Canadian Urological Association Guideline on Perioperative Thromboprophylaxis

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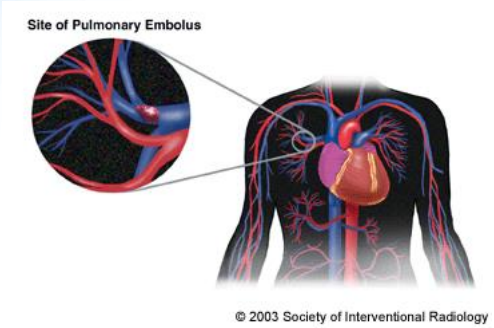
Disclosures

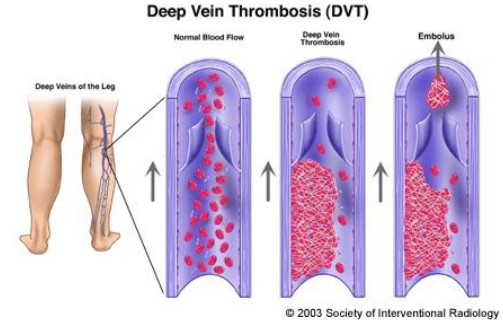
Author Name	Advisory Boards	Speaker's Bureau	Payment/ Honoraria	Grants/ Research Support	Clinical Trials	Investments	Patents
Philippe Violette	None	None	SIU, CUA	None	None	None	none
Luke T. Lavallée	Ferring, Sanofi			Sanofi			
Wassim Kassouf		Astellas, AstraZeneca, Janssen, Merk, Roche		Astellas, AstraZeneca, Janssen, Merk, Roche			
Peter L. Gross	Pfizer, Leo		Bayer, BMS, Pfizer, LEO, Servier	BMS, Boeringer-Ingerheim, Pfizer	BMS, Pfizer, Bayer, Servier		
Bobby Shayagan		Abbvie, Astella, Janssen, Sanofi			Astellas, Janssen		

What do we need to know?

1. What is the tradeoff?
2. What are the risks with a given surgery?
3. How do patient factors fit in?
4. When do we start and how long to we give prophylaxis?

1 - What is the tradeoff?





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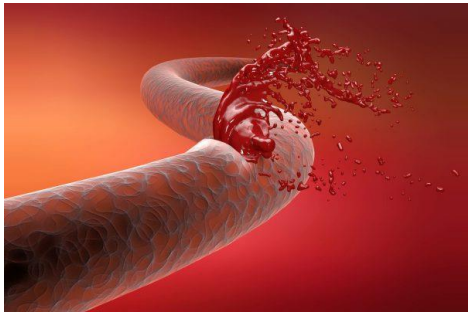


Use of pharmacolocical prophylaxis will decrease risk of symptomatic VTE by 50% and increase major bleed by 50% (relative effect)

Procedures that strongly favor prophylaxis

Surgery with high risk of VTE and low risk of bleed

VTE

Bleed

Procedures that strongly favor no prophylaxis

Surgery with low risk of VTE and high risk of bleed

Bleed

Procedures with close tradeoff of VTE and bleeding risk

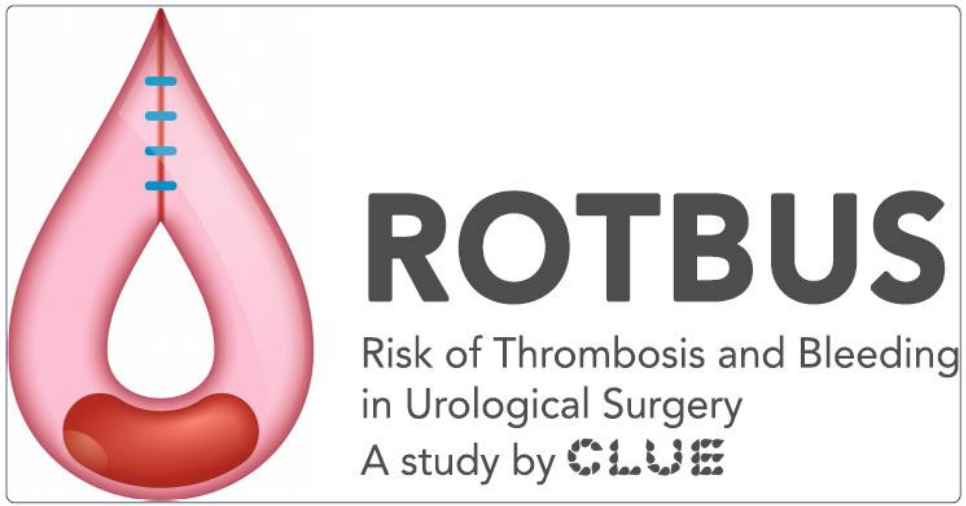
Surgery with similar risk of VTE and bleeding require discussion of patient values and preferences

↓50% symptomatic VTE

↑50% Major Bleed

2- What are the risks with a given surgery?

Baseline risks of VTE and bleeding



- Absolute risk of VTE and bleeding calculated for 31 urological procedures
- Provides “natural history” if no prophylaxis given
- Risks of VTE change with patient risk strata
- Relative effect of prophylaxis modifies this baseline risk

Syst Rev 2014;336:995.
Eur Urol 2018 Feb;73(2):236-41.
Eur Urol 2018 Feb;73(2):242-51.

3 - Patient-related risk

Patient level factor	Effect on VTE risk (RR)	Risk stratification
None		Low risk
Age >75 years	2-fold	Moderate risk
BMI ≥ 35	2-fold	Moderate risk
VTE in a first degree relative (parents, full siblings, or children)	2-fold	Moderate risk
Any 2 factors above	4-fold	High risk
Personal history of VTE	4-fold	High risk

Tikkinen et al. *Syst Rev* 2014;336:995

A priori definitions of net benefit used to make recommendations

Net benefit	Recommendation	Note
Pharmacological prophylaxis		
≥10 per 1000	STRONG in FAVOR	If based on moderate or high-quality evidence
≥10 per 1000	WEAK in FAVOR	If based on low or very low-quality evidence
≥5-10 per 1000	WEAK in FAVOR	In borderline situations we always favored prophylaxis as case fatality is higher for VTE than for bleeding
≥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 FAVOR	
<2.5 per 1000	WEAK AGAINST	

Strong vs. weak recommendation

Strong recommendation

- For patients: Most people in this situation would want recommended course (>80%)
- For urologists: Most patients should receive this course of action
  - Informed consent

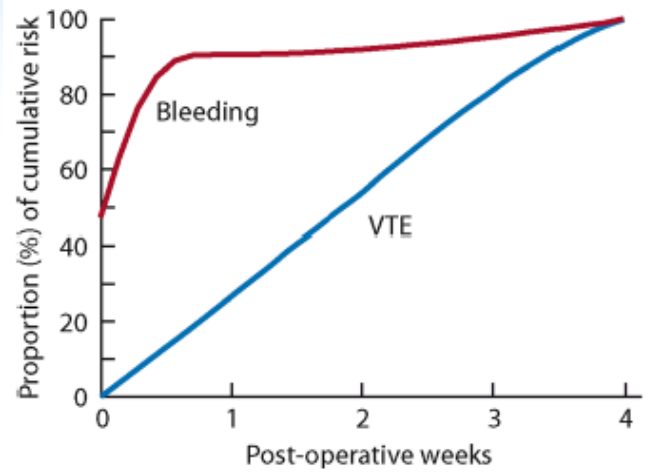
Weak recommendation

- For patients: Most people in this situation would want recommended course, but many would not
- For urologists: Different choices will be appropriate for different patients; value and preference sensitive
  - Shared decision-making

What about timing of prophylaxis?

- When do we start?
- How long to we give?

4- What about timing of prophylaxis?



Post-operative days

	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%

Risk of major bleed is highest on the day of surgery then decreases

Risk of symptomatic VTE is constant over 1 month

<u>Optimal net benefit timing:</u>

- Start morning POD1 and continue for 28 days post-op
  - Decrease risk of major bleed more than increase risk of symptomatic VTE in the first day, still get benefit of prophylaxis over the 4 weeks duration

EAU guideline → CUA guideline

Adopt?

Adapt?

de Novo?

[Original Research **Education, Research, and Quality Improvement**]

CHEST

Adaptation of Trustworthy Guidelines Developed Using the GRADE Methodology

A Novel Five-Step Process

Annette Kristiansen, MD; Linn Brandt, MD; Thomas Agoritsas, MD; Elie A. Akl, MD, PhD, MPH; Eivind Berge, MD, PhD; Johan Bondi, MD, PhD; Anders E. Dahm, MD, PhD; Lars-Petter Granan, MD, PhD; Sigrun Halvorsen, MD, PhD; Pål-Andre Holme, MD, PhD; Anne Flem Jacobsen, MD, PhD; Eva-Marie Jacobsen, MD, PhD; Ignacio Neumann, MD; Per Morten Sandset, MD, PhD; Torunn Sætre, MD, PhD; Arnljot Tveit, MD, PhD; Trond Vartdal, MD, PhD; Gordon Guyatt, MD, FCCP; and Per Olav Vandvik, MD, PhD

[Original Research **Education, Research, and Quality Improvement**]

CHEST

Applying New Strategies for the National Adaptation, Updating, and Dissemination of Trustworthy Guidelines

Results From the Norwegian Adaptation of the Antithrombotic Therapy and the Prevention of Thrombosis, 9th Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Annette Kristiansen, MD; Linn Brandt, MD; Thomas Agoritsas, MD; Elie A. Akl, MD, PhD, MPH; Eivind Berge, MD, PhD; Anne Flem Jacobsen, MD, PhD; Lars-Petter Granan, MD, PhD; Sigrun Halvorsen, MD, PhD; Gordon Guyatt, MD, FCCP; and Per Olav Vandvik, MD, PhD

Modified ADAPTE used for this guideline

1. Met in person, decided on scope, and discussed methodological elements of the guideline to be adopted
2. Each panel member independently reviewed each EAU recommendation, methodology, source documents and appendices
3. Each member independently assigned one of 3 possible actions for each of the 32 recommendations (adopt, exclude, modify).
4. Modification based on:
   a) the balance between benefits and harms
   b) confidence in the estimates of the effect of the interventions under consideration
   c) extent of assumed variability in patient values and preferences
   d) resource and health equity considerations
5. Decisions regarding adoption, exclusion, modification, and new topics were agreed upon by Panel consensus.

Result of ADAPTE process

- On first iteration 14 of 32 recommendations were kept without modification
  - In subsequent we combined 14 into 11 recommendations
- From the 18 of 32 recommendations to be modified
  - 4 were excluded as outside of desired scope and replaced with one clinical principle
  - 14 were combined into 7

In summary

- CUA guideline includes 18 recommendations and 1 clinical principle

Excecutive summary CUA guideline

Abbreviated summary of CUA recommendations for postoperative VTE prophylaxis

#	Surgery	Pharmacological prophylaxis		Mechanical prophylaxis
		Risk stata	Strength and direction	Strength and direction
1	Radical cystectomy (open or robotic)	All	Strong for	Weak for
2	Open prostatectomy (without extended PLND)	Low	Weak for	Weak for
		Moderate or high	Strong for	Weak for
3	Open prostatectomy (extended PLND)	All	Strong for	Weak for
4	Robotic or laparoscopic prostatectomy (no PLND)	Low	Strong against	Weak against
		Moderate or high	Weak against	Weak for
5	Robotic or laparoscopic prostatectomy (standard PLND)	Low	Strong against	Weak for
		Moderate	Weak against	Weak for
		High	Weak for	Weak for
6	Robotic or laparoscopic prostatectomy (extended PLND)	Low	Weak against	Weak for
		Moderate	Weak for	Weak for
		High	Strong for	Weak for
7	Open - Radical nephrectomy - Partial nephrectomy - Nephroureterectomy	All	Weak for	Weak for
8	Laparoscopic - Radical nephrectomy	Low or moderate	Weak against	Weak for
		High	Weak for	Weak for
9	Laparoscopic - Partial nephrectomy	Low or moderate	Weak against	Weak for
		High	Strong for	Weak for
10	Robotic - Partial nephrectomy	Low	Weak against	Weak for
		Moderate	Weak for	Weak for
		High	Strong for	Weak for
11	RPLND for testicular germ cell cancer	All	Weak for	Weak for
12	Ambulatory day surgery	All	Strong against	Weak against
13	TURP	All	Weak against	Weak against
14	Nephrectomy for benign disease	Low or moderate	Weak against	Weak against
		High	Weak for	Weak for
15	Continence and prolapse surgery	All	Weak against	Weak against

PLND: pelvic lymph node dissection; TURP: transurethral resection of the prostate; VTE: venous thromboembolism.

Excecutive summary CUA guideline cont'd

Abbreviated summary of CUA recommendations for peri-procedure management of anticoagulants and antiplatelet agents

#	Preoperative agent	Stop days prior	Start days post	Notes
16	Antiplatelets	7 days	4 days	Excludes patients at very high risk of thrombosis: - DES within six months - BMS within six weeks - TIA or stroke within 30 days - New VTE within 1 month - Severe thrombophilia - Cage-ball mechanical heart valves
17	Direct oral anticoagulant	3 days	4 days	
17	Warfarin	5 days	4 days	
17	LMWH			
	- Twice daily formulation	12 hours	4 days	
	- Once daily formulation	24 hours	4 days	
17	Fondaparinux	24 hours	4 days	

Severe thrombophilia defined as anti-thrombin deficiency, protein C deficiency, antiphospholipid antibody, or other as identified by appropriate specialist. BMS: bare metal stent; DES: drug-eluting stent; LMWH: low molecular weight heparin; TIA: transient ischemic attack; VTE: venous thromboembolism.

18: Patients at very high risk of thrombosis in whom surgery can be delayed should have surgery delayed until the period of very high risk is over (strong recommendation, high-quality evidence).

Clinical principle: For patients at very high risk of thrombosis in whom surgery cannot be delayed, our panel recommends multidisciplinary discussion and an individualized treatment plan.