Tromboseprofylakse ved artroskopisk kirurgi

Jørn Dalsgaard Nielsen

Hvorfor tromboseprofylakse?

For 30 år siden var kirurgi den hyppigste årsag til venetrombose og lungeemboli under indlæggelse

Årsager til venøs tromboembolisk sygdom (VTE)

Blandt faktorer, som disponerer til VTE, er kirurgi stadig den vigtigste enkeltfaktor.

Nordström M et al.
J Intern Med 1992;232:155.

Heit JA et al.
Arch Intern Med. 2002;162:1245–8.

VTE: >50 risk factors

Surgery. Trauma. High age. Partus and puerperium. Perivenous inflammation. Radioisotope exposure. Intravenous catheters. Chemotherapy. Malignant diseases. Antitrombin deficiency. Protein C deficiency. Protein S deficiency. Faktor V Leiden mutation. Prothrombin mutation. Heparin cofactor II deficiency. Lupus inhibitor. Cardiolipin antibody. Beta-2-glycoprotein-1-antibody. Severe factor XII deficiency. High factor VIII. High factor VII. Hypofibrinolysis. Homocysteinemi. Nephrotic syndrome. Inflammatory intestinal disease. Oral contraception and estrogen. Venous obstruction. Insufficient (use of) vein pump. High blod/plasma viscocity. Previous VTE. Other venous obstruction. Venous malformations. e.g. vena cava atresia. Paralysed limbs. Plaster casts. Immobilisation e.g. bed rest. Long journeys. Venous insufficiency. Varicous veins. Obesity. Pregnancy. Heart failure. Respiratory failure. Assisted ventilation. Dehydration. Myeloproliferative disease.

VTE-risiko ved kirurgi

Hoftefrakturkirurgi

Elektiv hofte- og knæalloplastik

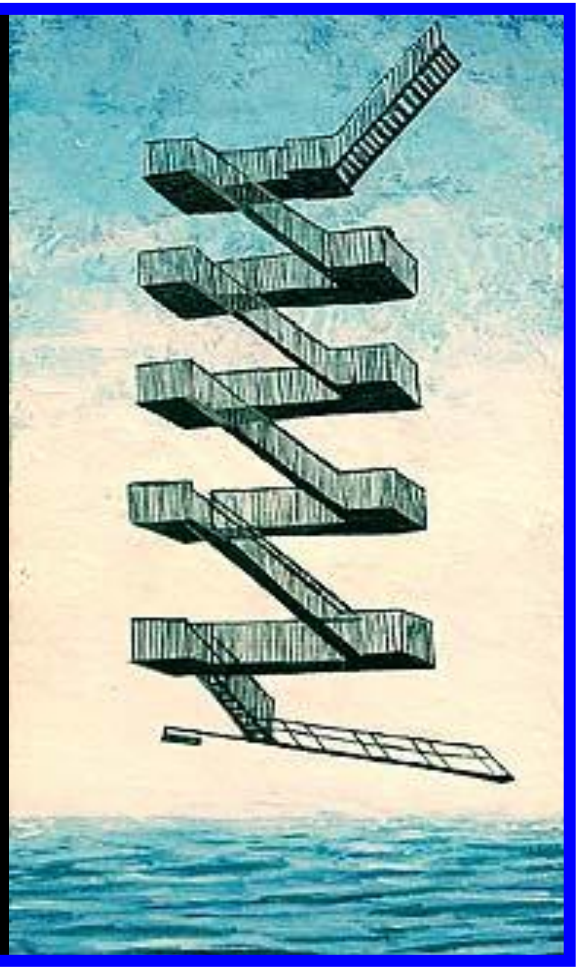
Kolorektalkirurgi

Ikke-malign abdominalkirurgi

..

..

Sammedagskirurgi



Profylaksemetoder

Hoftefrakturkirurgi

Elektiv hofte- og knæalloplastik

Kolorektalkirurgi

Ikke-malign abdominalkirurgi

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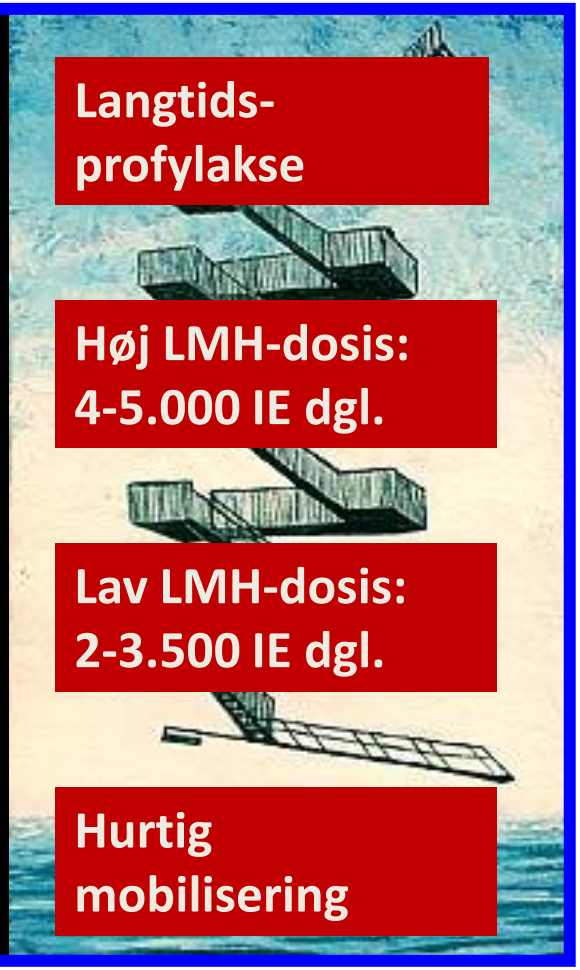
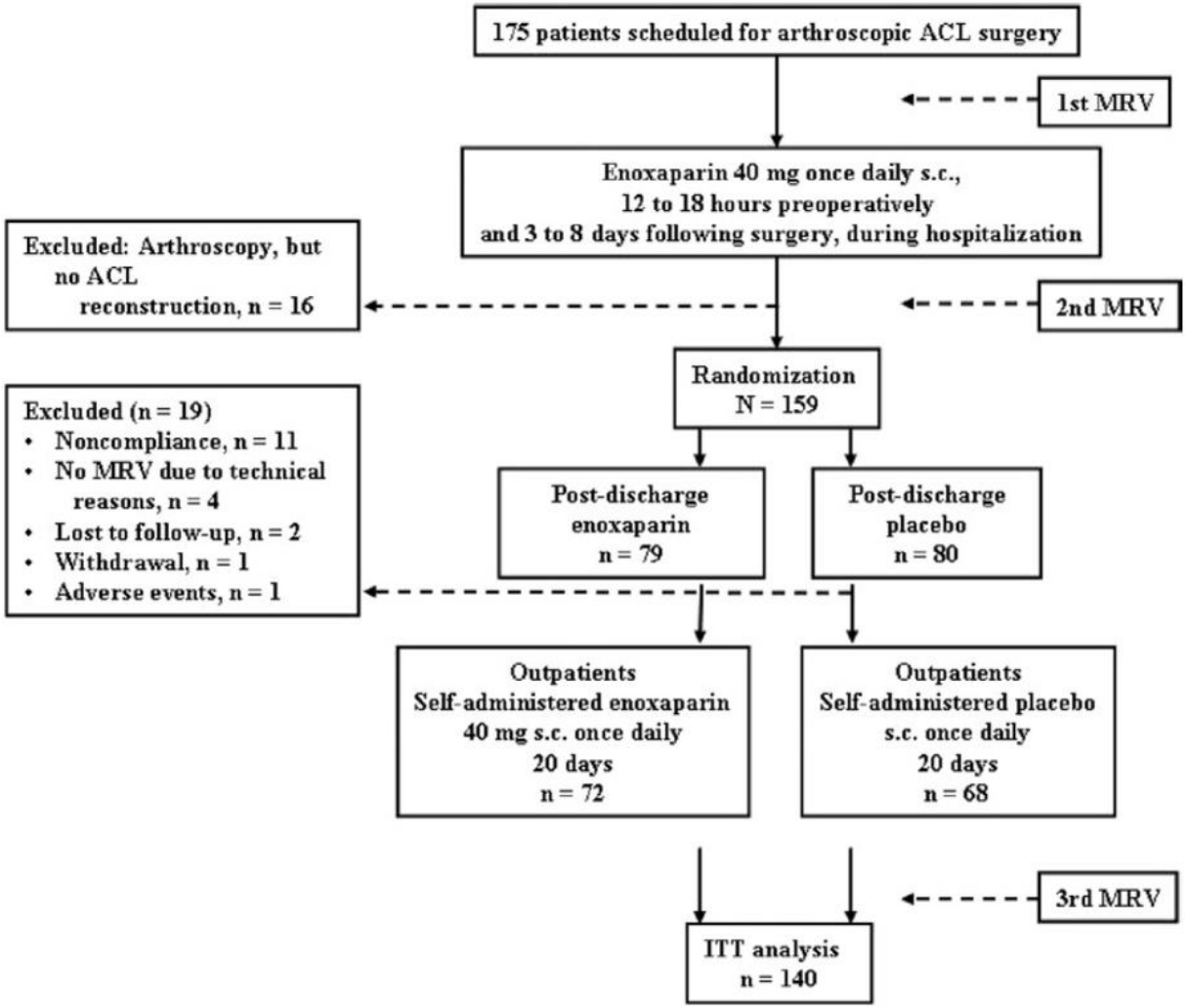
Sammedagskirurgi



Mekaniske metoder:

1. IPC
2. TED

Extended-Duration Thromboprophylaxis With Enoxaparin After Arthroscopic Surgery of the Anterior Cruciate Ligament: A Prospective, Randomized, Placebo-Controlled Study



Marlovits et al. Arthroscopy 2007;23:696-702

Extended-Duration Thromboprophylaxis With Enoxaparin After Arthroscopic Surgery of the Anterior Cruciate Ligament: A Prospective, Randomized, Placebo-Controlled Study

End-points, n (%)	Postdischarge Thromboprophylaxis* Enoxaparin (n = 72)	Postdischarge Thromboprophylaxis* Placebo (n = 68)	*P* Value†
Efficacy endpoints			
Total DVT	2 (2.8)	28 (41.2)	<.001
Femoral DVT	1 (1.4)	6 (8.8)	.044
Lower leg DVT	2 (2.8)	28 (41.2)	<.001
Popliteal DVT	2 (2.8)	12 (17.6)	.003
PE	0 (0)	0 (0)	—
Safety end-points			
Major bleeding	0 (0)	0 (0)	—
Minor bleeding‡	13 (2.5)	10 (2.0)	.595
Other adverse events	0 (0)	0 (0)	—

*All patients received in-hospital thromboprophylaxis with enoxaparin for 3 to 8 days before randomization.

Marlovits et al. Arthroscopy 2007;23:696-702

CHEST Supplement

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Prevention of VTE in Orthopedic Surgery Patients

Recommendation

4.0. For patients undergoing knee arthroscopy without a history of prior VTE, we suggest no thromboprophylaxis rather than prophylaxis (Grade 2B).

Falck-Ytter et al. Chest 2012; 141(2)(Suppl):e278S–e325S

NICE National Institute for Health and Care Excellence

April 2008 - Update: discussions between NICE and the British Orthopaedic Association

Discussions have taken place between the National Institute for Health and Clinical Excellence (NICE) and the British Orthopaedic Association (BOA) on the issues generated by the NICE guideline on the prevention of venous thrombo-embolism (VTE). It was concluded that as the guidance was generic, further information should be made available to allow orthopaedic surgeons to understand the relevance of the guidelines to their practice.

This page was last updated: **30 March 2010**

Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy (Review)

Ramos J, Perrotta C, Badariotti G, Berenstein G

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 3

Analysis 1.1. Comparison 1 Prophylactic treatment (all LMWH) versus no treatment, Outcome 1 Participants with thrombotic events (both clinical and through diagnostic procedure).

Review: Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy

Comparison: 1 Prophylactic treatment (all LMWH) versus no treatment

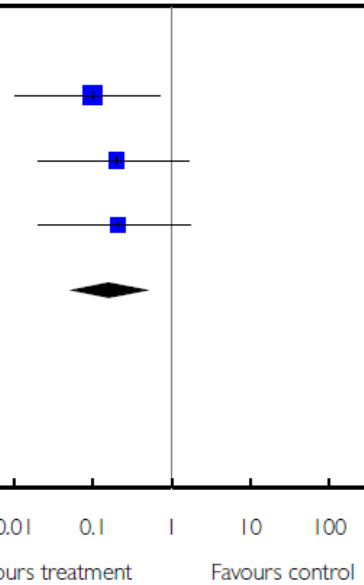
Outcome: 1 Participants with thrombotic events (both clinical and through diagnostic procedure)

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Canata 2003	0/18	0/18		0.0 [0.0, 0.0]
Michot 2002	1/66	10/64		0.10 [0.01, 0.74]
Roth 1995	1/61	5/61		0.20 [0.02, 1.66]
Wirth 2001	1/117	5/122		0.21 [0.02, 1.76]
Total (95% CI)	**262**	**265**		**0.16 [0.05, 0.52]**

Total events: 3 (Treatment), 20 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.34$, df = 2 (P = 0.84); $I^2 = 0.0\%$

Test for overall effect: Z = 3.01 (P = 0.0026)



Ramos J et al. Cochrane Database Syst Rev 2008;(4):CD005259

Analysis 1.2. Comparison 1 Prophylactic treatment (all LMWH) versus no treatment, Outcome 2 Participants with clinical thrombotic events.

Review: Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy

Comparison: 1 Prophylactic treatment (all LMWH) versus no treatment

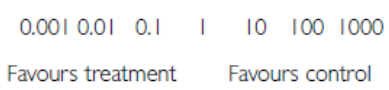
Outcome: 2 Participants with clinical thrombotic events

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
Canata 2003	0/18	0/18		0.0 [0.0, 0.0]
Michot 2002	0/66	0/64		0.0 [0.0, 0.0]
Roth 1995	1/61	1/63		1.03 [0.07, 16.15]
Wirth 2001	0/117	3/122		0.15 [0.01, 2.85]
Total (95% CI)	**262**	**267**		**0.42 [0.06, 3.14]**

Total events: 1 (Treatment), 4 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.92$, df = 1 (P = 0.34); $I^2 = 0.0\%$

Test for overall effect: Z = 0.84 (P = 0.40)



Ramos J et al. Cochrane Database Syst Rev 2008;(4):CD005259

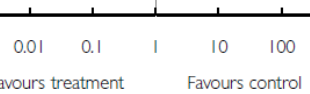
Analysis 1.3. Comparison 1 Prophylactic treatment (all LMWH) versus no treatment, Outcome 3 Participants with adverse events.

Review: Interventions for preventing venous thromboembolism in adults undergoing knee arthroscopy

Comparison: 1 Prophylactic treatment (all LMWH) versus no treatment

Outcome: 3 Participants with adverse events

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 All adverse events					
Canata 2003	3/18	2/18		16.8 %	1.50 [0.28, 7.93]
Michot 2002	8/66	4/64		35.2 %	1.94 [0.61, 6.12]
Roth 1995	7/61	1/61		10.9 %	7.00 [0.89, 55.20]
Wirth 2001	7/117	5/122		37.1 %	1.46 [0.48, 4.47]
Subtotal (95% CI)	**262**	**265**		**100.0 %**	**1.92 [0.97, 3.80]**
Total events: 25 (Treatment), 12 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.88$, df = 3 (P = 0.60); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.88 (P = 0.060)					
2 Minor bleedings					
Canata 2003	3/18	2/18		23.4 %	1.50 [0.28, 7.93]
Michot 2002	8/66	4/64		49.2 %	1.94 [0.61, 6.12]
Roth 1995	5/61	1/61		14.5 %	5.00 [0.60, 41.55]
Wirth 2001	3/117	1/122		12.9 %	3.13 [0.33, 29.65]
Subtotal (95% CI)	**262**	**265**		**100.0 %**	**2.23 [0.99, 4.99]**
Total events: 19 (Treatment), 8 (Control)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.94$, df = 3 (P = 0.82); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.95 (P = 0.052)					



Ramos J et al. Cochrane Database Syst Rev 2008;(4):CD005259

Cochrane-analysens konklusioner

The incidence of DVT during arthroscopy varies from 3.1% to 17.9% in a meta-analysis by Ilahi et al. However, the question we are looking for an answer to is: what is the clinical relevance of distal thrombosis diagnosed through sonogram?
The literature is not conclusive in this area.

The number needed to treat to benefit (NNTB) (17) relates to asymptomatic DVT, and the number needed to harm (NNTH) (20) is about a clinical event. Assuming a ratio of asymptomatic distal DVT to clinically apparent DVT of 1:10 to 1:20, the NNTB to prevent a clinical event would range from 170 to 340.

We conclude that the physician needs to discuss these benefits and possible complications with the patient until new studies are performed. It is essential that future studies stratify patients according to their risk factors, and also stratify arthroscopic procedures.

Ramos J et al. Cochrane Database Syst Rev 2008;(4):CD005259

Low-Molecular-Weight Heparin versus Compression Stockings for Thromboprophylaxis after Knee Arthroscopy (KANT Study)

- **Patients**
  - 1761 consecutive patients undergoing knee arthroscopy
- **Design**
  - Open, randomized study
- **Intervention**
  - Patients were randomly assigned to wear full-length graduated compression stocking for 7 days (660 patients) or
  - to receive a once-daily subcutaneous injection of LMWH nadroparin, 3800 anti-Xa IU for 7 days (657 patients) or
  - nadroparin, 3800 anti-Xa IU for 14 days (444 patients).
- The data and safety monitoring board prematurely stopped the 14-day heparin group after the second interim analysis.

Camporese et al. Ann Intern Med. 2008;149:73-82.

Low-Molecular-Weight Heparin versus Compression Stockings for Thromboprophylaxis after Knee Arthroscopy (KANT Study)

Table 2. **Efficacy and Safety Results at Eighth-Day Color-Coded Doppler Ultrasonography***

Variable	7-d GCS (*n* = 660), *n* (%)	7-d LMWH (*n* = 657), *n* (%)	14-d LMWH [95% CI] (*n* = 444), *n* (%)†	Absolute Difference (95% CI), 7-d GCS vs. 7-d LMWH, *percentage points*	*P* Value‡
Primary efficacy end point	21 (3.2)	6 (0.9)	4 (0.9 [0.4 to 2.3])	2.3 (0.7 to 4.0)	0.005
Death	0	0	0	0	
Symptomatic PE (nonfatal)	2 (0.3)	2 (0.3)	2 (0.5 [0.1 to 1.6])	0	
Asymptomatic proximal DVT	7 (1.1)	2 (0.3)	0	0.8 (−0.1 to 1.6)	
Symptomatic proximal DVT	1 (0.2)	0	1 (0.2 [0.0 to 1.3])	0.2 (−0.1 to 0.4)	
Symptomatic distal DVT	11 (1.7)	2 (0.3)	1 (0.2 [0.0 to 1.3])	1.4 (0.3 to 2.4)	
Secondary efficacy end point§	31 (4.7)	12 (1.8)	11 (2.5 [1.4 to 4.4])	2.9 (1.0 to 4.8)	0.005
Asymptomatic distal DVT	10 (1.5)	6 (0.9)	7 (1.6 [0.8 to 3.2])	0.6 (−0.6 to 1.8)	
Primary safety end point	2 (0.3)	6 (0.9)	2 (0.5 [0.1 to 1.6])	−0.6 (−1.5 to 0.2)	–
Major bleeding event	1 (0.2)‖	2 (0.3)¶	1 (0.2 [0.0 to 1.3])**	−0.2 (−0.7 to 0.4)	
Clinically relevant bleeding event	1 (0.2)††	4 (0.6)‡‡	1 (0.2 [0.0 to 1.3])§§	−0.5 (−1.4 to 0.3)	
Secondary safety end point‖‖	22 (3.3)	29 (4.4)	18 (4.1 [2.6 to 6.3])	−1.1 (−3.2 to 1.0)	–
Minor bleeding event	20 (3.0)	23 (3.5)	16 (3.6 [2.2 to 5.8])	−0.5 (−2.4 to 1.4)	

DVT = deep venous thrombosis; GCS = graduated compression stockings; LMWH = low-molecular-weight heparin; PE = pulmonary embolism.
* All events occurred in the operated leg.
† Stopped after the second interim analysis.
‡ We analyzed only data on the primary and secondary end points. Additional details are reported for descriptive purposes only. All *P* values are 2-tailed (Fisher exact test).
§ Secondary efficacy end point = primary efficacy end point + asymptomatic distal DVT.
‖ Large hematoma of the operated leg associated with a hemoglobin decrease of 39 g/L.
¶ Hemarthrosis requiring re-intervention with 600-mL blood joint drainage and large hematoma of the operated leg associated with a hemoglobin decrease of 25 g/L.
** Gastrointestinal hemorrhage requiring admission and transfusion of 3 units of packed red blood cells.
†† Hemarthrosis with 130-mL blood joint drainage.
‡‡ Hemarthroses with 170-, 200-, 270-, and 300-mL blood joint drainage.
§§ Hemarthrosis with 250-mL blood joint drainage.
‖‖ Secondary safety end point = primary safety end point + minor bleeding events.

Camporese et al. Ann Intern Med. 2008;149:73-82.

Incidence of symptomatic VTE after elective knee arthroscopy

- A retrospective cohort study of elective arthroscopic knee procedures during a twenty-seven-month period (January 1, 2006, through March 31, 2008)
- Use of the administrative database identified 21,794 arthroscopic knee procedures.
- The occurrence of a symptomatic DVT or PE within ninety days after surgery was identified.
- Mortality and the cause of death were captured with use of electronic medical records.
- Patient charts were reviewed for confirmation of DVT, PE, or death.
- Patients who had a history of a venous thromboembolism or who had received anticoagulation therapy within fourteen days prior to the index surgery were excluded.

Maletis et al. J Bone Joint Surg Am. 2012;94:714-20

Incidence of symptomatic VTE after elective knee arthroscopy

Results

- The study cohort comprised 20,770 patients who met the inclusion criteria.
- 51 patients developed a DVT
  - (0.25%; 95% confidence interval, 0.18% to 0.31%)
- 35 patients developed a pulmonary embolism
  - (0.17%; 95% confidence interval, 0.11% to 0.22%)
- 9 patients (0.04%) died within ninety days of surgery
  - Only 1 death was confirmed to have resulted from a PE

Maletis et al. J Bone Joint Surg Am. 2012;94:714-20

The burden of arthroscopy of the knee

A CONTEMPORARY ANALYSIS OF DATA FROM THE ENGLISH NHS

- Prospectively collected admissions data, routinely collected on every English NHS patient, were analysed to determine the rates of complications within 30 days (including reoperation and re-admission), 90-day symptomatic venous thromboembolism and all-cause mortality.
- There were 301,701 operations performed between 2005 and 2010 – an annual incidence of 9.9 per 10,000 English population.
- Of these, 16,552 (6%) underwent ligament reconstruction and 106,793 (35%) underwent meniscal surgery.

Jameson et al. J Bone Joint Surg Br 2011;93-B:1327–33.

The burden of arthroscopy of the knee

A CONTEMPORARY ANALYSIS OF DATA FROM THE ENGLISH NHS

Table III. Complications following arthroscopy of the knee in the English NHS (2005 to 2010)

Complication*	Number of patients (%)
Orthopaedic re-admission	1662 (*0.55*)
Any wound complication	677 (*0.22*)
Unplanned re-operation	1033 (*0.34*)
Lower leg fasciotomy for compartment syndrome	13 (*0.00*)
Myocardial infarction	48 (*0.02*)
Lower respiratory tract infection	72 (*0.02*)
Cerebrovascular event (including transient)	52 (*0.02*)
Acute renal failure	40 (*0.01*)
VTE event within 90 days†	580 (*0.19*)
DVT	369 (*0.12*)
Non-fatal PE	224 (*0.08*)
Fatal PE	6 (*0.00*)
Death (all-cause, in-hospital) within 90 days	47 (*0.02*)

* complication within 30 days unless stated

† VTE, venous thromboembolism; DVT, deep-vein thrombosis; PE, pulmonary thromboembolism. Some patients had both DVT and PE

Jameson et al. J Bone Joint Surg Br 2011;93-B:1327–33.

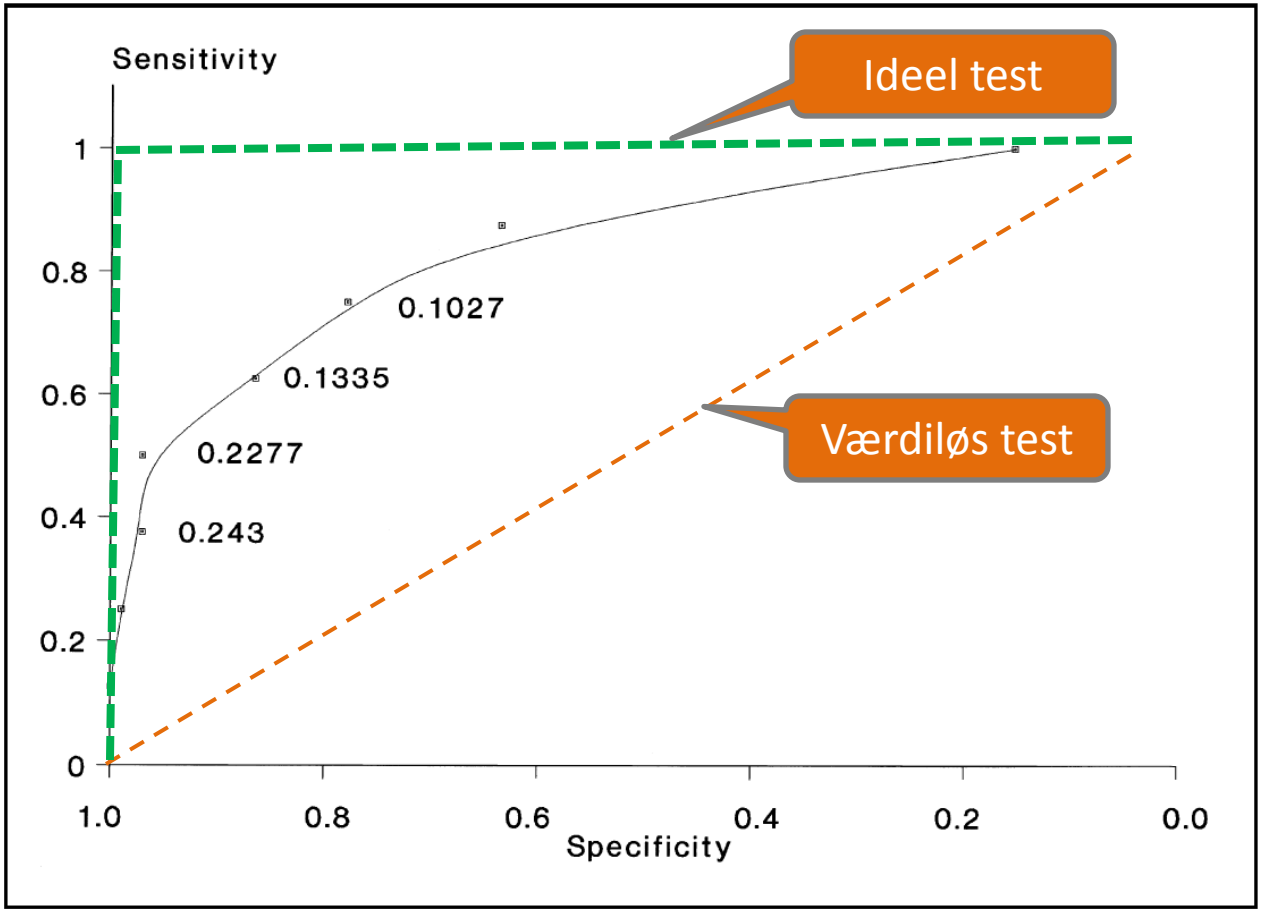
Risk factors of DVT in elective knee arthroscopy

Risk Factors	Relative Risk	95% Confidence Interval
Age > 65 years	2.314	0.601-8.914
Past DVT	8.167	2.341-28.492
Chronic Venous Insufficiency	0.978	0.131-7.320
Obesity (BMI > 30)	2.46	0.641-9.445
Tourniquet time > 30 min	2.302	0.582-9.104
Hormonal Replacement or Oral Contraception	3.444	0.811-14.635

DVT = 0.0059 + 0.0407 (tourniquet time[>30 min]) + 0.0968 (obesity [BMI>30]) + 0.125 (age[>65 years]) - 0.0381 (CEAP2-4) + 0.439 (past DVT) + 0.0996 (hormonal replacement therapy/oral contraception)

Delis et al. Thromb Haemost 2001; 86: 817–21

Risk factors of DVT in elective knee arthroscopy



Delis et al. Thromb Haemost 2001; 86: 817–21

Risk factors of DVT [illegible] rthroscopy

Alt for få
som basis for en
algoritme

Risk Factors	[illegible] n=102 [illegible]r (100%)	[illegible]VT (+) [illegible]=8 or (8%)	Patients DVT (-) n=94 or (92.2%)
Age > 65 yrs	24 (23.5)	4 [illegible]50)	20 (21.3)
Obesity (BMI>30)	21 (20.6)	3 ([illegible]7.5)	14 (14.9)
Smoking	24 (23.5)	0 (0)	24 (24.5)
Oral Contraception or Hormone Replacement	9 (8.8)	2 [illegible]25)	7 (7.5)
Chronic Venous Insufficiency$_{CEAP\ 2\text{-}4}$ [24]	13 (12.7)	1 ([illegible]2.5)	12 (12.8)
Previous DVT*	4 (3.9)	2 ([illegible]25)*	2 (2.1)*

Delis et al. Thromb Haemost 2001; 86: 817–21

Fremtiden……?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Arthroscopic instrument
Viewing scope
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ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Prevention of VTE in Orthopedic Surgery Patients

Recommendation

4.0. For patients undergoing knee arthroscopy without a history of prior VTE, we suggest no thromboprophylaxis rather than prophylaxis (Grade 2B).

Falck-Ytter et al. Chest 2012; 141(2)(Suppl):e278S–e325S

Tromboseprofylakse med rivaroxaban ved knæartroskopi

- 467 patienter, som fik foretaget knæartroskopi, fik tromboseprofylakse med
  - Bemiparin i 3 uger *eller*
  - Rivaroxaban 10 mg i 3 uger
- Endepunkt: Symptomatisk, objektivt verificeret DVT
  - Ingen patienter fik DVT
- Rivaroxaban blev seponeret hos 1 patient pga epistaxis

Muñoa et al. Musculoskelet Surg 2013, Jul 14. Epub ahead of print

Perioperativ Regulering af Antitrombotisk Behandling (PRAB)

» Retningslinjer for

Perioperativ regulering af antitrombotisk behandling

Udarbejdet af Dansk Selskab for Trombose og Hæmostase – et tværfagligt selskab med fagområde under Organisationen af Lægevidenskabelige Selskaber

www.dsth.dk

Blødningsrisiko ved indgreb under vedligeholdt VKA-behandling

Lav risiko	Intermediær risiko	Høj risiko
Kataraktoperation Mundhulekirurgi Tandekstraktion Kutan kirurgi Pacemakerimplantation Ledpunktur TUR-P ved laserablation Endoskopiske lavrisikoprocedurer	Indgreb, hvor risikoen hverken er lav eller høj, f.eks.: Anlæggelse af centralt venekateter Angiografi Bronkoskopi Større kirurgi, generelt	Neuraksial blokade Neurokirurgi Endoskopiske højrisikoprocedurer Leverbiopsi og andre dybe biopsier med grov kanyle Operation i områder med rig vaskularisering, inflammation eller talrige adhærencer

VKA-behandling:		
INR i terapeutisk niveau	**INR gerne <2,0 (max 2,5)**	**INR <1,5**

Orthopedics. 2010 Feb;33(2):82-6. doi: 10.3928/01477447-20100104-08.

Arthroscopy on anticoagulated patients: a retrospective evaluation of postoperative complications.

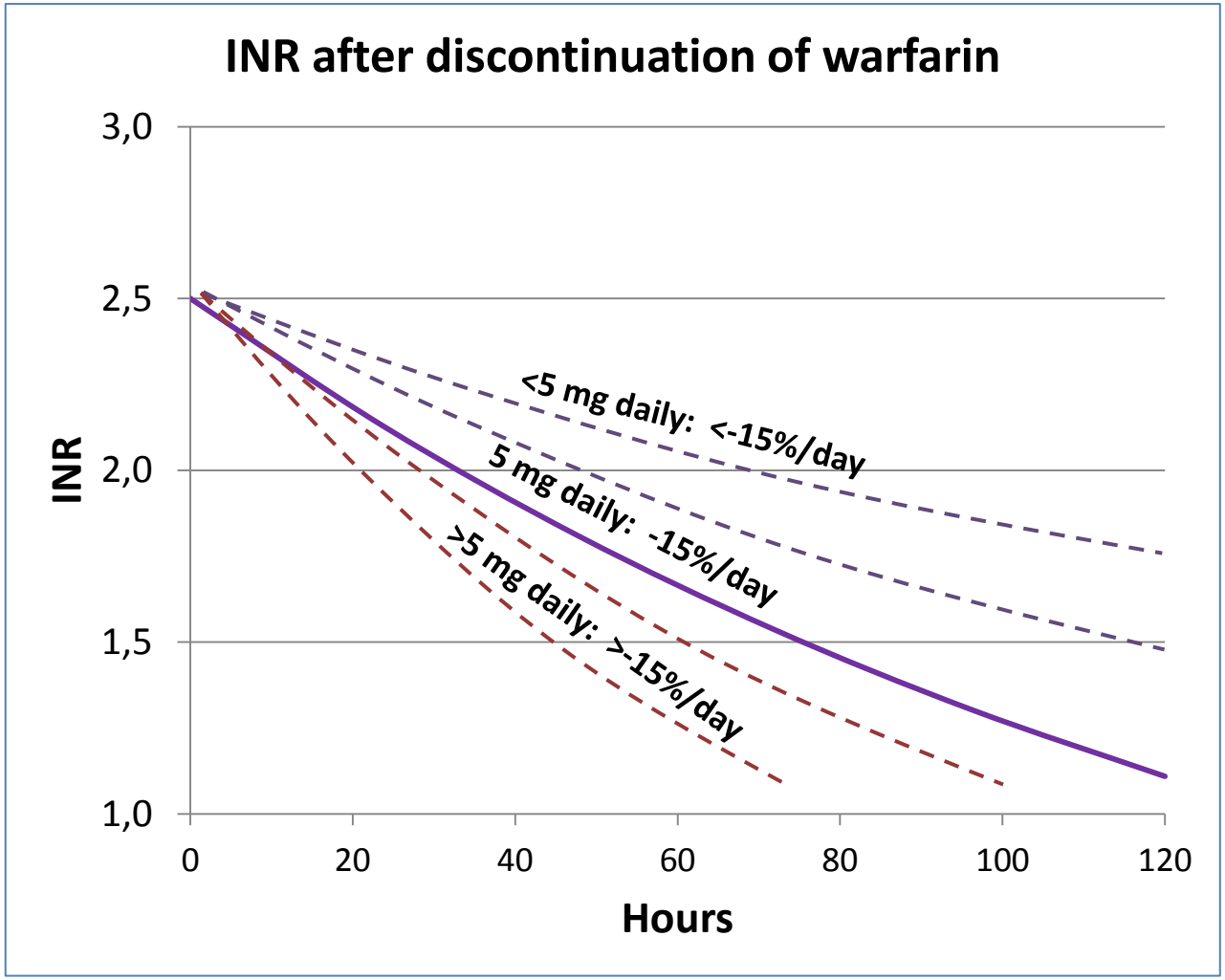
Flanigan DC, Muchow R, Orwin J, Graf B.

24 patients met the inclusion criteria. All had abnormal INR levels at time of surgery. Four patients were operated on emergently for septic joints, and 20 patients had elective arthroscopic procedures (10 knees, 10 shoulders).

There were no major intraoperative bleeding problems. Seven patients had minor postoperative surgical complications: 2 prolonged effusions and 5 prolonged ecchymosis.

Oral warfarin appeared to be a safe alternative to manipulating anticoagulation during the preoperative period for simple arthroscopic procedures. Minor bleeding complications consisting of ecchymosis were seen, but no medical complications were identified.

Changes in INR after discontinuation of warfarin



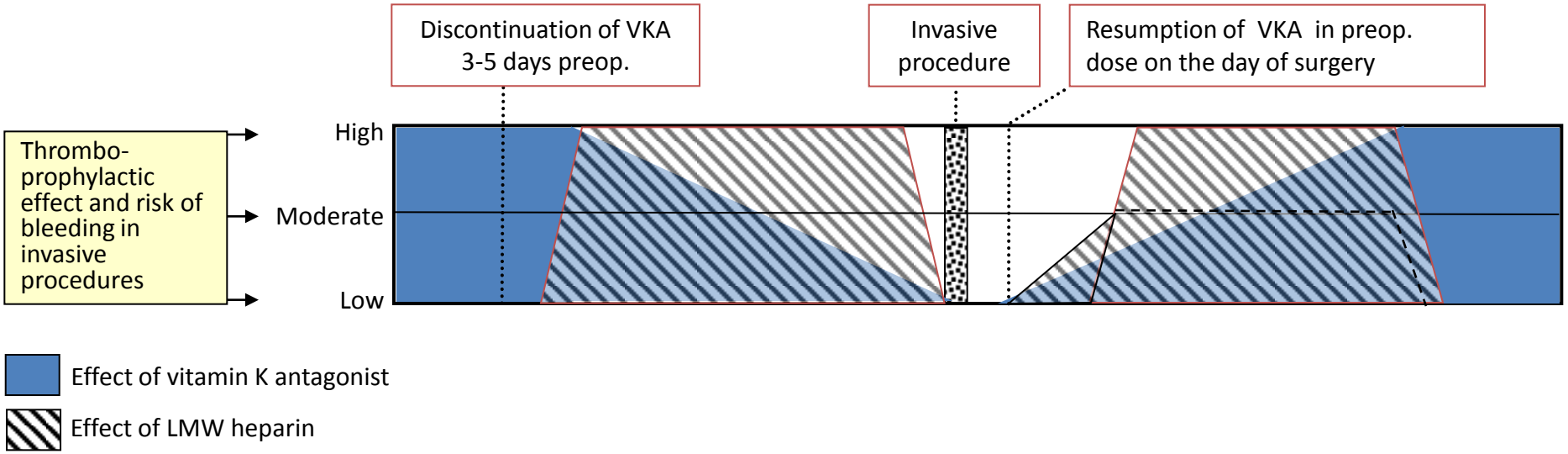
Revertering af VKA-behandling

	Tid til fuld effekt	
Sep. VKA	≥3 d.	VKA har lang halveringstid
Vit. K	1½ d.	Langsom syntese af koag.faktorer
FFP	2 t.	Optøning, infusion af stort volumen
PCC	5 m.	Alle manglende faktorer til stede
rFVIIa	partiel effekt	Stadig mangel på FII, FIX og FX

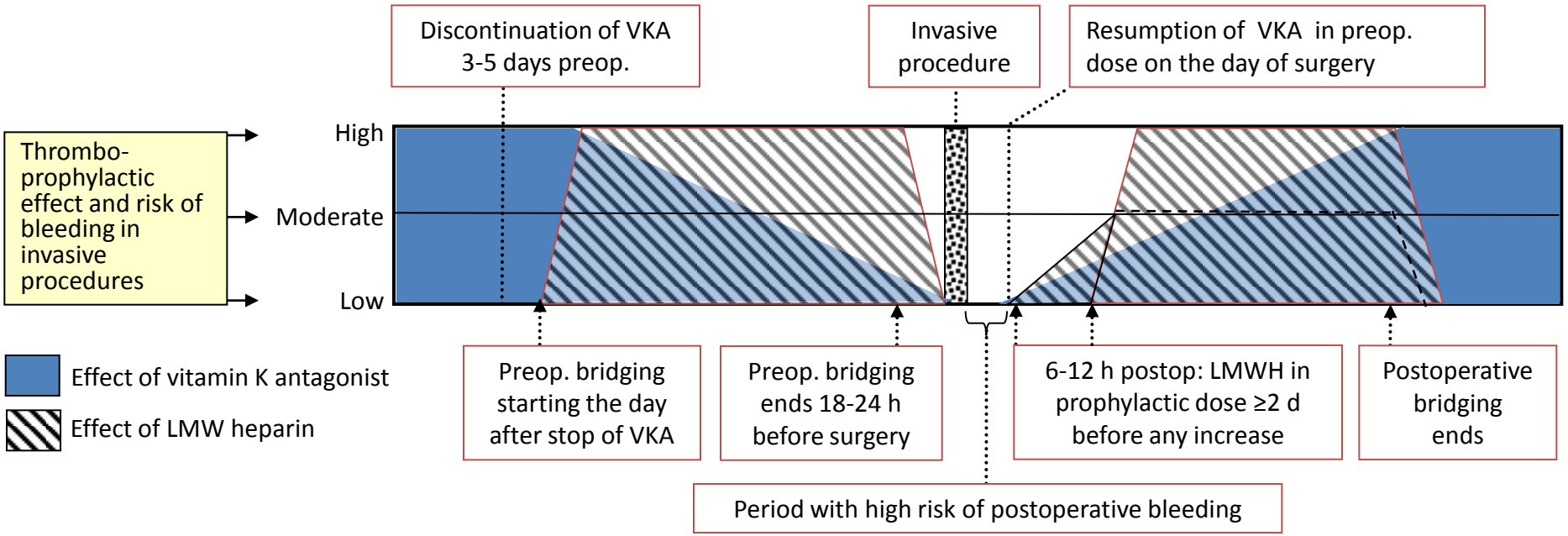
Patienters tromboserisiko ved de tre almindeligste indikationer for VKA-behandling

Trombose-risiko	Indikation for VKA-behandling		
	Mekaniske hjerteklapper	Atrieflimren	Venøs tromboemboli
Høj	Nylig (<6 mdr.) apopleksi eller TCI Alle mitralklapproteser Ældre (kugleventil eller enkelt vippeskive) aortaklapproteser	Nylig (<3 mdr.) apopleksi eller TCI. CHADS2-score på 5-6. Reumatisk hjerteklapsygdom.	Nylig (<3 mdr.) VTE. Trombofili - højrisikofaktorer, fx mangel på antitrombin, protein C eller protein S, homozygot faktor V Leiden, lupusantikoagulans eller multiple risikofaktorer.
Moderat	Dobbelt vippeskive aortaklap + >=1 af følgende risikofaktorer: atrieflimren, tidligere apopleksi eller TCI, hypertension, diabetes, hjerteinsufficiens, alder >75 år	CHADS2-score på 3-4.	VTE for 3-12 mdr siden. Recidiverende VTE. Aktiv cancer. Trombofili - lavrisikofaktorer, fx heterozygoti for faktor V Leiden eller protrombin G20210A
Lav	Dobbelt vippeskive aortaklap uden supplerende risikofaktorer	CHADS2-score på 0-2.	1 tilfælde af VTE for >12 mdr. siden og ingen supplerende risikofaktorer

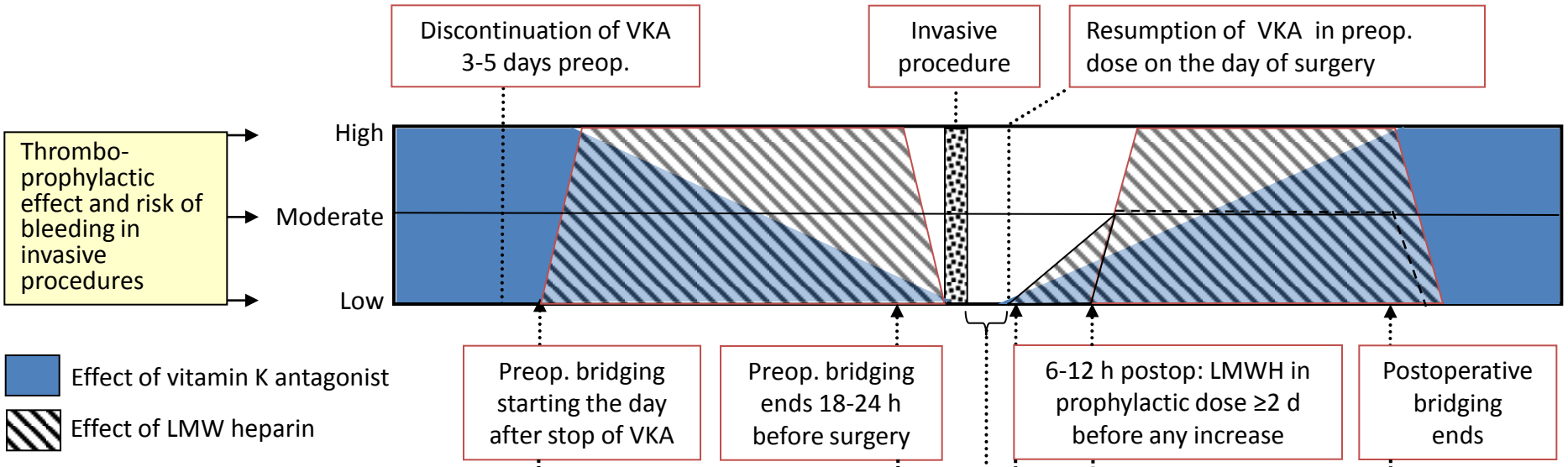
Principles of heparin bridging of VKA



Principles of heparin bridging of VKA



Principles of heparin bridging of VKA



Patients with high TE risk*	Therapeutic dose of LMWH	No LMWH	proph dose	Therapeutic dose of LMWH
Low - intermediate TE risk	No LMWH		Prophylactic dose of LMWH	

* Mainly patients with mechanical heart valves or recent TE

Low dose of LMWH: 4.000-5.000 IU once daily (depending on brand)
Therapeutic dose of LMWH: 100 IU/kg b.i.d.

Postoperativ genoptagelse af behandling med vitamin K-antagonist (VKA)

- VKA genoptages, så snart pt. kan indtage tabletter, gerne allerede på operationsdagen
- VKA-behandlingen genoptages med samme dosis, som patienten fik inden indlæggelsen
- **Alle** VKA-patienter skal have LMWH postoperativt:
  - Lavrisikopatienter: profylaksedosis af LMWH startende 6-12 timer postoperativt, gives indtil INR >2,0
  - Højrisikopatienter: profylaksedosis af LHWM startende 6-12 timer postoperativt med stigning til terapeutisk dosis efter 1-3 døgn, afhængig af blødning, gives indtil INR er i terapeutisk niveau

Perioperative regulation of dabigatran

Dabigatran 150 mg b.i.d.*	Creatinine clearance	Interventional bleeding risk	
		Low	High
Preoperatively	>50 ml/min	Stop 1½ day preop.	Stop 3 days preop.
	30-50 ml/min**	Stop 2 days preop.	Stop 4 days preop.
Postoperatively	>50 ml/min	1-4 h. postop.: 110 mg followed by 110 mg b.i.d. Dose may be increased after 2-3 days§	6-12 h. postop.: 75 mg followed by 75 mg b.i.d. Dose may be increased after 4-5 days§
	30-50 ml/min**	1-4 h. postop.: 75 mg followed by 110 mg o.d. Dose may be increased after 2-3 days§	6-12 h. postop.: 75 mg followed by 75 mg o.d. Dose may be increased after 4-5 days§

*Reduce preoperative interval with 1/3 if the patient preoperatively had prophylactic dose of dabigatran.
** This also applies to patients over 75 years with normal renal function.
§ Increase of dose relates to patients who received preoperative therapeutic dose.

Perioperative regulation of rivaroxaban

Rivaroxaban 20 mg once daily*	Creatinine clearance	Interventional bleeding risk	
		Low	High
Preoperatively	>50 ml/min	Stop 1 day preop.	Stop 2 days preop.
	30-50 ml/min	Stop 1½ day preop.	Stop 3 days preop.
Postoperatively	>30 ml/min	6-10 h. postop.: 10 mg followed by 10 mg o.d. Dose may be increased after 2-3 days§	8-12 h. postop.: 10 mg followed by 10 mg o.d. Dose may be increased after 4-5 days§

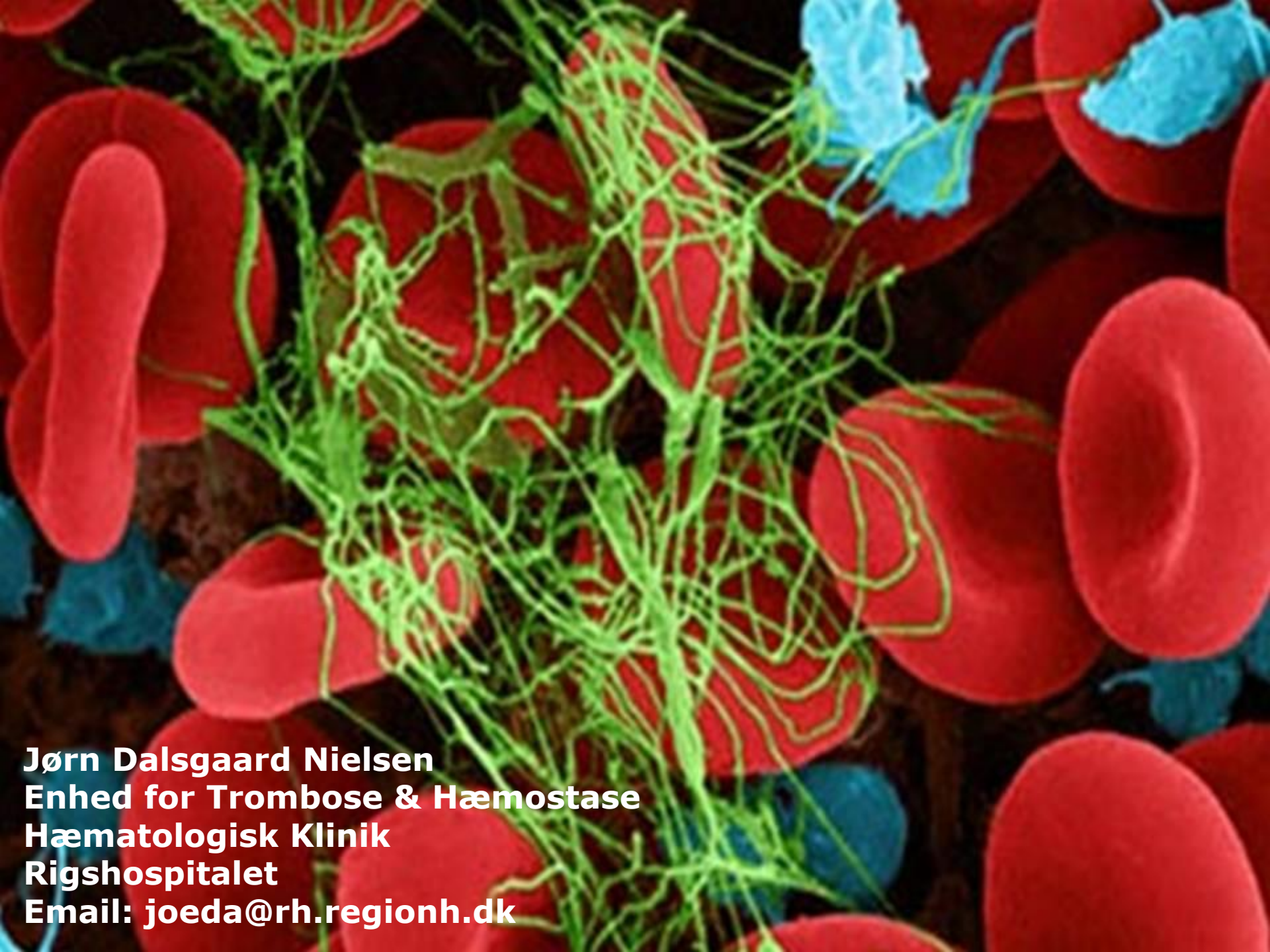
*Reduce preoperative interval with 1/3 if the patient preoperatively had prophylactic dose of rivaroxaban.
§ Increase of dose relates to patients who received preoperative therapeutic dose.

Perioperative regulation of apixaban

Apixaban 5 mg b.i.d.*	Creatinine clearance	Interventional bleeding risk	
		Low	High
Preoperatively	>30 ml/min	Stop 1½ day preop.	Stop 3 days preop.
Postoperatively	>30 ml/min	12-24 h. postop.: 2.5 mg followed by 2.5 mg b.i.d. Dose may be increased after 2-3 days§	12-24 h. postop.: 2.5 mg followed by 2.5 mg b.i.d. Dose may be increased after 4-5 days§

*Reduce preoperative interval with 1/3 if the patient preoperatively had prophylactic dose of rivaroxaban.

§ Increase of dose relates to patients who received preoperative therapeutic dose.



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