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## Guidelines for deep-vein thrombosis prevention in hip arthroplasty in 2019

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Oostende – 25.04.19 -



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### HIGHLIGHTS

- Many guidelines – little consensus ?
- Are guidelines obsolete ?
- Do real-life data outweigh randomized trials ?
- How to move towards precision medicine ?
- In practice, what can be proposed ?

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### MANY GUIDELINES

ACCP 2012	• Prevention of VTE in orthopedic surgery patients, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.
AAOS 2012	• American Academy of Orthopedic Surgeons Clinical Practice Guidelines
NICE 2018	• National Institute for Health and Care Excellence
ESA 2018	• European guidelines on perioperative venous thromboembolism prophylaxis: Day surgery and fast-track surgery, Mechanical prophylaxis

Chest 2012; 141(2)(Suppl):e278S–e325S  
J Bone Joint Surg Am. 2012;94:746-7  
NICE 2018. [www.nice.org.uk/guidance/NG89](http://www.nice.org.uk/guidance/NG89)  
Eur J Anaesthesiol 2018; 35:134-138

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### THROMBOPHOPHYLAXIS AFTER PRIMARY HIP ARTHROPLASTY

#### Choice of prophylaxis regimen

ACCP 2012	• LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, low-dose unfractionated Heparin, adjusted-dose vitamin K antagonist, aspirin (all Grade 1B) , or • An intermittent pneumatic compression device (IPCD) (Grade 1C) • LMWH (in preference, Grade 2C)
AAOS 2012	• No recommendations regarding the use of a specific prophylaxis regimen
NICE 2018	• LMWH for 10 days followed by aspirin (75 or 150 mg) for a further 28 days or LMWH for 28 days combined with anti-embolism stockings, or • Rivaroxaban or Apixaban or Dabigatran
ESA 2018	• Aspirin in patients without a high VTE risk

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### THROMBOPHOPHYLAXIS AFTER PRIMARY HIP ARTHROPLASTY

#### Duration of prophylaxis regimen

ACCP 2012	• For a minimum of 10 to 14 days • We suggest extending thromboprophylaxis in the outpatient period for up to 35 days from the day of surgery rather than for only 10 to 14 days (Grade 2B)
AAOS 2012	• No recommendation regarding the duration of the prophylaxis
NICE 2018	• For 28 days
ESA 2018	• A minimum of 7 days (Grade 1B)

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### THROMBOPHOPHYLAXIS AFTER PRIMARY HIP ARTHROPLASTY

#### Mechanical prophylaxis

ACCP 2012	• IPCD (Grade 1C) as one of the options • We suggest dual prophylaxis with an antithrombotic agent and an IPCD during the hospital stay (Grade 2C) • IPCD if increased risk of bleeding
AAOS 2012	• Mechanical compressive devices if pharmacological interventions contraindicated
NICE 2018	• Combined with LMWH for 28 days as one of the options • Anti-embolism stockings (GCS) until discharge if pharmacological interventions contraindicated
ESA 2018	• Use of IPCD over GCS if pharmacological interventions contraindicated • Recommendation against the routine use of mechanical thromboprophylaxis if pharmacological thromboprophylaxis • Combined mechanical and pharmacological prophylaxis is suggested in selected patients at very high risk of VTE

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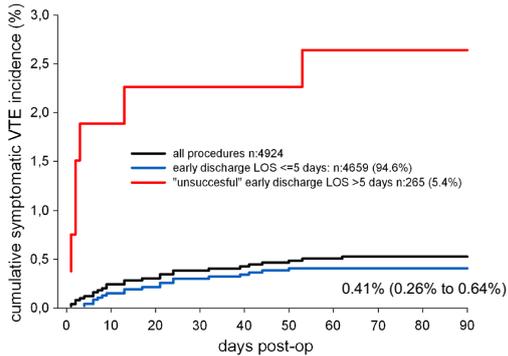
### WHY DISCREPANCIES BETWEEN GUIDELINES ?

- Composition of the individual development group
- Focus on overall VTE rates, or symptomatic VTE, or PE only
- Inclusion of only RCTs and systematic reviews or inclusion also of observational cohorts
- Controversy on the precise estimates of the true risk of bleeding

### MOST GUIDELINES ARE OBSOLETE

- Most guidelines rely heavily on the results of RCTs from 1990 to 2010 with:
  - Median length of hospital stay of 8 – 12 days
  - Outdated surgical and anesthetic techniques,
  - No focus on early mobilization

### LOW RATES OF VTE AFTER FAST-TRACK THA AND TKA WITH THROMBOPROPHYLAXIS ONLY DURING HOSPITALISATION IN PATIENTS WITH LOS ≤5 DAYS



### REAL-LIFE DATA OUTWEIGH RANDOMIZED TRAILS: RESULTS OF OBSERVATIONAL STUDIES LEADING TO CHANGE IN PROPHYLAXIS RECOMMENDATIONS

- In 2013 change in the Danish National recommendations for prophylaxis allowing in-hospital-only prophylaxis in fast-track THA and TKA if LOS is ≤ 5 days,

### REAL-LIFE DATA OUTWEIGH RANDOMIZED TRAILS: THE COMEBACK OF ASPIRIN IS SUPPORTED BY COHORT STUDIES

- Retrospective cohort study of a large administrative database (USA)
- Patients hospitalized for primary THA or TKA, 2009- 2012
- Objective: to compare rates of VTE in patients who received aspirin (ASA) with rates in patients who received anticoagulants (AC)

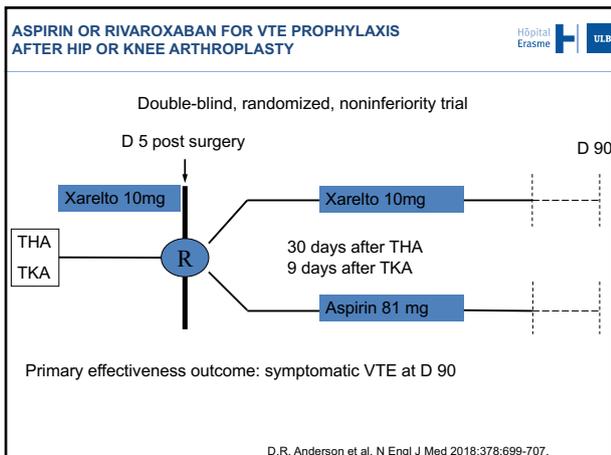
Overall VTE rate after THA			
ASA only	AC only	ASA + AC	Total
0.16%	0.42%	0.51%	0.41%

#### Risk of VTE after THA, multivariable model

	Adjusted odds ratio (95% CI)
Aspirin only (vs. Anticoagulant or anticoagulant + aspirin)	0.82 (0.45, 1.51)

### EUROPEAN GUIDELINES ON PERIOPERATIVE VENOUS THROMBOEMBOLISM PROPHYLAXIS: DAY SURGERY AND FAST-TRACK SURGERY

- Recommendations should be tailored from the assessment of both patient and procedure-related risk factors
- Use of aspirin in patients without a high VTE risk (Grade 2C)
- Use of pharmacological prophylaxis with low molecular weight heparins (Grade 2B) in patients with additional risk factors



### ASPIRIN OR RIVAROXABAN FOR VTE PROPHYLAXIS AFTER HIP OR KNEE ARTHROPLASTY: EPCAT II TRIAL

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Table 3. Primary Effectiveness and Safety Outcomes, According to Surgical Procedure.

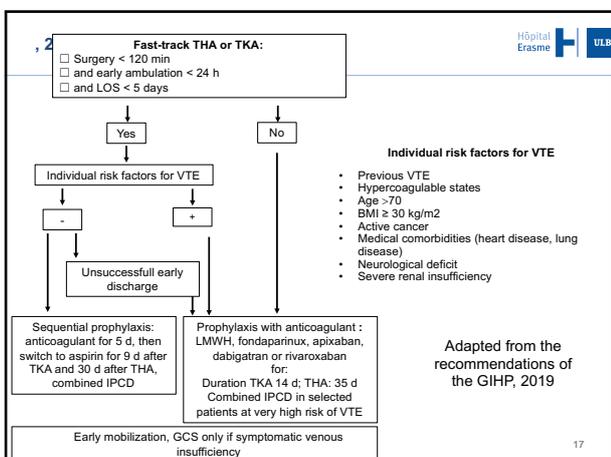
Outcome	Total Hip Arthroplasty			Total Knee Arthroplasty		
	Rivaroxaban (N=902)	Aspirin (N=902)	P Value	Rivaroxaban (N=815)	Aspirin (N=805)	P Value
	no. (%)			no. (%)		
Venous thromboembolism	5 (0.55)	4 (0.44)	1.00*	7 (0.86)	7 (0.87)	1.00†
Pulmonary embolism	2 (0.22)	2 (0.22)		4 (0.49)	3 (0.37)	
Proximal deep-vein thrombosis	1 (0.11)	1 (0.11)		3 (0.37)	3 (0.37)	
Pulmonary embolism and proximal deep-vein thrombosis	2 (0.22)	1 (0.11)		0	1 (0.12)	
Major bleeding	3 (0.33)	3 (0.33)	1.00	2 (0.25)	5 (0.62)	0.29
All bleeding‡	7 (0.78)	11 (1.22)	0.48	10 (1.23)	11 (1.37)	0.83

Aspirin was not significantly different from the direct oral anticoagulant after an initial 5-day postoperative course of rivaroxaban.

D.R. Anderson et al. N Engl J Med 2018;378:699-707. 14

- ### MOVING TOWARDS PRECISION MEDICINE
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- Individual risk factors for VTE include:
    - Advance age
    - Previous VTE
    - Family history of VTE
    - Hypercoagulable states
    - Active cancer
    - Multiple medical comorbidities (heart disease, lung disease, diabetes)
    - Morbid obesity (BMI ≥ 40 kg/m<sup>2</sup>)
    - Immobility (limited weight bearing)
  - Interaction of individual risk factors for VTE in a given patient
  - No risk stratification system has been shown to effectively guide thromboprophylaxis strategies after arthroplasty
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- Many guidelines – little consensus ?
  - Are guidelines obsolete ?
  - Do real-life data outweigh randomized trials ?
  - How to move towards precision medicine ?
  - In practice, what can be proposed ?
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- ### CONCLUSIONS
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- Most guidelines are obsolete
  - Thromboprophylaxis should be tailored from the assessment of both patient and procedure-related risk factors
    - Low-risk patients: anticoagulant for 5 days then aspirin
    - Higher-risk patients: extended prophylaxis with an anticoagulant
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## WHAT DO WE NEED ?

- To validate a risk stratification system to distinguish between low-risk and higher-risk patients
- To definitely establish the place of aspirin in de-escalation randomized trial:
  - Non inferiority regarding efficacy
  - Superiority regarding safety