LOW MOLECULAR WEIGHT HEPARIN

“THE STANDARD VALUE”

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UNIVERSITY OF IOANNINA, IOANNINA, GREECE
POSTOPERATIVE VENOUS THROMBOEMBOLISM (VTE)
CLASSIFIED AS:
DEEP VEIN THROMBOSIS (DVT) OR
PULMONARY EMBOLISM (PE)
REVIEW OF THE LITERATURE INDICATES THAT, WITHOUT PROPHYLAXIS, THE INCIDENCE OF VENOGRAPHICALLY CONFIRMED DVT IS:

- 42% TO 57% AFTER THA (TOTAL HIP ARTHROPLASTY)
- 41% TO 85% AFTER TKA (TOTAL KNEE ARTHROPLASTY)
- 46% TO 75% AFTER HFS (HIP FRACTURE SURGERY)
The importance of VTE prevention after orthopaedic surgery

THE OVERALL EFFECT OF VTE AFTER ORTHOPAEDIC SURGERY IS SUBSTANTIAL

PHARMACOLOGIC THROMBOPROPHYLAXIS IS ESTABLISHED AS THE STANDARD OF CARE FOR THESE PATIENTS
UNFRACTIONATED HEPARIN (UFH)

HEPARIN FOLLOWING ITS DISCOVERY IN 1916 AND EARLY CLINICAL TRIALS IN THE 1930s AND 1940s, IT BECAME THE MAINSTAY OF PREVENTION AND TREATMENT OF VENOUS THROMBOEMBOLISM

THE THROMBOPLASTIC ACTION OF CEPHALIN
JAY McLEAN
From the Physiological Laboratory of the Johns Hopkins University
Received for publication, June 15, 1916

Jay McLean (1890-1957)
HOWEVER, **UFH** HAS A NUMBER OF PHARMACOKINETIC AND BIOLOGICAL **LIMITATIONS** THAT HAMPER ITS CLINICAL USE:

1. **MUST BE GIVEN PARENTERALLY, USUALLY BY CONTINUOUS INTRAVENOUS INFUSION,**

2. **AND TREATMENT REQUIRES FREQUENT MONITORING OF THE ACTIVATED PARTIAL THROMBOPLASTIN TIME (aPTT)**
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- The first LMWHs were introduced for the treatment of VTE more than 30 years ago.
- LMWHs are derived from unfractionated heparin (UFH) via chemical or enzymatic depolymerization.

Structures of the repeating disaccharide motifs in heparin.
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

GENERATING **FRAGMENTS** WITH MOLECULAR WEIGHTS BETWEEN 1,000 & 10,000 DALTON (MEAN 4,000 TO 5,000 DALTON)
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

- THE ANTICOAGULANT EFFECT OF UFH IS MEDIATED BY THE ACTIVATION OF ANTITHROMBIN, WHICH INHIBITS MULTIPLE COAGULATION ENZYMES, MAINLY THROMBIN (FACTOR IIa) AND FACTOR Xa.

To inactivate thrombin, UFH forms a ternary complex with antithrombin and thrombin.
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWHs produce their anticoagulant effect mainly by inhibiting **factor Xa**.

Because of their lower molecular weight, LMWH species are unable to form the ternary complexes with antithrombin and thrombin.
1. PHARMACOKINETICS OF UFH ARE INFLUENCED BY ITS BINDINGS TO PLASMA PROTEIN, ENDOTHELIAL CELL SURFACES, MACROPHAGES, AND OTHER ACUTE PHASE REACTANTS

2. LMWH HAS DECREASED BINDING TO NONANTICOAGULANT RELATED PLASMA PROTEINS
ADVANTAGES OF LMWH OVER UFH

✅ NO NEED FOR LABORATORY MONITORING

When given on a weight-adjusted basis, the LMWH anticoagulant response is predictable and reproducible.

✅ HIGHER BIOAVAILABILITY

Given subcutaneously in low doses, the recovery of anti-Factor Xa activity approaches 100 percent, as compared with about 30 percent with UFH.
ADVANTAGES OF LMWH OVER UFH

- LONGER PLASMA HALF-LIFE
  - 4 TO 6 HOURS vs 0.5 TO 1 HOUR
  - RENAL (SLOWER) VS HEPATIC CLEARANCE

- LESS INHIBITION OF PLATELET FUNCTION
  POTENTIALLY LESS BLEEDING RISK

- LESS HEPARIN-ASSOCIATED OSTEOPENIA
ADVANTAGES OF LMWH OVER UFH

- LOWER INCIDENCE OF HIT SYNDROME
- LESS INTERACTION WITH PLATELET FACTOR 4
- FEWER HEPARIN-DEPENDENT IgG ANTIBODIES
MONITORING OF LMWH

• UNNECESSARY IN MAJORITY OF PATIENTS

• MAY BE USEFUL IN SPECIFIC INSTANCES
  – RENAL INSUFFICIENCY (CREATININE >2.0 mg/dl)
  – OBESE PATIENTS WITH ALTERED DRUG PK
  – MAJOR BLEEDING RISK FACTORS
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWHS ARE DISTINCT CHEMICAL ENTITIES:

THE UNITED STATES FOOD AND DRUG ADMINISTRATION (FDA), THE EUROPEAN MEDICINE EVALUATION AGENCY (EMEA), AND THE WORLD HEALTH ORGANIZATION (WHO), CLASSIFY EACH LMWH AS A DISTINCT DRUG

UNIQUE PHARMACOKINETIC & PHARMACODYNAMIC PROFILES
## PREVENTION OF VTE IN ORTHOPAEDIC SURGERY PATIENTS

<table>
<thead>
<tr>
<th>LMWH</th>
<th>RECOMMENDED DOSES *</th>
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<tbody>
<tr>
<td>Dalteparin (Fragmin ®)</td>
<td>5000 U 8–12 hr before surgery and once daily starting 12 hr after</td>
</tr>
<tr>
<td>Enoxaparin (Clexane ®)</td>
<td>3000 U twice daily starting 12–24 hr after surgery or 4000 U once daily starting 10–12 hr before surgery</td>
</tr>
<tr>
<td>Nadroparin (Fraxiparine ®)</td>
<td>40 U/kg starting 2 hr before surgery and once daily after surgery</td>
</tr>
<tr>
<td>Tinzaparin (Innohep ®)</td>
<td>50 U/kg 2 hr before surgery and once daily after surgery or 75 U/kg once daily starting 12–24 hr after surgery</td>
</tr>
<tr>
<td>Bemiparin (Ivor ®)</td>
<td>3500 U 2 hr before surgery and once daily starting 6 hr after</td>
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* GIVEN SUBCUTANEOUSLY
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

MAJOR ORTHOPEDIC SURGERY: THA, TKA, HFS

<table>
<thead>
<tr>
<th>AUTHORS</th>
<th>JOURNAL</th>
<th>Author</th>
<th>JOURNAL</th>
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LOW MOLECULAR WEIGHT HEPARINS (LMWH)

ESTIMATED INCIDENCE VTE FOR LMWH AND NO PROPHYLAXIS FOR MAJOR ORTHOPEDIC SURGERY
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWH vs LOW-DOSE UNFRACTIONED HEPARIN (LDUH)

- **64** RANDOMIZED CONTROL TRIALS (**RCTs**)
- **> 23000** pts, (**2800** ARTHROPLASTY AND HFS cases)
- **LMWH WAS SUPERIOR TO LDUH** WITH FEWER
  - PE (RR 0.78; CI 0.49–1.24) AND
  - DVT (RR 0.80; CI 0.73–0.88) AND
  - LESS MAJOR BLEEDING (RR 0.91; CI 0.75–1.09)
# LOW MOLECULAR WEIGHT HEPARINS (LMWH)

<table>
<thead>
<tr>
<th></th>
<th>ACCP 2012</th>
<th>ICS 2013</th>
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<tbody>
<tr>
<td></td>
<td>LMWH</td>
<td>LDUH</td>
</tr>
<tr>
<td>THA</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TKA</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HFS</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>GRADE</td>
<td>1C</td>
<td>1C</td>
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</tbody>
</table>

**ACCP**: AMERICAN COLLEGE OF CHEST PHYSICIANS  
**ICS**: INTERNATIONAL CONSENSUS STATEMENT  
**GRADE 1C**: STRONG RECOMMENDATION,  
LOW OR VERY LOW-QUALITY EVIDENCE
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWH vs VITAMIN K ANTAGONIST (VKA)

- > 10 RANDOMIZED CONTROL TRIALS (RCTs)
- COMPARED LMWH TO VKA (MAINLY WARFARIN)
- > 9000 pts, FOR INITIAL PROPHYLAXIS (14 DAYS)
- > 1200 pts, FOR EXTENDED PERIOD (6 WEEKS)

MOST OF THESE TRIALS, STARTED LMWH SHORTLY BEFORE SURGERY (<12 PERIOPERATIVELY) WHICH INCREASES THE RISK OF BLEEDING SUBSTANTIALLY
# LOW MOLECULAR WEIGHT HEPARINS (LMWH) vs VKAs

<table>
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<tr>
<th>AUTHORS</th>
<th>JOURNAL</th>
<th>No PATIENTS</th>
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</thead>
<tbody>
<tr>
<td>Hull R</td>
<td>N Engl J Med 1993</td>
<td>569 pts</td>
</tr>
<tr>
<td>RD Heparin</td>
<td>J Bone Joint Surg Am 1994</td>
<td>969 pts</td>
</tr>
<tr>
<td>Leclerc JR</td>
<td>Ann Intern Med 1996</td>
<td>670 pts</td>
</tr>
<tr>
<td>Heit JA</td>
<td>Thromb Haemost 1997</td>
<td>860 pts</td>
</tr>
<tr>
<td>Francis CW</td>
<td>J Bone Joint Surg Am 1997</td>
<td>580 pts</td>
</tr>
<tr>
<td>Colwell CW Jr</td>
<td>J Bone Joint Surg Am 1999</td>
<td>3011 pts</td>
</tr>
<tr>
<td>Hull R</td>
<td>Arch Intern Med 2000</td>
<td>1472 pts</td>
</tr>
<tr>
<td>Samama CM</td>
<td>Arch Intern Med 2002</td>
<td>1279 pts</td>
</tr>
</tbody>
</table>

The LMWH was found to be more effective or at least as effective for preventing asymptomatic DVT with a slight increase in hemorrhagic complications.
**LOW MOLECULAR WEIGHT HEPARINS (LMWH) vs VKAs**

**LECLERC JR. ANN INTERN MED. 1996; 124(7): 619-626**

- ENOXAPARIN (30 mg sc EVERY 12 HOURS) OR ADJUSTED-DOSE WARFARIN (INR, 2.0 TO 3.0) STARTED AFTER SURGERY (TKA)

- STUDY MEDICATIONS WERE ADMINISTERED FOR 14 DAYS

<table>
<thead>
<tr>
<th></th>
<th>ENOXAPARIN (n=206)</th>
<th>WARFARIN (n=211)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL DVT</td>
<td>76 (36.9 %)</td>
<td>109 (51.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>PROXIMAL DVT</td>
<td>24 (11.7%)</td>
<td>22 (10.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>MAJOR BLEEDING *</td>
<td>7/336 (2.1%)</td>
<td>6/334 (1.8%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* DATA BASED ON INCIDENCE OCCURRING IN THE INTENTION-TO-TREAT POLULATION
NS : NOT SIGNIFICANT
Low Molecular Weight Heparins (LMWH) vs VKAs

Extended Venous Thromboembolism Prophylaxis After Total Hip Replacement

A Comparison of Low-Molecular-Weight Heparin With Oral Anticoagulant

Charles Marc Samama, MD, PhD; Muriel Vray, PhD; Jeanne Barré, MD; Jean-Noël Fiessinger, MD; Nadia Rosencher, MD; Thomas Lecompte, MD; Gérard Potron, MD; Joseph Basile, MD; Russell Hull, MBBS, MSc; Denise Desmichels, PhD; for the SACRE Study Investigators

Arch Intern Med 2002; 162

1279 Patients randomly assigned after THA to fixed-dose subcutaneous LMWH or adjusted-dose ACENOCOUMAROL (INR, 2-3) for a 6-weeks

The primary end point was a confirmed symptomatic thromboembolic event, a major hemorrhage, or death
# LOW MOLECULAR WEIGHT HEPARINS (LMWH) vs VKAs

<table>
<thead>
<tr>
<th></th>
<th>LMWH</th>
<th>ACENOCOUMAROL</th>
<th>X²</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE</td>
<td>15/643 (2.3%)</td>
<td><strong>21/636 (3.3%)</strong></td>
<td>P = .03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95% CI -0.8% to 2.8%</td>
</tr>
<tr>
<td>MAJOR BLEEDING</td>
<td>9/643 (1.4%)</td>
<td><em><em>35</em> /636 (5.5%)</em>*</td>
<td>P = .001</td>
</tr>
<tr>
<td>FAILURE RATE</td>
<td>24/643 (3.7%)</td>
<td><strong>53/636 (8.3%)</strong></td>
<td>P = .001</td>
</tr>
</tbody>
</table>

* TWO DEATHS

A SIGNIFICANTLY HIGHER BENEFIT-RISK RATIO WAS OBSERVED FOR PTS UNDERGOING THA WHO RECEIVED EXTENDED PROPHYLAXIS WITH LMWH VS ACENOCOUMAROL

LMWH PROPHYLAXIS WAS AT LEAST AS EFFECTIVE AS VKAS BUT WITH A MARKED IMPROVEMENT IN SAFETY
IN PATIENTS UNDERGOING MAJOR ORTHOPEDIC SURGERY,
VKAS ARE LESS EFFECTIVE THAN LMWH, WITHOUT ANY SIGNIFICANT DIFFERENCE IN THE BLEEDING RISK
LOW MOLECULAR WEIGHT HEPARIN (LMWH) vs VKAs

IN PATIENTS UNDERGOING MAJOR ORTHOPEDIC SURGERY

**VKAs** WERE **LESS EFFECTIVE** AND **NO SAFER** THAN **LMWH**
IN PREVENTING TOTAL DVT AND PROXIMAL DVT

**VKAs ARE HARDER TO USE**

1. Narrow Therapeutic Range (mild degree of overdose may lead to hemorrhage)
2. High Interpatient Variability (no standard dose)

Need for frequent **INR** monitoring _bridging anticoagulation_ for invasive procedures
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWH vs FONTAPARINUX

SYNTHETIC PENTASACCHARIDE THAT BIND TO ANTITHROMBIN AND INHIBIT THE ACTION OF FACTOR Xa
LOW MOLECULAR WEIGHT HEPARIN (LMWH) vs FONTAPARINUX

**N ENGL J MED 2001;345:1298-304**

**FONDAPARINUX COMPARED WITH ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM AFTER HIP-FRACTURE SURGERY**

Bengt I. Eriksson, M.D., Kenneth A. Bauer, M.D., Michael R. Lassen, M.D., and Alexander G.G. Turpie, F.R.C.P., for the Steering Committee of the Pentasaccharide in Hip-Fracture Surgery Study*

**PENTASACCHARIDE IN HIP – FRACTURE SURGERY STUDY**
**PENTHIFRA STUDY**

**LANCET 2002; 359: 1715–20**

**Postoperative fondaparinux versus preoperative enoxaparin for prevention of venous thromboembolism in elective hip-replacement surgery: a randomised double-blind comparison**

Michael Rud Lassen, Kenneth A Bauer, Bengt I Eriksson, Alexander G G Turpie, for the European Pentasaccharide Hip Elective Surgery Study (EPHESUS) Steering Committee*

**EUROPEAN PENTASACCHARIDE HIP ELECTIVE SURGERY STUDY**
**EPHESUS STUDY**
Postoperative fondaparinux versus postoperative enoxaparin for prevention of venous thromboembolism after elective hip-replacement surgery: a randomised double-blind trial

Alexander G G Turpie, Kenneth A Bauer, Bengt I Eriksson, Michael R Lassen, for the PENTATHLON 2000 Study Steering Committee

FONDAPARINUX COMPARED WITH ENOXAPARIN FOR THE PREVENTION OF VENOUS THROMBOEMBOLISM AFTER ELECTIVE MAJOR KNEE SURGERY

Kenneth A. Bauer, M.D., Bengt I. Eriksson, M.D., Michael R. Lassen, M.D., and Alexander G.G. Turpie, F.R.C.P., for the Steering Committee of the Pentasaccharide in Major Knee Surgery Study

N ENGL J MED 2001;345:1305-10
LOW MOLECULAR WEIGHT HEPARIN (LMWH) vs FONTAPARINUX

ARCH INTERN MED 2002;162

Fondaparinux vs Enoxaparin for the Prevention of Venous Thromboembolism in Major Orthopedic Surgery

A Meta-analysis of 4 Randomized Double-blind Studies

Alexander G. G. Turpie, FRCP; Kenneth A. Bauer, MD; Bengt I. Eriksson, MD, PhD; Michael R. Lassen, MD; for the Steering Committees of the Pentasaccharide Orthopedic Prophylaxis Studies

INCIDENCE OF VTE BY DAY 11

<table>
<thead>
<tr>
<th></th>
<th>TOTAL VTE</th>
<th>SYMPTOMATIC VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LMWH</strong></td>
<td>371/2703 (13.7%)</td>
<td>15/3608 (0.4 %)</td>
</tr>
<tr>
<td><strong>FONTAPARINUX</strong></td>
<td>182/2682 (6.8%)*</td>
<td>22/3603 (0.6 %)</td>
</tr>
</tbody>
</table>

ODDS REDUCTION OF 55.2% (95% CI, 45.8% TO 63.1%)  * P <.001
LOW MOLECULAR WEIGHT HEPARIN (LMWH) vs FONDAPARINUX

SAFETY OUTCOMES

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fondaparinux Group (n = 3616)</th>
<th>Enoxaparin Group (n = 3621)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment period (up to day 11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal bleeding</td>
<td>0</td>
<td>1 (0.0)</td>
</tr>
<tr>
<td>Bleeding in critical organ</td>
<td>0</td>
<td>1 (0.0)</td>
</tr>
<tr>
<td>Bleeding leading to another operation</td>
<td>12 (0.3)</td>
<td>8 (0.2)</td>
</tr>
<tr>
<td>Bleeding with a bleeding index $\geq 2^\uparrow$</td>
<td>84 (2.3)</td>
<td>53 (1.5)</td>
</tr>
<tr>
<td>Any transfusion†</td>
<td>1950 (53.9)</td>
<td>1864 (51.5) $^\delta$</td>
</tr>
<tr>
<td>Wound infection</td>
<td>37 (1.0)</td>
<td>29 (0.8)</td>
</tr>
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</table>

ALTHOUGH, THE INCIDENCE OF CLINICALLY RELEVANT BLEEDING (LEADING TO DEATH OR REOPERATION OR IN A CRITICAL ORGAN) DID NOT DIFFER BETWEEN GROUPS, MAJOR BLEEDING OCCURRED MORE FREQUENTLY IN FONDAPARINUX - GROUP ($P = .008$)

TURPIE G.G.A ET AL: ARCH INTERN MED 2002;162
LOW MOLECULAR WEIGHT HEPARIN (LMWH) vs FONTAPARINUX

PENTAMAKS STUDY

TKR SAFETY: BLEEDING

PENTASACCHARIDE IN MAJOR KNEE SURGERY STUDY (2001)
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

ESSENTIAL OF SURGERY

RELATIVELY LOW VALUE → ON THE PREVENTION OF VENOGRAPHIC THROMBOSIS

RELATIVELY HIGH VALUE → ON MINIMIZING BLEEDING COMPLICATIONS
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

VTE PREVENTION IN ORTHOPAEDIC SURGERY

FOR HOW LONG
THE INCIDENCE OF THROMBOEMBOLIC EVENTS DOES NOT STABILIZE UNTIL APPROXIMATELY 10 WEEKS AFTER THR

WHITE ET AL. ARCH INTERN MED. 1998
Incidence and Time Course of Thromboembolic Outcomes Following Total Hip or Knee Arthroplasty

Richard H. White, MD; Patrick S. Romano, MD, MPH; Hong Zhou, PhD; Juan Rodrigo, MD; William Bargar, MD

INCIDENCE OF THROMBOEMBOLIC EVENTS WITHIN 3 MOS OF SURGERY

<table>
<thead>
<tr>
<th></th>
<th>TOTAL VTE</th>
<th>AFTER HOSPITAL DISCHARGE</th>
<th>MEAN TIME OF DIAGNOSIS</th>
</tr>
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<tbody>
<tr>
<td>PRIMARY THA 19586 PTS</td>
<td>556 (2.8 %)</td>
<td>76 %</td>
<td>17th DAY</td>
</tr>
<tr>
<td>PRIMARY TKA 24059 PTS</td>
<td>508 (2.1 %)</td>
<td>47 %</td>
<td>7th DAY</td>
</tr>
</tbody>
</table>
Prolonged Enoxaparin Therapy to Prevent Venous Thromboembolism After Primary Hip or Knee Replacement

By Philip C. Comp, MD, PhD, Theodore E. Spiro, MD, Richard J. Friedman, MD, Thomas L. Whitsett, MD, Gerhard J. Johnson, MD, Geoffrey A. Gardiner Jr., MD, Glenn C. Landon, MD, and Maurice Jove, MD, for the Enoxaparin Clinical Trial Group

THE JOURNAL OF BONE & JOINT SURGERY 2001: 83-A

968 Patients - THA or TKA, postop enoxaparin sc (30mg bid) for 7 to 10 days,

873 then 21 days of double-blind outpatient treatment with either enoxaparin (40 mg qd) or a placebo.
RESULTS

THE 7 TO 10 - DAY REGIMEN OF 30 mg OF ENOXAPARIN bid FOR PATIENTS TREATED WITH THA IS SUBOPTIMAL

A SUBSTANTIAL THERAPEUTIC BENEFIT BY PROLONGING ENOXAPARIN TREATMENT (40 mg qd) FOR ADDITIONAL 3 WEEKS POSTOP (TOTAL OF 4 WEEKS OF ENOXAPARIN TREATMENT)

COMP CP. THE JOURNAL OF BONE & JOINT SURGERY 2001: 83-A
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

VTE PREVENTION IN ORTHOPAEDIC SURGERY

WHEN SHOULD PROPHYLAXIS BEGIN
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

CURRENT CLINICAL PRACTICE

EUROPE

12 HOURS PREOPERATIVELY - 40 mg ONCE DAILY

RECOGNIZES THAT DVT TYPICALLY ORIGINATES PERIOPERATIVELY AND THAT PRE-OPERATIVE PROPHYLAXIS MAY OPTIMIZE THE ANTITHROMBOTIC EFFECTIVENESS
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

CURRENT CLINICAL PRACTICE

USA - CANADA

12 – 24 HOURS POSTOPERATIVELY 30 mg TWICE DAILY

DELAYED INITIATION OF PROPHYLAXIS WITH LMWH IS STANDARD PRACTICE TO MINIMIZE BLEEDING RISK
Timing of Initial Administration of Low-Molecular-Weight Heparin Prophylaxis Against Deep Vein Thrombosis in Patients Following Elective Hip Arthroplasty

A Systematic Review

Russell D. Hull, MBBS; Graham F. Pineo, MD; Paul D. Stein, MD; Andrew F. Mah, BSc; Susan M. MacIsaac, M Ola E. Dahl, MD, PhD; William A. Ghali, MD, MPH; Matthew S. Butcher, BSc; Rollin F. Brant, PhD;
David Bergqvist, MD, PhD; Karly Hamulyák, MD; Charles W. Francis, MD; Victor J. Marder, MD; Gary E. Raskob,

THE PRACTICE IN THE USA AND CANADA OF DELAYED INITIATION OF LMWH 12 - 24 HOURS POSTOP RESULTS:

- SUBOPTIMAL ANTITHROMBOTIC EFFECTIVENESS
- NO SUBSTANTIVE SAFETY ADVANTAGE
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWHs have been evaluated extensively for VTE prophylaxis in all clinical conditions and their efficacy has been documented in dozens of RCT and in several meta-analyses.
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LMWHS ARE **EFFECTIVE AND SAFE** FOR VTE PROPHYLAXIS IN MAJOR ORTHOPEDIC SURGERY AND ARE PROBABLY THE **MOST COMMONLY USED** PROPHYLACTIC AGENT IN EUROPE AND THE 2**ND** USED AGENT IN N. AMERICA
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

LWMH ARE CONSIDERED TO BE:

THE **REFERENCE ANTICOAGULANT** AGENTS AND THE **ACTIVE COMPARATOR** IN MOST TRIALS OF NEW ANTICOAGULANTS FOR **VTE** PROPHYLAXIS IN THE CONTEXT OF MAJOR ORTHO SURGERY
LOW MOLECULAR WEIGHT HEPARINS (LMWH)

WE SUGGEST THE USE OF LMWH IN PREFERENCE TO THE OTHER AGENTS, THAT HAS SIMILAR OR SUPERIOR PROPERTIES OF EFFECTIVE PROPHYLAXIS COMBINED WITH LITTLE RISK OF BLEEDING & Extensive Clinical Experience

9TH ED: ACCP GUIDELINES, CHEST 2012
Prevention of VTE in Orthopedic Surgery Patients
1. NEW ORAL ANTICOAGULANTS (FACTOR Xa & THROMBIN INHIBITORS) ARE BEING DEVELOPED TO IMPROVE THE EFFICACY AND SAFETY OF VTE PROPHYLAXIS

2. WHETHER THESE AGENTS WILL ULTIMATELY SUPPLANT THE WIDESPREAD APPLICATION OF LMWH TO ORTHO – PAEDIC SURGERY REMAINS TO BE SEEN
DEPARTMENT OF ORTHOPAEDIC SURGERY,
UNIVERSITY OF IOANNINA, SCHOOL OF MEDICINE, IOANNINA, GREECE