Prosthetic Heart Valves In Pregnancy

3rd ESC & SHA Joint Meeting

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Case

• 35 year old female
• H/O degenerative Mitral Valve Disease with significant MR
• S/P failed MV repair in 2009
• S/P MVR with Tissue valve in 2012
TTE- Transmitial
Case

- 35 year old female
- H/O degenerative Mitral Valve Disease with significant MR
- S/P failed MV repair in 2009
- S/P MVR with Tissue valve in 2012
  - at another hospital, in another city
- In 06.2015
  - 22\textsuperscript{nd} week
  - Progressive DOE & exercise intolerance for mild to moderate activity over the last couple of weeks
  - No fever, chills r sweating
  - Medication: Iron, MVT and Folate supplement
3D- en face
3D- ventricular view
TTE- Transmitral
• What’s possible etiology?
• What’s next?

• Started on UFH → Warfarin + ASA & diuretic

• For logistic issues, pt. requested referral back to previous hospital
INTRODUCTION

• Prosthetic heart valves (PHV’s)
  – Mechanical (MHV) or
  – Bioprosthetic, heterografts and homografts (BHV)

• Complications of MHV’s in pregnancy
  1. Valve thrombosis
  2. Thromboembolic events.
     • Therapeutic anticoagulation throughout pregnancy is essential
     • No adequate prospective controlled trials →
       – Optimum anticoagulant regimen uncertain
  3. Maternal and fetal complications with different anticoagulant regimens
     • Bleeding
     • Birth defects

• Failure/ Rapid Degeneration of Bioprosthetic valves:
  • No long term anticoagulation (unless other thromboembolic risk factors)
  • Significantly higher incidence of valve failure than mechanical valves
    – Particularly young women

• Endocarditis: Both
Valve Thrombosis (VT) and Thromboembolism (TE)

• Potentially life-threatening
• Hypercoagulable state of pregnancy increases the risk of valve thrombus formation among women with PHV’s:
  1. Type
  2. Location of prosthetic valve

3. **Clinical features:**
   a. H/O prior thromboembolic event
   b. A. fibrillation
   c. Prosthesis in *mitral position*
   d. *Multiple* prosthetic valves
   e. LV dysfunction
Type of PHV

• **Mechanical prosthetic heart valves:**
  – higher thromboembolic risk than BHV’s or homografts
  – newer generation MHV’s → lower thromboembolic risk
  – risk of thromboembolism increased with unfractionated heparin and, to a lesser degree, with LMWH compared with warfarin

• **Bioprosthetic valves:**
  – Usually No long term chronic anticoagulation unless other thromboembolic risk factors present.
  – Aspirin recommended, and continued during pregnancy.
Ninth ed: ACCP evidence-based clinical practice guidelines:

**Antithrombotic therapy** in patients with **bioprosthetic heart valves**

- For the first three months after bioprosthetic mitral valve replacement (MVR), vitamin K antagonist (VKA) therapy (target INR, 2.5; range, 2.0-3.0) is suggested over no VKA therapy.
- For the first three months after surgical bioprosthetic aortic valve replacement (AVR) in patients who are in sinus rhythm and have no other indication for VKA therapy, aspirin (50 to 100 mg/day) is suggested over VKA therapy.
- For the first three months after transcatheter aortic bioprosthetic valve implantation, aspirin (50 to 100 mg/d) plus clopidogrel (75 mg/d) is suggested over VKA therapy and over no antiplatelet therapy.
- For the first three months after mitral valve repair with an annular ring in patients who are in sinus rhythm, antiplatelet therapy is suggested over VKA therapy.
- After the first three months following bioprosthetic valve replacement in patients in normal sinus rhythm, aspirin therapy is suggested over no aspirin therapy.
- In patients undergoing aortic valve repair, aspirin (50 to 100 mg/d) is suggested over VKA therapy.

ACC/AHA guideline summary: **Antithrombotic therapy** in patients with **bioprosthetic heart valves**

Class I - There is evidence and/or general agreement that antithrombotic therapy is indicated in patients with bioprosthetic heart valves in the following settings:

- Warfarin to achieve a goal INR of 2.0 to 3.0 after:
  1. Aortic valve replacement (AVR) if risk factors* are present.
  2. MVR with a bioprosthesis if risk factors* are present.

- Role of aspirin:
  1. After AVR or MVR with no risk factors* at a dose of 75 to 100 mg/day
  2. After AVR or MVR in patients with risk factors* who cannot take warfarin, at a dose of 75 to 325 mg/day.

  3. In addition to warfarin, in patients with risk factors* at a dose of 75 to 100 mg/day.

Class IIa - The weight of evidence or opinion is in favor of the usefulness of antithrombotic therapy in patients with bioprosthetic heart valves in the following setting:

- In the first three months after AVR or MVR in patients with no risk factors*, warfarin to achieve a goal INR of 2.0 to 3.0.

Joint Task Force on the Management of Valvular Heart Disease of ESC & European Association for Cardio-Thoracic Surgery (EACTS)


- VKA **should be** considered for the first 3 months after *mitral or tricuspid bioprosthesis* placement.

- **May be** considered in the first 3 months following *aortic bioprosthetic* valve replacement
### Guidelines for anticoagulation therapy in pregnant women with mechanical heart valves

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>ACC/AHA&lt;sup&gt;6&lt;/sup&gt;</th>
<th>ACCP&lt;sup&gt;67&lt;/sup&gt;</th>
<th>ESC&lt;sup&gt;56&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Oral anticoagulants</td>
<td>Can be used throughout pregnancy, with substitution by dose-adjusted UFH or LMWH during weeks 6–12 of gestation if preferred by the patient</td>
<td>Can be used throughout pregnancy in high-risk* patients, with substitution by LMWH or UFH close to term (time frame not specified but normally 48 h before delivery)</td>
<td>If the warfarin dose is ≤5 mg daily, oral anticoagulants throughout pregnancy is the safest regimen (associated with &lt;3% embryopathy)</td>
</tr>
<tr>
<td>Heparin derivatives</td>
<td>Monitored UFH or LMWH might be options throughout gestation or during weeks 6–12 of gestation. LMWH dose should be adjusted to give an anti-factor Xa activity 0.7–1.2 U/ml 4–6 h after administration</td>
<td>Dose-adjusted and monitored LMWH or UFH throughout pregnancy or during weeks 6–12 of gestation is acceptable. In low-risk patients, LMWH should be given twice daily and the dose adjusted to achieve the manufacturer’s peak inhibition of factor Xa 4 h after subcutaneous injection</td>
<td>LMWH or UFH during weeks 6–12 of gestation should be considered if high-dose warfarin is required to maintain therapeutic anticoagulation. LMWH dose should be adjusted to give an anti-factor Xa activity of 0.8–1.2 U/ml 4–6 h after administration</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Low-dose aspirin in addition to anticoagulation during the second and third trimesters</td>
<td>Low-dose aspirin in addition to anticoagulation in high-risk* patients</td>
<td>Aspirin in addition to anticoagulation is not recommended</td>
</tr>
<tr>
<td>Anticoagulation target</td>
<td>INR 3 for all patients with mechanical prosthetic heart valves</td>
<td>INR 2–3 for patients with bileaflet aortic valves without high-risk features*</td>
<td>No INR target recommendation</td>
</tr>
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*First-generation prostheses, mitral valve prostheses, history of thromboembolism, atrial fibrillation, or left ventricular dysfunction. Abbreviations: ACCP, American College of Chest Physicians; ESC, European Society of Cardiology; INR, international normalized ratio; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.


*Nat. Rev. Cardiol.* doi:10.1038/nrcardio.2012.69
A Comparison of Aspirin with Placebo in Patients Treated with Warfarin after Heart-Valve Replacement


METHODS:

• In a RDBPC trial:
  – Efficacy and safety of adding aspirin (100 mg/day) to Warfarin (target INR 3.0 to 4.5)
  – 370 patients with
    • mechanical heart valves or
    • tissue valves plus atrial fibrillation or a history of thromboembolism.
RESULTS

• 186 patients → aspirin and 184 → placebo - F/U 4 years (average, 2.5)

  • **Major systemic embolism or death from vascular causes** occurred in 6 aspirin-treated patients (1.9%/ year) and 24 placebo-treated patients (8.5%/ year) →
    – *risk reduction with aspirin, 77% (P<0.001)*

  • **Major systemic embolism, nonfatal intracranial hemorrhage, or death from hemorrhage or vascular causes:** 12 patients aspirin (3.9%/ year) and 28 patients placebo (9.9%/ year) →
    – *risk reduction, 61% (P = 0.005)*

  • **Major systemic embolism or death from any cause:** 13 patients (4.2%) and 33 patients (11.7%), respectively →
    – *risk reduction, 65% (P<0.001)*

  • **Death from all causes** 9 patients (2.8%) and 22 patients (7.4%), respectively →
    – *risk reduction, 63% (P = 0.01)*

• **Bleeding:** 71 patients in aspirin group (35%); 49 in placebo group (22%) →
  – *increase in risk, 55% (P = 0.02)*

• **Major bleeding:** 24 and 19 patients, respectively →
  – *increase in risk, 27% (P = 0.43)*
Cumulative Risk of Major Systemic Embolism or Death from Vascular Causes

ASA: 1.9% /year
Placebo: 8.9%/year

77% Risk reduction (P<0.001)
Cumulative Risk of Major Systemic Embolism, Nonfatal Intracranial Hemorrhage, Death from Hemorrhage, or Death from Vascular Causes

ASA: 3.9%/ year  → RR 61% (P= 0.005)
Placebo 9.9%/ year
CONCLUSIONS

• In patients with MHV’s and high-risk patients with prosthetic tissue valves, the addition of Aspirin to Warfarin reduced:
  – mortality, (from vascular causes), &
  – major systemic embolism.

• Although, increase in bleeding → risk combined treatment was more than offset by considerable benefit.
Summery

• Number of pregnant women with PHV is generally small.
• Important before Pregnancy:
  – risks associated with specific valvular conditions
  – types of prosthetic valves and
  – need for anticoagulation in pregnancy
• All treatments have an impact on both mother and fetus →
  – all treatments to be optimized for both
• Data from prospective or randomized studies are absent
• Guidelines for optimal management are based on evidence of Level C
• Careful planning and a multi-disciplinary approach to management of women with complex valvular disease → avoiding complications.
Thanks

End