DV T Prophylaxis in Lower Extremity Surgery

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PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL
Conflicts of Interest

- **Consultant**
  - Boston Scientific (non-compensated)
  - Cordis Corporation (non-compensated)

- **Equity**
  - Embolitech

July 2018
44 yo WM Amateur Competitive Athlete

Long history of left foot pain due to repetitive trauma
  - Rugby, Soccer

Undergoes complex left foot reconstructive surgery October 2011

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At the end of 2 weeks, patient notes left calf swelling and discomfort

No CP, SOB, Cough, DOE, hemoptysis, syncope
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Some improvement with limb elevation

PMH: Minor GERD, not requiring medication

No tobacco ever

No recent illness

Exam completely normal except for minimal left mid-posterior calf tenderness with deep palpation
Left Leg
Venous Duplex Ultrasonography LLE
Venous Duplex Ultrasonography LLE
Should Patients Who Have Undergone THA/TKA Receive Routine Pharmacoprophylaxis for DVT Prevention?

A debate as old as Father Time...
What **Don’t** Orthopaedic Surgeons Believe?

DVT/PE occur commonly after total joint arthroplasty

There is no reliable evidence to suggest that anticoagulation is superior to aspirin as a pharmacoprophylactic strategy

This topic is only of interest to pharmaceutical manufacturers and non-surgeon vascular medicine specialists
Aspirin Versus Anticoagulation for Prevention of Venous Thromboembolism Major Lower Extremity Orthopedic Surgery: A Systematic Review and Meta-Analysis

Frank S. Drescher, MD\textsuperscript{1,*}, Brenda E. Sirovich, MD, MS\textsuperscript{2}, Alexandra Lee, MS\textsuperscript{3}, Daniel H. Morrison, MD, MS\textsuperscript{4}, Wesley H. Chiang, MS\textsuperscript{2}, Robin J. Larson, MD, MPH\textsuperscript{1}

Records identified through electronic database searching Medline and CINAHL: n=275

Records screened for eligibility (n=298)

Full-text records assessed for eligibility (n=45)

Studies included in quantitative synthesis (meta-analysis) (n=8)

Records excluded by abstract & title review:
Wrong design n=151
Wrong intervention n=67
Wrong comparison n=19
Wrong population n=7
Other reasons n=9

Records excluded by full text review:
Wrong design n=31
Wrong intervention n=3
Wrong comparison n=2
No usable data=1

Other sources:
AOCQ guidelines n=6
AOCQ meetings (2003-10) n=2
AOSK meetings 2010-11) n=9
ASH meetings (2007-10) n=1
ClinicalTrials.gov n=1
Cochrane library n=2
Reference review n=2

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ASA vs Anticoagulant Impact on DVT Rates

# Aspirin Versus Anticoagulation for Prevention of Venous Thromboembolism Major Lower Extremity Orthopedic Surgery: A Systematic Review and Meta-Analysis

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## ASA vs Anticoagulant on Bleeding

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Aspirin</th>
<th>Anticoagulant</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Total Weight</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td><strong>Hip fracture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gent 1996</td>
<td>2</td>
<td>128</td>
<td>8</td>
<td>125</td>
</tr>
<tr>
<td>Powers 1989</td>
<td>4</td>
<td>66</td>
<td>11</td>
<td>65</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>192</td>
<td>190</td>
<td>25.9%</td>
<td>0.32 [0.13, 0.77]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>6</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong>: Tau² = 0.66; Chi² = 0.15, df = 1 (P = 0.70); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.54 (P = 0.01)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hip or knee arthroplasty</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harris 1982</td>
<td>1</td>
<td>51</td>
<td>75</td>
<td>6.2%</td>
</tr>
<tr>
<td>Josefsson 1987</td>
<td>9</td>
<td>40</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>Lotke 1996</td>
<td>6</td>
<td>166</td>
<td>8</td>
<td>146</td>
</tr>
<tr>
<td>Westrich 2006</td>
<td>1</td>
<td>138</td>
<td>0</td>
<td>139</td>
</tr>
<tr>
<td>Woolson 1991</td>
<td>1</td>
<td>72</td>
<td>7</td>
<td>60</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>465</td>
<td>471</td>
<td>70.5%</td>
<td>0.63 [0.33, 1.21]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>18</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong>: Tau² = 0.09; Chi² = 4.63, df = 4 (P = 0.33); I² = 14%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.40 (P = 0.16)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong> (95% CI)</td>
<td>657</td>
<td>661</td>
<td>100.0%</td>
<td>0.52 [0.31, 0.86]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td>24</td>
<td>55</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heterogeneity</strong>: Tau² = 0.64; Chi² = 6.52, df = 6 (P = 0.37); I² = 8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 2.55 (P = 0.01)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 1.47, df = 1 (P = 0.23); I² = 32.0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Do Guidelines Help?

EJA

European Guidelines on perioperative venous thromboembolism prophylaxis

Executive summary

Aspirin

- We recommend the use of aspirin as an option for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (Grade 1B). {11}
- We suggest the use of aspirin for VTE prevention after total hip arthroplasty, total knee arthroplasty and hip fracture surgery (high-risk procedures) in patients without high VTE risk (Grade 2C).
Prevention of VTE in Orthopedic Surgery Patients

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest 2012;141 (2) (Supple):e278S-e325S
2.1.1. In patients undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA), we recommend use of one of the following for a minimum of 10 to 14 days rather than no antithrombotic prophylaxis: low-molecular-weight heparin (LMWH), fondaparinux, apixaban, dabigatran, rivaroxaban, low-dose unfractionated heparin (LDUH), adjusted-dose vitamin K antagonist (VKA), aspirin (all Grade 1B), or an intermittent pneumatic compression device (IPCD) (Grade 1C).
2.4. For patients undergoing major orthopedic surgery, 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).

2.5. In patients undergoing major orthopedic surgery, we suggest using dual prophylaxis with an antithrombotic agent and an IPCD during the hospital stay (Grade 2C).
We suggest the use of pharmacologic agents and/or mechanical compressive devices for the prevention of venous thromboembolism in patients undergoing elective hip or knee arthroplasty, and who are not at elevated risk beyond that of the surgery itself for venous thromboembolism or bleeding. Current evidence is unclear about which prophylactic strategy (or strategies) is/are optimal or suboptimal. Therefore, we are unable to recommend for or against specific prophylactics in these patients.
No! I Don’t Think the Guidelines Help!!!
What about Anticoagulation Following Knee Arthroscopy/Casting?

Thromboprophylaxis after Knee Arthroscopy and Lower-Leg Casting

Raymond A. van Adrichem, M.D., Banne Nemeth, M.D., Ale Algra, M.D., Ph.D., Saskia le Cessie, Ph.D., Frits R. Rosendaal, M.D., Ph.D., Inger B. Schipper, M.D., Ph.D., Rob G.H.H. Nelissen, M.D., Ph.D., and Suzanne C. Cannegieter, M.D., Ph.D.

What about Anticoagulation Following Knee Arthroscopy/Casting?

Two parallel, open-label multicenter randomized trials:

- POT-KAST—Patients undergoing knee arthroscopy randomized to 8 days of SQ LMWH vs no LMWH
- POT-CAST—Patients wearing a LL cast randomized to SQ LMWH for duration of cast vs no LMWH

Primary Endpoint

- Symptomatic VTE within 3 months
- Major bleeding within 3 months

What about Anticoagulation Following Knee Arthroscopy/Casting?

<table>
<thead>
<tr>
<th>Outcome</th>
<th>POT-KAST Trial</th>
<th>POT-CAST Trial</th>
<th>Absolute Difference in Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment Group</td>
<td>Control Group</td>
<td>Relative Risk (95% CI)</td>
</tr>
<tr>
<td></td>
<td>(N = 731)</td>
<td>(N = 720)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Primary outcome: thromboembolism</td>
<td>5</td>
<td>3</td>
<td>1.6 (0.4 to 6.8)</td>
</tr>
<tr>
<td></td>
<td>(0.2 to 1.6)</td>
<td>(0.1 to 1.2)</td>
<td>(0.3 to 1.2)</td>
</tr>
<tr>
<td></td>
<td>0.7 (95% CI)</td>
<td>1.4 (95% CI)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Deep-vein thrombosis</td>
<td>4</td>
<td>2</td>
<td>0.3 (0.5 to 1.1)</td>
</tr>
<tr>
<td></td>
<td>(0.1 to 1.4)</td>
<td>(0.1 to 1.0)</td>
<td>percentage points</td>
</tr>
<tr>
<td></td>
<td>0.5 (95% CI)</td>
<td>0.8 (95% CI)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>1</td>
<td>0 (0.6 to 0.7)</td>
</tr>
<tr>
<td></td>
<td>(0 to 0.8)</td>
<td>(0 to 0.8)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Deep-vein thrombosis and pulmonary embolism</td>
<td>0</td>
<td>0</td>
<td>0 (0.5 to 0.5)</td>
</tr>
<tr>
<td></td>
<td>(0 to 0.5)</td>
<td>(0 to 0.5)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Primary safety outcome: major bleeding</td>
<td>1</td>
<td>1</td>
<td>1 (0.1 to 15.7)</td>
</tr>
<tr>
<td></td>
<td>(0 to 0.8)</td>
<td>(0 to 0.8)</td>
<td>percentage points</td>
</tr>
<tr>
<td>Secondary safety outcome: clinically relevant non-major bleeding</td>
<td>1</td>
<td>0.1</td>
<td>0.3 (0 to 3.1)</td>
</tr>
<tr>
<td></td>
<td>(0 to 0.8)</td>
<td>(0.1 to 1.2)</td>
<td>percentage points</td>
</tr>
</tbody>
</table>
So, How Do I Approach This Clinical Scenario?

**Total Hip/Knee Arthroplasty in Standard Risk Patient**
- Mechanical Prophylaxis Peri-Op
- ASA 81 mg/d for 35 days post-op OR
- DOAC po for 28-35 days OR
- LMWH sq for 28-35 days

**Total Hip/Knee Arthroplasty in High Risk Patient**
- Mechanical Prophylaxis Peri-Op
- DOAC po for 28-35 days OR
- LMWH sq for 28-35 days

**Total Hip/Knee Arthroplasty in High **Bleeding** Risk Patient**
- Mechanical Prophylaxis Peri-Op
- ASA 81 mg/d for 35 days post-op OR
- No post-procedure antithrombotic/anticoagulant
Remember our 44 yo WM Amateur Competitive Athlete

Long history of left foot pain due to repetitive trauma
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Undergoes complex left foot reconstructive surgery October 2011

Placed in full calf plaster cast for 2 weeks

At the end of 2 weeks, patient notes left calf swelling and discomfort

No CP, SOB, Cough, DOE, hemoptysis, syncope
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Some improvement with limb elevation

PMH: Minor GERD, not requiring medication

No tobacco ever

No recent illness

Exam completely normal except for minimal left mid-posterior calf tenderness with deep palpation
What Would You Do Now?

1. Anticoagulate with LMWH-Warfarin

2. Anticoagulate with Warfarin

3. Aspirin 81 mg po qD

4. Serial duplex ultrasound surveillance

5. Nothing
Here’s What I Did...

I recommended anticoagulation with LMWH-Warfarin for 3 months

Patient was reluctant

I told him that the risk of PE without propagation is very low, and we began duplex ultrasound surveillance
48 hours later....

First surveillance duplex ultrasound unchanged...

- No proximal DVT
- Persistent mid-left calf peroneal DVT

Continued on current plan...next surveillance in 4 days
3 days later....

Sudden onset pleuritic left upper chest and shoulder discomfort

No cough, hemoptysis, palpitations, syncope

Left calf edema resolved, as had discomfort
CTA of the Lungs
Unbelievable, right? What Else...
SITE: Left upper lobe.

HISTOLOGIC TYPE (modified WHO classification): Adenocarcinoma, bronchioloalveolar, non-mucinous (10%), acinar, moderately differentiated (10%), papillary (40%), and micropapillary (40%).

TUMOR SIZE (MAXIMUM DIAMETER): 3.4 cm.

TUMOR CONFIGURATION: Single nodule.

STATUS OF VISCERAL PLEURA: Tumor does not invade visceral pleura.

BRONCHIAL RESECTION MARGIN: Negative (surgical clearance: 3.7 cm).

VASCULAR RESECTION MARGIN: Contains metastatic adenocarcinoma in a small perivascular lymph node. No tumor is present within the vessel wall or in perivascular soft tissue.

PARENCHYMAL (STAPLE) MARGIN: Negative.

BLOOD VESSEL INVASION: Absent.

LYMPHATIC VESSEL INVASION: Absent.

TUMOR LYMPHOCYTE INFILTRATION: Present, mild to moderate in degree.

TUMOR NECROSIS: Absent.

LYMPH NODES:
4 of 8 peribronchial lymph nodes contain tumor.
3 of 3 hilar lymph nodes contain tumor.

LYMPH NODE EXCISION, AP WINDOW PACKET LEVEL 6:
Metastatic adenocarcinoma in one of one lymph node (1/1).
My Most Important Piece of Information

If you love lobster....