Supplementary article data

Thromboembolic and major bleeding events in relation to perioperative bridging of vitamin K antagonists in 649 fast-track total hip and knee arthroplasties

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Appendix

Guidelines on perioperative bridging

Department 1, 2 and 3 (n_{VKA} = 194 (29.8%))

Risk stratification and dosing according to Danish society of Thrombosis and Haemostasis guidelines:

Before 2010 Individual risk assessment based on type of cardiac valve, atrial flutter with previous stroke TIA, hypertension, diabetes, age, genetic disposition to VTE		
After 2011 High risk		
Mechanical heart valves: - ischemic stroke or TIA < 6 months - mitral valve prosthesis - older aortic valves	Atrial fibrillation: - CHADS2 score 4–6 - ischemic stroke or TIA < 6 months - rheumatic valve disease	VTE - VTE <3 months - recurrent VTE - thrombophilia – high risk e.g. protein C or S deficiency, homozygotes factor V Leiden, lupusanticoagulants or a combination - High malignant cancer
TIA: transient ischemic attack VTE: venous thromboembolic event		

Treatment algorithm

Before 2011	Preoperatively	Day of surgery	Postoperatively	
Moderate/high risk [a]	1 day after cessation of VKA	6–12 hours postop.	1. postop day	≥2. postop. days (until INR >2.0)
VTE				
	dalteparin 200 UI/kg x 1/day	dalteparin 5000 IU	dalteparin 5000 IU	dalteparin 200 UI/kg x 1/day
	enoxaparin 1.5mg/kg x 1/day	enoxaparin 40 mg	enoxaparin 40 mg	enoxaparin 1,5mg/kg x 1/day
	tinzaparin 175 UI/kg x 1/day	tinzaparin 4500 UI	tinzaparin 4500 UI	tinzaparin 175 UI/kg x 1/day
Cardiac valve/arterial embolism				
	dalteparin 100UI/kg x 2/day	dalteparin 5000 IU	dalteparin 5000 IU	dalteparin 100UI/kg x 2/day
	enoxaparin 1.5mg/kg x 2/day	enoxaparin 40 mg	enoxaparin 40 mg	enoxaparin 1.5mg/kg x 2/day
Dosis reduction in case of impaired renal function with clearance < 30 mL/min or weight < 50 kg [a] Preoperative bridging not recommended in low risk patients, postoperative bridging as in moderate/high risk. IU: international units, h: hours kg: kilograms, INR: international normalized ratio				

After 2011	Preoperatively			Day of surgery	Postoperatively	
	Preop. day ≥3	Preop. day 2	Preop. day 1	Day 0	Postop. day 1	Postop. day ≥2
High risk						
dalteparin	100 IU /kg x 2	100 IU /kg x 2	100 IU /kg x 1	5000 IU 6–12 h postop.	100 IU /kg x 1	100 IU /kg x 2/day until INR >2.0
tinzaparin	100 IU/kg x 2	100 IU /kg x 2	100 IU /kg x 1	4500 IU 6–12 h postop.	100 IU /kg x 1	100 IU /kg x 2/day until INR >2.0
enoxaparin	1 mg/kg x 2	1 mg/kg x 2	1 mg/kg x 1	40 mg 6–12 h postop.	1 mg/kg x 1	1 mg/kg x 2/day until INR >2.0
Moderate/low risk						
dalteparin	0	0	0	5000 IU 6–12 h postop.	5000 UI	5000 UI /day until INR >2.0
tinzaparin	0	0	0	4500 IU 6–12 h postop.	4500 UI	4500 IU /day until INR >2.0
enoxaparin	0	0	0	40 mg 6–12 h postop.	40 mg	40 mg/day until INR >2.0
IU: international units h: hours kg: kilograms INR: international normalized ratio						

Department 4 (n_{VKA} = 81 (12.5%))

Local guidelines

High risk
2010–2011: Mechanical heart valve, atrial fibrillation with CHADS2 ≥2 venous thromboembolism <6 months
2012–2013: Mechanical heart valve, atrial fibrillation with stroke or CHA2DS2-VASc ≥4 venous thromboembolism <3 months
Low/moderate risk
2010–2011: atrial fibrillation CHADS2 <2 or venous thromboembolism >6 months
2012–2013: Mechanical heart valve, atrial fibrillation with no stroke and CHA2DS2-VASc <4 venous thromboembolism >3 months

Treatment algorithm 2010–2013

	Preoperatively		Day of surgery		Postoperatively	
	Preop. day 4/7 [a]	Preop. day 2	Preop. day 1	Day 0	Postop. day 1–5	Postop. day >5
High risk	cessation of VKA	tinzaparin 175 IU /kg x 1 (max. 18,000 IU/day)	tinzaparin 3500 UI in the evening	tinzaparin 3500 IU 6–12 h postop.	tinzaparin 175 IU /kg x 1 (max. 18,000 IU/day)	tinzaparin 175 IU /kg x 1 (max. 18,000 IU/day) until INR >2.0 for 2 days
Low/moderate risk	cessation of VKA	tinzaparin 3500 UI	tinzaparin 3500 IU	tinzaparin 3500 IU 6–12 h postop.	tinzaparin 3500 IU/day	tinzaparin 3500 IU/day until INR >2.0 for 2 days

[a] 4 for warfarin/ 7 for coumarins, IU: international units, h: hours, kg: kilograms, INR: international normalized ratio.

Department 5 (n_{VKA} = 100 (15.4%))

Local guideline

Individual based risk assessment based upon Danish Society of Thrombosis and Haemostasis guidelines (see department 1,2 and 3).

Treatment algorithm

Moderate/high risk [a]	Preoperatively	Day of surgery	Postoperatively	
	1 day after cessation of VKA	6–12 hours postop.	1. postop. day	≥ 2. postop. days (until INR >2.0)
VTE	dalteparin 200 UI/kg x 1/day	dalteparin 5000 IU	dalteparin 5000 IU	dalteparin 200 UI/kg x 1/day
Cardiac valve/arterial embolism	dalteparin 100UI/kg x 2/day	dalteparin 5000 IU	dalteparin 5000 IU	dalteparin 100UI/kg x 2/day

Dosis reduction in case of impaired renal function with clearance < 30 mL/min or weight < 50 kg.
[a] Preoperative bridging not recommended in low risk patients, postoperative bridging as in moderate/high risk.
IU: international units kg: kilograms INR: international normalized ratio

Department 6 (n_{VKA} = 92 (14.2%))

Local guideline

High risk (always preop. bridging)	Moderate risk (preop. bridging depending on clinical assessment)	Low risk (no preop. bridging)
Any mechanical heart valve Atrial fibrillation with one of the following: ischemic stroke or TIA hypertension cardiac insufficiency/left ventricular dysfunction diabetes age > 75 years Thrombophilia High malignancy cancer VTE < 3 months	Atrial fibrillation without other complications and age 65–75 years VTE > 3 and < 12 months	Atrial fibrillation without other complications and age <65 years VTE no more than once and >12 months Biologic mitral valve

TIA: transient ischemic attack, VTE: venous thromboembolic event

Treatment algorithm

Preoperatively		Day of surgery	Postoperatively
2 days after cessation of VKA	1 day preop.	6–8 hours postop.	until INR >2
dalteparin 2500 UI x 2 daily	dalteparin 2500 UI x 2 daily (last dose >12 hours preop.)	dalteparin 2500 IU x 2	dalteparin 2500 IU x 2

IU: international units, INR: international normalized ratio

Department 7 (n_{VKA} = 91 (14.0%)

Local guideline

Preoperative bridging in all-patients with VKA

Treatment algorithm

Preoperatively		Day of surgery	Postoperatively	
4 days preop.	2 days after cessation of VKA	1 day preop.	6–8 hours postop.	until INR >2 for 2 days
Cessation of VKA	dalteparin 5000 UI x1 daily	no bridging	dalteparin 5000 IU x1 if sufficient hemostasis	dalteparin 5000 IU x 1/day

In case of renal affection with creatinine >200 dalteparin 100 IU/kg x1
IU: international units, INR: international normalized ratio

Department 8 (n_{VKA} = 91 (14.0%))

Local guidelines

Risk assessment 2010–2012
- High risk: Atrial fibrillation with cardiac disposition, previous VTE, diabetes, cardiac insufficiency. Other conditions (VTE or cardiac valve) depending on clinical assessment.

Risk assessment after 2012
- High risk (preop. bridging)
  - Atrial fibrillation with:
    - ischemic stroke or TIA
    - mitral stenosis
    - prosthetic valve
  - Atrial fibrillation with two of the following:
    - cardiac insufficiency
    - hypertension
    - diabetes
    - age >75 years
    - ejection fraction < 35%
  - Mechanical heart valve
  - Heart valve surgery < 3 months
  - VTE < 3 months or with cancer/thrombophilia
- Low risk (no preop. bridging)
  - Atrial fibrillation without other complications and age < 65 years
  - VTE no more than once and > 12 months
  - Biologic mitral valve

TIA: transient ischemic attack VTE: venous thromboembolic event

Treatment algorithms

	5 days preop.	Preoperatively 2 days after cessation of VKA	1 day preop.	Day of surgery 6–8 hours postop.	Postoperatively until INR > 2
2010–2012					
High risk	cessation of VKA	enoxaparin 1 mg/kg x 2/day	enoxaparin 1 mg/kg x1	enoxaparin 1 mg/kg x 1	enoxaparin 1 mg/kg x 2/day
Low risk	cessation of VKA	enoxaparin 40mg x 2 daily	enoxaparin 40 mg x1	enoxaparin 40 mg x 1	enoxaparin 40 mg x 2/day
2013					
High risk	cessation of VKA	dalteparin 100 IU/kg x 2	dalteparin 100 IU/kg x 1 (24 hours preop.)	dalteparin 5000 IU x 1	dalteparin 5000 IU x1/day
Low risk	cessation of VKA	–	–	–	–

INR: international normalized ratio, IU: international units