A pregnant patient with a prosthetic valve

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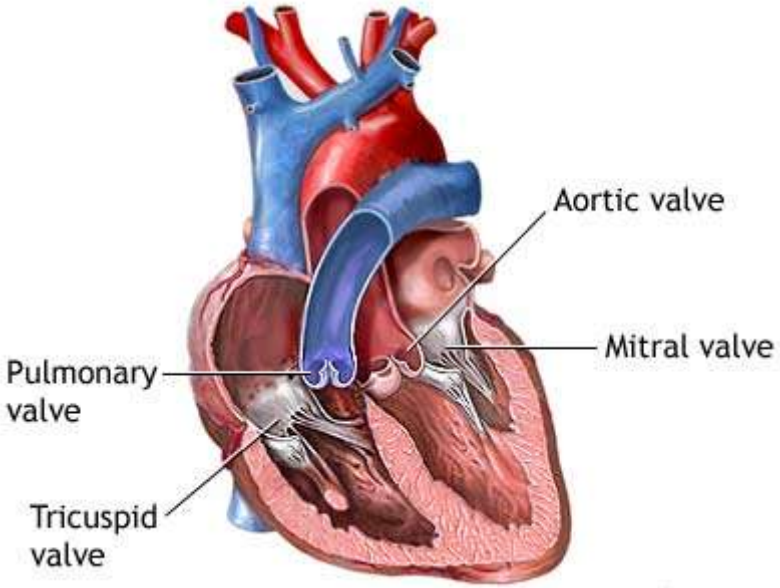
*C.V. was born the 24th May 1980

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. Bollati[1], W. Grosso Marra[1], I. Sheiban[1], F.Gaita[1], V. Donvito[2], T. Todros[2]. [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

Risk class	Risk of pregnancy by medical condition
I	No detectable increased risk of maternal mortality and no/mild increase in morbidity.
II	Small increased risk of maternal mortality or moderate increase in morbidity.
III	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.
IV	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.

Modified from Thorne *et al.*[72]
WHO = World Health Organization

ESC Guidelines on the management of cardiovascular diseases during pregnancy
in press

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

III	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.

Maternal predictors of neonatal events in women with heart disease

1. Baseline NYHA class >II or cyanosis[12]
2. Maternal left heart obstruction[12,76]
3. Smoking during pregnancy[12,37]
4. Multiple gestation[13,37]
5. Use of oral anticoagulants during pregnancy[12]
6. Mechanical valve prosthesis[37]

Modified from Siu *et al.*[12] (CARPREG investigators); Khairy *et al.*[76]; Drenthen/Pieper *et al.*[37] (ZAHARA investigators).
NYHA = New York Heart Association.

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Modified WHO classification of maternal cardiovascular risk: application

Conditions in which pregnancy risk is WHO I
• Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse
• Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage).
• Atrial or ventricular ectopic beats, isolated
Conditions in which pregnancy risk is WHO II or III
WHO II *if otherwise well and uncomplicated)*
• Unoperated atrial or ventricular septal defect
• Repaired tetralogy of Fallot
• Most arrhythmias
WHO II–III *(depending on individual)*
• Mild left ventricular impairment
• Hypertrophic cardiomyopathy
• Native or tissue valvular heart disease not considered WHO I or IV
• Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with BAV
• Repaired coarctation
WHO III
• Mechanical valve
• Systemic right ventricle
• 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 (pregnancy contraindicated)
• Pulmonary arterial hypertension of any cause
• Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV)
• Previous peripartum cardiomyopathy with any residual impairment of left ventricular function
• Severe mitral stenosis, severe symptomatic aortic stenosis
• Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve
• Native severe coarctation

Adapted from Thorne *et al.*[73]
LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; WHO = World Health Organization.

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

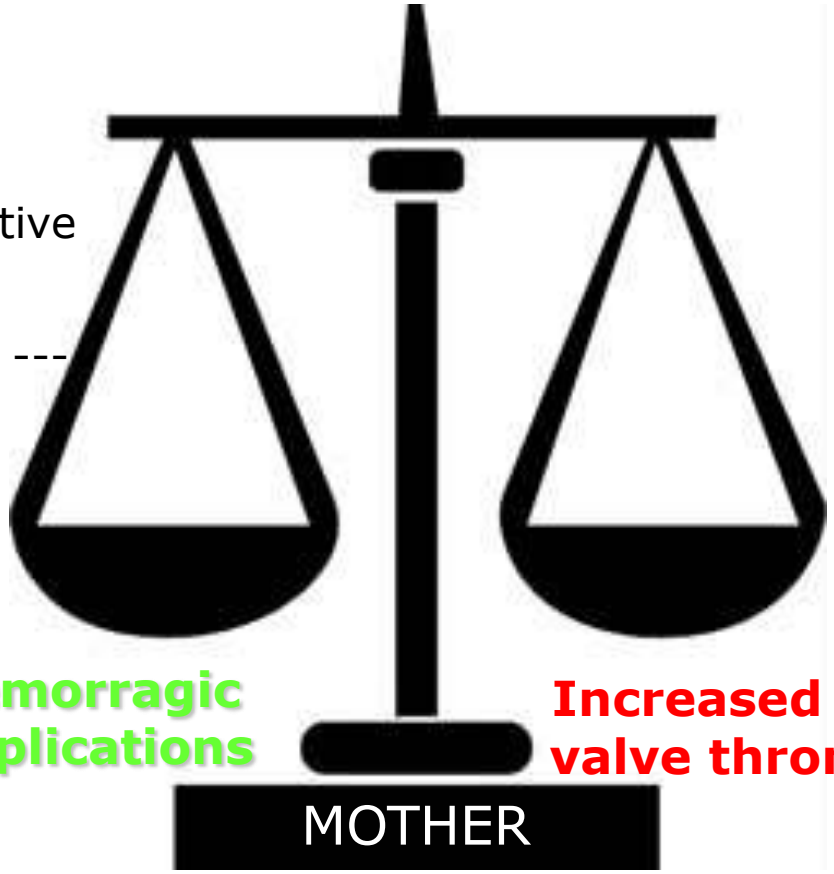
Haemodynamically, women with well-functioning mechanical valves tolerate pregnancy well.

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?

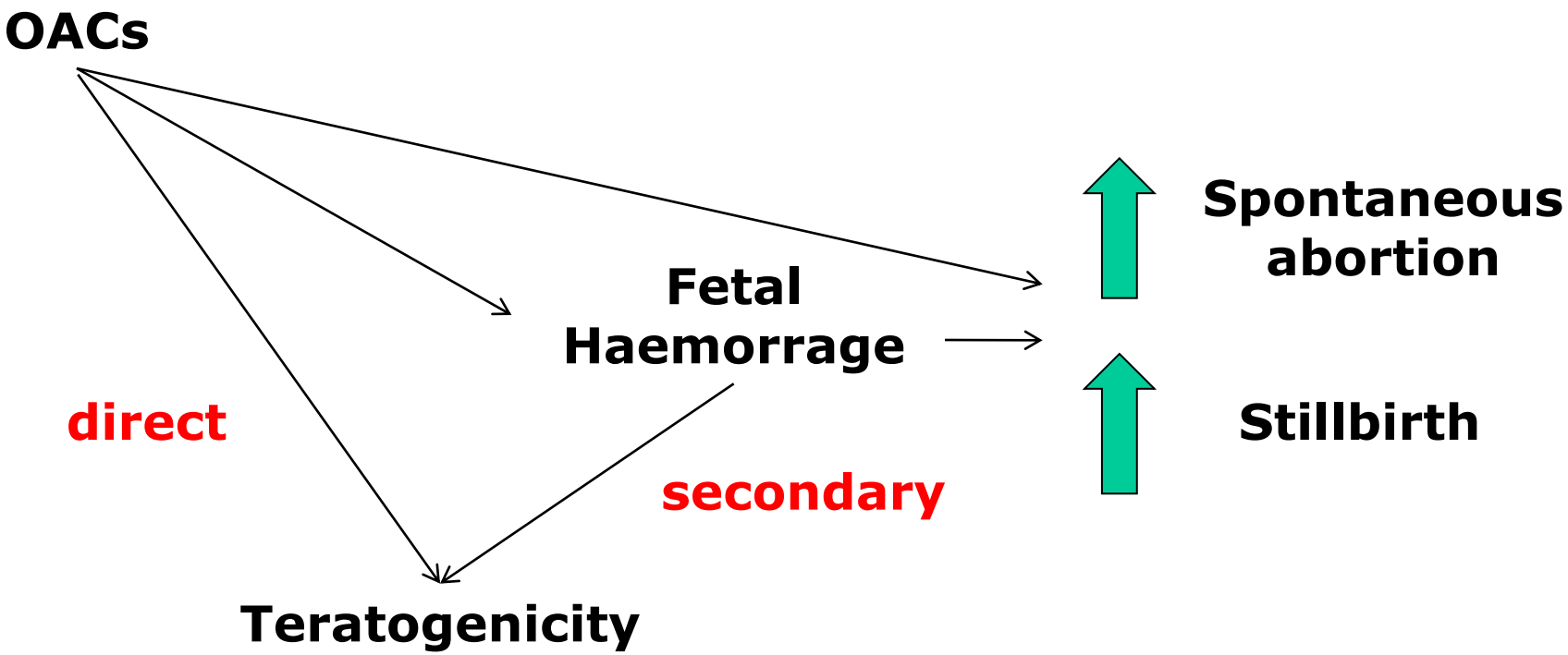
The need for **anticoagulation therapy** raises concerns because of:

Oral anticoagulation therapy: provide effective protection against thromboembolism but --- cross the placenta



Heparin-type drugs do not cross the placenta but are less effective in protection against thromboembolism

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



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, arrthymias)? No

4) Prior pregnancies? No

5) Therapy? Out of therapy

Physical examina

ECG: Normal sinus

TTE: Normal left ve function of mechani significant regurgita

Comparison of dose-related differences in pregnancy outcomes in women with mechanical heart valves treated with warfarin.

	Vitale et al.[2] (recruitment period Dec 1987–May 1997)		Cotrufo et al.[18] (recruitment period Jan 1987–Jan 2000)	
	Warfarin dose ≤5 mg	Warfarin dose >5 mg	Warfarin dose ≤5 mg	Warfarin dose >5 mg
Pregnancies, n	33	25	38	33
Fetal anomalies, n (%)				
Warfarin embryopathy	0 (0)	2 (8)	1 (3)	2 (6)
Other	0 (0)	1[a] (4)	0 (0)	1 (3)[a]
Spontaneous abortion[b], n (%)	4 (12.1)	18 (72)	2 (5)	21 (6)
Stillbirths[c], n (%)	0 (0)	1 (4)	0 (0)	5 (15)
Live births – no abnormalities, n (%)	29 (88)	3 (12)	35 (92)	6 (18)
Maternal thromboembolic complications, n (%)	1 (3.0)	1 (4)	0 (0)	0 (0)

[a] Ventricular septal defect.
[b] Spontaneous abortion defined as loss <28 weeks (Vitale); <20 weeks (Cotrufo).
[c] Stillbirth defined as loss after 28 weeks gestation (Vitale); after 20 weeks (Cotrufo).

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.

	Maternal thromboembolic complications %	**Spontaneous abortions %**	**Congenital fetal anomalies %**
OAC throughout [1-7]	2.4-3.9	26	6.4
Unfractionated heparin 1st trimester + OACs [1-7] •Heparin use between 6-12 wk •Heparin use after 6 wek	9.2-10.3	23.2 15 35	3.4 0 11
Unfractionated heparin throughout	33	23	0
LMWH throughout	9	7.4	0
LMWH 1st trimester + OACs (limited data) [1-7]	3.6	9.1	0

1 Vitale N, J Am Coll Cardiol 1999 May;33(6):1637–41. 2 Fuster V Circulation 1982;66(Suppl 1):157–61. 3 Yeh TJ Circulation 1967;35(Suppl 1):77–81. 4 Chan WS Arch Intern Med 2000 Jan 24;160(2):191–6. 5 Nassar AH, Am J Obstet Gynecol 2004 Sep ;191(3):1009–13. 6 Meschengieser SS. Heart 1999 Jul;82(1): 23–6. 7 Lee JH J Korean Med Sci 2007 Apr;22(2):258–61

LABOUR/DELIVERY

Last menstrual period: February 10th 2009. Positive pregnancy test.

6-12°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

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The therapeutic antifactor Xa range is:0.8–1.2 U/mL

LABOUR/DELIVERY

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

33° week. Planned vaginal delivery was decided.

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

October 28th she stopped enoxaparin and October 29th (37 weeks gestation) She had an uneventful induced vaginal delivery resulting in delivery of a healthy boy (Apgar 5/7).

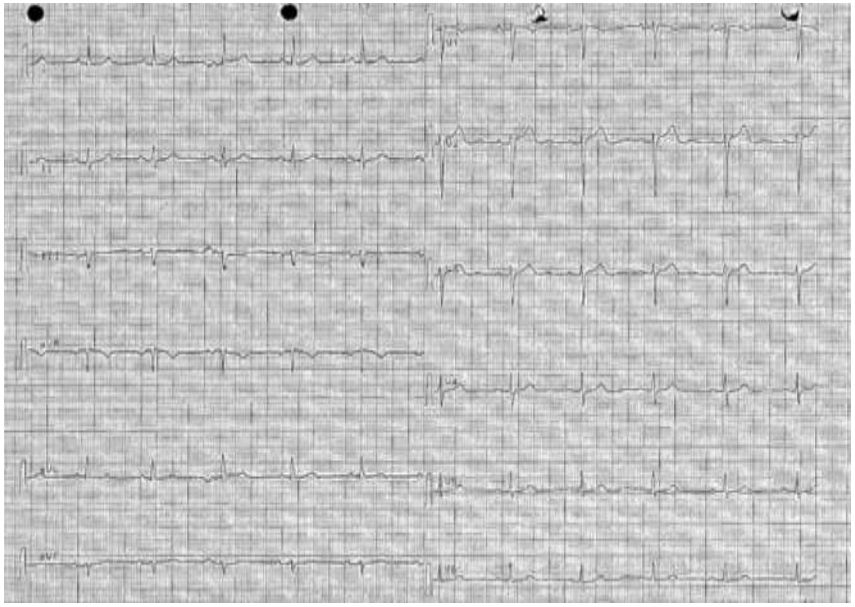
POSTPARTUM PERIOD

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



ECG: normal sinus rythm

CT scan of head: no lesion

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Torino, 02/11/2009

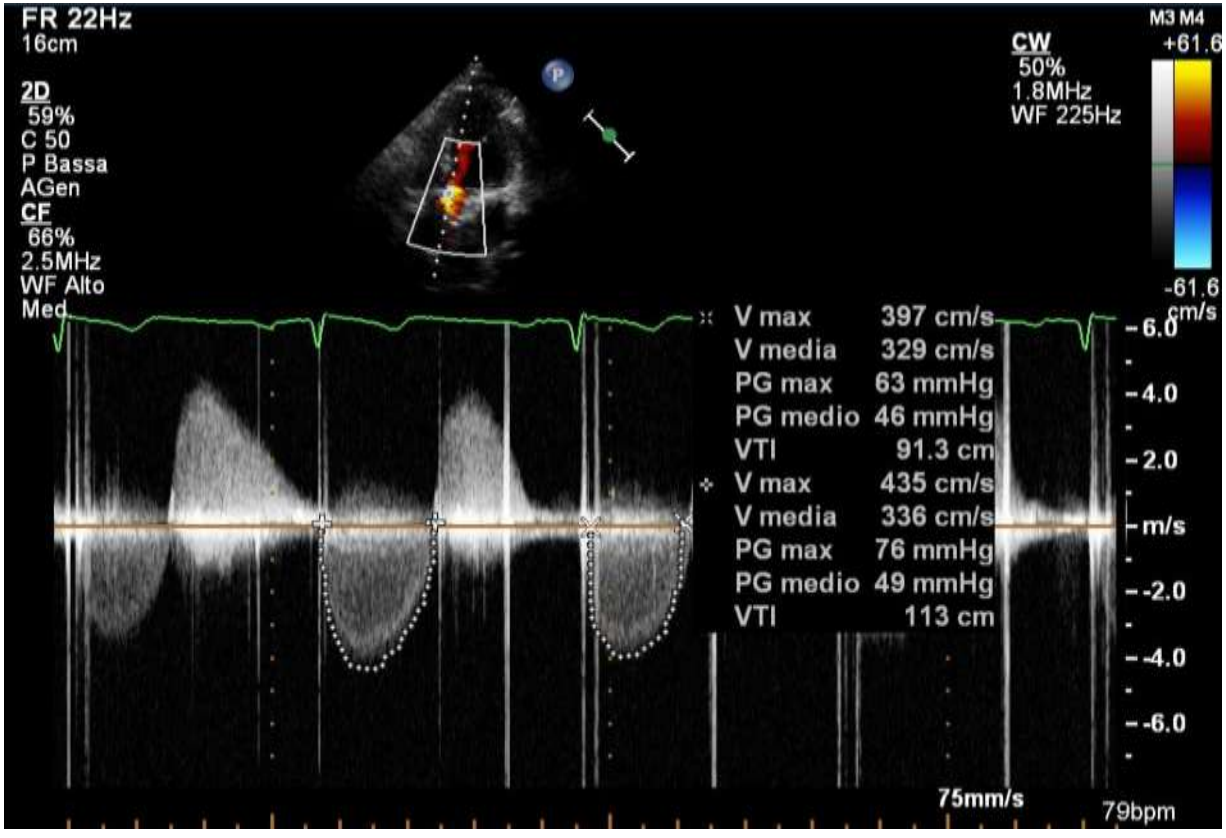
65469.2009.3

TC CRANIO [8779936/472]

All'esame TC del cranio, eseguito in urgenza, non sono documentabili evidenti lesioni a carattere focale del parenchima encefalico né segni di emorragie cerebro-meningee. Il sistema ventricolare è in asse, di dimensioni nei limiti di norma.

Transthoracic Doppler echocardiography

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?

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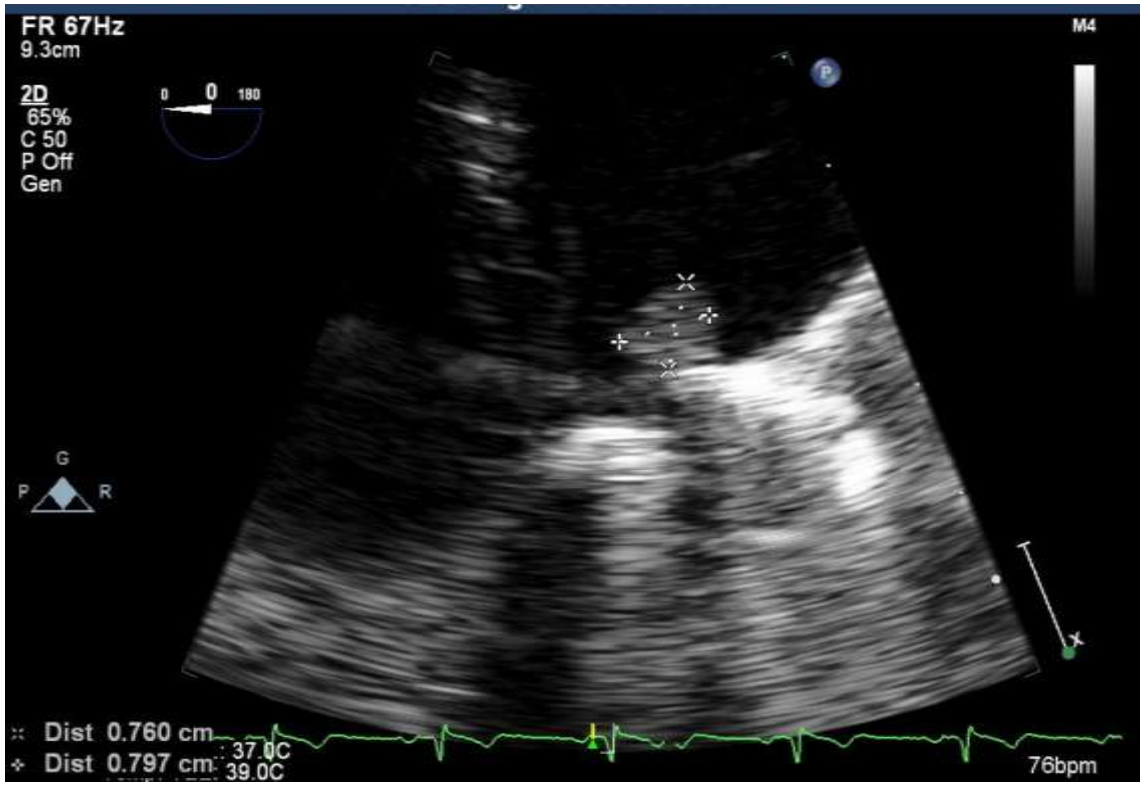
Transoesophageal echocardiography

Revealed a thrombus (about 8 x 6 mm) located between the two prostheses, causing intermittent aortic valve malfunction

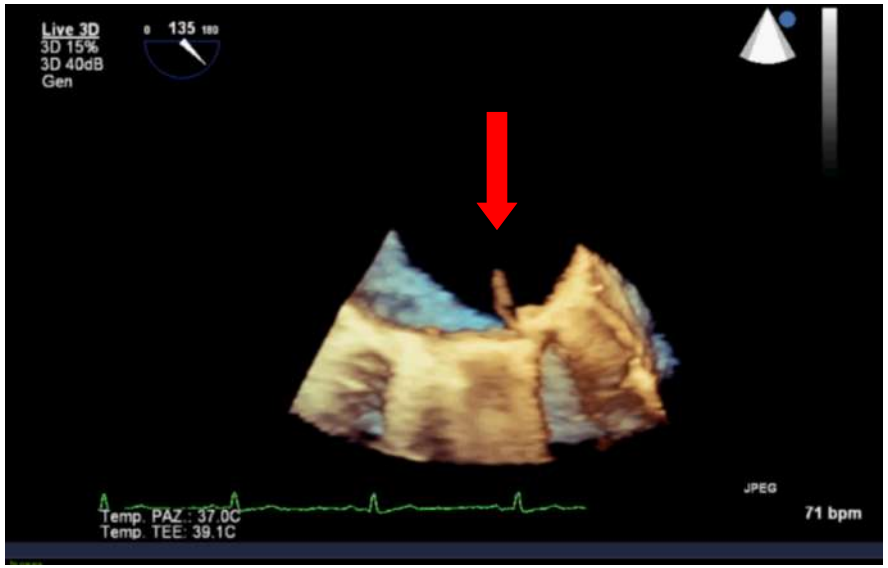


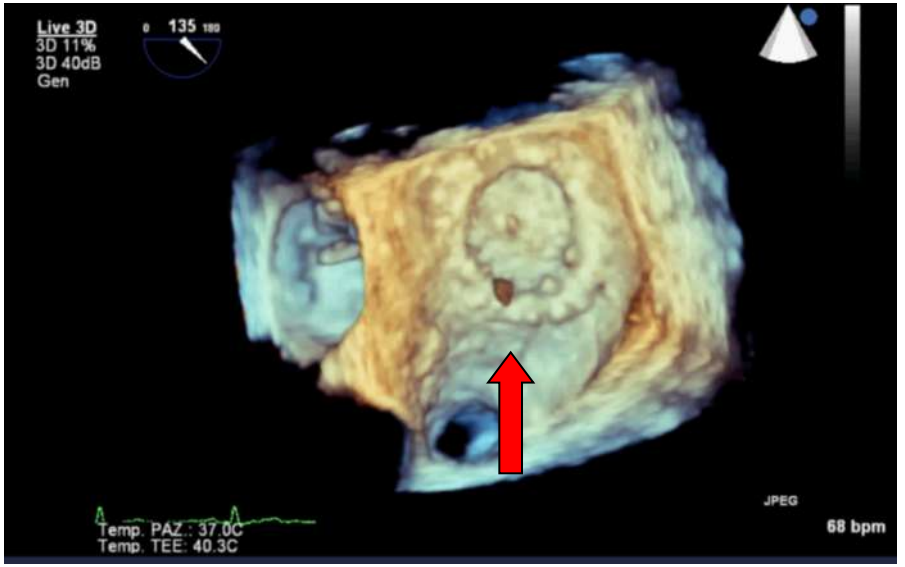
Due to the stable clinical condition, no thrombolytic therapy was started, but intravenous unfractioned heparin was initiated and maintained.

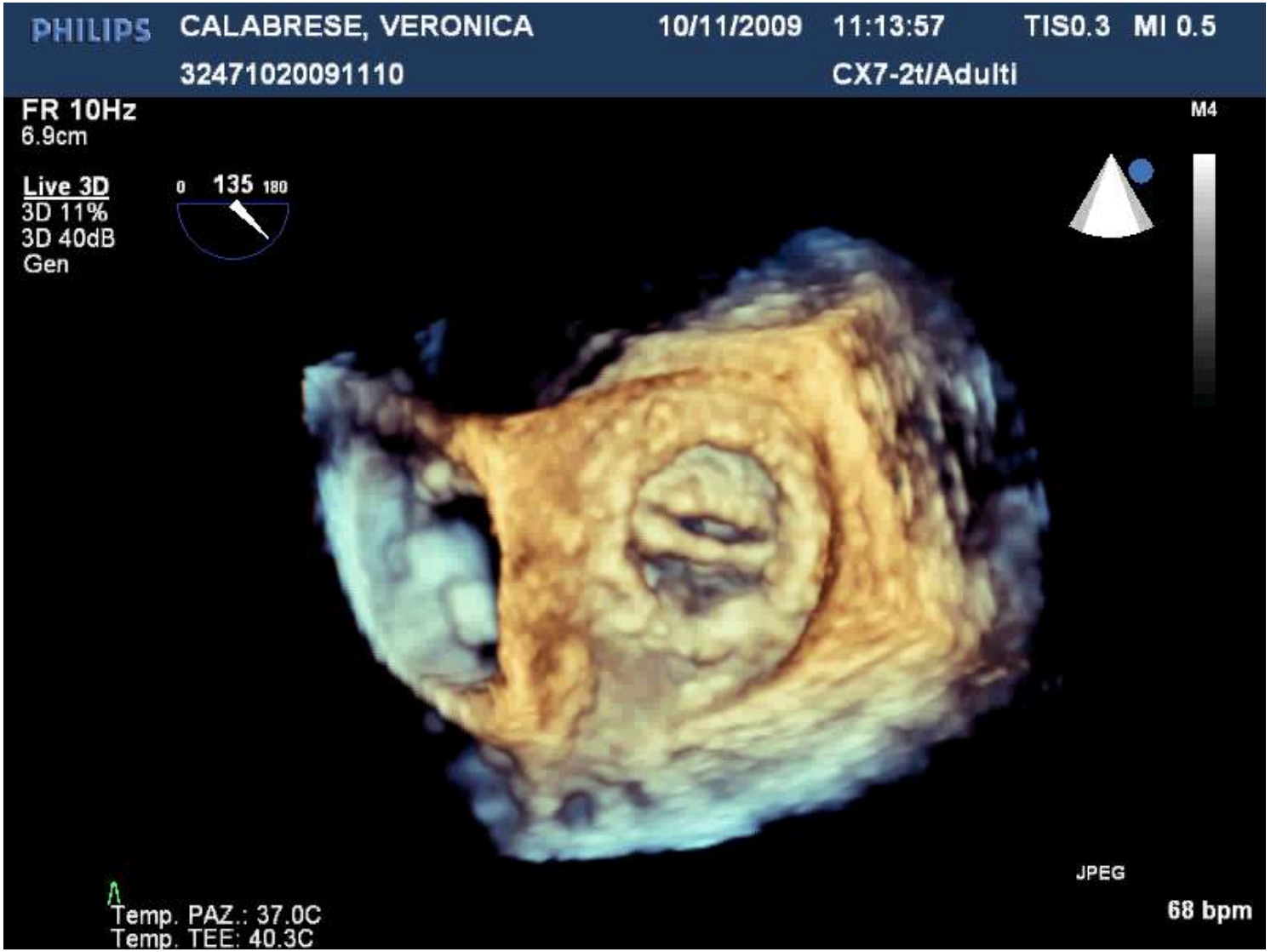
3 days later

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.

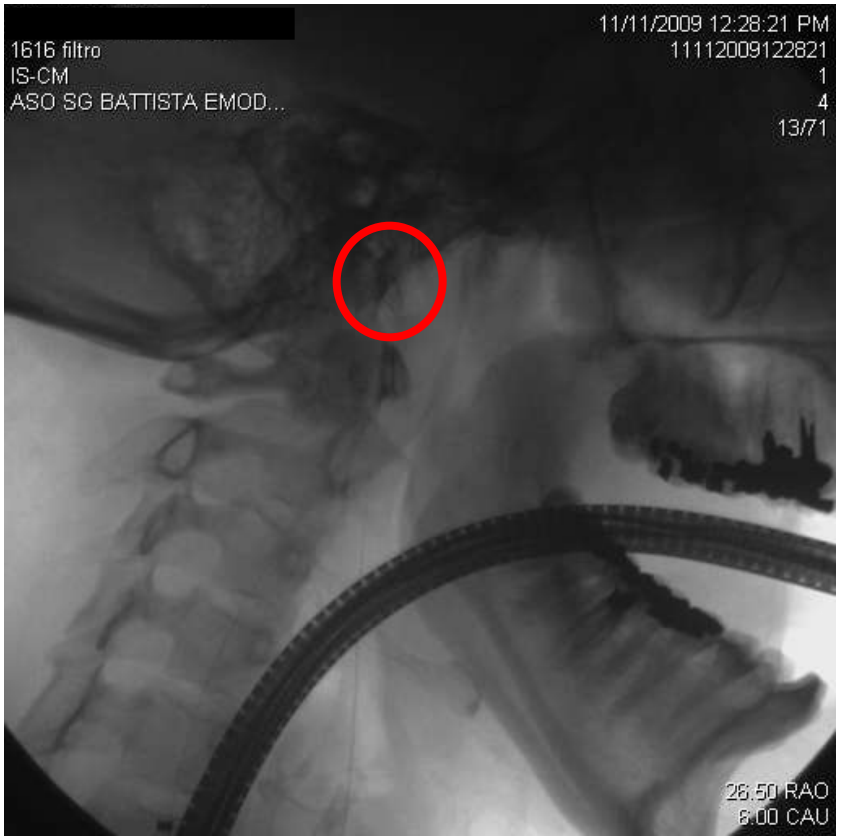
Another smaller thrombus (7mm) was evident adhering to the aortic prosthesis annulus, without prosthesis malfunction.

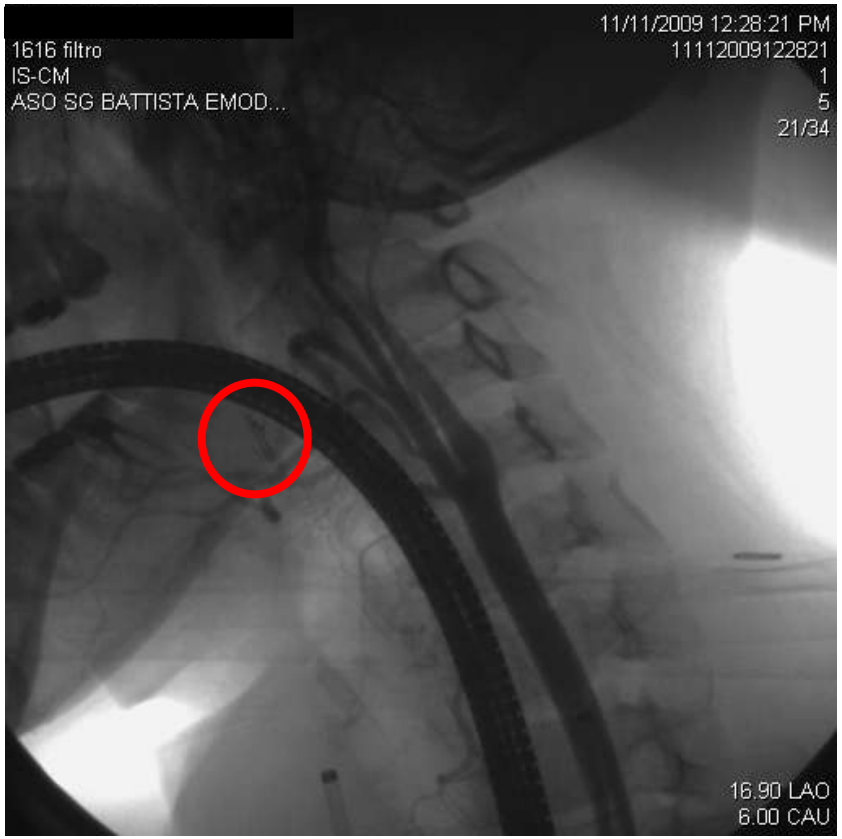




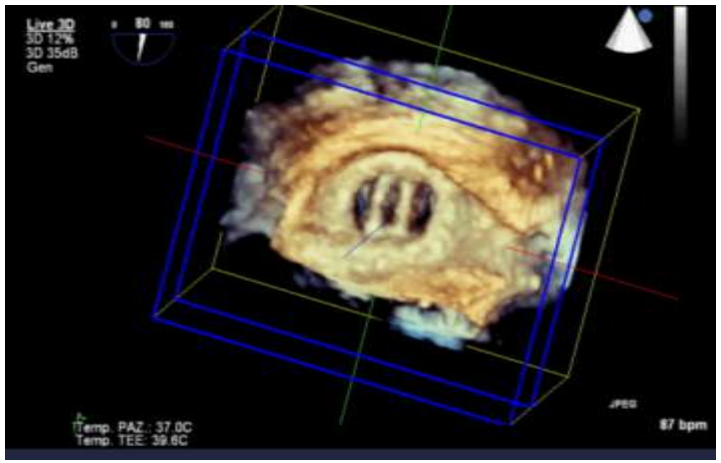

PHILIPS
CALABRESE, VERONICA
10/11/2009
11:13:57
TIS0.3
MI 0.5
32471020091110
CX7-2t/Adulti
FR 10Hz
6.9cm
M4
Live 3D
3D 11%
3D 40dB
Gen
0
135
180
JPEG
Temp. PAZ.: 37.0C
Temp. TEE: 40.3C
68 bpm

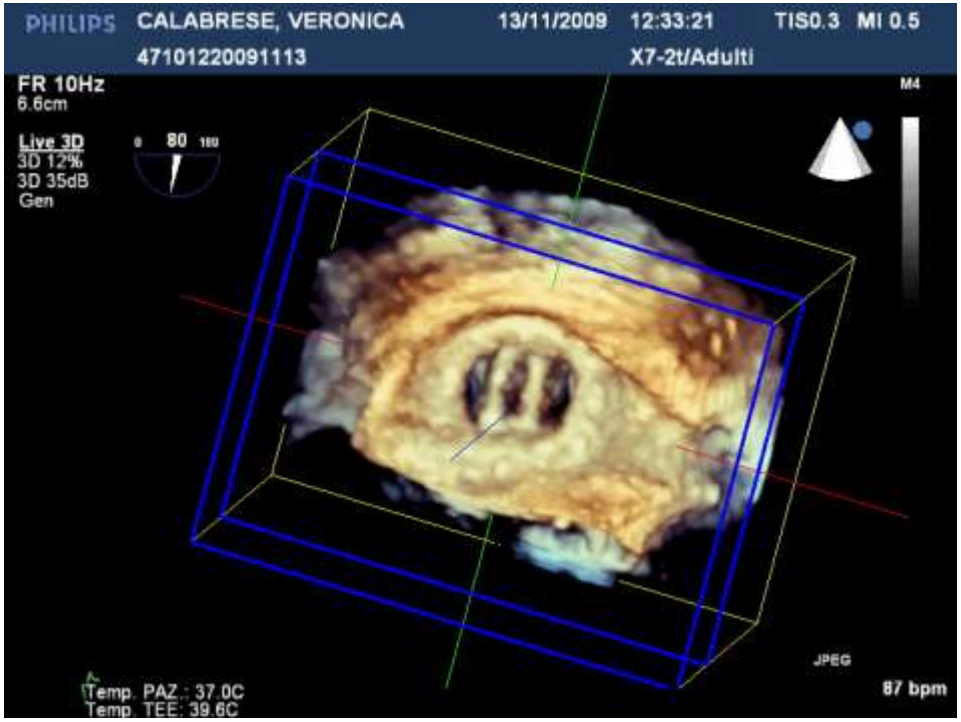
Due to the high embolic risk, alteplase was given as a bolus (0.27 mg/kg) and intravenous infusion (0.6mg/kg in 30min). To minimize the risk of cerebral embolization, carotid filters (Filter Wire EZ, Boston Scientific) were placed in both common carotid arteries.





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.

Where did we went wrong?

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

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Mechanical valves		
OACs are recommended during the second and third trimesters until the 36th week. ✓	I	C
Change of anticoagulation regimen during pregnancy should be implemented in hospital. ✗	I	C
If delivery starts while on OACs, caesarean delivery is indicated.	I	C
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. ✓	I	C
In pregnant women managed with LMWH, the post-dose anti-Xa level should be assessed weekly. ✗	I	C
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. ✗	I	C
Immediate echocardiography is indicated in women with mechanical valves presenting with dyspnoea and/or an embolic event. ✓	I	C
Continuation of OACs should be considered during the first trimester if the warfarin dose required for therapeutic anticoagulation is <5 mg/day (or phenprocoumon <3 mg/day or acenocoumarol <2 mg/day), after patient information and consent.	IIa	C
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 >5 mg/day (or phenprocoumon >3 mg/day or acenocoumarol >2mg/day). ✓	IIa	C
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 <5 mg/day (or phenprocoumon <3 mg/day or acenocoumarol <2 mg/day).	IIb	C
Continuation of OACs may be considered between weeks 6 and 12 in patients with a warfarin dose required for therapeutic anticoagulation >5 mg/day (or phenprocoumon >3 mg/day or acenocoumarol >2 mg/day).	IIb	C
LMWH should be avoided, unless anti-Xa levels are monitored.	III	C

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