

VTE PREVENTION FOR SURGICAL PATIENTS

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REASONS TO PROPHYLAX

1. Prevent DVT and PE
2. Enhance cost-effectiveness
3. Minimize medicolegal liability

FAILURE TO PROPHYLAX: ACCORDING TO ACCP

“Rationale”

- 1) VTE incidence has declined
- 2) Concern about bleeding complications
- 3) VTE not perceived as important problem

(CHEST 2001; 119: 132S-175S)

PROPHYLAXIS MODALITIES

Mechanical

Graduated Compression Stockings

Intermittent Pneumatic Compression

Combined GCS / IPC

IVC Filter

Pharmacologic

Heparins

Warfarin

Combined Mechanical — Pharmacologic

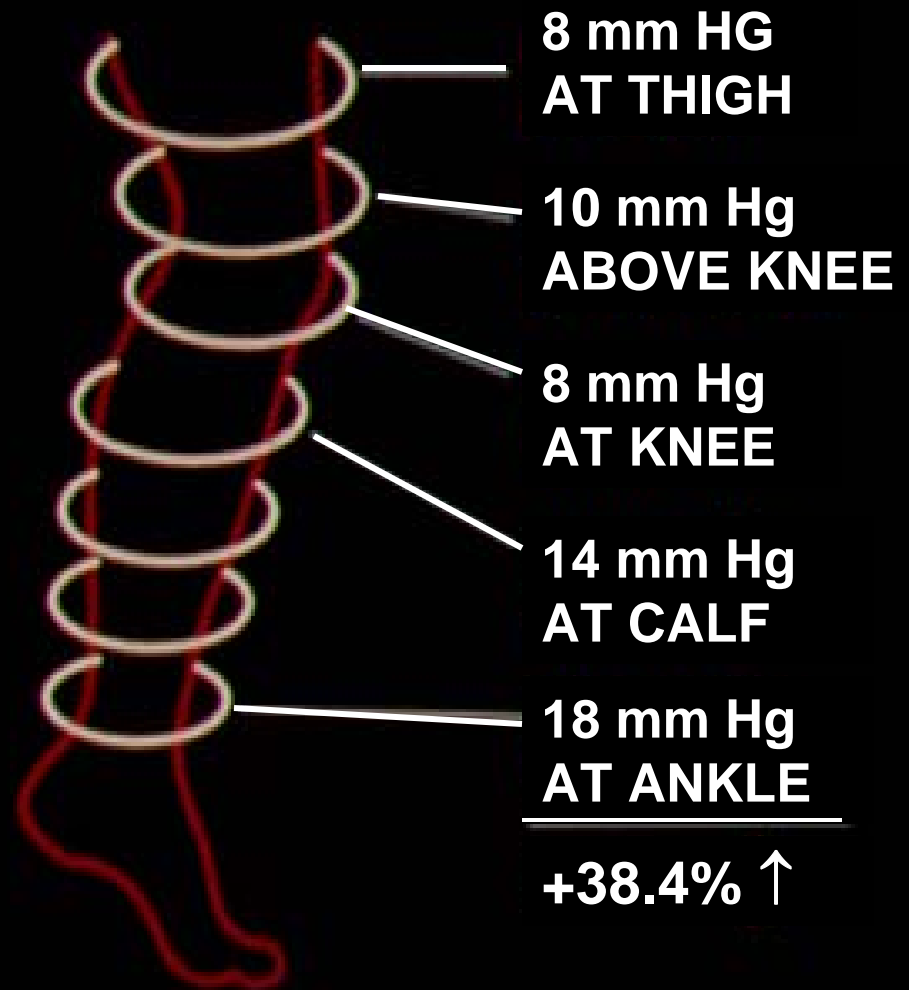
MECHANICAL PROPHYLAXIS

- 1) **GCS:** ↑ venous blood flow
- 2) **IPC:** ↑ venous blood flow;
↑ endogenous fibrinolysis
- 3) **IVC Filter:** mechanical barrier
prevents PE,
but does not halt
thrombotic process

Anti-Embolism Stockings

Structural Features

- Graduated Compression
- Proven Pressure Pattern



PNEUMATIC COMPRESSION BOOTS

STIMULATE ENDONGENOUS

FIBRINOLYSIS

Decrease PAI - 1

Increase TPA Activity

(Comerota AJ. Ann Surgery 1997; 226:306)

INTERMITTENT PNEUMATIC COMPRESSION

Meta-Analysis in Postop Patients

- 2,270 patients in 15 randomized trials
- IPC devices reduced DVT risk by 60% (Relative Risk 0.40, 95% CI 0.29-0.56, $p < 0.001$)

(Urbankova J. Thromb Haemost 2005; 94: 1181-5)

HIGH FAILURE RATE OF “FOOT PUMPS”

- Trauma Patients: 21% DVT
(J Trauma 1999; 47: 25-32)
- TKR Patients: 65% DVT
(JBJS [Br] 1999; 81-B: 654-659)

Advantages of LMWH Over UFH

EFFECT

CONSEQUENCE

Much Less Protein Binding → More Predictable Dose Response

Cleared Primarily by Renal Mechanism → Longer Plasma Half-Life

Much Less Binding to Osteoblasts → Less Osteopenia

Less Binding to PF4 → Lower Risk of HIT

GENERAL SURGERY

- Heparin 5,000 units SC q8h
(begin 2h preop)
- Enoxaparin 40 mg SC q24h
(begin 2h preop)
- Dalteparin 5,000 units SC q24h
(begin 12h preop, or give 2,500
units 2h preop)

ORTHOPEDIC SURGERY

- Enoxaparin 40 mg SC q24h
- Enoxaparin 30 mg SC q12h
- Dalteparin 5,000 units SC q24h
- Fondaparinux 2.5 mg SC q24h
- Warfarin, target INR 2.0-3.0

Derivation of Pentasaccharides

Unfractionated Heparin

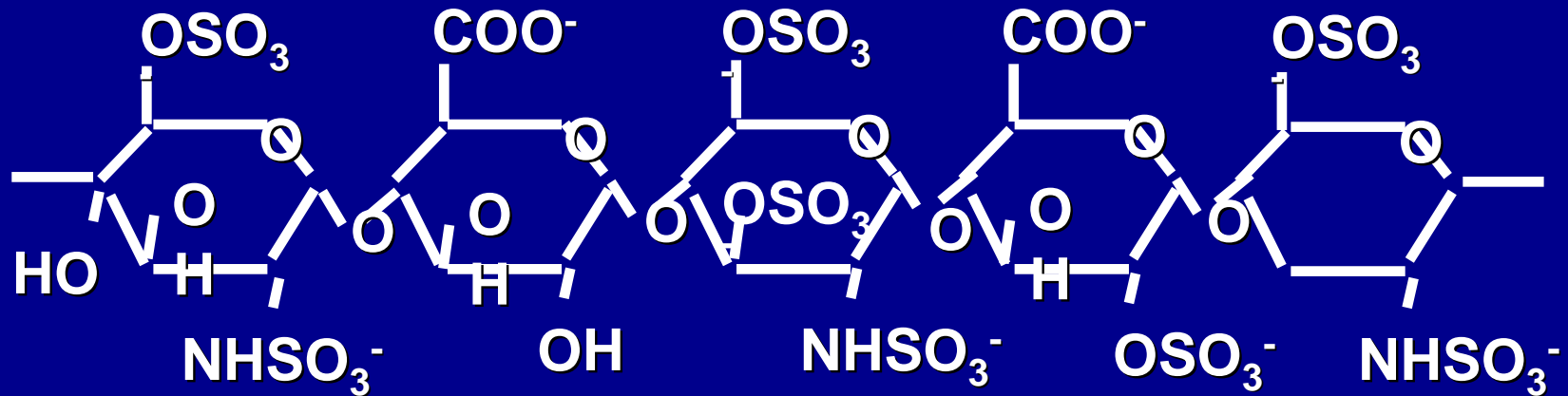


Low Molecular Weight Heparin



Pentasaccharides

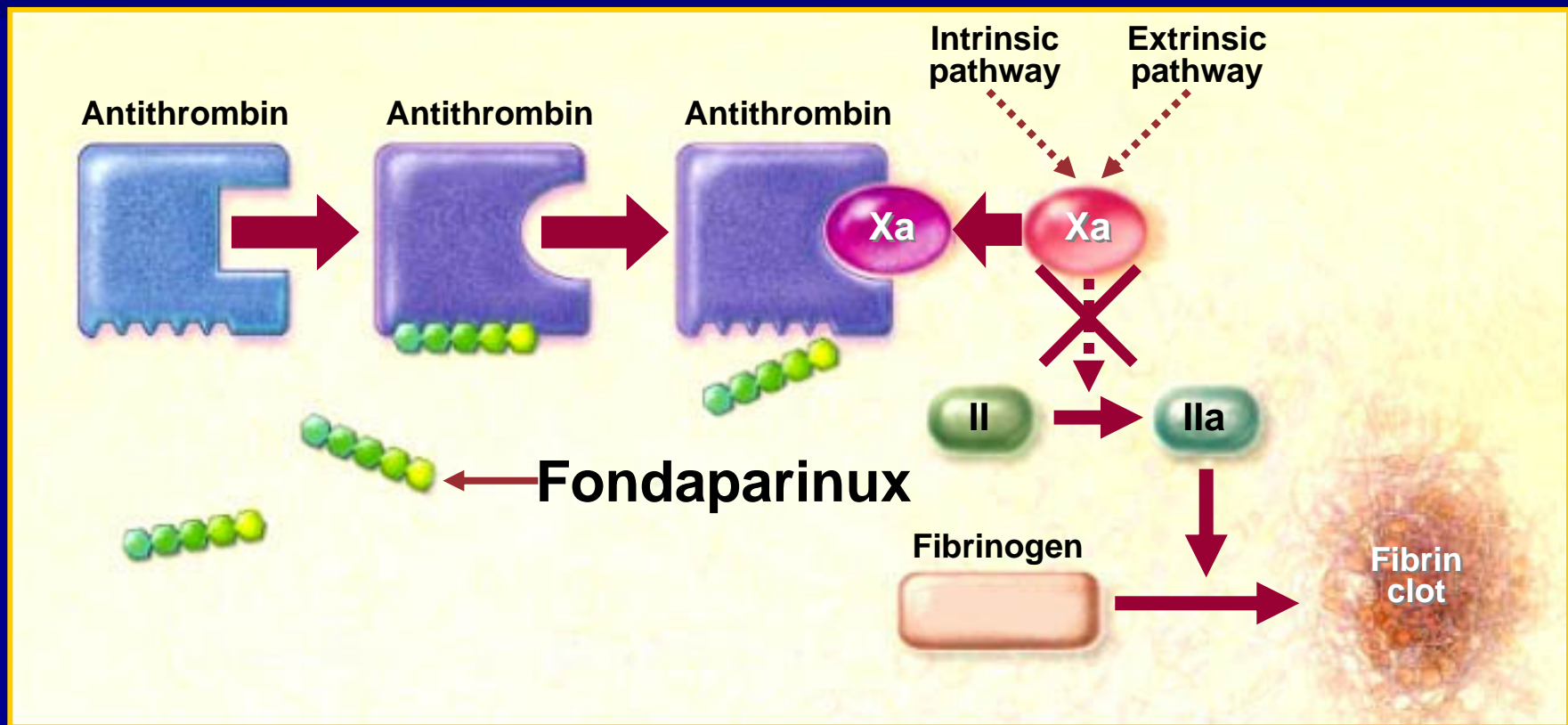
HEPARIN: Minimal AT-III Binding Pentasaccharide



(Choay et al Ann NY Acad Sci 370: 644, 1981)

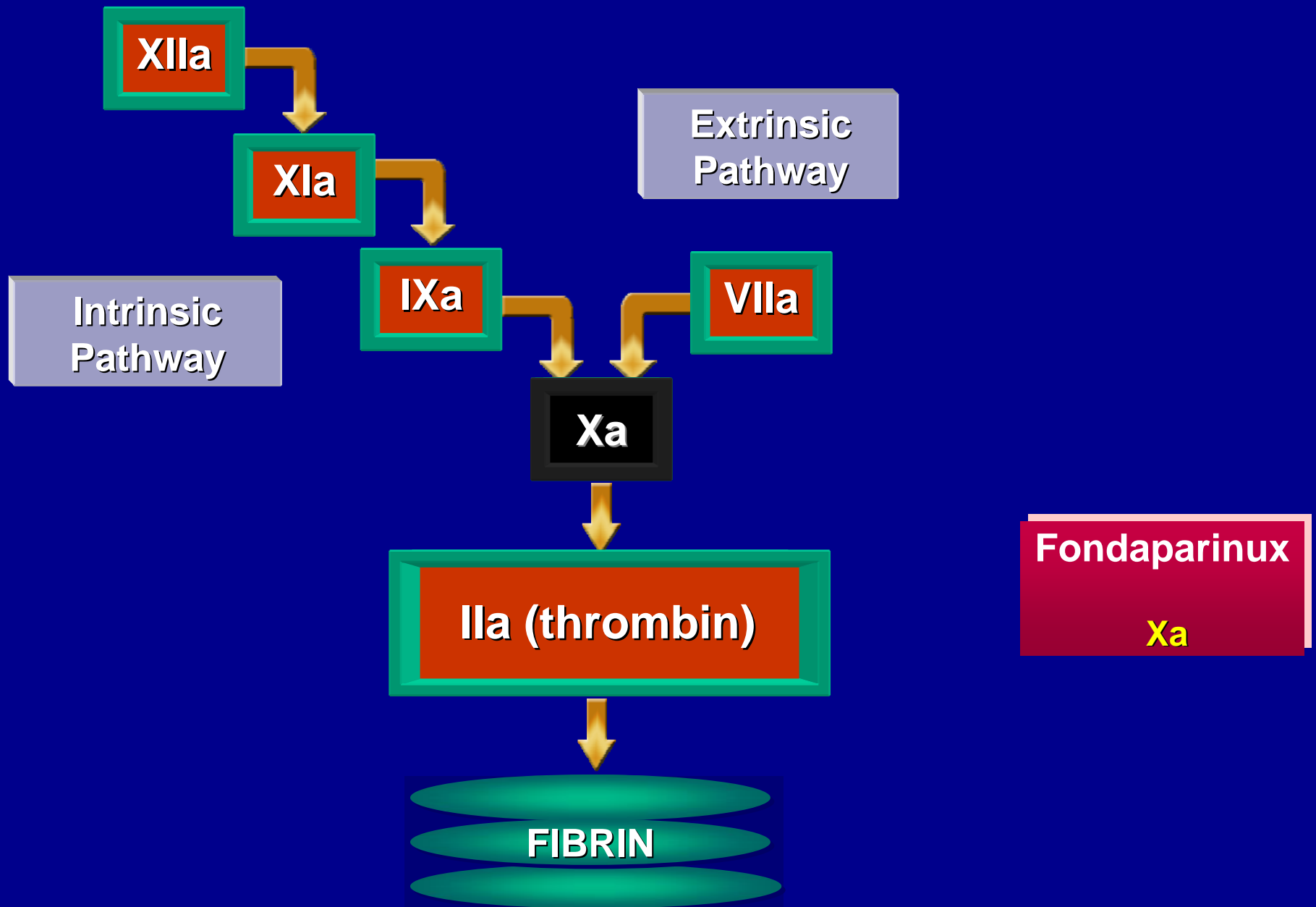
Pentasaccharide: Mechanism

Produces an Irreversible Conformational Change in Antithrombin, Which Binds to and Inhibits Factor Xa



Turpie et al. *N Engl J Med* 2001;344:619-625

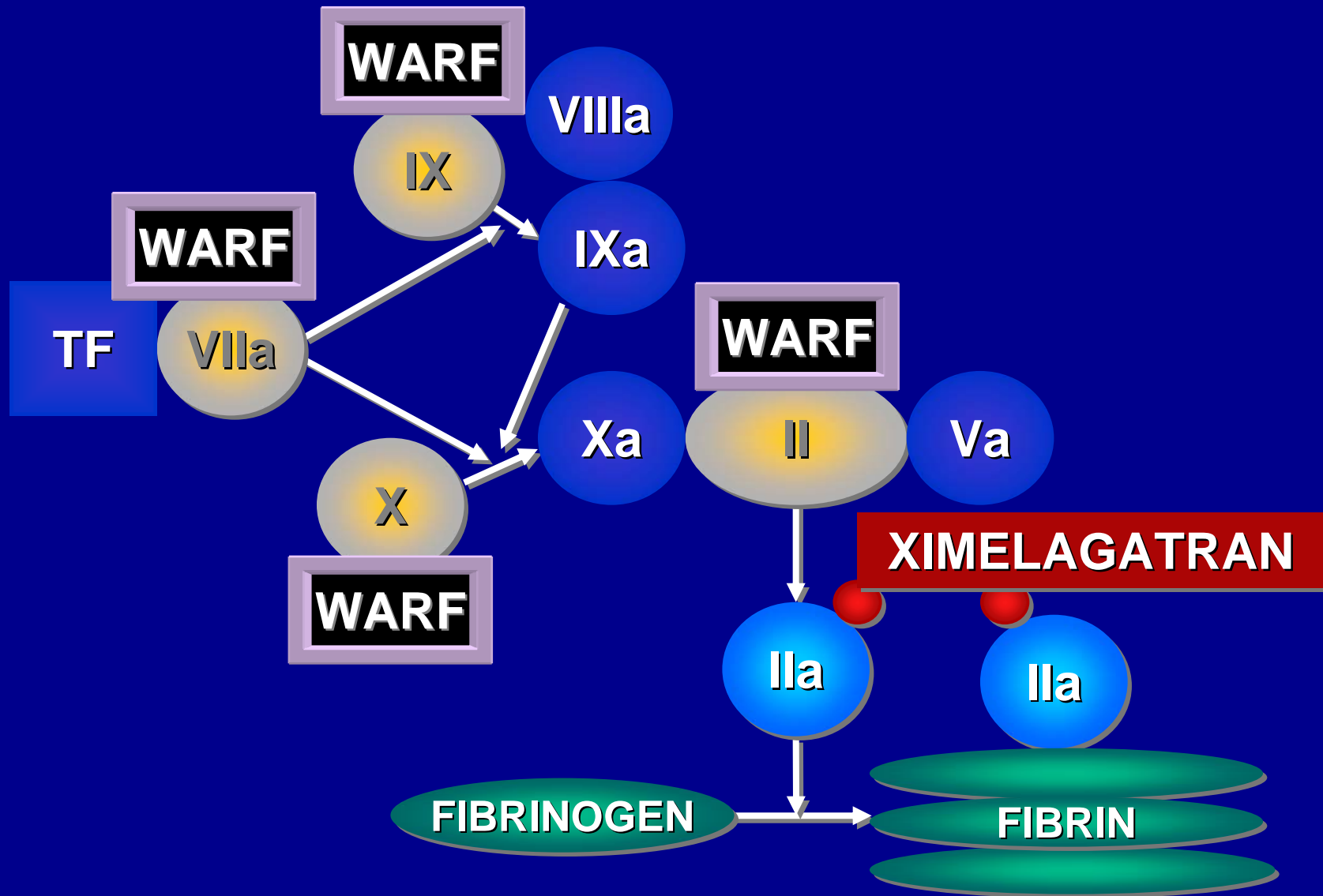
Xa Inhibitors: Pentasaccharides



FONDAPARINUX

- Pentasaccharide (5-sugar moiety)
- Synthetic
- Selectively binds to ATIII to potentiate neutralization of factor Xa
- Elimination half-life 17-21 hours
- Daily SC dosing
- Renally cleared
- FDA approved: hip fracture, THR, TKR

ORAL ANTICOAGULANTS



PREVENT VTE AFTER MAJOR ORTHOPEDIC SURGERY

Suggested Strategy

- 1) Universal prophylaxis with LMWH or fondaparinux or warfarin \pm pneumatic compression.
- 2) Extend prophylaxis 4 weeks postop.
- 3) No ultrasound of legs unless symptoms develop.

ENOXAPARIN VERSUS WARFARIN

(THR Patients; N = 3,011)

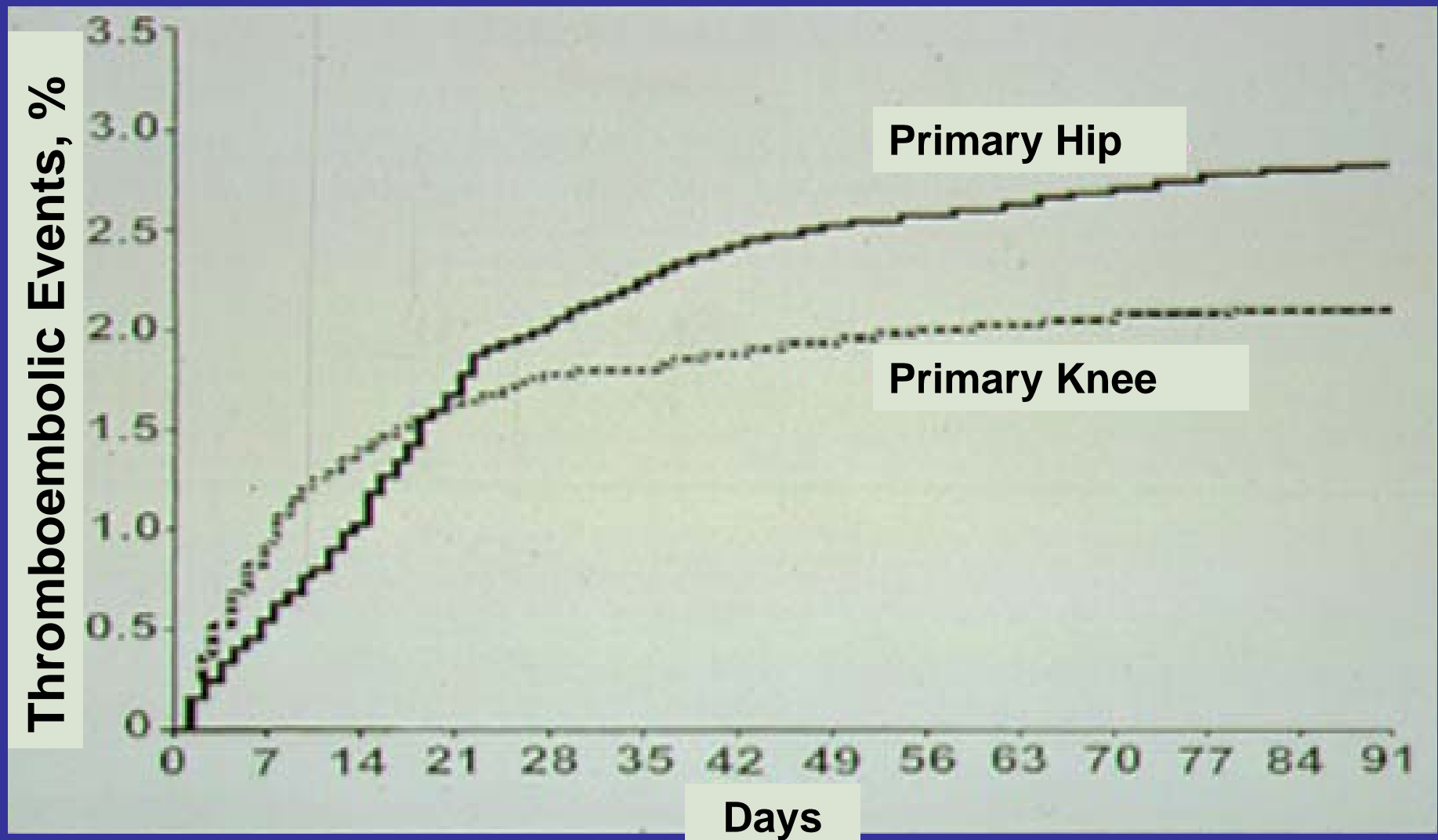
- Enoxaparin 30 mg BID
- Warfarin: target INR = 2.0 - 3.0

Average 7-day hospitalization;
enoxaparin VTE = 0.3%, versus
warfarin VTE = 1.1% (p=0.008).

Enoxaparin major bleeds = 1.2%,
versus **Warfarin major bleeds = 0.5%**
(p=0.06)

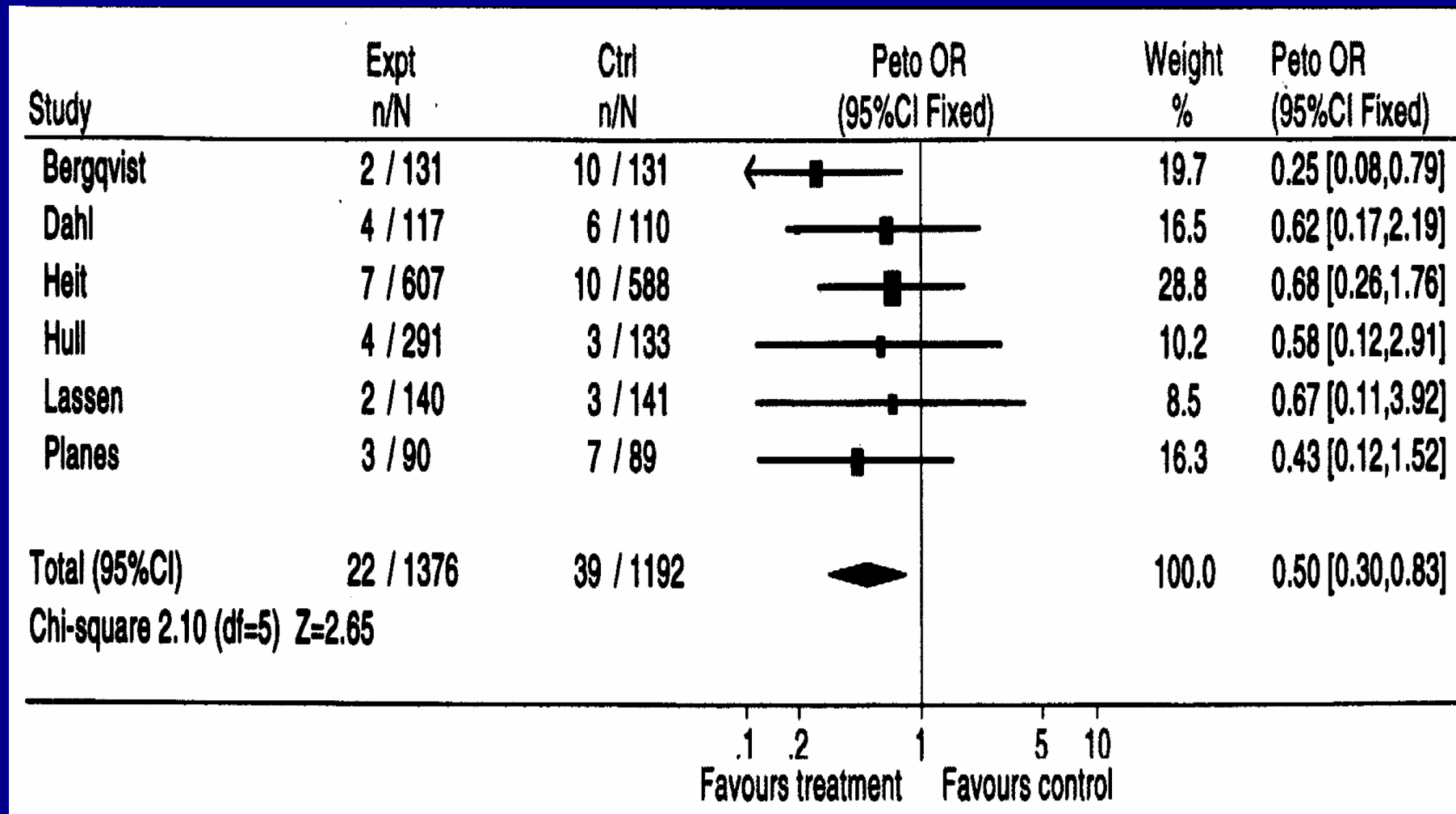
(JBJS 1999; 81-A: 932-939)

HIP / KNEE VTE INCIDENCE



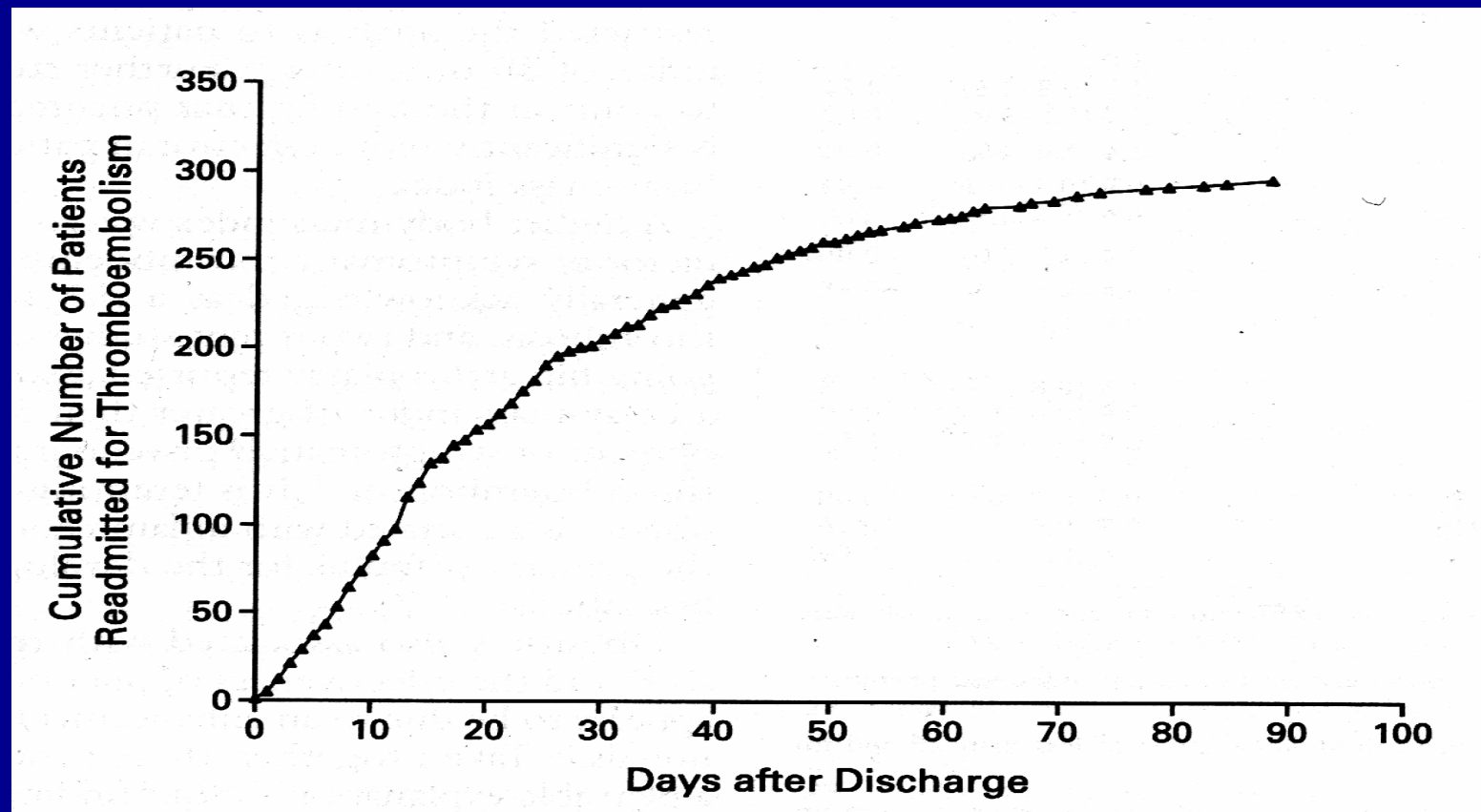
(Arch Intern Med 1998; 158: 1525)

EXTENDED DURATION LMWH REDUCES RATE OF SYMPTOMATIC VTE



(Cohen AT et al. Thromb Haemost 2001; 85:940)

TIME COURSE AFTER THA FOR HOSPITAL READMISSION (N=297)



(White RH et al. NEJM 2000; 343: 1758-64)

PROTECTION AGAINST VTE READMISSION AFTER TKA

- 1) Lean body weight
- 2) Pneumatic compression
- 3) Warfarin after discharge

(White RH et al. NEJM 2000; 343: 1758-64)

NEUROSURGERY

Despite maximal intensive prophylaxis, Neurosurgery has replaced Orthopedic Surgery as BWH's #1 Service for postoperative DVT/PE.

VTE AFTER NEUROSURGERY

BWH Experience

497 pts: 429 Primary and 68 Metastatic
Clinically Overt DVT/ PE

Overall rate: **3.7%**

Craniotomy for primary brain tumor: **9.5%**

Craniotomy for metastatic brain tumor: **19%**

(J Thrombosis Thrombolysis 1999; 8: 139-142)

LMWH FOR ELECTIVE NEUROSURGERY

N = 307

Enoxaparin 40 mg daily vs. Placebo
Bilateral leg venography pre-discharge
No pneumoboosts

Placebo: 32% DVT rate

Enoxaparin: 17% DVT rate

Major Bleeding: 3% each group

(Agnelli et al; NEJM 1998; 339:80-85)

LOW RATE OF VENOUS THROMBOEMBOLISM
AFTER CRANIOTOMY FOR BRAIN TUMOR
USING MULTIMODALITY PROPHYLAXIS

Samuel Z. Goldhaber, MD

Kelly Dunn, BA

Marie Gerhard-Herman, MD

John K. Park, MD, PhD

Peter McL. Black, MD, PhD

(CHEST 2002; 105: 1416-1419)

CRANIOTOMY FOR BRAIN TUMOR TRIAL

GCS, IPC

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graph TD; A[GCS, IPC] --> B[Randomize (Double-Blind)]; B --> C[Enoxaparin 40 mg daily]; B --> D[Miniheparin 5,000 q 12h];
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Randomize
(Double-Blind)

Enoxaparin
40 mg daily

Miniheparin
5,000 q 12h

ASCERTAINMENT OF DVT

(N = 150)

All patients, regardless of symptoms, underwent pre-discharge ultrasonography of deep leg veins.

RESULTS (N = 150)

- 1) No patient developed symptomatic DVT or PE.
- 2) 14 (9.3%) developed asymptomatic DVT.
- 3) 10 of 14 were isolated calf DVT.
- 4) Only 1 ICH.

TAKE-HOME POINTS

- 1) Multimodality approach was key:
 - A) Mechanical Prophylaxis
 - B) Pharmacologic Prophylaxis
 - C) Venous U/S as a “fail-safe” backup

- 2) Ultrasound was crucial in these patients, many unaware or unable to complain of leg discomfort.

CABG CONTROVERSY

“Individualize

prophylaxis according

to level of risk”

REASONS TO SHUN CABG PROPHYLAXIS PROTOCOLS

- Post-CABG PE is rare
- Heparin during CPB protects (but what about OP-CABG?)
- Heparin injections are uncomfortable, cost money, and may cause bleeding

REASONS FOR PROTOCOL

Post-CABG PE may be difficult or impossible to identify antemortem:

- Normal HR / BP
- Normal ECG
- Vague symptoms
- Easy to ascribe to pericarditis, costochondritis, deconditioning
- 1/2 DVTs occur in non-harvest leg

IS THIS A BIG PROBLEM?

- 20% postop DVT/PE, mostly calf DVT, mostly asymptomatic
- 1% postop symptomatic PE (nonfatal)
- 0.1% fatal postop PE

(Goldhaber SZ et al. Am J Cardiol 1995; 76: 993-6)

CLINICAL PE / DVT INCIDENCE

Post CABG

736 / 66,180 (1.1%)

(Thromb Haemostas 2003; 90: 446-455)

CABG RE-ADMISSIONS

PE / DVT account for
133 / 2,111 cases
(6.3%)

(JAMA 2003;290:773-780)

PNEUMO BOOTS WORKED
POST-CABG WHEN ADDED
TO MINIHEP

(N=2,551)

62% reduction in clinical PE:

4.0%  1.5%

(CHEST 1996; 109:82-85)

DVT PREVENTION

- Surgical teams have done a better job than internal medicine teams.
- Making prevention routine and mandatory is the best protection.
- Multiple effective measures are available to prevent DVT.
- New drugs and computerized order entry will prevent even more DVTs than ever before.