A pregnant patient with a prosthetic valve

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C.V. was born the 24th May 1980
Rheumatic fever during childhood
Normal development until adulthood.
At the age of 25 years she underwent a double valve replacement (aortic and mitral) with mechanical valves

Sorin Bicarbon 21
Sorin Bicarbon 27

*Courtesy of M. Bollati¹, W. Grosso Marra¹, I. Sheiban¹, F.Gaita¹, V. Donvito², T. Todros². ¹ Division of Cardiology, University of Torino, Molinette Hospital. ² Division of Internal Medicine, O. San Anna, Torino.
She had excellent results after surgery. NYHA I. TTE: Normal left ventricular systolic function. LV Ejection fraction: 60%. Regular function of the mechanical valves.

At the age of 28 years the patient came to us for preconceptional counselling.

Preconceptional counselling has to address:
1. The risk for the mother
2. The risk for the fetus
3. The maternal life expectancy
4. The risk of recurrence in the offspring
According to the WHO risk classification, what is the maternal cardiovascular risk of this patient?

**Modified WHO classification of maternal cardiovascular risk: principles**

<table>
<thead>
<tr>
<th>Risk class</th>
<th>Risk of pregnancy by medical condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>No detectable increased risk of maternal mortality and no/mild increase in morbidity.</td>
</tr>
<tr>
<td>II</td>
<td>Small increased risk of maternal mortality or moderate increase in morbidity.</td>
</tr>
<tr>
<td>III</td>
<td>Significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium.</td>
</tr>
<tr>
<td>IV</td>
<td>Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues, care as for class III.</td>
</tr>
</tbody>
</table>

ESC Guidelines on the management of cardiovascular diseases during pregnancy

*Modified from Thoms et al.*

*WHO = World Health Organization*
According to the WHO risk classification, what is the maternal cardiovascular risk of this patient?

1. RISK CLASS 1
2. RISK CLASS 2
3. RISK CLASS 3
4. RISK CLASS 4
1. **RISK CLASS 1**
2. **RISK CLASS 2**
3. **RISK CLASS 3**
4. **RISK CLASS 4**

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### Maternal predictors of neonatal events in women with heart disease

<table>
<thead>
<tr>
<th>Event</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Baseline NYHA class &gt;II or cyanosis [7]</td>
<td></td>
</tr>
<tr>
<td>2. Maternal left heart obstruction [5,36]</td>
<td></td>
</tr>
<tr>
<td>3. Smoking during pregnancy [12,27]</td>
<td></td>
</tr>
<tr>
<td>4. Multiple gestation [11,27]</td>
<td></td>
</tr>
<tr>
<td>5. Use of oral anticoagulants during pregnancy [7]</td>
<td></td>
</tr>
<tr>
<td>6. Mechanical valve prosthesis [7]</td>
<td></td>
</tr>
</tbody>
</table>

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Modified from Siu et al. [12], CARPREG investigators, Khairi et al. [56], Drenthen/Peper et al. [37] (ZAHARA investigations). NYHA = New York Heart Association.

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**Modified WHO classification of maternal cardiovascular risk: application**

<table>
<thead>
<tr>
<th>Risk Class</th>
<th>Conditions in which pregnancy risk is WHO I</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Uncomplicated, small or mild</td>
</tr>
<tr>
<td></td>
<td>- pulmonary stenosis</td>
</tr>
<tr>
<td></td>
<td>- patent ductus arteriosus</td>
</tr>
<tr>
<td></td>
<td>- mitral valve prolapse</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Class</th>
<th>Conditions in which pregnancy risk is WHO II or III</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td>Unoperated atrial or ventricular septal defect</td>
</tr>
<tr>
<td></td>
<td>- Repaired tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>- Most arrhythmias</td>
</tr>
<tr>
<td></td>
<td>WHO II-III (depending on individual)</td>
</tr>
<tr>
<td>3.</td>
<td>Mitral left ventricular impairment</td>
</tr>
<tr>
<td></td>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td></td>
<td>Native or tissue valvular heart disease not considered WHO I or IV</td>
</tr>
<tr>
<td>4.</td>
<td>Marfan syndrome without aortic dilatation</td>
</tr>
<tr>
<td>5.</td>
<td>Aortic &lt;45 mm in aortic disease associated with BAV</td>
</tr>
</tbody>
</table>

### WHO III

- Medical valve
- Systemic right arterial
- Fontan circulation
- Cyanotic heart disease (unrepaired)
- Other complex congenital heart disease
- Aortic dilatation 40–45 mm in Marfan syndrome
- Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve

### Conditions in which pregnancy risk is WHO IV

- Pulmonary arterial hypertension of any cause
- Severe systemic ventricular dysfunction (LVEF <30%, NYHA II–IV)
- Previous percutaneous cardiomyoplasty with any residual impairment of left ventricular function
- Severe mitral stenosis, severe symptomatic aortic stenosis
- Marfan syndrome with aortic dilatation >45 mm
- Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve
- Native severe coarctation

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ESC Guidelines on the management of cardiovascular diseases during pregnancy
Why are the maternal and offspring risks elevated in a patient with a prosthetic valve?

Haemodynamically, women with well-functioning mechanical valves tolerate pregnancy well.

The physiological changes of pregnancy induce a prothrombotic environment, reinforcing the requirement for effective anticoagulation.
Why are the maternal and offspring risks elevated in a patient with a prosthetic valve?

The need for **anticoagulation therapy** raises concerns because of:

- Oral anticoagulation therapy: provide effective protection against thromboembolism but do not cross the placenta.
- Heparin-type drugs do not cross the placenta but are less effective in protection against thromboembolism.

**Increased risk of valve thrombosis**

**Haemorrhagic complications**

**MOTHER**
Why are the maternal and offspring risks elevated in a patient with a prosthetic valve?

- OACs
- Fetal Haemorrhage
- Spontaneous abortion
- Stillbirth

- direct
- secondary

- Teratogenicity

Offspring complications
How can we estimate the magnitude of the maternal and fetal risk in this patient?

**History:**

1) Symptoms? No. 2) Functional capacity? NYHA I
3) Prior cardiac events (heart failure, TIA/Stroke, arrhythmias)? No
4) Prior pregnancies? No
5) Therapy? Out of therapy

**Physical examination:**

**ECG:** Normal sinus

**TTE:** Normal left valve function of mechani

significant regurgita
There are several regimens for pregnant women with mechanical heart valves. Which will be your choice?

1. Unfractioned heparin throughout pregnancy
2. Unfractionated heparin (UFH) and warfarin combination
3. LMWH and warfarin combination
4. LMWH throughout the pregnancy
5. Warfarin throughout pregnancy
Counseling

We discuss with the patient the different therapeutic options and we planned our strategy:

1) The importance of very early diagnosis of pregnancy was stressed (if she misses a menstrual period she should be tested immediately for pregnancy)

2) Discontinuation of OAC between weeks 6 and 12 and replacement by LMWH twice daily (with dose adjustment according to weight and target anti-Xa level)
The character and magnitude of the risk depend on the anticoagulation regimen used during pregnancy and the quality of anticoagulation control.

<table>
<thead>
<tr>
<th>Anticoagulation Regimen</th>
<th>Maternal Thromboembolic Complications %</th>
<th>Spontaneous Abortions %</th>
<th>Congenital Fetal Anomalies %</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAC throughout [1-7]</td>
<td>2.4-3.9</td>
<td>26</td>
<td>6.4</td>
</tr>
<tr>
<td>Unfractionated heparin 1st trimester + OACs [1-7]</td>
<td>9.2-10.3</td>
<td>23.2</td>
<td>3.4</td>
</tr>
<tr>
<td>• Heparin use between 6-12 wk</td>
<td></td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>• Heparin use after 6 week</td>
<td></td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Unfractionated heparin throughout</td>
<td>33</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>LMWH throughout</td>
<td>9</td>
<td>7.4</td>
<td>0</td>
</tr>
<tr>
<td>LMWH 1st trimester + OACs (limited data) [1-7]</td>
<td>3.6</td>
<td>9.1</td>
<td>0</td>
</tr>
</tbody>
</table>

Last menstrual period: February 10\textsuperscript{th} 2009. Positive pregnancy test.

6-12\textdegree weeks: she discontinued coumadin and started enoxaparin 6000 U.I (1mg/kg body weight) twice daily subcutaneously. The anti Xa level was repeatedly checked:
What is the optimal sampling time of anti-Xa level?

- Immediately after injection
- 12 hours after injection
- 4-6 hours after injection
- Sampling time is not relevant
The therapeutic antifactor Xa range is: 0.8–1.2 U/mL

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- Immediately after injection
- 12 hours after injection
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6-12\textdegree weeks: she discontinued coumadin and started enoxaparin 6000 U.I (1mg/kg body weight) twice daily subcutaneously. The anti Xa level was repeatedly checked: March 24\textsuperscript{th} 0.8, April 17\textsuperscript{th}: 0.9 May 26\textsuperscript{th} :0.77

Visit + Tranthoracic Echo was performed at 12\textdegree- 16\textdegree- 24\textdegree - 29\textdegree weeks. (Fetal echo was performed 21\textdegree -29\textdegree weeks)

33\textdegree week. Planned vaginal delivery was decided.

34\textdegree week she discontinued coumadin and started enoxaparin 6000 U.I (1mg/kg body weight) twice daily subcutaneously.

October 28\textsuperscript{th} she stopped enoxaparin and October 29\textsuperscript{th} (37 weeks gestation) She had an uneventful induced vaginal delivery resulting in delivery of a healthy boy (Apgar 5/7).
The enoxaparin was restarted 12 hours after the delivery. She was discharged three days after delivery. She still was taking enoxaparin 6000 U.I twice daily and coumadin (INR <2). The anti-Xa level was not checked.

The same day the patient came to the emergency department complaining of sudden but self-resolving diplopia. Physical examination was negative for signs of heart failure. A grade 2/4 aortic diastolic murmur was heart
Differential Diagnosis?

- TIA in atrial fibrillation
- Intracerebral Hemorrhage in a patient on oral anticoagulation therapy + LMWH
- TIA in Prosthesis malfunction
CT scan of head: no lesion

ECG: normal sinus rythm
Severe aortic prosthesis regurgitation due to incomplete leaflet apposition, with a significantly increased prosthetic aortic transvalvular gradient (peak velocity 4.4 m/s, peak gradient 76mmHg, mean gradient 49mmHg), whereas the mitral valve prosthesis appeared normal.
Differential Diagnosis?

- TIA in atrial fibrillation
- Intracerebral Hemorrhage in a patient on oral anticoagulation therapy + LMWH
- TIA in Prosthesis malfunction
Revealed a thrombus (about 8 x 6 mm) located between the two prostheses, causing intermittent aortic valve malfunction.

Due to the stable clinical condition, no thrombolytic therapy was started, but intravenous unfractioned heparin was initiated and maintained.
Transoesophageal echocardiogram revealed:
a decreased aortic transvalvular gradient (peak 35mmHg), but
an oval thrombus (with length 15mm and width 2mm) was
detected adhering to the mitral prosthesis and fluctuating
through the prosthetic valve.

Another smaller thrombus (7mm) was evident adhering to the
aortic prosthesis annulus, without prosthesis malfunction.
Due to the high embolic risk, alteplase was given as a bolus (0.27 mg/kg) and intravenous infusion (0.6mg/kg in 30min). To minimize the risk of cerebral embolization, carotid filters (Filter Wire EZ, Boston Scientific) were placed in both common carotid arteries.
No complication occurred during and after the procedure, and after evidence of thrombus dissolution 30min after the end of alteplase infusion at transoesophageal echocardiography, filters were removed.

The patient continued intravenous heparin + coumadin until achievement of therapeutic international normalized ratio range (2.5–3.5) and she was asymptomatic when discharged the following week.
Oral anticoagulant (OACs) therapy until 5 week gestation

We stopped OACs between weeks 6 and 12 and replacement by LMWH twice daily. The change of anticoagulation regimen was done at home.

We stopped OACs at the 34 week gestation and replacement by LMWH twice daily. The vaginal delivery was planned.

24 hours prior delivery we stopped LMWH. LMWH was restarted 12 h after delivery. OACs was restarted after 3 day and patient discharged in double therapy OACs +LMWH
### ESC Guidelines on the management of cardiovascular diseases during pregnancy

**Mechanical valves**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>OACs are recommended during the second and third trimesters until the 36th week.</td>
<td>✓</td>
<td>I C</td>
</tr>
<tr>
<td>Change of anticoagulation regimen during pregnancy should be implemented in hospital.</td>
<td>✗</td>
<td>I C</td>
</tr>
<tr>
<td>If delivery starts while on OACs, caesarean delivery is indicated.</td>
<td></td>
<td>I C</td>
</tr>
<tr>
<td>OAC should be discontinued and dose-adjusted UFH (a PTT ≥2× control) or adjusted-dose LMWH (target anti-Xa level 4–6 hours post-dose 0.8-1.2 U/mL) started at the 36th week of gestation.</td>
<td>✓</td>
<td>I C</td>
</tr>
<tr>
<td>In pregnant women managed with LMWH, the post-dose anti-Xa level should be assessed weekly.</td>
<td>✗</td>
<td>I C</td>
</tr>
<tr>
<td>LMWH should be replaced by intravenous UFH at least 36 hours before planned delivery. UFH should be continued until 4–6 hours before planned delivery and restarted 4–6 hours after delivery if there are no bleeding complications.</td>
<td>✗</td>
<td>I C</td>
</tr>
<tr>
<td>Immediate echocardiography is indicated in women with mechanical valves presenting with dyspnoea and/or an embolic event.</td>
<td>✓</td>
<td>I C</td>
</tr>
<tr>
<td>Continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is &lt;5 mg/day (or phenprocoumon &lt;3 mg/day or acenocoumarol &lt;2 mg/day), after patient information and consent.</td>
<td>IIa C</td>
<td></td>
</tr>
<tr>
<td>Discontinuation of OAC between weeks 6 and 12 and replacement by adjusted-dose UFH (a PTT ≥2× control; in high risk patients applied as intravenous infusion) or LMWH twice daily (with dose adjustment according to weight and target anti-Xa level 4–6 hours post-dose 0.8–1.2 U/mL) should be considered in patients with a warfarin dose required of &gt;5 mg/day (or phenprocoumon &gt;3 mg/day or acenocoumarol &gt;2mg/day).</td>
<td>✓</td>
<td>IIa C</td>
</tr>
<tr>
<td>Discontinuation of OACs between weeks 6 and 12 and replacement by UFH or LMWH under strict dose control (as described above) may be considered on an individual basis in patients with warfarin dose required for therapeutic anticoagulation &lt;5 mg/day (or phenprocoumon &lt;3 mg/day or acenocoumarol &lt;2 mg/day).</td>
<td>IIb C</td>
<td></td>
</tr>
<tr>
<td>Continuation of OACs may be considered between weeks 6 and 12 in patients with a warfarin dose required for therapeutic anticoagulation &gt;5 mg/day (or phenprocoumon &gt;3 mg/day or acenocoumarol &gt;2 mg/day).</td>
<td>IIb C</td>
<td></td>
</tr>
<tr>
<td>LMWH should be avoided, unless anti-Xa levels are monitored.</td>
<td>III C</td>
<td></td>
</tr>
</tbody>
</table>
1 years follow up

NYHA I. TTE: Normal left ventricular systolic function. LV Ejection fraction: 60%. Regular function of the mechanical valves.

Take home message

Pregnancy in women with mechanical heart valves is (very)? high risk. The role of the clinician is to discuss the pros and cons of the available options and when the strategy has been decided be very caution because just one mistake can change the outcome.
Grazie