents the overall quality of evidence.

The strength of a recommendation reflects the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects. GRADE classifies recommendations as strong or weak [12]. Strong recommendations mean that all or virtually all informed patients would choose the recommended management and that clinicians can structure their interactions with patients accordingly. Weak recommendations mean that patients' choices will vary according to their values and preferences, and that clinicians must ensure that patients' care is in keeping with their values and preferences through shared decision-making. Strength of recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence (certainty in estimates), and nature and variability of values and preferences.

Post-operative thromboprophylaxis and peri-operative management of antithrombotic agents in urology are discussed seperately. Specific methods are presented in the context of the relevant recommendations.

3. GUIDELINE

3.1 Thromboprophylaxis post-surgery

*3.1.1 **Introduction***

This guideline provides procedure and patient risk-specific guidance weighing the benefit of reduced VTE with the harm of increased bleeding. The Panel provides recommendations for numerous urologic procedures with a simple and practical patient risk stratification scheme.

*3.1.2 **Outcomes and definitions***

The Panel defined non-fatal and fatal symptomatic VTE and non-fatal and fatal major bleeding as key outcomes. Venous thromboembolism was defined as symptomatic DVT or PE and major bleeding was defined as bleeding requiring re-operation or intervention (such as angioembolisation). Transfusion, indwelling catheter, or change in hemoglobin levels were not considered as part of "major bleeding".

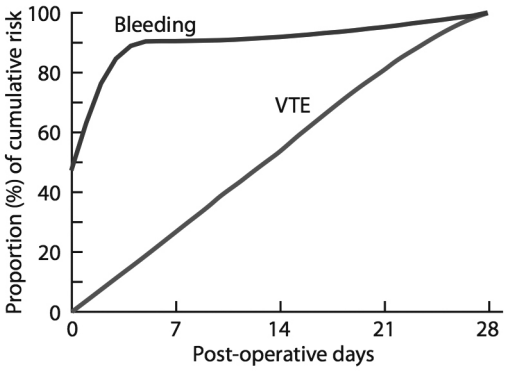
*3.1.3 **Timing and duration of thromboprophylaxis***

High-quality evidence suggests that, of the cumulative risk during the first four weeks post-surgery, approximately 50% of major bleeds occur between surgery and the next morning and approximately 90% during the first four post-surgical days. In contrast, the risk of VTE is almost constant during these first four post-surgical weeks (Figure 1) [1, 13-15].

There are no direct comparisons of the same agent administered before versus after surgery. Recent studies with direct-acting oral anticoagulants (DOACs) in orthopedic surgery have, however, suggested that, relative to starting low molecular weight heparin (LMWH) before surgery, prophylaxis can begin 24 hours after surgery without an increase in VTE but with a decrease in bleeding complications [16, 17]. Given these findings, in addition to the compelling rationale regarding the relative timing of bleeds versus thrombosis (Figure 1), we recommend administration of thromboprophylaxis beginning the day after surgery.

One could argue that prophylaxis be started even later than this, especially in procedures with high bleeding risk. The extent to which an even later start would decrease the effectiveness of thromboprophylaxis is, however, open to question. Given that the further the patient is from surgery the greater the net benefit of prophylaxis (as bleeding risks decreases), while the risk of VTE is just as great in the fourth week after surgery as in the first, the optimal duration of pharmacological prophylaxis is approximately four weeks post-surgery [1, 13-15].

Figure 1: Proportion of cumulative risk (%) of VTE and major bleeding by week since surgery during the first four post-operative weeks



	Proportion of 28-day cumulative bleeding risk
Operation day	47.4%
Post-operative day 1	63.3%
Post-operative day 2	76.6%
Post-operative day 3	84.9%
Post-operative day 4	89.2%
Post-operative day 28	100.0%

Figure modified from: Tikkinen KA, *et al.* Systematic reviews of observational studies of risk of thrombosis and bleeding in urological surgery (ROTBUS): introduction and methodology. *Syst Rev* 2014;3:150. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

*3.1.4 **Basic principles for recommending (or not recommending) post-surgery thromboprophylaxis***

Considerations in the administration of thromboprophylaxis include the relative effect of prophylaxis on key outcomes, baseline risk of key outcomes, as well as patient-related risk (and protective) factors. Finally, one must consider the quality of evidence (certainty in estimates) as well as the relative importance of the relevant outcomes.

3.1.4.1 Effect of prophylaxis on key outcomes

The Panel performed several meta-analyses of RCTs in urology, general surgery, gynecology, and gastrointestinal surgery to inform relative risk estimates of thromboprophylaxis [1, 8, 9]. These meta-analyses demonstrated that anticoagulants (such as LMWH) reduce the relative risk of VTE by approximately 50% and increase the relative risk of major bleeding by approximately 50% [1, 8, 9]. These meta-analyses also demonstrated 50% VTE risk reduction for mechanical prophylaxis [1, 8, 9]. An earlier meta-analysis informing the risk estimates for direct-acting oral anticoagulants yielded similar estimates: a decrease in the relative risk of VTE by approximately 50% and an increase of major bleeding by approximately 50% [18]. The evidence regarding pharmacological prophylaxis was judged as high-quality but low-certainty for mechanical prophylaxis because studies used surrogate outcomes, had very few events, unblinded patients and assessors, and provided almost no information on intermittent pneumatic compression (low-quality evidence) [1, 8, 9].

3.1.4.2 Baseline risk of key outcomes

The Panel performed a series of systematic reviews to provide estimates of absolute risk of symptomatic VTE and bleeding requiring re-operation in urologic surgery [1, 8, 9]. The cited publications, with minor modifications, provide the evidence summary used to develop these recommendations.

3.1.4.3 Patient-related risk (and protective) factors

The Panel conducted a comprehensive literature search addressing VTE and bleeding risk factors in the context of urology, general surgery, gynecology, and gastro intestinal surgery [1]. A model was developed for VTE risk based on the studies reporting the most relevant and high-quality evidence [19-27] (Table 1). However, this model has not been validated and clinicians may consider other factors, including the length of the surgical procedure, oral contraception, immobility, spinal cord injury, and inheritable blood disorders such as

antiphospholipid antibody syndromes, factor V Leiden, antithrombin, protein C or S deficiencies, when making decisions. The Panel's search did not reveal studies demonstrating convincing and replicable risk factors for bleeding [1]; therefore, bleeding risk was not stratified by patient specific factors.

Table 1: Venous thromboembolism (VTE) according to patient risk factors

	Risk	Likelihood of VTE
Low risk	No risk factors	1x
Medium risk	Any one of the following: age 75 years or more; Body mass index 35 or more; VTE in 1st degree relative (parent, full sibling, or child).	2x
High risk	Prior VTE Patients with any combination of two or more risk factors	4x

3.1.4.4 From evidence to recommendations

When creating recommendations, the Panel first calculated the net benefit (absolute reduction in VTE risk – absolute increase in bleeding risk) and thereafter considered quality of evidence, separately for both pharmacological and mechanical prophylaxis. The Panel made strong recommendations only if the quality of evidence was moderate or high and net benefit fulfilled threshold criteria (see below); otherwise, the Panel made weak recommendations.

When calculating the net benefit, twice the weight was assigned for major bleeding as for 'any symptomatic VTE'. The most comprehensive guideline published in the field, the American College of Chest Physicians (ACCP) guideline on "Prevention of VTE in Nonorthopedic Surgical Patients" considered symptomatic VTE and major bleeding as having the same weight. However, they included transfusions in their definition of major bleeding [28] which the Panel considered less relevant because: 1) studies often did not report transfusions, 2) criteria for transfusion vary widely between studies, and use of transfusion may have limited relation to underlying bleeding, and 3) transfusions are less important to patients than are reoperations. Given this guideline's focus on only the more severe bleeds – those that require re-operation – the greater weight on preventing bleeding is appropriate.

For each procedure (and separately for each patient risk factor stratum), the net benefit of using pharmacological thromboprophylaxis (benefit from VTE reduction – harm from bleeding) was calculated. After considering the net benefit and quality of evidence, the thresholds presented in Table 2 were indentified.

Table 2: Thresholds of net benefit and quality of evidence used when creating recommendations

Net benefit*	Recommendation	Note
Pharmacological prophylaxis		
≥ 10 per 1000	STRONG in FAVOUR	If based on moderate or high-quality evidence
≥ 10 per 1000	WEAK in FAVOUR	If based on low or very low-quality evidence
≥ 5-10 per 1000	WEAK in FAVOUR	In borderline situations prophylaxis was always favoured as case fatality is higher for VTE than for bleeding [8, 9]
≥ 1-5 per 1000	WEAK AGAINST	
< 1 per 1000	WEAK AGAINST	If based on low or very low-quality evidence
< 1 per 1000	STRONG AGAINST	If based on moderate or high-quality evidence
Mechanical prophylaxis		
≥ 2.5 per 1000	WEAK in FAVOUR	
< 2.5 per 1000	WEAK AGAINST	

* Net benefit is equal to absolute reduction in VTE risk minus absolute increase in bleeding risk (with twice the weight for major bleeding as for VTE). The net benefit is positive when the value of reduced VTE is greater than increased bleeding.

These thresholds reflect value and preference considerations for which there is limited evidence available [29]. A recent multinational study found that the median threshold net benefit at which women with a history of VTE were willing to accept use of heparin to prevent VTE during pregnancy or the post-partum period is 30 in 1,000 [30]. In that study, the use of prophylaxis spanned the entire duration of pregnancy and continued during the

post-partum period. As post-surgery prophylaxis has a much shorter duration, and is thus less burdensome, our threshold of strong recommendation when net benefit is 10 in 1,000 or more is consistent with this evidence. As mechanical prophylaxis is typically used for a shorter duration than the Panel recommend for pharmacological prophylaxis [31], a lower threshold for mechanical prophylaxis was used.

Making a recommendation regarding thromboprophylaxis requires trading off VTE reduction against bleeding increase, and thus placing a relative value on the two events. A serious bleed (defined as bleeding requiring re-operation or intervention) was considered twice as important as a VTE (defined as symptomatic DVT or PE) event. For patients who feel very differently about this relative value judgment, the Panel's recommendations may not be optimal.

3.1.5 General statements for all procedure-specific recommendations

Consistent with GRADE guidance [32], a single good practice statement was made in which the supporting evidence is compelling, though indirect, and which was not summarised systematically. This association between early ambulation and decreased post-operative complications, in particular decrease in VTE, and early discharge from hospital is convincing. Further, early ambulation has no important adverse consequences. Therefore, the Panel believes that early ambulation for all patients after surgery represents good clinical practice.

The following apply to all recommendations for pharmacologic prophylaxis:

- All recommendations are based on a starting time of the morning after surgery.
- The optimal duration of prophylaxis for all recommendations is approximately four weeks post-surgery.
- There are number of acceptable alternatives for pharmacologic prophylaxis (Table 3).

Table 3: Alternative regimens for pharmacological prophylaxis

Pharmacological agent	Dosage*
Low molecular weight heparins:	
Dalteparin	5,000 IU injection once a day
Enoxaparin	40 mg injection once a day
Tinzaparin	3,500/4,500 IU injection once a day
Unfractionated heparin	5,000 IU injection two or three times a day
Fondaparinux†	2.5 mg injection once a day
Direct acting oral anticoagulants†:	
Dabigatran	220 mg tablet once a day
Apixaban	2.5 mg tablet once a day
Edoxaban	30 mg tablet once a day
Rivaroxaban	10 mg tablet once a day

** Dosages may not apply in renal impairment.*

† Fondaparinux and direct acting oral anticoagulants have not been sufficiently studied in urology to warrant on-label use for post-surgery thromboprophylaxis.

3.1.6 Recommendations

Ambulatory day surgery

R1. In all patients undergoing minor ambulatory day surgery (for example, circumcision, hydrocelectomy and vasectomy), the Panel recommends against use of pharmacological prophylaxis (***strong, moderate-quality evidence***), and against use of mechanical prophylaxis (***strong, moderate-quality evidence***).

Note: The Panel is of the opinion that these patients have risk of VTE close to the general population with an increased risk of bleeding.

Open radical cystectomy

R2. In all patients undergoing open radical cystectomy, the Panel recommends use of pharmacological prophylaxis (***strong, moderate or high-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

Robotic radical cystectomy

R3. In all patients undergoing robotic radical cystectomy, the Panel suggests use of pharmacological prophylaxis (***weak, low-quality evidence***), and suggest use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

Table 4: Procedure-specific evidence summaries with recommendations for radical cystectomies

Procedure	Outcome	Baseline risk among 1000 patients		Net benefit per 1000 patients with pharmacological prophylaxis*	Certainty in estimate	Recommendations for pharmacological prophylaxis	Recommendations for mechanical prophylaxis
Cystectomy, Open	Venous thromboembolism	Low-risk	29	13	Moderate	Strong, for	Weak, for
		Medium-risk	58	27	High	Strong, for	Weak, for
		High risk	116	56	High	Strong, for	Weak, for
	Bleeding requiring reoperation		3.0		Moderate/ High		
Cystectomy, Robotic	Venous thromboembolism	Low-risk	26	11	Low	Weak, for	Weak, for
		Medium-risk	52	24	Low	Weak, for	Weak, for
		High risk	103	50	Low	Weak, for	Weak, for
	Bleeding requiring reoperation		3.0		Low		

* Net benefit is equal to absolute reduction in VTE risk minus absolute increase in bleeding risk (with twice the weight for major bleeding as for VTE). For instance, in medium-risk patients undergoing open radical cystectomy, use of pharmacological prophylaxis, such as LMWH, beginning first post-surgery day for four weeks decreases absolute risk of VTE by 29 per 1,000 and increases absolute risk of bleeding by 0.8 per 1,000 (Figure 1). As twice the weight for major bleeding was assigned as for VTE, the net benefit is 27 per 1,000.

Laparoscopic radical prostatectomy

R4. For patients undergoing laparoscopic radical prostatectomy without pelvic lymph node dissection (PLND), for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis (***strong, moderate-quality evidence***) and suggests against use of mechanical prophylaxis (***weak, low-quality evidence***); for those at moderate and high risk, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate or high quality evidence***) and suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R5. For patients undergoing laparoscopic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis (***strong, moderate-quality evidence***); for those at medium risk, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at high risk, the Panel recommends use of pharmacologic prophylaxis (***strong, high-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R6. For patients undergoing laparoscopic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at medium risk, the Panel suggests use of pharmacologic prophylaxis (***weak, high-quality evidence***); for those at high risk, the Panel recommends use of pharmacologic prophylaxis (***strong, high-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

Open radical prostatectomy

R7. For patients undergoing open radical prostatectomy without PLND or with standard PLND, for those at low risk of VTE, the use of pharmacologic prophylaxis is suggested (***weak, moderate-quality evidence***); for those at medium and high risk, the use of pharmacologic prophylaxis is recommended (***strong, moderate or high-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R8. For all patients undergoing open radical prostatectomy with extended PLND, the Panel recommends use of pharmacologic prophylaxis (***strong, moderate or high-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

Robotic radical prostatectomy

R9. For patients undergoing robotic radical prostatectomy without PLND, for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis (***strong, moderate-quality evidence***) and suggests against use of mechanical prophylaxis (***weak, low-quality evidence***); for those at medium and high risk, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***) and suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R10. For patients undergoing robotic radical prostatectomy with standard PLND, for those at low risk of VTE, the Panel recommends against use of pharmacologic prophylaxis (***strong, moderate-quality evidence***); for those at medium risk, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at high risk, the Panel suggests use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R11. For patients undergoing robotic radical prostatectomy with extended PLND, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at medium risk, the Panel suggests use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at high risk, the Panel recommends use of pharmacologic prophylaxis (***strong, moderate-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

Table 5: Procedure-specific evidence summaries with recommendations for radical prostatectomies

Procedure	Outcome	Baseline risk among 1000 patients		Net benefit per 1000 patients with pharma-cological prophylaxis*	Certainty in estimate	Recommendations for pharma-cological prophylaxis	Recommendations for mechanical prophylaxis
Prostatectomy, Laparoscopic without pelvic lymph node dissection (PLND)	Venous thrombo-embolism	Low-risk	4.0	-1.7	Moderate	Strong - against	Weak – against
		Medium-risk	8.0	0.30	Moderate	Weak - against	Weak - for
		High-risk	15	4.0	High	Weak - against	Weak - for
	Bleeding requiring reoperation		7.0		Moderate		
Prostatectomy, Laparoscopic with standard PLND	Venous thrombo-embolism	Low-risk	8.0	-1.3	Moderate	Strong - against	Weak - for
		Medium-risk	15	2.2	Moderate	Weak - against	Weak - for
		High-risk	30	10	High	Strong - for	Weak - for
	Bleeding requiring reoperation		10		Moderate		
Prostatectomy, Laparoscopic with extended PLND	Venous thrombo-embolism	Low-risk	15	0.10	Moderate	Weak - against	Weak - for
		Medium-risk	30	7.6	High	Weak - for	Weak - for
		High-risk	60	23	High	Strong - for	Weak - for
	Bleeding requiring reoperation		14		Moderate		
Prostatectomy, Open without PLND	Venous thrombo-embolism	Low-risk	10	4.5	Moderate	Weak - for	Weak - for
		Medium-risk	20	9.5	Moderate	Strong - for	Weak – for
		High-risk	39	19	High	Strong - for	Weak - for
	Bleeding requiring reoperation		1.0		Moderate		

Prostatectomy, Open with standard PLND	Venous thrombo-embolism	Low-risk	20	8.9	Moderate	Weak – for	Weak - for
		Medium-risk	39	18	High	Strong - for	Weak - for
		High-risk	79	38	High	Strong -for	Weak - for
	Bleeding requiring reoperation		2.0		Moderate		
Prostatectomy, Open with extended PLND	Venous thrombo-embolism	Low-risk	39	18	Moderate	Strong - for	Weak - for
		Medium-risk	79	38	High	Strong - for	Weak - for
		High-risk	157	77	High	Strong - for	Weak - for
	Bleeding requiring reoperation		2.0		Moderate		
Prostatectomy, Robotic without PLND	Venous thrombo-embolism	Low-risk	2.0	-1.1	Moderate	Strong - against	Weak - against
		Medium-risk	5.0	0.40	Moderate	Weak - against	Weak - for
		High-risk	9.0	2.4	Moderate	Weak - against	Weak - for
	Bleeding requiring reoperation		4.0		Moderate		
Prostatectomy, Robotic with standard PLND	Venous thrombo-embolism	Low-risk	5.0	-0.7	Moderate	Strong - against	Weak - for
		Medium-risk	9.0	1.3	Moderate	Weak - against	Weak - for
		High-risk	19	6.3	Moderate	Weak - for	Weak - for
	Bleeding requiring reoperation		6.0		Moderate		
Prostatectomy, Robotic with extended PLND	Venous thrombo-embolism	Low-risk	9.0	0.3	Moderate	Weak - against	Weak - for
		Medium-risk	19	5.3	Moderate	Weak - for	Weak - for
		High-risk	37	14	Moderate	Strong - for	Weak - for
	Bleeding requiring reoperation		8.0		Moderate		

Nephrectomy

R12. For patients undergoing laparoscopic partial nephrectomy, for those at low and medium-risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, low-quality evidence***); for those at high risk, the Panel recommends use of pharmacologic prophylaxis (***strong, moderate-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R13. For all patients undergoing open partial nephrectomy, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

R14. For patients undergoing robotic partial nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at medium risk, the Panel suggests use of pharmacologic prophylaxis (***weak, moderate-quality evidence***); for those at high risk, the Panel recommends use of pharmacologic prophylaxis (***strong, high-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R15. For patients undergoing laparoscopic radical nephrectomy, for those at low or medium risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low-quality evidence***); for those at high risk, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

R16. For patients undergoing open radical nephrectomy, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***); and for all patients, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R17. For all patients undergoing radical nephrectomy with thrombectomy, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

R18. For all patients undergoing open nephroureterectomy, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

Table 6: Procedure-specific evidence summaries with recommendations for kidney procedures for cancer

Procedure	Outcome	Baseline risk among 1000 patients		Net benefit per 1000 patients with pharma-cological prophylaxis*	Certainty in estimate	Recommendations for pharma-cological prophylaxis	Recommendations for mechanical prophylaxis
Nephrectomy, Laparoscopic partial	Venous thrombo-embolism	Low-risk	11	-3.4	Low	Weak - against	Weak – for
		Medium-risk	21	1.6	Low	Weak - against	Weak – for
		High-risk	42	12	Moderate	Strong - for	Weak - for
	Bleeding requiring reoperation		17		Low/ Moderate		
Nephrectomy, Open partial	Venous thrombo-embolism	Low-risk	10	4.5	Very low	Weak - for	Weak – for
		Medium-risk	20	9.5	Very low	Weak - for	Weak – for
		High-risk	39	19	Very low	Weak - for	Weak - for
	Bleeding requiring reoperation		1.0		Moderate		
Nephrectomy-Robotic partial	Venous thrombo-embolism	Low-risk	10	2.4	Moderate	Weak - against	Weak – for
		Medium-risk	19	6.9	Moderate	Weak - for	Weak – for
		High-risk	39	17	high-quality	Strong - for	Weak - for
	Bleeding requiring reoperation		5.0		Moderate		
Nephrectomy, Laparoscopic radical	Venous thrombo-embolism	Low-risk	7.0	0.9	Very low	Weak - against	Weak – for
		Medium-risk	13	3.9	Very low	Weak - against	Weak – for
		High-risk	26	10	Very low	Weak - for	Weak - for
	Bleeding requiring reoperation		5.0		Very low		
Nephrectomy, Open radical	Venous thrombo-embolism	Low-risk	11	5.2	Low	Weak - for	Weak – for
		Medium-risk	22	11	Low	Weak - for	Weak – for
		High-risk	44	22	Low	Weak - for	Weak - for
	Bleeding requiring reoperation		0.5		Very low		
Radical nephrec-tomy with thrombec-tomy	Venous thrombo-embolism	Low-risk	29	4.0	Very low	Weak - for	Weak - for
		Medium-risk	58	19	Very low	Weak - for	Weak - for
		High-risk	116	48	Very low	Weak - for	Weak - for
	Bleeding requiring reoperation		20		Very low		
Open nephro-ureterectomy	Venous thrombo-embolism	Low-risk	16	7.7	Very low	Weak - for	Weak - for
		Medium-risk	31	15	Very low	Weak - for	Weak - for
		High-risk	62	31	Very low	Weak - for	Weak - for
	Bleeding requiring reoperation		0.5		Very low		

R19. For all patients undergoing primary nerve sparing RPLND, the Panel suggests use of pharmacologic prophylaxis (***weak, very low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

Table 7: Procedure-specific evidence summaries with recommendations for primary nerve sparing retroperitoneal lymph node dissection

Procedure	Outcome	Baseline risk among 1000 patients		Net benefit per 1000 patients with pharma-cological prophylaxis*	Certainty in estimate	Recommendations for pharma-cological prophylaxis	Recommendations for mechanical prophylaxis
Primary nerve sparing retroperitoneal lymph node dissection	Venous thrombo-embolism	Low-risk	23	10	Very low	Weak - for	Weak – for
		Medium-risk	45	21	Very low	Weak - for	Weak – for
		High-risk	91	44	Very low	Weak - for	Weak - for
	Bleeding requiring reoperation		2.0		Very low		

Non-cancer urological procedures

R20. For all patients undergoing transurethral resection of the prostate (TURP) or equivalent procedures, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low-quality evidence***); for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis (***weak, low-quality evidence***); and for those at high risk, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, low-quality evidence***).

R21. For patients undergoing laparoscopic donor nephrectomy or open donor nephrectomy, for those at low risk of VTE, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low or low-quality evidence***), and suggests against use of mechanical prophylaxis (***weak, very low or low-quality evidence***); for medium risk patients, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low or low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low or low-quality evidence***); and for high risk patients, the Panel suggests use of pharmacologic prophylaxis (***weak, very low or low-quality evidence***), and suggests use of mechanical prophylaxis until ambulation (***weak, very low or low-quality evidence***).

R22. For all patients undergoing open prolapse surgery or reconstructive pelvic surgery, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low-quality evidence***); for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis (***weak, very low or low-quality evidence***); while for those at high risk, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, very low or low-quality evidence***).

R23. For all patients undergoing percutaneous nephrolithotomy, the Panel suggests against use of pharmacologic prophylaxis (***weak, very low-quality evidence***); for those at low or medium risk of VTE, the Panel suggests against use of mechanical prophylaxis (***weak, very low-quality evidence***); while for those at high risk, the Panel suggests use of mechanical prophylaxis until ambulation (***weak, very low-quality evidence***).

Table 8: Procedure-specific evidence summaries (with recommendations) for non-cancer procedures

Procedure	Outcome	Baseline risk among 1000 patients		Net benefit per 1000 patients with pharma-cological prophylaxis*	Certainty in estimate	Recommendations for pharma-cological prophylaxis	Recommendations for mechanical prophylaxis
Transurethral resection of the prostate (TURP) or equivalent	Venous thrombo-embolism	Low-risk	2.0	-0.1	Low	Weak - against	Weak - against
		Medium-risk	4.0	0.9	Low	Weak - against	Weak - against
		High-risk	8.0	2.9	Low	Weak - against	Weak - for
	Bleeding requiring reoperation		2.0		Very low		
Donor nephrectomy, laparoscopic	Venous thrombo-embolism	Low-risk	4.0	1.5	Low	Weak - against	Weak – against
		Medium-risk	7.0	3.0	Low	Weak - against	Weak – for
		High-risk	14	6.5	Low	Weak - for	Weak - for
	Bleeding requiring reoperation		1.0		Low		
Donor nephrectomy, open	Venous thrombo-embolism	Low-risk	3.0	1.0	Very low	Weak - against	Weak – against
		Medium-risk	7.0	3.0	Very low	Weak - against	Weak – for
		High-risk	13	6.0	Very low	Weak - for	Weak – for
	Bleeding requiring reoperation		1.0		Very low		
Recipient nephrectomy, open	Venous thrombo-embolism	Low-risk	13	-5.6	Very low	Weak - against*	Weak - for
		Medium-risk	27	1.4	Very low	Weak - against*	Weak – for
		High-risk	53	14	Very low	Weak – for*	Weak - for
	Bleeding requiring reoperation		23		Very low		
Prolapse surgery, open	Venous thrombo-embolism	Low-risk	2.0	-1.1	Low	Weak - against	Weak – against
		Medium-risk	3.0	-0.6	Low	Weak - against	Weak – against
		High-risk	7.0	1.4	Low	Weak - against	Weak – for
	Bleeding requiring reoperation		4.0		Very low		
Reconstructive pelvic surgery (including sling surgery for stress urinary incontinence and vaginal prolapse surgery)	Venous thrombo-embolism	Low-risk	1.0	-1.1	Very low	Weak - against	Weak – against
		Medium-risk	3.0	-0.1	Very low	Weak - against	Weak – against
		High-risk	5.0	0.9	Very low	Weak - against	Weak - for
	Bleeding requiring reoperation		3.0		Very low		
Percutaneous nephrolitho-tomy	Venous thrombo-embolism	Low-risk	2.0	-3.7	Very low	Weak - against	Weak – against
		Medium-risk	4.0	-2.7	Very low	Weak - against	Weak – against
		High-risk	7.0	-1.2	Very low	Weak - against	Weak - for
	Bleeding requiring reoperation		9.0		Low		

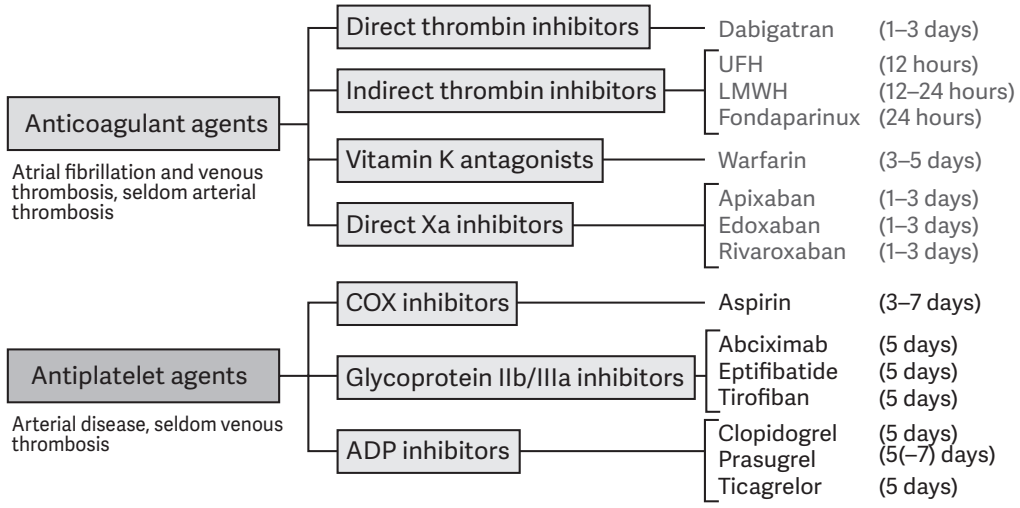
* The Panel understands that patients will receive anticoagulation in the peri-operative period. The recommendations against refer to extended prophylaxis.

3.2 Peri-operative management of antithrombotic agents in urology

3.2.1 ***Introduction***

In principle, there are four options to manage use of antithrombotic agents (Figure 2) during the peri-operative period: 1) to defer surgery until antithrombotic agents are not needed, 2) stop antithrombotic agents prior to surgery and restart some time after surgery, 3) continue through the surgical procedure, or 4) administer alternative antithrombotic agents that may still reduce the risk of thrombosis but with less risk of bleeding than agents patients are currently using ("bridging").

Figure 2: The most widely used antithrombotic agents in patients undergoing urologic surgery
Required period of stopping drug before surgery (if desired) provided in parentheses.



3.2.2 ***Evidence summary***

Earlier major guidelines addressing perioperative management of antithrombotic agents in surgery [2, 33-35] preceded recent major studies, including large, rigorous randomised trials [15, 36-38]. With respect to anti-platelet agents, a recent large, rigorous randomised trial comparing aspirin to placebo has demonstrated that aspirin increases post-operative bleeding without reducing arterial thrombotic events [15]. These results provide indirect evidence for antiplatelet agents other than aspirin. Although the absence of large, rigorous placebo-controlled trials to inform recommendations for other antiplatelet agents constitutes a limitation, given similar antithrombotic and bleeding profiles, the indirect evidence provides useful information to inform our recommendations.

Recommendations that preceded the recent much higher-quality evidence often recommended, in the peri-operative context, substitution of alternative agents for the antithrombotic agents patients were using on a regular basis [39]. The recent evidence has demonstrated that bridging increases bleeding without preventing thrombosis. The Panel therefore essentially have two recommendations for patients receiving antithrombotic agents regularly and contemplating surgery: 1) discontinue antithrombotic therapy for the period around surgery, or 2) in those with a temporary very high risk of thrombosis, delay surgery until that risk decreases. If it is not possible to delay, continuing antithrombotic therapy or bridging through surgery may be advisable.

3.2.3 ***Recommendations***

Five days is an appropriate time to stop antiplatelet agents before surgery while the optimal time to stop varies across anticoagulants (for details, see Figure 2).

R24. In all patients receiving antiplatelet agents (aspirin, clopidogrel, prasugrel, ticagrelor), except those with very high risk of thrombosis (see recommendations 26 and 27), the Panel recommends stopping antiplatelet agents before surgery and not initiating any alternative antithrombotic therapy (***strong, high-quality evidence***).

R25. In patients in whom antiplatelet agents have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk – typically four days post-surgery – rather than withholding for longer periods (***strong, moderate-quality evidence***).

R26. In patients with very high risk of thrombosis receiving antiplatelet agents (those with: drug-eluting stent placement within six months; bare metal stent placement within six weeks; transient ischemic attack (TIA) or

stroke within 30 days) in whom surgery can be delayed, the Panel recommends delaying surgery (***strong, high-quality evidence***).

R27. In patients with very high risk of thrombosis receiving antiplatelet agents (those with: drug-eluting stent placement within six months; bare metal stent placement within six weeks; TIA or stroke within 30 days) in whom surgery cannot be delayed, the Panel suggests continuing the drugs through surgery (***weak, low-quality evidence***).

R28. In all patients receiving anticoagulant agents (unfractionated heparin, low molecular weight heparin, warfarin, fondaparinux, dabigatran, apixaban, rivaroxaban, edoxaban), except those with very high risk of thrombosis (see recommendation 26), the Panel recommends stopping drugs before surgery (see Figure 2) and not initiating any alternative antithrombotic therapy (***strong, high-quality evidence***).

Note: Patients with creatinine clearance < 30 ml/min should not receive dabigatran, apixaban, rivaroxaban or edoxaban.

R29. In patients in whom anticoagulants have been stopped before surgery, the Panel recommends restarting when bleeding is no longer a serious risk – typically four days post-surgery – rather than withholding for longer periods (***strong, moderate-quality evidence***).

R30. In patients with a new VTE, it is recommended that surgery is delayed for at least one month, and if possible three months, to permit discontinuation of anticoagulation pre-operatively, rather than operating within one month of thrombosis (***strong, high-quality evidence***).

R31. In patients receiving any anticoagulant with a severe thrombophilia, such as antithrombin deficiency and antiphospholipid antibody syndrome, the Panel suggests anticoagulation with either heparin or low molecular weight heparin through surgery, rather than stopping anticoagulation before and after surgery (***weak, low-quality evidence***).

R32. In patients with high-risk mechanical prosthetic heart valves, such as cage-ball valves, receiving warfarin, the Panel recommends bridging with LMWH prior and subsequent to surgery, rather than discontinuing anticoagulation peri-operatively (***strong, high-quality evidence***).

Anticoagulation in these patients involves stopping the warfarin five days prior, commencing LMWH four days prior, omitting LMWH on the day of surgery, and recommencing LMWH and warfarin after surgery.

4. RESEARCH RECOMMENDATIONS

The evidence base for this guideline is limited. Much of the evidence regarding baseline risk is low, or very low quality [8, 9]. Prospective observational studies to establish baseline risk of VTE and bleeding in a wide variety of urologic procedures, as well as addressing patient risk factors for both thrombosis and bleeding, will be necessary to create more definite guidelines. Examples of procedures in which the evidence base is particularly limited include robotic cystectomy, laparoscopic radical nephrectomy, open nephroureterectomy, TURP and prolapse surgery. To confidently establish the baseline risk of VTE and bleeding for specific surgery will require studies that meet certain methodologic standards, such as comprehensive characterisation of the patient populations and follow-up times, documentation of the prophylaxis used, and explicit criteria with demonstration of reproducibility of judgments for documentation of DVT, PE, and bleeding assessments. Furthermore, the optimal timing and duration of thromboprophylaxis remains unclear. Timing and duration questions will be best addressed by large-scale randomised trials.

5. REFERENCES

1. Tikkinen, K.A., *et al.* Systematic reviews of observational studies of risk of thrombosis and bleeding in urological surgery (ROTBUS): introduction and methodology. Syst Rev, 2014. 3: 150. http://www.ncbi.nlm.nih.gov/pubmed/25540016
2. Violette, P.D., *et al.* Guideline of guidelines: thromboprophylaxis for urological surgery. BJU Int, 2016. 118: 351. http://www.ncbi.nlm.nih.gov/pubmed/27037846
3. Forrest, J.B., *et al.* AUA Best Practice Statement for the prevention of deep vein thrombosis in patients undergoing urologic surgery. J Urol, 2009. 181: 1170. http://www.ncbi.nlm.nih.gov/pubmed/19152926
4. Scarpa, R.M., *et al.* Clinically overt venous thromboembolism after urologic cancer surgery: Results from the @RISTOS Study. Eur Urol, 2007. 51: 130. https://www.ncbi.nlm.nih.gov/pubmed/16942832
5. Pridgeon, S., *et al.* Venous thromboembolism (VTE) prophylaxis and urological pelvic cancer surgery: a UK national audit. BJU Int, 2015. 115: 223. http://www.ncbi.nlm.nih.gov/pubmed/25756135
6. Weinberg, A., *et al.* Nationwide practice patterns for the use of venous thromboembolism prophylaxis among men undergoing radical prostatectomy. World J Urol, 2014. 32: 1313. http://www.ncbi.nlm.nih.gov/pubmed/24292076
7. Benyo, M., *et al.* Present practice of thrombosis prophylaxis of radical prostatectomy in a European country: a Hungarian multicenter study. Urol Int, 2014. 92: 289. http://www.ncbi.nlm.nih.gov/pubmed/24280912
8. Tikkinen, K.A., *et al.* Procedure-specific risks of thrombosis and bleeding in urological cancer surgery: systematic review and meta-analysis. Eur Urol, 2017 (in press).
9. Tikkinen, K.A., *et al.* Procedure-specific risks of thrombosis and bleeding in urological non-cancer surgery: systematic review and meta-analysis. Eur Urol, 2017 (in press).
10. Guyatt, G.H., *et al.* GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, 2008. 336: 924. http://www.ncbi.nlm.nih.gov/pubmed/18436948
11. Guyatt, G.H., *et al.* What is “quality of evidence” and why is it important to clinicians? BMJ, 2008. 336: 995. http://www.ncbi.nlm.nih.gov/pubmed/18456631
12. Guyatt, G.H., *et al.* Going from evidence to recommendations. BMJ, 2008. 336: 1049. http://www.ncbi.nlm.nih.gov/pubmed/18467413
13. Amin, A.N., *et al.* Retrospective administrative database study of the time period of venous thromboembolism risk during and following hospitalization for major orthopedic or abdominal surgery in real-world US patients. Hosp Pract, 2011. 39: 7. http://www.ncbi.nlm.nih.gov/pubmed/21576893
14. Sweetland, S., *et al.* Duration and magnitude of the postoperative risk of venous thromboembolism in middle aged women: prospective cohort study. BMJ, 2009. 339: b4583. http://www.ncbi.nlm.nih.gov/pubmed/19959589

15. Devereaux, P.J., *et al.* Aspirin in patients undergoing noncardiac surgery. N Engl J Med, 2014. 370: 1494.
http://www.ncbi.nlm.nih.gov/pubmed/24679062
16. Lassen, M.R., *et al.* Apixaban versus enoxaparin for thromboprophylaxis after knee replacement (ADVANCE-2): a randomised double-blind trial. Lancet, 2010. 375: 807.
https://www.ncbi.nlm.nih.gov/pubmed/20206776
17. Lassen, M.R., *et al.* Apixaban versus enoxaparin for thromboprophylaxis after hip replacement. N Engl J Med, 2010. 363: 2487.
https://www.ncbi.nlm.nih.gov/pubmed/21175312
18. Neumann, I., *et al.* Oral direct Factor Xa inhibitors versus low-molecular-weight heparin to prevent venous thromboembolism in patients undergoing total hip or knee replacement: a systematic review and meta-analysis. Ann Intern Med, 2012. 156:710.
https://www.ncbi.nlm.nih.gov/pubmed/22412038
19. Hansson, P.O., *et al.* Deep vein thrombosis and pulmonary embolism in the general population: 'The Study of Men Born in 1913'. Arch Intern Med, 1997. 157: 1665.
http://www.ncbi.nlm.nih.gov/pubmed/9250227
20. Tosetto, A., *et al.* Prevalence and risk factors of non-fatal venous thromboembolism in the active population of the VITA Project. J Thromb Haemost, 2003. 1: 1724.
http://www.ncbi.nlm.nih.gov/pubmed/12911584
21. Edmonds, M.J., *et al.* Evidence-based risk factors for postoperative deep vein thrombosis. ANZ J Surg, 2004. 74: 1082.
http://www.ncbi.nlm.nih.gov/pubmed/15574153
22. Stein, P.D., *et al.* Venous thromboembolism according to age: the impact of an aging population. Arch Intern Med, 2004. 164: 2260.
http://www.ncbi.nlm.nih.gov/pubmed/15534164
23. Weill-Engerer, S., *et al.* Risk factors for deep vein thrombosis in inpatients aged 65 and older: a case–control multicenter study. J Am Geriatr Soc, 2004. 52: 1299.
http://www.ncbi.nlm.nih.gov/pubmed/15271117
24. Caprini, J.A. Thrombosis risk assessment as a guide to quality patient care. Dis Mon, 2005. 51: 70.
http://www.ncbi.nlm.nih.gov/pubmed/15900257
25. Rogers, S.O. Jr., *et al.* Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg, 2007. 204: 1211.
http://www.ncbi.nlm.nih.gov/pubmed/17544079
26. Parkin, L., *et al.* Body mass index, surgery, and risk of venous thromboembolism in middle-aged women: a cohort study. Circulation, 2012. 125: 1897.
http://www.ncbi.nlm.nih.gov/pubmed/22394567
27. Pannucci, C.J., *et al.* A validated risk model to predict 90-day VTE events in postsurgical patients. Chest, 2014. 145: 567.
http://www.ncbi.nlm.nih.gov/pubmed/24091567
28. Gould, M.K., *et al.* Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 2012. 141: e227S.
http://www.ncbi.nlm.nih.gov/pubmed/22315263
29. MacLean, S., *et al.* Patient values and preferences in decision making for antithrombotic therapy: a systematic review: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 2012. 141: e1S.
http://www.ncbi.nlm.nih.gov/pubmed/22315262
30. Bates, S.M., *et al.* Women's values and preferences and health state valuations for thromboprophylaxis during pregnancy: A cross-sectional interview study. Thromb Res, 2016. 140: 22.
https://www.ncbi.nlm.nih.gov/pubmed/27500301
31. Craigie, S., *et al.* Adherence to mechanical thromboprophylaxis after surgery: a systematic review and meta-analysis. Thromb Res, 2015. 136: 723.
http://www.ncbi.nlm.nih.gov/pubmed/26140737
32. Guyatt, G.H., *et al.* Guideline panels should seldom make good practice statements: guidance from the GRADE Working Group. J Clin Epidemiol, 2016. 80: 3.
https://www.ncbi.nlm.nih.gov/pubmed/27452192

33. Douketis, J.D., *et al.* Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 2012. 141: e326S. http://www.ncbi.nlm.nih.gov/pubmed/22315266
34. National Clinical Guideline Centre – Acute and chronic conditions (UK). Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in patients admitted to hospital. London: Royal College of Physicians (UK); 2010.
35. Culkin D.J., *et al.* Anticoagulation and antiplatelet therapy in urological practice: ICUD/AUA review paper. J Urol, 2014. 192: 1026. https://www.ncbi.nlm.nih.gov/pubmed/24859439
36. Douketis, J.D., *et al.* Perioperative bridging anticoagulation in patients with atrial fibrillation. N Engl J Med, 2015. 373: 823. http://www.ncbi.nlm.nih.gov/pubmed/26095867
37. Steinberg, B.A., *et al.* Use and outcomes associated with bridging during anticoagulation interruptions in patients with atrial fibrillation: findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). Circulation, 2015. 131: 488. http://www.ncbi.nlm.nih.gov/pubmed/25499873
38. Douketis, J.D., *et al.* Perioperative bridging anticoagulation during dabigatran or warfarin interruption among patients who had an elective surgery or procedure. Substudy of the RE-LY trial. Thromb Haemost, 2015. 113:625. https://www.ncbi.nlm.nih.gov/pubmed/25472710
39. Rose, A.J., *et al.* A call to reduce the use of bridging anticoagulation. Circ Cardiovasc Qual Outcomes, 2016. 9: 64. 2016. 9:64. https://www.ncbi.nlm.nih.gov/pubmed/26715651

6. CONFLICT OF INTEREST

All members of the Thromboprophylaxis working panel have provided disclosure statements on all relationships that they have that might be perceived to be a potential source of a conflict of interest. This information is publically accessible through the European Association of Urology website: http://www.uroweb.org/guidelines/. This document was developed with the financial support of the European Association of Urology. No external sources of funding and support have been involved. The EAU is a nonprofit organisation and funding is limited to administrative assistance and travel and meeting expenses. No honoraria or other reimbursements have been provided.

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