KPHI VENOUS THROMBOEMBOLISM (VTE) PREVENTION GUIDELINE TEAM CLINICAL RECOMMENDATIONS *(FINAL DRAFT 4/23/09)*

DISCLAIMERS

- The information provided is an attempt to identify and synthesize the best scientific evidence available as of the date of this report. Such efforts as evidence identification, selection, appraisal and synthesis require judgment. As such, persons with similar skills in scientific evidence review may reasonably reach different conclusions about the strength of the evidence and what we may conclude from that evidence.
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Purpose & Applicability of Recommendations

- The KPHI VTE Prevention Clinical Recommendations are evidence-based DVT prophylaxis options and recommendations developed to assist in the management of patients undergoing total knee and hip replacement surgery. It was the consensus of KPHI VTE Prevention guideline team that clinically significant VTE includes all pulmonary embolisms, deep vein thrombi proximal to the popliteal vein and all symptomatic DVTs, even if distal. Asymptomatic distal DVTs may not represent clinically significant events.
- Population information based on studies utilized in this review follows the Evidence Synthesis

Clinical Recommendations

1. **Based on our evidence review and evidence synthesis the KPHI VTE Prevention Guideline Team recommends that mechanical compression devices be used in conjunction with recommended pharmacological agents (enoxaparin, warfarin, fondaparinux or aspirin), continuing at least through discharge, to achieve the lowest possible DVT rates in THR and TKR surgery.** (LOE: Fair for reduction of overall DVT rates; Inconclusive for reduction of symptomatic DVT, proximal DVT and PE rates.**)**

Notes:

a. **Pharmacological Agents**: The guideline team favors the use of enoxaparin over fondaparinux because of what appears to be an increased risk of major bleeding with the use of fondaparinux. (LOE: Inconclusive, but suggestive)

b. **Dosing:** The following recommendations are based on dosing used in clinical trials and from drug labels (LOE: Inconclusive, but suggestive).
   - **Enoxaparin**: Hip = 30 mg bid or 40 mg once daily (starting 12-24 hours after surgery; Knee = 30 mg bid (starting 12-24 hours after surgery.
     - The dosage of enoxaparin should be adjusted for level of renal function.
   - **Fondaparinux**: 2.5mg given subcutaneously once daily.
     - Fondaparinux is not recommended in patients with GFR of <30ml/min.
   - **Aspirin**: 325 mg enteric coated twice daily

c. **Duration:** The following recommendations are based on study data and consensus of the KPHI VTE Prevention Guideline Team (LOE: Inconclusive).
   - **Pharmacological Agents —**The KPHI VTE Prevention Guideline Team recommends that until further evidence is available, decisions

Abbreviations

- **AACP:** American Academy of Chest Physicians
- **AAOS:** American Academy of Orthopedic Surgery
- **ARR:** Absolute Risk Reduction
- **ASA: Aspirin**
- **CI**: Confidence Interval
- **CECT**: Continuous Enhanced Circulation Therapy
- **DVT**: Deep Vein Thrombosis
- **INR**: International Normalized Ratio
- **IPC**: Intermittent Pneumatic Compression
- **KPHI**: Kaiser Permanente Hawaii
- **LMWH**: Low Molecular Weight Heparin (eg, **enoxaparin**)
- **LOE**: Level of Evidence
- **NSAIDS**: Non-steroidal anti-inflammatory drugs
- **PE**: Pulmonary Embolism
- **RCT**: Randomized Controlled Trial
- **RRR**: Relative Risk Reduction
- **SCD**: Sequential Compression Device
- **THA**: Total Hip Arthroplasty
- **TKA**: Total Knee

regarding the extension of VTE prophylaxis beyond hospitalization be individualized following risk assessment. Current national guideline recommendations are provided in Tables 1-3 below for reference. **(It should be note that the AAOS and ACCP guidelines are not in agreement. Some guideline recommendations listed in the tables are not supported by valid evidence.)**

- **Mechanical Devices** — Mechanical devices should be applied and monitored by trained staff immediately postoperatively and worn constantly during hospitalization except for cleaning or when walking in all patients undergoing THR or TKR surgery. There is insufficient evidence to make recommendations regarding use of mechanical devices following hospital discharge.

d. Warfarin:

- Warfarin is an acceptable alternative for VTE prophylaxis especially if the patient has been on maintenance warfarin prior to surgery for other reasons.
- The KPHI VTE Prevention Guideline Team does not favor the use of warfarin for VTE prophylaxis because of the increased risk of VTE from delay of first administration of warfarin to achievement of therapeutic drug levels.
- If warfarin is used, it should be continued post-discharge for at least 14 days and preferably for 4 to 6 weeks with a goal of INR 2-3.

2. The KPHI VTE Prevention Guideline Team recommends against the use of aspirin alone for VTE prophylaxis in THR and TKR surgery. (LOE: Fair for lack of efficacy)

Arthroplasty
- **THR**: Total Hip Replacement
- **TKR**: Total Knee Replacement
- **VTE**: Venous Thromboembolism

Evidence Tags

Levels of Evidence (LOEs)
- Good: For therapy, more than one valid and clinically useful RCT
- Fair: For therapy, at least one valid and clinically useful RCT
- Inconclusive: For therapy, conflicting grade B-U studies, B-U studies with inconclusive efficacy results for clinically meaningful outcomes or grade U studies for safety
- Consensus: Valid, clinically useful evidence is lacking, but consensus of the KPHI guideline team has been achieved

Evidence Grades (Applied to Each Study)
- Grade A: Useful
- Grade B: Possibly Useful
- Grade B-U: Possible to Uncertain Usefulness
- Grade U: Uncertain Validity and/or Usefulness

Table 1: ACCP Recommendations for Duration of VTE Prophylaxis **(It should be note that the AAOS and ACCP guidelines are not in agreement. Some guideline recommendations listed in this table are not supported by valid evidence.)**

Reference: ANTITHROMBOTIC AND THROMBOLYTIC THERAPY 8TH ED: ACCP GUIDELINES, CHEST 2008; 133.)

3.5.3.1. For patients undergoing THR or TKR ACCP guidelines suggest thromboprophylaxis with one of the recommended options for at least 10days.

3.5.3.2. For patients undergoing THR, ACCP guidelines suggest that thromboprophylaxis be extended beyond 10 days and up to 35 days after surgery. The recommended options for extended thromboprophylaxis in THR include LMWH, warfarin or fondaparinux.

3.5.3.3. For patients undergoing TKR, ACCP guidelines suggest that thromboprophylaxis be extended beyond 10 days and up to 35 days after surgery. The recommended options for extended thromboprophylaxis in TKR include LMWH, warfarin or fondaparinux.

Table 2: AAOS Recommendations for Duration of VTE Prophylaxis **(It should be noted that the AAOS and ACCP guidelines are not in agreement. Some guideline recommendations listed in this table are not supported by valid evidence.)**

Reference: American Academy of Orthopaedic Surgeons clinical guideline on prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. Rosemont (IL): American Academy of Orthopaedic Surgeons (AAOS); 2007. Available at http://www.aaos.org/Research/guidelines/guide.asp accessed on 4/9/09.

[Note: the following more recent reference contains identical information to that obtained from the AAOS website. Johanson NA, Lachiewicz PF, Lieberman JR, Lotke PA, Parvizi J, Pellegrini V, Stringer TA, Tornetta P 3rd, Haralson RH 3rd, Watters WC 3rd. Prevention of symptomatic pulmonary embolism in patients undergoing total hip or knee arthroplasty. J Am Acad Orthop Surg. 2009 Mar;17(3):183-96.]

3.1 **Post-operatively, patients should be considered for continued mechanical prophylaxis until discharge to home.**

3.3.1 **Patients at standard risk of both PE and major bleeding** should be considered for one of the chemoprophylactic agents evaluated in this guideline, including (*in alphabetical order*):
a. Aspirin, 325 mg 2x/day (reduce to 81 mg 1x/day if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.
b. LMWH, dose per package insert, starting 12-24 hours post-operatively (or after an indwelling epidural catheter has been removed), for 7-12 days (N.B., the LMWHs have not been sufficiently evaluated for longer periods to allow recommendation beyond this period).
c. Synthetic pentasaccharides (e.g.,fondaparinux), dose per package insert, starting 12-24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7-12 days (N.B., the synthetic pentasaccharides have not been sufficiently evaluated for longer periods to allow recommendation beyond this periodd. Warfarin, with an INR goal of ≤2.0, starting either the night before or the night after surgery, for 2-6 weeks.

3.3.2 **Patients at elevated (above standard) risk of PE and at standard risk of major bleeding** should be considered for one of the following chemoprophylactic agents (*in alphabetical order*):
a. LMWH, dose per package insert, starting 12-24 hours post-operatively (or after an indwelling epidural catheter has been removed), for 7-12 days (N.B., the LMWHs have not been sufficiently evaluated for longer periods to allow recommendation beyond this period).
b. Synthetic pentasaccharides, dose per package insert, starting 12-24 hours postoperatively (or after an indwelling epidural catheter has been removed), for 7-12 days (N.B., the synthetic pentasaccharides have not been sufficiently evaluated for longer periods to allow recommendation beyond this period).
c. Warfarin, with an INR goal of ≤2.0, starting either the night before or the night after surgery, for 2-6 weeks.

3.3.3 **Patients at standard risk of PE and at elevated (above standard) risk of major bleeding [listed in guideline as history of bleeding disorder, history of recent hemorrhagic stroke, history of recent GI bleed]** should be considered for one of the following chemoprophylactic agents (*in alphabetical order*):
a. Aspirin, 325 mg 2x/day (reduce to 81 mg 1x/day if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.
b. Warfarin, with an INR goal of ≤2.0, starting either the night before or the night after surgery, for 2-6 weeks.
c. None

3.3.4 **Patients at elevated (above standard) risk of both PE and major bleeding** should be considered for one of the following chemoprophylactic agents (*in alphabetical order*):
a. Aspirin, 325 mg 2x/day (reduce to 81 mg 1x/day if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.
b. Warfarin, with an INR goal of ≤2.0, starting either the night before or the night after surgery, for 2-6 weeks.
c. None

Table 3: AHRQ List of Considerations and Relative Contraindications for VTE Prophylaxis (see http://www.ahrq.gov/qual/vtguide/)

- Intracranial hemorrhage within last year.
- Craniotomy within 2 weeks
- Intraocular surgery within 2 weeks.
- Gastrointestinal, genitourinary hemorrhage within the last month.
- Thrombocytopenia (<50K) or coagulopathy (prothrombin time >18 seconds).
- End stage liver disease.
- Active intracranial lesions/neoplasms.
- Hypertensive urgency/emergency.
- Post-operative bleeding concerns (Scheduled return to OR within the next 24 hours: major ortho: 24 hours leeway; spinal cord or ortho spine: 7 days leeway; general surgery, status post transplant, status post trauma admission: 48 hours leeway.

EVIDENCE SYNTHESIS

EFFICACY

Clinical Questions

1. What is the evidence that thromboembolism or DVT prophylaxis with various agents reduces mortality and clinically significant morbidity in hip and knee replacement surgery?
2. What is the evidence regarding timing of anticoagulant prophylaxis for appropriate agents when used for prevention of thromboembolism in hip and knee replacement surgery?
    a. What is the evidence regarding starting anticoagulant prophylaxis?
    b. What is the evidence regarding duration of anticoagulant prophylaxis?

1. Mechanical Devices **THR, TKR Surgery** **Efficacy**	**Evidence Synthesis: The evidence for efficacy of mechanical compression devices alone for preventing symptomatic or proximal DVT or PE in patients undergoing knee or hip replacement surgery is inconclusive.** We were able to find 3 valid studies (grade B-U) utilizing mechanical devices. However, the studies are not sufficient to make a conclusive recommendation based on a body of evidence. Although the studies provide evidence for efficacy of mechanical devices for reducing overall DVT rates they do not provide conclusive evidence of efficacy specific to prevention of symptomatic DVT, proximal DVT or PE. ▪ Gelfer 06 (grade B-U) reported superiority of Continuous Enhanced Circulation Therapy (CECT) + 100 mg aspirin over enoxaparin in reducing the overall rates of DVT in THR and TKR surgery. Further studies are required to confirm the results of this single study. o The overall DVT rate was 17/60, 28.3%; 95 % CI (17% to 39%) with enoxaparin versus 4/61, 6.6%; 95% CI (0.4% to 12.8%) for CECT; p=0.002. o For proximal DVTs the rate was 10% with enoxaparin and 1.6% with CECT+ASA; p = 0.49. o For PE there was one event with 1 enoxaparin and no events with CECT. ▪ Haas 90 (grade B-U) reported clinically and statistically significant lower rates of distal DVTs in total knee replacement surgery patients with sequential compression compared to aspirin alone. But there is insufficient evidence to conclude that this is clinically relevant because the difference between the groups for proximal DVT and PE rates was not statistically significant. o Distal DVT rate with sequential compression devices (SCD) was 22% vs. 47% with aspirin alone; p< 0.01. o DVT rates in the surgically uninvolved extremity were 0% with SCD and 22% with aspirin alone; p<0.01. o The incidence of small and medium size DVT lesions was not significantly different between the groups; however the incidence of large lesions was 30.6% in the aspirin group and 5.6% in the compression group; p<0.01. ▪ Westrich 06 (grade B-U) reported overall DVT rates in TKR surgery rates in the mechanical compression and enoxaparin group of 14.1% versus 17.8% in the mechanical compression and ASA group; ARR 1.36%; 95% CI (-6.83% to 9.55%); p=0.27. Rates in both groups are significantly lower than the 41% to 85% DVT incidence rates reported in the literature for no VTE prophylaxis and the reported distal DVT rate of 47% (Haas 90) for aspirin alone. o Mechanical compression was initiated in the recovery room; 325 mg of enteric-coated aspirin twice daily was started the night prior to surgery;

	enoxaparin was started ~48 hours after removal of the epidural catheter).
2. Aspirin Alone in **THR, TKR Surgery** **Efficacy**	**Evidence Synthesis: The evidence for efficacy of aspirin alone for preventing symptomatic or proximal DVT or PE in patients undergoing knee or hip replacement surgery is inconclusive.** We found 1 valid study (grade B-U) that reported clinically and statistically significant lower rates of distal DVTs in total knee replacement surgery patients with sequential compression compared to aspirin alone. However there is insufficient evidence to conclude that this is clinically relevant because there was no statistically significant difference between the groups for proximal DVT and PE. ▪ Haas 90 (grade B-U) reported — o The distal DVT rate with sequential compression devices (SCD) was 22% vs. 47% with aspirin alone; p< 0.01. o DVT rates in the surgically uninvolved extremity were 0% with SCD and 22% with aspirin alone; p<0.01. o The incidence of small and medium size DVT lesions was not significantly different between the groups; however the incidence of large lesions was 30.6% in the aspirin group and 5.6% in the compression group; p<0.01.
3. Warfarin vs LMWH **THR, TKR Surgery** **Efficacy**	**Evidence Synthesis: The evidence for efficacy of LMWH versus warfarin for preventing symptomatic or proximal DVT or PE in patients undergoing knee or hip replacement surgery is inconclusive.** **THR Surgery**: We found 0 valid studies comparing LMWH to warfarin in THR surgery. **TKR Surgery**: We found 1 valid study (grade B-U), comparing warfarin to enoxaparin for DVT prophylaxis in TKR surgery. The overall DVT rate with enoxaparin was lower than with warfarin; however, the evidence is insufficient regarding efficacy in preventing symptomatic or proximal DVT and PE. ▪ LeClerc 96 (grade B-U) in a study of 670 patients undergoing TKR surgery reported a statistically significant overall decreased DVT rate with enoxaparin when compared to warfarin; ARR 14.8%; 95% CI (5.3% to 24.1%). However, the study did not report a statistically significant difference in proximal DVT rates (warfarin vs enoxaparin: 10.4% vs 11.7%; ARR 1.2%, 95% CI (-7.2% to 4.8%). The confidence intervals may reflect low power of the study (ie, too few events to show a statistically significant difference if there was one).
4. Fondaparinux vs LMWH **THR, TKR Surgery** **Efficacy**	**Evidence Synthesis: The evidence for efficacy of fondaprinux versus LMWH for preventing symptomatic or proximal DVT or PE in patients undergoing knee or hip replacement surgery is inconclusive. There is fair evidence for greater efficacy of fondaparinux compared to LMWH for reducing overall DVT rates in patients undergoing TKR surgery.** **THR Surgery**: We found 0 valid studies addressing the use of fonduparinux vs LMWH in THR surgery. **TKR Surgery**: We found 1 valid study (grade B-U) reporting that use of fondaparinux resulted in a decreased overall rate of DVTs; however, the reduction was due to primarily to a decrease

	in distal DVTs. ▪ Bauer 01 (grade B-U) in a study of 1049 patients undergoing elective total knee replacement surgery reported: o The overall rate of DVTs with fondaparinux was 12.5% vs 27.8%, with enoxaparin; ARR 15.3% favoring fondaparinux; 95% CI (9.3 to 22.3); p<0.001. o The rates for proximal DVTs were 2.4% with fondaparinux and 5.4% for enoxaparin; ARR 3%; 95% CI (-0.4 to 7.60); p=0.06.

EVIDENCE SYNTHESIS

SAFETY

Clinical Question

1. What is the evidence regarding bleeding from thromboembolism prophylaxis with the various appropriate agents?

1. Warfarin vs LMWH **THR, TKR Surgery** **Safety**	**Evidence Synthesis: The evidence for safety of LMWH versus warfarin for patients undergoing hip or knee replacement surgery is inconclusive.** **THR Surgery:** We found 1 study (grade U) reporting major hemorrhage with warfarin and enoxaparin in patients receiving DVT prophylaxis for total hip replacement surgery. ▪ Francis 97 (grade U) in a study of 580 patients undergoing total hip replacement surgery found a statistically significant increased risk of bleeding at the operative site with dalteparin (2500 units subcutaneously starting 2 hours prior to surgery, second dose 2500 units in the evening of surgery and 5000 units thereafter) compared to warfarin (started in the evening before surgery, 5 mg if patients were less than 57 kg and 7.5 mg if greater than 57 kg). Operative site bleeding rates were 4% in the daltaparin group versus 1% with warfarin; ARR 3%; p = 0.03. Importantly, the mean achieved INR in the warfarin group was <2.2. Major bleeding complications occurred in 2% of the dalteparin group and 1% of the warfarin group; p-value not reported. **TKR Surgery:** We found 1 valid study (grade B-U) reporting major hemorrhage with warfarin and enoxaparin in patients receiving DVT prophylaxis for total knee replacement surgery. ▪ LeClerc 96 (grade B-U) in a study of 670 patients undergoing total knee replacement surgery reported bleeding rates of 1.8% for warfarin vs 2.1 % for enoxaparin , ARR 0.3% (-2.4% to 1.8%). The evidence for a difference in bleeding rates between warfarin and enoxaparin is inconclusive based on a consideration of the rates and 95% CIs of study patients. Review of confidence intervals indicates that the difference in bleeding rates could have been as great as 2.4% favoring warfarin or up to 1.8% favoring enoxaparin. o Major hemorrhage was defined as overt bleeding that 1) decreased the hemoglobin level by 20 g/L or more, 2) necessitated transfusion of 2 or more units of packed red cells, 3) required hemarthrosis evacuation, 4) required discontinuation of prophylaxis, or 5) interrupted physiotherapy for at least 24 hours.
3. Extended Use of LMWH (8 to 21 days) **THR, TKR Surgery** **Safety**	**Evidence Synthesis: The evidence for safety of extended use (for 8 to 21 days after the first week of surgery) of LMWH following THR or TKR surgery is inconclusive.** We found 1 valid study (grade B-U) reporting major hemorrhage rates for extended use of LMWH in THR and TKR surgery. ▪ Comp 01 (grade B-U for safety) in a study of 873 patients undergoing THR or TKR surgery reported that extended use of enoxaparin compared to saline (extended prophylaxis for 8 to 21 days after the first week of surgery) did not pose a major hemorrhagic risk (<0.5% over the subsequent 3 weeks). Authors reported 0% (0/441) major hemorrhages (death, transfusion of 2 or more units of blood products, decrease in hemoglobin of >=2.0g/dL, serious or life-threatening clinical event, event requiring surgical intervention, retroperitoneal, intracranial, intraocular hemorrhage) in the enoxaparin group and 0.2% (1/432) in the saline group. 95% CI for difference between

	groups was -0.22% to 0.68% for all patients and -.43% to 1.33% for TKR surgery patients. o Limitation of the study: The rate of bleeding during the first week postoperatively was not formally evaluated; patients were randomized after the first postoperative week.
4. Fondaparinux vs Enoxaparin **THR, TKR Surgery** **Safety**	**Evidence Synthesis: The evidence for safety of fondaparinux versus LMWH in THR or TKR surgery is inconclusive but the evidence is suggestive of increased bleeding with fondaparinux.** We found 1 valid study (grade B-U) and 2 studies (grade U) comparing bleeding rates with fondaparinux versus enoxaparin for DVT prevention in THR and TKR surgery. ▪ Bauer 01 (grade B-U) in a study of 1049 patients undergoing TKR surgery reported higher bleeding rates with use of fondapariux than with use of enoxaparin. Bleeding index was higher in the fondaparinux group. No difference was reported in fatal bleeding, critical organ bleeding, bleeding leading to reoperation. Higher bleed rates were reported for bleeding leading to reoperation with rates for fondaparinux and enoxaparin of 0.4% and 0.2% respectively. Rates of bleeding index rates >/= 2 were higher in fondaparinux than with enoxaparin with rates of 1.7% and 0 respectively. Discontinuation of fondaparinux because of bleeding occurred in 3 of 9 patients who experienced overt bleeding. Postoperative transfusion rates were 42.9% in the fondaparinux group vs 38.1% in the enoxaparin group; no p-values or confidence intervals were reported. ARR favoring enoxaparin for postoperative transfusion was 4.8%, 95% CI, (-1.38% to 10.46%); p = 0.1471. ▪ Lassen 02 (grade U) in a study of 2309 subjects undergoing THR surgery found inconclusive evidence regarding differences between fondaparinux and enoxaparin in bleeding rates (based on rates of bleeding index >/=2); review of CIs indicates that bleeding index rates could differ as much as 1.77% favoring enoxaparin or up to 1.28% favoring fondaparinux. Rates of bleeding index >/=2 were 3.68% in the fondaparinux group versus 3.4% in the enoxaparin group, ARR 0.24%, 95% CI (-1.28% to 1.77%). ▪ Turpie Lancet 02 (grade U) in an RCT of 2275 subjects undergoing total hip replacement surgery reported a borderline statistically significant and possibly clinically significant increase in bleeding rates (bleeding index) of fondaparinux when compared to enoxaparin. The rate of bleeding index >/= 2% was 18/1128=1.6% in the fondaparinux group versus a rate of 8/1129=0.71% in the enoxaparin group; ARI for fondaparinux 0.89%, 95% CI (0.01% to 1.77%), p=0.051. The rate of bleeding leading to reoperation was 2 of 1128 subjects (0.2%) in the fondaparinux group versus a rate of 2 of 1129 (0.2%) in the enoxaparin group, ARI = 0%. Fatal bleeding: fondaparinux vs enoxaparin = 0 in each group; bleeding into a critical organ: fondaparinux vs enoxaparin = 0 vs 1; ARI = 0.1%.

POPULATION DESCRIPTION FOR INCLUDED STUDIES

Bauer 01	Ages 57-77, undergoing elective TKR surgery, mostly primary surgeries, mean weight 89 kg. Baseline characteristics were similar: approximately half women; general anesthesia used in 71% to 75% of cases; most surgeries were of similar duration (about 2 hrs); 12% of fondaparinux patients and 16% of enoxaparin patients were taking NSAIDs or aspirin.
Comp 01	Ages 64-66 undergoing elective THR or TKR surgery, mostly primary surgeries for osteoarthritis. Excluded previous DVTs. Slightly higher proportion of females than males. Otherwise, baseline characteristics were similar: BMI 28-31; general or IV anesthesia 69% to 71%.
Francis 97	Ages 63-64 yrs undergoing THR surgery, mostly primary surgeries. Baseline characteristic were similar: mean weight ~80kg, ~53% female, ~10% previous DVT. Duration of surgery ~162mins, 63-67% general anesthesia vs regional, ~90% white.
Gelfer 06	Mean age ~68 yrs undergoing THR or TKR surgery. Patients with previous VTE were excluded. Most baseline characteristics were similar except for diabetes mellitus (17% in the enoxaparin group versus 5% in the CECT group) and ischemic heart disease (20% enoxaparin group) versus 8% (CECT group); BMI~29.
Haas 90	Age ~70 undergoing THR or TKR surgery. Similar baseline characteristics: weight ~77kg, ~67% female, ~61% THR patients, surgery time (median) 85 minutes.
Lassen 02	Age 66-67, undergoing THR surgery. Similar baseline characteristics: 53% women; weight 75kg; duration surgery 2.4 h; ~61% regional anesthesia; 88% first surgery.
LeClerc 96	Age 63-64 yrs undergoing THR surgery. Baseline characteristics were similar: ~53% female, mean weight ~80kg, ~10% previous DVT; duration of surgery ~ 162mins, ~ 63-67% general anesthesia vs regional.
Turpie Lancet 02	Age ~67 undergoing THR surgery. Similar baseline characteristics: male ~47%; mean weight ~80kg; prior DVT 5-6%; primary THA 84-87%; revision 13-16%; general anesthesia 67-72%; duration of surgery 2.45 hrs.
Westrich 06	Age ~69 undergoing TKR surgery. Patients with previous VTE were excluded. Similar baseline characteristics: male 36%; weight ~79 kg; tourniquet time ~134 minutes.

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