Thromboprophylaxis

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2nd Nordic Course in

Advanced Renal Cancer Surgery

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Introduction

- Surgery induces hypercoagulable state
- Complications of renal surgery include venous thromboembolism (VTE) – composed of deep vein thrombosis (DVT) and pulmonary embolism (PE)
- Bleeding is opposite surgical complication of VTE
- Thromboprophylaxis is a trade-off between decreased risk of VTE and increased risk of bleeding

Thrombo-prophylaxis

- Substantial practice variation in the use of thromboprophylaxis, both within and between countries

Sterious J Urol 2013

Pridgeon BJU Int 2015

Recommendations?

- No consensus on the use of thromboprophylaxis
- Risks known to vary between procedures, but magnitude is uncertain
- EAU had procedure-specific guideline
- Much of the evidence regarding baseline risk is low quality

VTE / Bleeding

What are the elements of risk?

Baseline risk ('natural history') of surgical outcomes

The effect of treatment (prophylaxis)

Patient related risk (and protective) factors

Baseline risk of surgical outcomes

Procedure	Risk of VTE (low- high risk), %	Bleeding requiring reoperation
Open radical cystectomy	2.9-11.6	0.3
Robotic radical cystectomy	2.6-10.3	0.3
RALP without PLND	0.2-0.9	0.4
RALP with extended PLND	0.9-3.7	0.8
Open radical prostatectomy without PLND	1.0-3.9	0.1
Open radical prostatectomy with PLND	3.9-15.7	0.2

- Big variation in the risk of symptomatic VTE between the procedures

Baseline risk of surgical outcomes

Procedure	Risk of VTE (low- high risk), %	Bleeding requiring reoperation
Nephrectomy, Laparoscopic partial	1.1-4.2	1.7
Nephrectomy, Open partial	1.0-3.9	0.1
Nephrectomy- Robotic partial	1.0-3.9	0.5
Nephrectomy, Laparoscopic radical	0.7-2.6	0.5
Nephrectomy, Open radical	1.1-4.4	0.05
Radical nephrectomy with thrombectomy	2.9-11.6	2.0
Open nephroureterectomy	1.6-6.2	0.05

- Nephrectomy is not one procedure when it comes to the risk of VTE

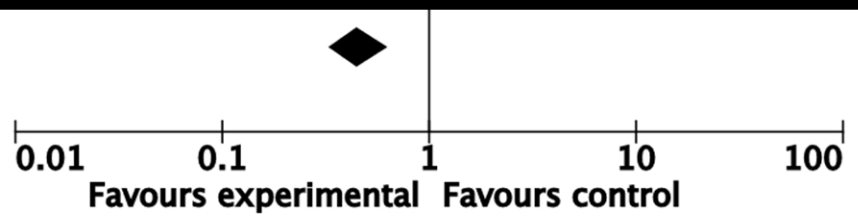
Effect of thromboprophylaxis: Heparin vs. no prophylaxis

Nonfatal PE

~50% decrease

Total (95% CI)	**7014**	**6842**	**100.0%**	**0.46 [0.34, 0.62]**
Total events	58	120		

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 18.22$, df = 25 (P = 0.83); $I^2 = 0\%$
Test for overall effect: Z = 4.96 (P < 0.00001)
Test for subgroup differences: $Chi^2 = 0.12$, df = 1 (P = 0.73), $I^2 = 0\%$

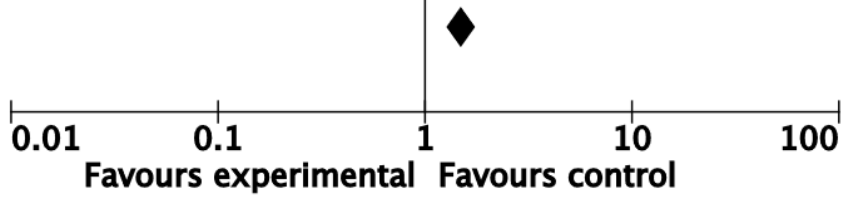


Nonfatal bleeding

~50% increase

Total (95% CI)	**6355**	**6295**	**100.0%**	**1.51 [1.29, 1.76]**
Total events	382	232		

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 34.63$, df = 35 (P = 0.49); $I^2 = 0\%$
Test for overall effect: Z = 5.16 (P < 0.00001)
Test for subgroup differences: $Chi^2 = 1.18$, df = 1 (P = 0.28), $I^2 = 15.0\%$



Lavikainen et al. *Ann Surg* 2023 updated from Tikkinen et al. *Eur Urol* 2018

Likelihood of venous thromboembolism (VTE) according to patient risk factors

	RISK	Likelihood of VTE
Low risk	No risk factors	1x
Medium risk	Any of the following: 75 years or more BMI 35 or more VTE in 1st degree relative	2x
High risk	Prior VTE Patients with any combination of two or more risk factors	4x

Tikkinen KAO EAU Guidelines 2022

When to use thrombo-prophylaxis?

When VTE risk is high and risk of bleeding is low -> use prophylaxis)

When VTE risk is low and risk of bleeding is high -> no prophylaxis

In real life, the trade-off is more complex because uncertainty in both bleeding and VTE estimates

Duration and starting of thromboprophylaxis

When do VTE and bleeding events happen?

How long duration of pharmacologic thromboprophylaxis?

Extended?

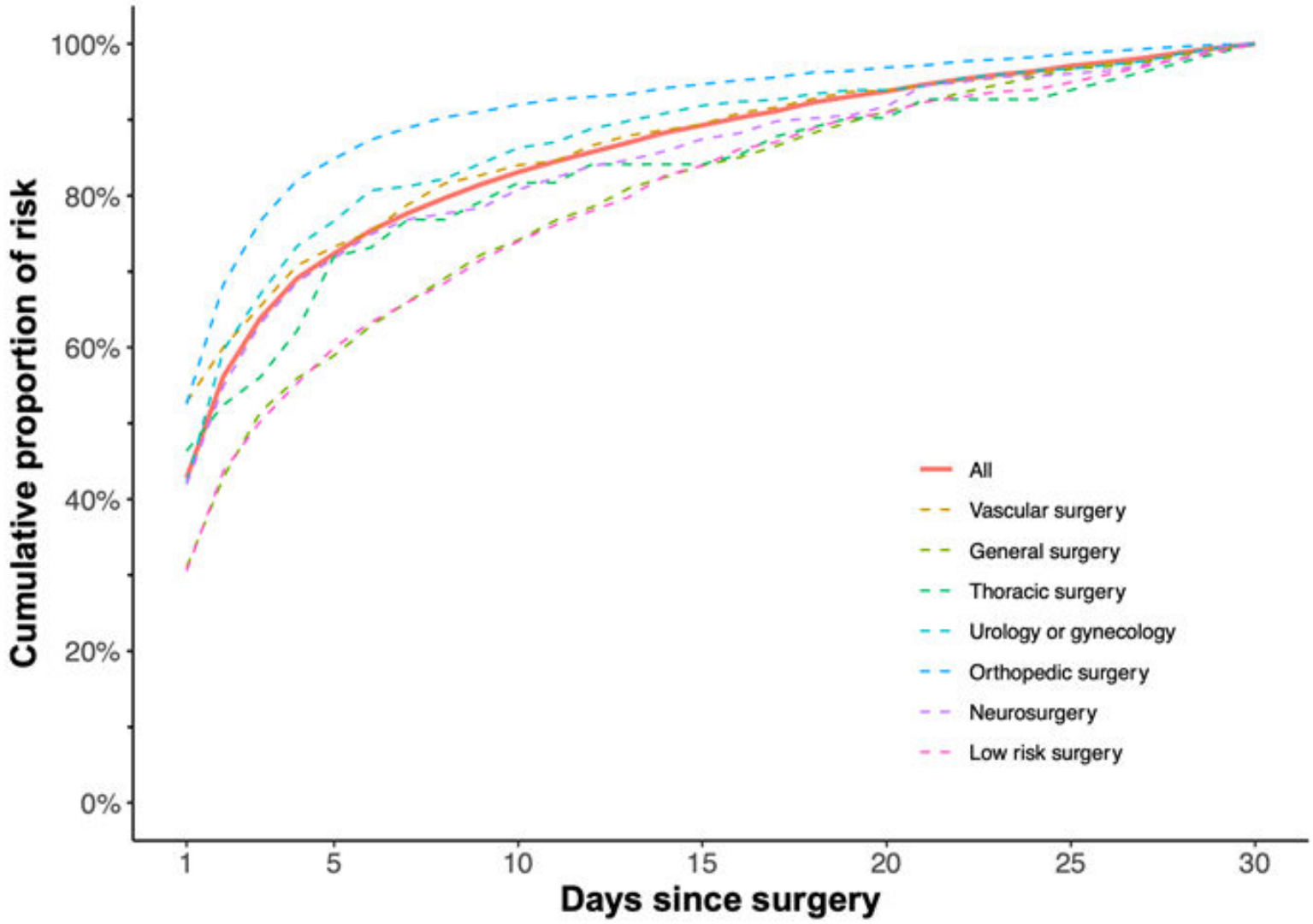
When to start pharmacologic thromboprophylaxis?

Beginning next morning after surgery?

Timing of bleeding

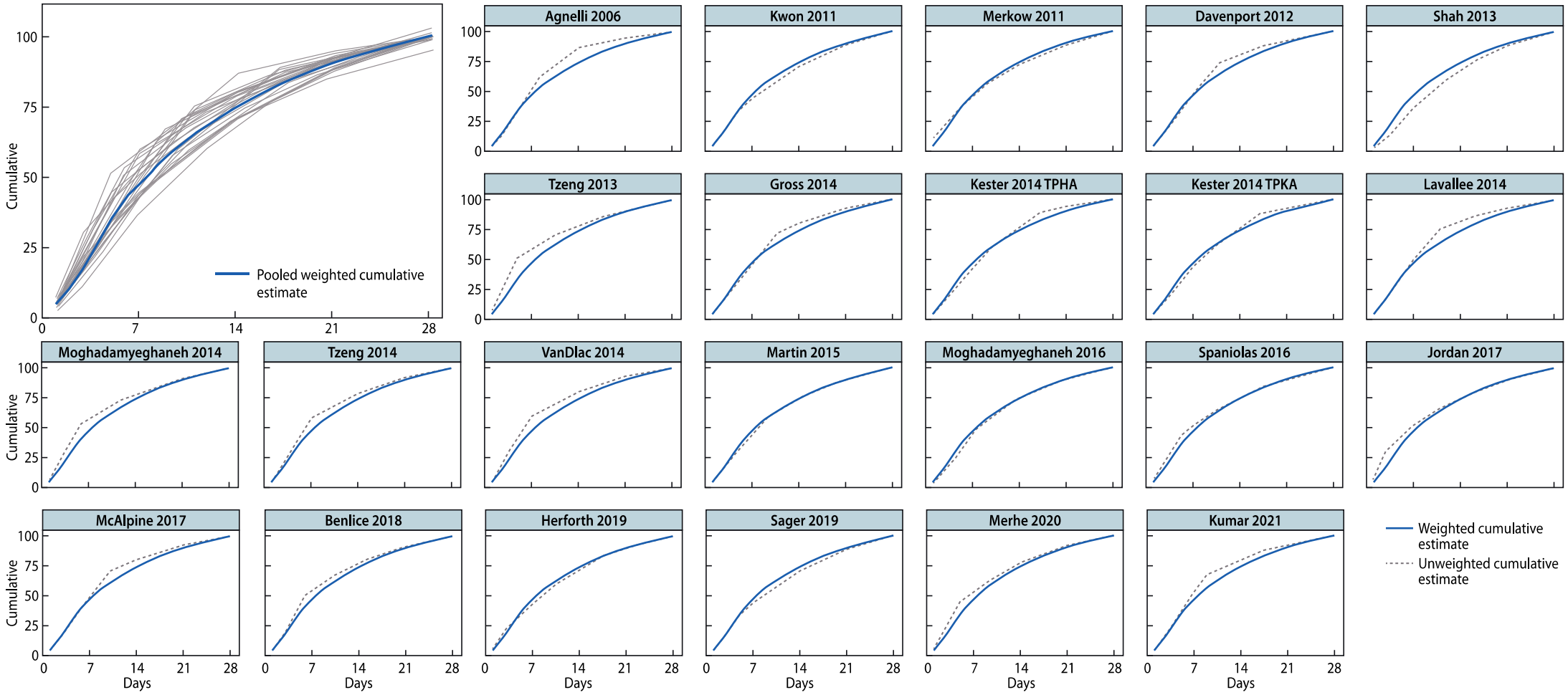
- Roughly 80% of the major bleeding events occur within a week

eFigure 4. Sensitivity Analysis of Cumulative Proportion of Risk for Major Bleeding by Surgical Specialty



Halme et al JAMA Open Network 2024

Timing of symptomatic VTE after Surgery:
a systematic review and meta-analysis



Tino Singh BJS 2023

Timing of symptomatic VTE

- 47.1% of the VTE events occurred during the first week post-surgery
- 26.9% during the second
- 15.8% during the third
- 10.1% during the fourth

Singh BJS 2023

Management of antithrombotic agents during perioperative period

1. To defer surgery until antithrombotics are not needed

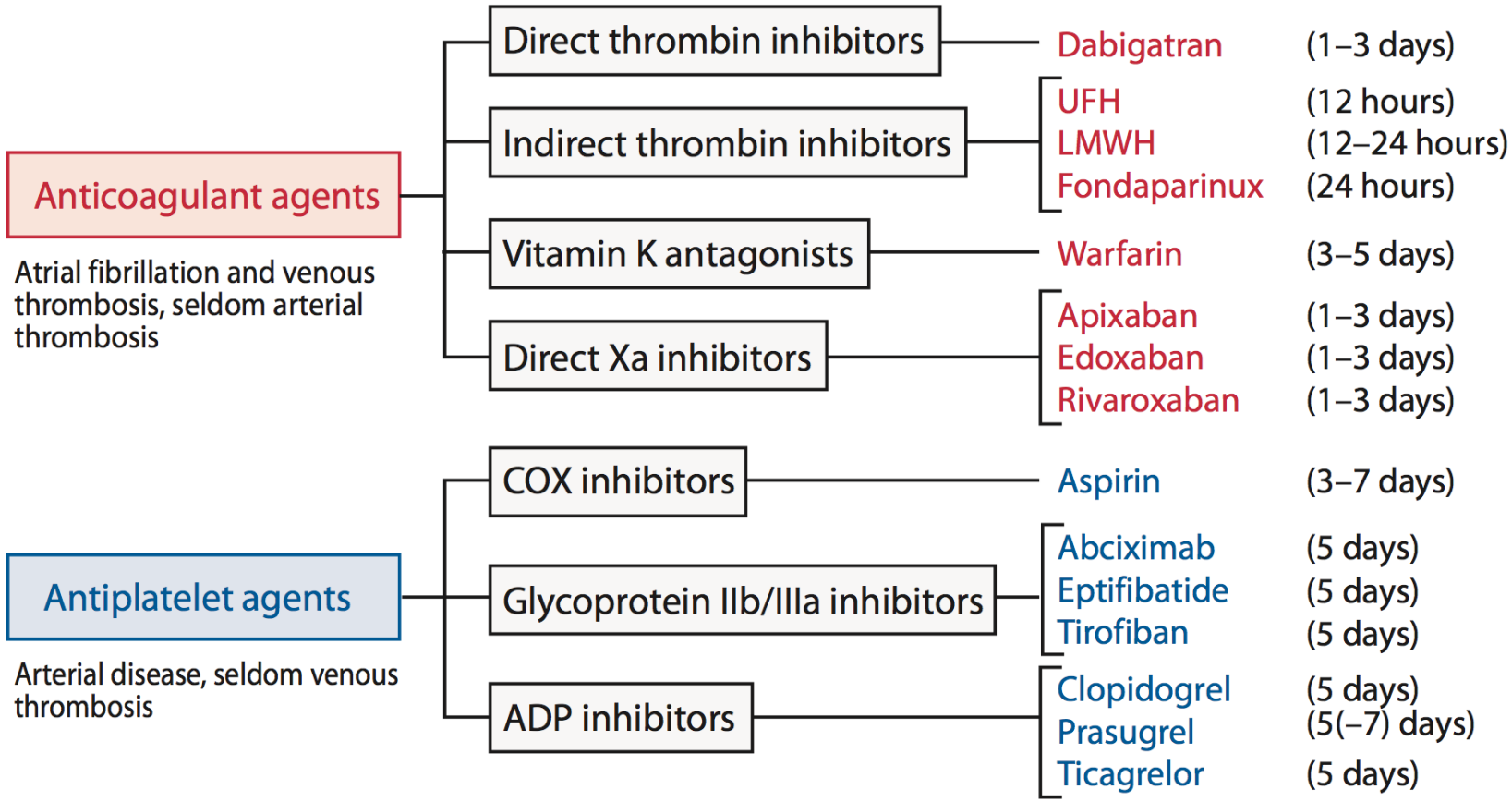
2. Stop antithrombotics prior to surgery and restart after surgery

3. Continue through the surgery

4. ”Bridge” antithrombotic agents

When should you stop antithrombotics?

5 days for antiplatelet agents, various times for anticoagulants



Procedure-specific recommendations for kidney procedures for cancer

Procedure	Baseline risk	Recommendations for pharmacological prophylaxis
Nephrectomy, Laparoscopic partial	Low risk	Weak - against
	Medium risk	Weak - against
	High risk	Strong - for
Nephrectomy, Open partial	Low risk	Weak - for
	Medium risk	Weak - for
	High risk	Weak - for
Nephrectomy- Robotic partial	Low risk	Weak - against
	Medium risk	Weak - for
	High risk	Strong - for
Nephrectomy, Laparoscopic radical	Low risk	Weak - against
	Medium risk	Weak - against
	High risk	Weak - for
Nephrectomy, Open radical	Low risk	Weak - for
	Medium risk	Weak - for
	High risk	Weak - for
Radical nephrectomy with thrombectomy	Low risk	Weak - for
	Medium risk	Weak - for
	High risk	Weak - for

Benefit of ”bridging” is questionable

- Aspirin before surgery and throughout the early postsurgical period increases the risk of major bleeding without reducing arterial thrombotic events Devereux NEJM 2014

- However, perioperative aspirin may be beneficial for patients with prior PCI Graham Ann Inter Med 2017

- Bridging with LMWH increases bleeding without preventing thrombosis Verma JAMA Surgery 2018
  Douketis NEJM 2014
  Steinberg Circulation 2015

Thromboprophylaxis Guidelines 2017-2022

European Society of Anaesthesiology and Intensive Care

VTE prophylaxis 2024 ->

- Based on same evidence
- Same investigators

EAU Guideline panel 2022 recommended

- Discontinue antithrombotic therapy for the period around surgery

- 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.

Tikkinen KAO EAU Guidelines 2022

EAU Guideline panel recommended

- Stop antiplatelet agents before surgery and do not initiate any alternative antithrombotic therapy
- Restart antiplatelets when bleeding is no longer a serious risk
  (e.g. 4 days after surgery)
- In patients with very high risk of thrombosis receiving antiplatelet agents in whom surgery can be delayed, delay surgery

Tikkinen KAO EAU Guidelines 2022

EAU Guideline panel recommended

- In patients receiving anticoagulant agents, except those with very high risk of thrombosis, stop drugs before surgery and do not initiate any alternative antithrombotic therapy

- In patients with a new VTE, surgery should be delayed to permit discontinuation of anticoagulation pre-operatively, rather than operating within 1 month of thrombosis

Tikkinen KAO EAU Guidelines 2022

Timing and duration of thromboprophylaxis

- No direct comparisons of the same agent administered before vs. after surgery
- Studies in orthopedic surgery suggested that prophylaxis can begin 24 hours after surgery without an increase in VTE but with a decrease in bleeding complications
- The EAU Guidelines recommend administration of thromboprophylaxis beginning the day after surgery.

Tikkinen KAO EAU Guidelines 2022

Summary

- When VTE risk is high and risk of bleeding low -> use prophylaxis
- When VTE risk is low and risk of bleeding high -> no prophylaxis
- In perioperative management, less is bridging needed

- Familiarize EAU Guidelines and surgeon friendly infographics on CLUE working group homepage

http://clueworkinggroup.com/2017/12/01/thromboprophylaxis-infographic