Challenging Cases in Anticoagulation: Pregnancy, Non-Cardiac Surgery, Prosthetic Valve Thrombosis

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IN ALL SETTINGS IN WHICH ANTICOAGULATION IS EMPLOYED, CERTAIN CONDITIONS CONFOUND AND ALTER REQUIRED INTENSITY OF ANTICOAGULATION AND/OR CLINICAL OUTCOME

- Atrial fibrillation
- Previous thromboembolism
- LV dysfunction
- Hypercoagulable conditions
- Relatively older generation, thrombogenic valves
- Mechanical tricuspid valves
- Multiple mechanical valves

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  - ***FEW DATA, FEW RANDOMIZED TRIALS***

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    - **Nasal hypoplasia, occular atrophy**
    - **Stippled epiphyses, mental impairment**

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  - Birth trauma, fetal intracranial hemorrhage
- **Post-partum** *begin 4-6 hrs post-partum,*
  Maternal hemorrhage *with heparin*

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HEPARIN UNFILTERED (UFH)

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  - Maternal hemorrhage, particularly at delivery (particularly when s.c. heparin is used, with prolonged availability c/w IV)

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LOW MOLECULAR WEIGHT HEPARIN (LMWH)

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  - Report of thromboemboli in 2/8 pregnant women with mechanical valves has resulted in initial labeling contraindication for mechanical valves, now altered to indication of lack of adequate study

ANTICOAGULATION DURING PREGNANCY IN WOMEN WITH MECHANICAL HEART VALVES (n=976 woman with 1234 pregnancies)

Anticoagulation regimen	Embryopathy (%)	Abortion (%)	TE (%)	Maternal death (%)
Only Vitamin K antag	6.4	25	3.9	1.8
Only Heparin	0	24	33	15
Low dose (5000 u sc bid/tid)	0	20	60	40
Adjusted dose (sc 1.5-2.5 xc)	0	25	25	6.7
Heparin first trimester, then vitamin K antagonists	3.4	25	9.2	4.2
Nothing or antiplatelet only	3.3	9.8	24	4.3

Chan WS et al Arch Intern Med 2000;160:191
ESC.EHJ 2003; 24:761. ACCP (SM Bates et al) Chest 2004;126:627S

ANTICOAGULATION FOR MECHANICAL HEART VALVES DURING PREGNANCY

The therapeutic choice of continuous intravenous or dose-adjusted subcutaneous UFH, or dose adjusted LMWH, throughout pregnancy or only during first trimester or through gestation weeks 6-12, or of continual oral warfarin throughout pregnancy, should be fully discussed with patient and her partner (fetal danger greater with warfarin, maternal danger greater with heparin).

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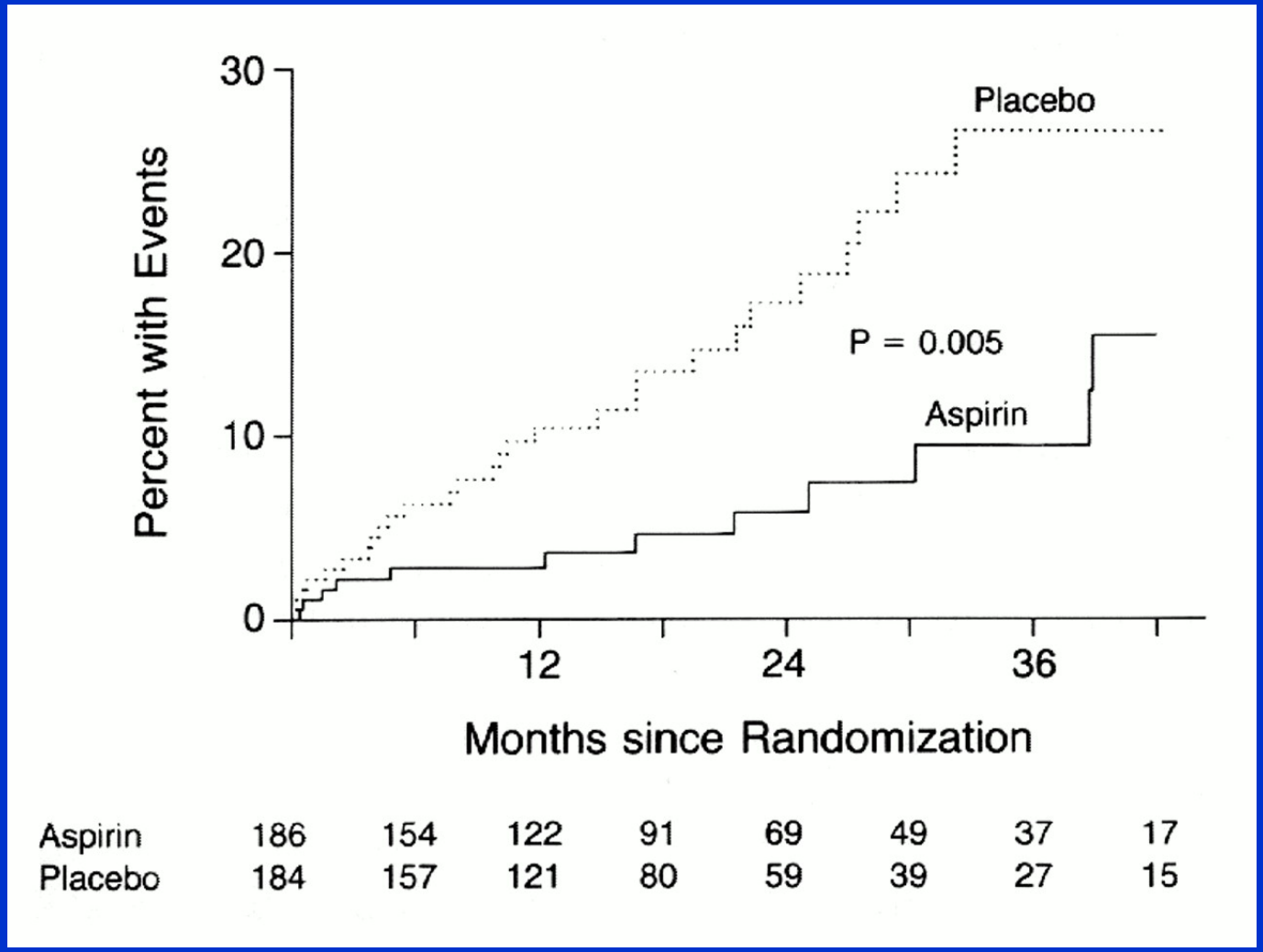
- **Adjunctive aspirin, though it crosses placenta and may be associated with abortion and fetal growth retardation, seems to cause relatively low absolute risk and can be continued if needed**

ASPIRIN or PLACEBO + WARFARIN for Mechanical Valves: Effect on Embolism, Intracranial Hemorrhage, Fatal Hemorrhage, or CV Death



Aspirin	186	154	122	91	69	49	37	17
Placebo	184	157	121	80	59	39	27	15

Turpie A et al. N Engl J Med 1993;329:524-529

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- **However, risks increase with heparin, e.g., cardiac catheterization with reinitiation of LMWH 12 hours after procedure is associated with 6% major hemorrhages**

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- If bleeding ***IS*** likely, **do** stop adjunctive antithrombotic treatments
  - Aspirin for 7 days
  - Clopidogrel for 5 days

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    - One study: 650 pts including 215 pts with mechanical valves
      - Thromboembolism = 0.62%
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  - **Do not use vitamin K1 to control anticoagulation**
    - **Hypercoagulable state**
    - **Use FFP if emergent need for control**

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- **Valve type**
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  - Inadequate anticoagulation in 50-75%
- **Diagnosis – if suspected clinically**
  - Echo (TTE for hemodynamic severity, TEE [or fluoro] for valve motion/clot burden)

PROSTHETIC HEART VALVE THROMBOSIS

- **Caveat**
  - ***Obstruction may involve pannus – may not be determinable pre-therapy***

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      - **INR range 0.5 higher than standard**
      - **+ aspirin**

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    - If partially successful, or if fibrinolysis not tolerable
      - s.c. UFH bid + warfarin (3 months, reevaluate)
        - » Success: warfarin as above
        - » Unsuccessful: surgery

PROSTHETIC HEART VALVE THROMBOSIS

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- **“Large” (>10mm) MV/AV clot by TEE and/or NYHA FC III-IV, relatively stable (= intermediate risk)**
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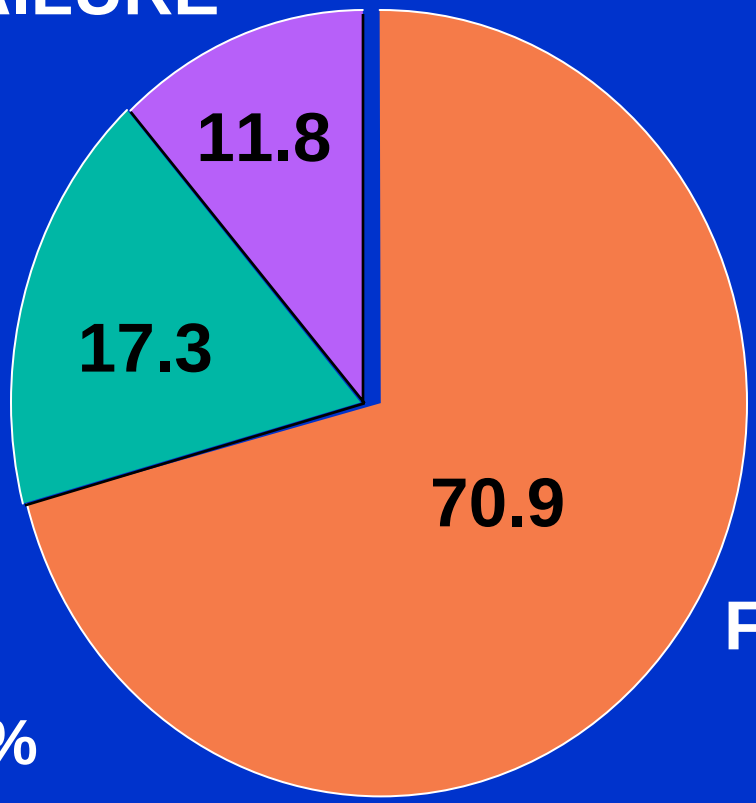
- **“Large” MV/AV clot, FC III-IV, unstable/critically ill, surgical risk high and/or surgery unavailable**
  - **Fibrinolysis (rescue)**

FIBRINOLYSIS FOR PROSTHETIC VALVE THROMBOSIS (N=127)



Mortality 12%
Hemorrhage 5%
Emboli 15%
Recurrence 19%

Roudaut et al., JACC 2003; 41:653

SURGERY FOR PROSTHETIC VALVE OBSTRUCTION (N=63: pannus=45, thrombus=18; initial thrombolysis=5)

Risk Factors for In-Hospital Mortality (=21%)

Factor	*P*
Cross clamp time	0.202
Total perfusion time	0.079
Preoperative atrial fibrillation	0.760
Preoperative renal insufficiency	0.673
Preoperative CVE	0.062
Emergency operation	0.514
PAP > 50 mmHg	0.635
Gender (female)	0.187
Tilting disk	0.532
LVESD	0.006
LVEDD	0.001
LVEF	0.001***
NYHA Class	
1-2	0.962
3-4	0.635

Toker et al. Int Heart J 2006; 47: 237-245)

Challenging Cases in Anticoagulation: Pregnancy, Non-Cardiac Surgery, Prosthetic Valve Thrombosis

1. Paucity of randomized trials
2. Most inferences drawn from observational series
3. Relevant drug labeling may differ from consensus standards
4. Should involve patients in full discussion of all decisions (considering degree of urgency of therapy)