Joint Replacement and Anticoagulation in the Post-Acute Setting

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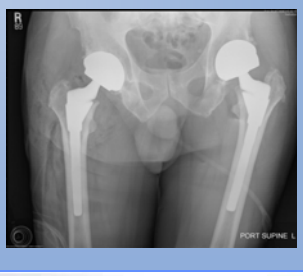
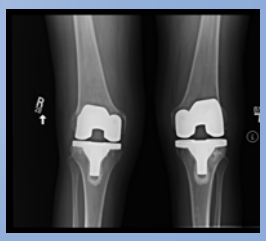
- No Financial Disclosures



Increasing Demand

The rate of TJA in the US has increased in the last two decades, and will likely increase further in the next two decades as a result of….

- Expanding and aging population
- The prevalence of osteoarthritis, trauma and obesity
- Cultural values of "Baby Boomers"
- Demonstrated Clinical Success



Increasing Demand

- Between 2005 and 2030 the prevalence of primary joint arthroplasty is expected to increase…
- Hip: 174% from 209,000 to 572,000 operations
- Knee: 673% from 450,000 to 3,480,000 operations
- Revisions: Hip 137% Knee 601%

Increasing Demand

- As length of hospital stays continue to decline, more venothrombolic events are occurring outside acute care setting.

Why is this topic so hard ?

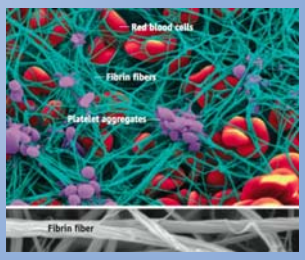
- Surgeons and non-surgeons can have tremendously different views of the risks, especially concerning bleeding
- Fatal PE is uncommon – 0.1-0.2 %
- May no longer be possible to have placebo-controlled trials

Why is this topic so hard ?

- Thromboembolic Disease (TED) Prevention
- What is the goal ?
  - Prevent asymptomatic DVT
  - Prevent symptomatic DVT
  - Prevent PE
  - Prevent fatal PE

TED prevention

- Risk/benefit ratio changes depending on which outcome you choose
- Willing to accept higher risk to prevent fatal PE than asymptomatic DVT



Tough Questions

- Does chemoprophylaxis prevent fatal PE ?
- Is DVT a good surrogate marker
- What are the current Orthopaedic guidelines ?

Tough Questions

- Is asymptomatic DVT detected by imaging a good surrogate marker for fatal PE?
  - Quinlan *et al.* compared incidence
    - Asymptomatic DVT in venographic studies
    - Symptomatic DVT in non-venographic studies
    - All received enoxaparin

Incidence of Asymptomatic DVT

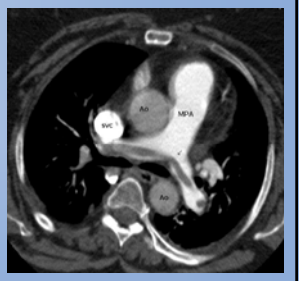
	THA	TKA
Total DVT	13.2 %	38.1 %
Proximal DVT	3 %	5.7 %
Distal DVT	10 %	32.2 %

What can we agree on ?

- LMWH and warfarin reduce the incidence of venographic DVT as compared to placebo
- Comparable or slightly higher bleeding rate with LMWH than warfarin
- Aspirin less effective for preventing venographic DVT – at least in hip

Tough Questions

- Does anti-coagulation prevent fatal PE ?



LMWH vs. Warfarin

- Colwell *et al.*
  - 3011 THA patients received adjusted-dose warfarin (goal INR 2.0-3.0) or enoxaparin (30 mg BID) for avg 7.3 days
  - No treatment post-discharge
  - Randomized, controlled, multi-center study followed for 3 months
  - End –point symptomatic TED

Colwell et al., *JBJS Am,* 1999;81:932-940

- <40 % achieved INR 2.0 by day 7
- 3.6 % enoxaparin and 3.7 % warfarin patients had symptomatic DVT
- 0.7 % in-hospital and 3 % post-discharge
- 0.9 % PE equal in the 2 groups

- 1 confirmed fatal PE in enoxaparin group
- 3 additional deaths ? PE
- ~ 0.1% fatal PE
- Overall mortality 0.6%, no difference
- Clinically significant bleeding 2X higher in enoxaparin group (1.2% vs. 0.5%) – mostly operative site
- Enoxaparin less TED in house but no difference at 3 months

ASA

- Lotke *et al.*
  - 3473 consecutive TKAs followed for minimum of 6 weeks
  - Rapid mobilization, foot pumps, regional anesthesia, epidural, ASA bid
  - 71 High risk patients received warfarin or LMWH

Lotke et al.,*Clin Orthop Relat Res.*2006;452:175-180

- Fatal PE rate 0.06 -0.14 %
- Overall mortality rate 0.26% at 6 weeks
- Non fatal PE 0.26 %
- Bleeding complications 0.4 %

TABLE 2. Prevalence of Fatal PE after THA and TKA

Study/year	Number of Patients	Procedure	Anticoagulant	Incidence (%)
Murray et al[29] 1996	130,000	THA	None/mix	0.1–0.2
Leiberman et al[24] 1997	1099	THA	Warfarin	0.1
Leclerc et al[22] 1998	1984	THA-TKA	LMWH	0.15
Westrich et al[44] 1999	2592	THA	Multimodal	0.04
Colwell et al[4] 1999	1516	THA	LMWH	0.13
Colwell et al[4] 1999	1495	THA	LMWH	0.13
PEPTCG[34] 2000	4089	THA-TKA	Aspirin	0.07
Williams et al[44] 2002	7155	THA	Mix	0.1
Gill et al[14] 2003	3048	TKA	Aspirin/mix	0.03–0.16
Turpie et al[42] 2004	3003	THA-TKA	LMWH	0.1
Turpie et al[42] 2004	3608	THA-TKA	Fondaparinux	0.1
Sarmiento and Goswami[38] 2005	1835	THA	Aspirin	0.1
Howie et al[16] 2005	44,088	THA	Mix	0.18
Howie et al[16] 2005	27,503	TKA	Mix	0.12
Gonzalez et al[15] 2005	2032	THA	Multimodal	0

THA = total hip arthroplasty; TKA = total knee arthroplasty; LMWM = low molecular weight heparin; PEPTCG = Pulmonary Embolism Prevention Trial Collaborative Group

- Murray *et al.*
  - Meta-analysis 93,000 patients
  - Fatal PE rate 0.1 % to 0.2 % even if no prophylaxis
  - End-point deaths within 3 months
  - Fatal PE and death rate decreased over last 30 years

Murry et al.*JBJS BR*,1996; 78-B:863-870.

Table II. The fatal PE (FPE) rate for different types of prophylaxis in studies starting in the 1970s, 80s and 90s. Differences between groups do not quite reach statistical significance (p = 0.051)

Prophylaxis	FPE	Patients	Rate (%)	95% Confidence limits
None	4	3432	*0.12*	*0.03* to *0.30*
Heparin	8	10 356	*0.08*	*0.03* to *0.15*
Warfarin	2	5162	*0.04*	*0.00* to *0.14*
Aspirin	3	2700	*0.11*	*0.02* to *0.32*
Dextran	7	2730	*0.26*	*0.10* to *0.53*

Table III. The death rate for different types of prophylaxis in studies starting in the 1970s, 80s and 90s. Differences between groups are not statistically significant (p = 0.2)

Prophylaxis	Deaths	Patients	Rate (%)	95% Confidence limits
None	10	3355	*0.30*	*0.14* to *0.55*
Heparin	40	10 105	*0.40*	*0.28* to *0.54*
Warfarin	11	3763	*0.29*	*0.15* to *0.52*
Aspirin	4	2649	*0.15*	*0.04* to *0.39*
Dextran	13	2618	*0.50*	*0.26* to *0.85*

Table I. The fatal PE and death rates with confidence limits (CL) in trials starting in different decades, with the death rate in 1991-2 in the UK calculated from the number of deaths identified by the National Confidential Enquiry into Perioperative Deaths (NCEPOD) (Campling et al 1993) and the number of THRs implanted during that period (Williams et al 1994)

Start of trial	Fatal PE	Patients	Rate (%)	95% Confidence limits	Deaths	Patients	Rate (%)	95% Confidence limits
1960s	129	20 190	*0.64*	*0.53* to *0.75*	237	21 501	*1.10*	*0.96* to *1.24*
1970s	143	40 207	*0.36*	*0.30* to *0.41*	434	39 199	*1.11*	*1.00* to *1.21*
1980s and 90s	27	23 511	*0.11*	*0.07* to *0.16*	69	18 204	*0.38*	*0.29* to *0.47*
NCEPOD					134	38 000	*0.35*	*0.29* to *0.41*

Does anti-coagulation prevent fatal PE ?

- Last 15 years death rate 0.38%, fatal PE 0.11%
- No significant difference in fatal PE rate with prophylaxis

Does anti-coagulation prevent fatal PE ?

- **Paxton *et al.***
  - Compared 957 Kaiser TKA pts. treated with low dose warfarin to 785 pts with no mech. or chemical proph.
  - Surgeon choice
  - INR 1.6 to 2.2 for 6 weeks
  - 3 month f/u

Paxton *et al.*, J. Arth. 2003

	Non-fatal PE	Deep Infection	Re-admission	Death	Subsequent surgery	Overall Complication
Control	0.3 %	0.3 %	0.9 %	0.3 %	0.3 %	2.2 %
Warfarin	0.1 %	0.6 %	1.8 %	0.1 %	1.1 %	4.7 %

No Fatal PE in either group

All-Cause Mortality

- **Sharrock *et al.***
  - Meta-analysis 1998 – 2007 of THA and TKA and TED prophyaxis
  - 6 wk or 3 month data on all-cause mortality
    - Grp A (15838) – LMWH, fondaparinux;
    - Grp B (7193) - regional anesthes, pneum comp and ASA;
    - Grp C (5006) –warfarin

Sharrock et al.*Clin Orthop Rel Res.*2008;466:714-721

	Group A (LMWH)	Group B (ASA, mech)	Group C (warfarin)
Nonfatal PE	0.6 %	0.35 %	0.52 %
mortality	0.41 %	0.19 %	0.4 %

A vs B significant at P<= .01 for mortality

- Now that we got that cleared up!

Risks

- What are the risks from anti-coagulation ?
  - Few studies examine long-term orthopedic bleeding complications
    - Additional surgery
    - Infection
    - Prosthetic loosening
    - stiffness

- Clarke *et al.*
  - Reviewed 17184 TKA pts.
  - 42 (0.24%) returned to the OR within 30 days for evacuation of a hematoma.
  - 12.3 % subsequent major surgery at 2 years vs. 0.6 % if no hematoma
  - 10.5 % deep infection at 2 years vs. 0.8 % if no hematoma

Clarke et al., JBJS-A, 90, 2008

- Morrey *et al.*
  - 150 pts. with suspected PE after THA
  - 47% managed with heparin had complication
  - 20% managed without heparin had complication

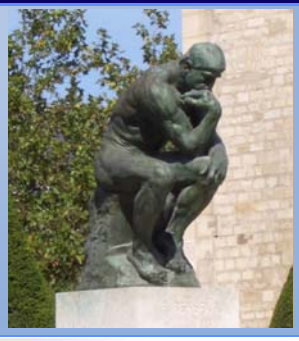
- Pts treated with heparin had increased risk
  - GI bleed
  - Hematologic complications
  - Prosthetic loosening
  - Hematoma
  - Revision surgery

- 31 pts had VQ nl or low prob but received heparin prior to VQ
  - 52 % had complications
  - 19% of pts with no PE and no heparin had complication

	+ PE	- PE
+ heparin	38 %	56 %
- heparin	2/5	18%

	+ heparin	- heparin
Death	6 %	4 %
GI bleed	7 %	0 %
Loosening	12 %	5 %
Hematoma	9 %	0 %
Revision < 10 yrs	15 %	6 %
Infection	6 %	5 %

So What Should We Do?



2 Sets of National TED Prevention Guidelines

- American College of Chest Physicians (ACCP) guidelines
  - more aggressive anticoagulation
  - emphasizes DVT prevention
- American Academy of Orthopaedic Surgery (AAOS) guidelines
  - stratified by TED risk and bleeding risk
  - emphasizes fatal PE prevention over DVT prevention

	Venographic DVT	PE	Bleeding Risk	Data quality	Risk Stratification
AACP Guidelines	More Focus	Less Emphasis	Less Concern	Better	Less
AAOS guidelines	Less Focus	More Emphasis	More Concern	Worse	More

AACP Guidelines

- ***Recommendations: Elective Knee Arthroplasty***
  - 3.2.1. For patients undergoing **elective TKA** (IA)
    - **LMWH** (1A)
    - **Fondaparinux (1A)**
    - **Adjusted-dose VKA** (target INR, 2.5; INR range, 2.0 to 3.0) (1A)
  - 3.2.2. The optimal use of **IPC** is an alternative option to anticoagulant prophylaxis (**Grade 1B**).
  - 3.2.3. We recommend **against** the use of any of the following as sole methods of thromboprophylaxis:
    - **Aspirin (1A)**
    - **Unfractionated heparin (1A)**
    - VFP (1B).

Chest 126, 3, Sept. 2004, supp.

AACP Guidelines

- 3.2.4. For patients undergoing TKR who have a high risk of bleeding we recommend :
  - Mechanical prophylaxis with IPC (IA)
  - VFP (IB)

AACP Guidelines

- ***Recommendations: Elective Hip Arthroplasty***
  - 3.1.1. For patients undergoing **elective THR**:
    - **LMWH** (at a usual high-risk dose, started 12 h before surgery or 12 to 24 h after surgery) (1A)
    - **fondaparinux** (2.5 mg started 6 to 24 h after surgery) (1A)
    - **adjusted-dose VKA** started preoperatively or the evening of surgery (INR target, 2.5; INR range, 2.0 to 3.0) (1A)
  - 3.1.2. We recommend **against** the use of **aspirin, dextran, LDUH, GCS, IPC, or VFP** as the only method of thromboprophylaxis in these patients (1A)

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AACP Guidelines

- 3.1.3. For patients undergoing THR who have a high risk of bleeding, we recommend prophylaxis with VFP or IPC (1A).

AACP Guidelines

- ***Recommendation: Screening for DVT***
  - 3.5.2. We recommend **against** the routine use of DUS screening at the time of hospital discharge in Asymptomatic patients following major orthopedic surgery (1A)
- ***Recommendations: Duration of Prophylaxis***
  - 3.5.3.1. We recommend that patients undergoing **THR, TKA, or HFS** receive thromboprophylaxis **for at least 10 days** (1A)
  - 3.5.3.2. We recommend that patients undergoing **THR** be given **extended prophylaxis beyond 10 days and for up to 35 days after surgery (1A)**. The recommended options include LMWH (1A), a VKA (1B), or fondaparinux (1C).

Chest 126, 3, Sept. 2004, supp.

AACP Guidelines

- 3.5.3.2. We suggest that patients undergoing **TKR** be given **extended prophylaxis beyond 10 days and for up to 35 days after surgery (2B)**. The recommended options include LMWH (1C), a VKA (1C), or fondaparinux (1C).

AACP Guidelines

- 3.5.3.2. We recommend that patients undergoing **HFS** be given **extended prophylaxis beyond 10 days and for up to 35 days after surgery (1A)**. The recommended options include LMWH (1C), a VKA (1C), or fondaparinux (1A).

AAOS Guidelines

- **AAOS Clinical Guideline on Prevention of Symptomatic PE in Patients Undergoing Total Hip or Knee Arthroplasty**

	Bleeding Risk	PE risk	Treatment	
1	standard	standard	**Aspirin, LMWH, synthetic pentasaccharides, and warfarin.**	**3B**
2	standard	↑	**LMWH, synthetic pentasaccharides, and warfarin.**	**3B**
3	↑	standard	**Aspirin, Warfarin, or none.**	**3C**
4	↑	↑	**Aspirin, Warfarin, or none.**	**3C**

Warfarin, with an INR goal of ≤2.0, starting either the night before or the night after surgery, for 2-6 weeks.

Aspirin, 325 mg 2x/day (reduce to 81 mg 1x/day if gastrointestinal symptoms develop), starting the day of surgery, for 6 weeks.

www.aaos.org/Research/guidelines/guide.asp

AAOS Guidelines

- **The following additional recommendations are based on the results of the objective AAOS Consensus Process in which the work group members participated.**
- ***Recommendation 1.1*** All patients should be assessed pre-operatively for elevated risk (greater than standard risk) of pulmonary embolism. (Level III, Grade B)
- ***Recommendation 1.2*** All patients should be assessed pre-operatively for elevated risk (greater than standard risk) of major bleeding. (Level III, Grade C)
- ***Recommendation 1.3*** Patients with known contraindications to anticoagulation should be considered for vena cava filter replacement. (Level V, Grade C)

AAOS Guidelines

- ***Recommendation 2.1*** Patients should be considered for intra-operative and/or immediate postoperative mechanical prophylaxis. (Level III, Grade B)
- ***Recommendation 2.2*** In consultation with the anesthesiologist, patients should be considered for regional anesthesia. (Level IV, Grade C)

AAOS Guidelines

- ***Recommendation 3.1*** Post-operatively, patients should be considered for continued mechanical prophylaxis until discharge to home. (Level IV, Grade C)
- ***Recommendation 3.2*** Post-operatively, patients should be mobilized as soon as feasible to the full extent of medical safety and comfort. (Level V, Grade C)
- ***Recommendation 3.4*** Routine screening for DVT or PE post-operatively in asymptomatic patients is not recommended. (Level III, Grade B)

AAOS Guidelines

- ***Recommendation 4.1*** Patients should be encouraged to progressively increase mobility after discharge to home. (Level V, Grade C)
- ***Recommendation 4.2*** Patients should be educated about the common symptoms of deep venous thrombosis and pulmonary embolism. (Level V, Grade B)

AAHKS VTE Survey

- 465 of 840 active AAHKS members returned questionnaires for a response rate of 55.4 % (95% confidence interval, ±5% sampling error)
- Current Practice
  - 99 % routinely use chemoprophylaxis following THA
  - 92 % routinely use chemoprophylaxis following TKA
  - 90 % routinely use mechanical prophylaxis following THA or TKA
  - 94 % routinely use chemoprophylaxis after discharge following THA or TKA

AAHKS VTE Survey

In-hospital Chemoprophylaxis choice :

	THA	TKA
Warfarin	47 %	46 %
LMWH	28 %	26 %
ASA	10 %	12 %
Fondaparinux	7 %	7 %

Post-discharge Chemoprophylaxis choice (Avg. 26 days):

	THA	TKA
Warfarin	35 %	39 %
LMWH	27 %	20 %
ASA	18 %	20 %
Fondaparinux	5 %	5 %

VTE Prevention Guidelines

Survey Results:	AAOS PE Guidelines	CHEST VTE Guidelines
Members Agree with:	82%	19%
Members Follow:	75%	40%
Members' Primary Hospitals Recognize:	31%	74%

Conclusions

- Complex issue with no clear answers
- Chemoprophylaxis may not prevent fatal PE or lower the overall mortality rate
- Consequences of bleeding complications are significant
- Most AAHKS members use chemoprophylaxis and mechanical measures

Recommendation

- Understand your goal
  - Prevent asymptomatic DVT?
  - Prevent symptomatic DVT?
  - Prevent PE?
  - Prevent fatal PE?
- Try to grasp local or regional Standard of Care..if possible.
- Carefully weigh bleeding risks vs benefits of chemoprophylaxis

Thank You