Mitral valve disease in pregnancy

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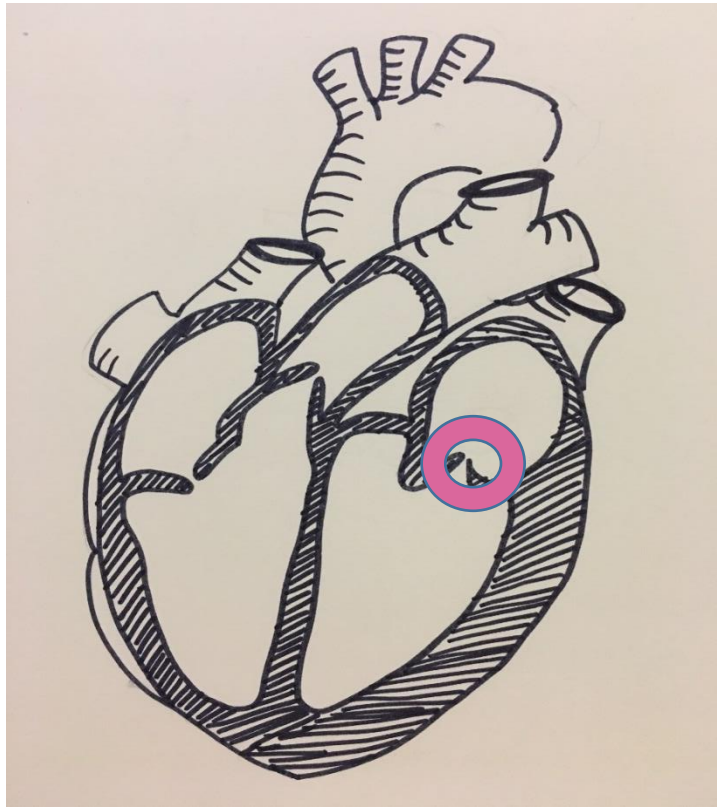
Rheumatic MV disease (MS and MR)
Prosthetic MV

- Pregnancy planning and pre pregnancy care
- Early pregnancy management (first trimester)
- Mid and late pregnancy care (second and third trimester)
- Planned delivery
- Post partum

Mitral Stenosis (MS)



Maternal risk

responsible for most of the morbidity and mortality of rheumatic heart disease during pregnancy

Obstetric and offspring risk

Acute heart failure during or just after delivery, prematurity, intrauterine growth restriction stillbirth

Markers of increased risk: (pre pregnancy)

- History of pulmonary edema, arrhythmias requiring treatment,
- transient ischemic attack, or stroke prior to pregnancy.
- Functional status by subjective (ie, New York Heart Association
- functional class) or objective measures (exercise testing).
- Central cyanosis (oxygen saturation <90 percent by oximetry).
- Mitral valve area, extent of mitral regurgitation, left ventricular
- systolic function.
- Systolic pulmonary artery pressure.

Indications for preconception intervention

- Valve intervention prior to conception is recommended in women with signifcant **(moderate or severe MS; mitral valve area ≤1.5 cm2**) who are **symptomatic or have reduced exercise capacity**

- The 2018 ESC guidelines recommended that asymptomatic women with moderate or severe MS should **avoid pregnancy and undergo prepregnancy intervention**, favoring a percutaneous approach
- In asymptomatic women with moderate or severe MS and normal pulmonary artery pressure, **we recommend exercise testing**

During pregnancy:

- Medication as needed (beta blockers and duritics)
- Intervention in high risk symptomatic patients despite medical therapy
- Biweekly follow up in Joint clinic (OB/Gyn – Cardiology)
- If needed B type natriuretic peptid (BNP)
- At least one Echo study at first visit and another in third trimester

Arrhythmia and Anticoagulation:

- Anticoagulation is recommended in those with **atrial fibrillation**, **left atrial thrombus, or prior embolism**. In those with signifcant MS and in sinus rhythm, anticoagulation is a consideration if there is spontaneous echocardiographic contrast in the left atrium, large left atrium (>60 mL/m2), or heart failure

- Sustained or **frequent palpitations** should be promptly investigated. Atrial fibrillation and other supraventricular tachycardia should be treated

Valve interventions:

- The procedure is best done after the period of organogenesis (>20 weeks) but prior to mid to late third trimester when the gravid uterus can interfere with catheter access and hemostasis with the femoral approach.

Delivery

- Planned or induced delivery is necessary
- almost all women with MS can undergo vaginal delivery with an assisted second stage
- Caesarian delivery is reserved for obstetric indications and in whom anticoagulation cannot be reversed
- One single dose of furosemide early post partum
- No endocarditis prophylaxis is needed

Post partum

- post-delivery “fluid shifts may be delayed in the presence of regional anesthesia.
- For those women who required ongoing anticoagulation, anticoagulation can be resumed once there is no evidence of early or late postpartum hemorrhage
- An exception is amiodarone, which affects the newborn thyroid, so breastfeeding is contraindicated during maternal use of amiodarone.
- Combination hormonal contraception should be avoided in women with valvular heart

Table 10 Management of native valvular heart disease (1)

Recommendations	Class	Level
Pre-pregnancy evaluation, including echocardiography, and counselling is recommended for any woman with known or suspected valvular disease.	I	C
Mitral stenosis		
In patients with symptoms or pulmonary hypertension, restricted activities and beta-1-selective blockers are recommended.	I	B
Diuretics are recommended when congestive symptoms persist despite beta-blockers.	I	B
Intervention is recommended before pregnancy in patients with MS and valve area <1.0 cm^2.	I	C
Therapeutic anticoagulation using heparins or VKA is recommended in case of atrial fibrillation, left atrial thrombosis, or prior embolism.	I	C

Table 10 Management of native valvular heart disease (2)

Recommendations	Class	Level
Intervention should be considered before pregnancy in patients with MS and valve area <1.5 cm^2.	IIa	C
Percutaneous mitral commissurotomy should be considered in pregnant patients with severe symptoms or systolic pulmonaryartery pressure >50 mmHg despite medical therapy.	IIa	C
Aortic stenosis		
Intervention is recommended before pregnancy in patients with severe aortic stenosis if:		
• they are symptomatic	I	B
• OR LV dysfunction (LVEF <50%) is present	I	C
• OR when they develop symptoms during exercise testing	I	C

Table 10 Management of native valvular heart disease (3)

Recommendations	Class	Level
Intervention should be considered before pregnancy in asymptomatic patients with severe AS when a fall in blood pressure below baseline during exercise testing occurs.	IIa	C
Balloon aortic valvuloplasty should be considered during pregnancy in patients with severe aortic stenosis and severe symptoms.	IIa	C
Chronic regurgitant lesions		
Surgical treatment is recommended before pregnancy in patients with severe aortic or mitral regurgitation with symptoms of impaired ventricular function or ventricular dilatation.	I	C
Medical therapy is recommended in pregnant women with regurgitant lesions when symptoms occur.	I	C

بررسی نتایج بارداری در زنان باردار مبتلا به تنگی دریچه میترال مراجعه کننده به بیمارستان های الزهرا و شهید چمران اصفهان از سال ۱۳۹۹-۱۳۹۰

نتایج:

۸۱ زن باردار مبتلا به تنگی دریچه میترال

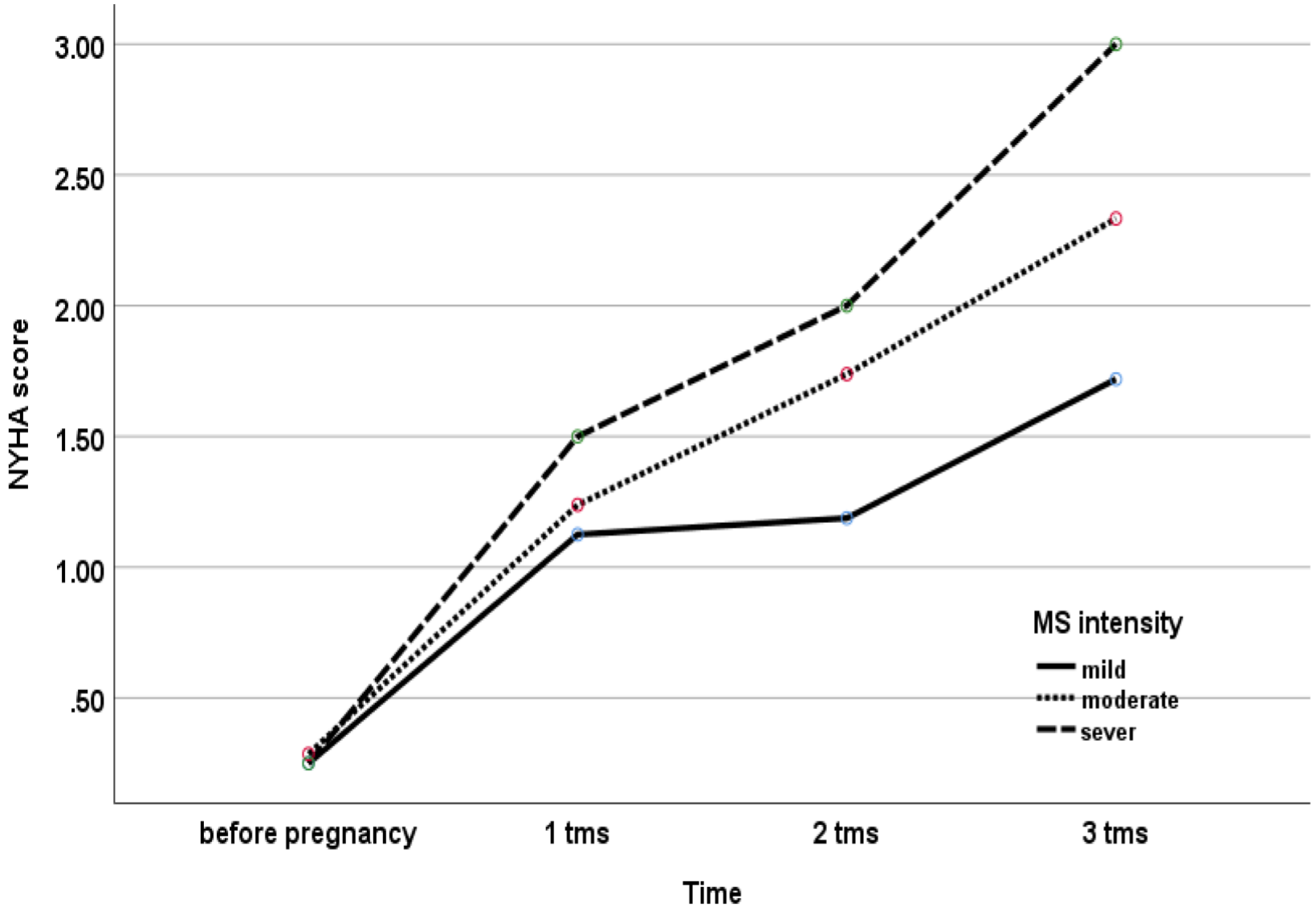
* زمان تشخیص بیماری :

۴۵ نفر (۵۵.۶٪) قبل بارداری
۳۶ نفر (۴۴.۴٪) در زمان بارداری

- شدت تنگی:

Very severs (زیر ۱cm) : ۴ نفر(۴.۹٪)
Severe (۱-۱.۵cm) : ۴۶ نفر(۵۶.۸٪)
Progressive (بالای ۱.۵ cm) : ۳۱ نفر(۳۸.۳٪)

متغیر		کل بیماران	شدت تنگی میترال			P
			پیش رونده 31 نفز	شدید 46 نفر	خیلی شدید 4 نفر	
زمان تشخیص	قبل بارادر	45(55.6)	21(67.7)	23(50)	1(25)	0.14
	حین بارداری	10(32.3)	10(32.3)	23(50)	3(75)	
میانگین سطح مقطع دریچه		1.47± 0.48	1.94 ± 0.39	1.22 ± 0.20	0.78 ± 0.13	<0.001
میانگین EF (درصد)		56.5± 6.9	56.9 ± 8.5	56.3 ± 5.6	56.3± 7.5	0.92
فشار خون ریوی		45.7 ± 16.41	38.23 ± 8.6	48.02 ± 16	75.75 ± 22.3	<0.001
PAP>50		25(30.9)	3(9.7)	18(39.1)	4(100)	<0.001
ریتم قلبی در بارداری	سینوسی	74(91.4)	28(90.3)	43(93.5)	3(75)	0.44
	AF	7(8.6)	3(9.7)	3(6.5)	1(25)	
بروز حوادث قلبی در بارداری		22(27.16)	5(15.6)	15(33.2)	2(66)	0.65
نیاز به انجام PTMC		13(16)	2(6.5)	9(19.6)	2(66)	0.046
بروز HF بعد از زایمان		2(2.5)	2(6.5)	0	0	0.24
بروز آریتمی بعد از زایمان		2(2.5)	1(3.2)	1(2.2)	0	0.99
ادم ریه		5(6.17)	1(3.2)	4(8.96)	0	0.64
آمبولی ریه		5(6.17)	1(3.2)	4(8.69)	0	0.64



نمودار ۱ : درصد گرید NYHA در طی بارداری

MS severity

جدول ۳ : توزیع فراوانی سرانجام جنینی و نوزادی در زنان مبتلا به تنگی دریچه میترال

متغیر	کل بیماران	شدت تنگی میترال			P
		Progressive 36 نفر	شدید (42 نفر)	خیلی شدید 3 نفر	
ختم بارداری با سزارین	70(86.4)	6(19.4)	4(8.7)	1(25)	0.21
میانگین سن ختم بارداری(هفته)	33.9± 8.1	34.2± 8.1	33.4 ± 8.5	36.3± 2.4	0.77
مرگ بعلت MS و عوارض آن	1(1.2)	0(0)	1(2.2)	0(0)	0.99
مرده زایی	1(1.2)	1(3.2)	0(0)	0(0)	0.43
سقط خود بخود	11(13.6)	4(12.9)	7(15.2)	0(0)	0.69
سقط درمانی	17(21)	6(19.4)	11(23.9)	0(0)	0.73
آنومالی حین تولد	7(8.6)	2(5.5)	5(11.4)	0(0)	0.57
میانگین نمره آپگار دقیقه 1	8.25 ± 1.23	8.44± 0.7	8.1± 1.51	8.5± 0.58	0.49
میانگین نمره آپگار دقیقه 5	9.50 ± 0.83	9.78 ± 0.44	9.2 ± 1.03	10 ± 1	0.27
میانگین وزن نوزاد در حین تولد	2645.5 ± 547	2784.2± 376.7	2564.8± 639.2	2537.5± 377.7	0.25
ابتلا به IUGR در بارداری	4(5.5)	2(7.4)	2(4.8)	0(0)	0.72
مدت اقامت در بیمارستان(روز)	5.5± 5.8	4.7± 0.98	5.61 ± 0.74	10.5± 6.5	0.16
نوع بی هوشی(عمومی)	65(80.2)	21(80.8)	41(95.3)	0(0)	0.26
حاملگی چند قلویی	2(2.5)	0(0)	2(4.3)	0(0)	0.56

عوارض جنینی:

- فراوانی انجام سزارین در کل بیماران ۷۰ مورد (۸۶.۴٪)
- ۶۵ نفر (۸۰.۲٪) تحت بیهوشی عمومی
- بروز مرده زایی ۱ مورد (۱.۲٪)
- سابقه سقط خودبخود ۱۱ مورد (۱۳.۶٪)
- سقط درمانی ۱۷مورد (۲۱٪)
- آنومالی حین تولد ۷ مورد (۸.۶٪)
- پره مچوریتی ۳ مورد(۳.۷٪)
- ابتلا به IUGR ۴ مورد (۴.۹٪)
- میانگین سن ختم بارداری ۸.۱ ±۳۳.۹ هفته(۳۶ نفر:۴۴.۴٪ PTL)
- میانگین وزن نوزادن در هنگام تولد ۵۴۷ ± ۲۶۴۵.۵ گرم (۲۷ نوزاد زیر ۲۵۰۰ گرم:۳۳.۳۳٪ LBW)
- میانگین مدت اقامت در بیمارستان ۵.۸ ±۵.۵ روز

Prosthetic valve and pregnancy

Hemostatic changes during normal pregnancy:

Concentration of coagulation factors ↑

Concentration of fibrinogen ↑

Platelet adhesiveness ↑

Obstruction venous return

Increased risk of thrombo-embolic events

Anticoagulation therapy during pregnancy

- Not routinely necessary in pregnant women

- When indication arises:

  -risk of fetal complications with vit K ant. (OAC)

  -changing dose requirements for anticoagulants

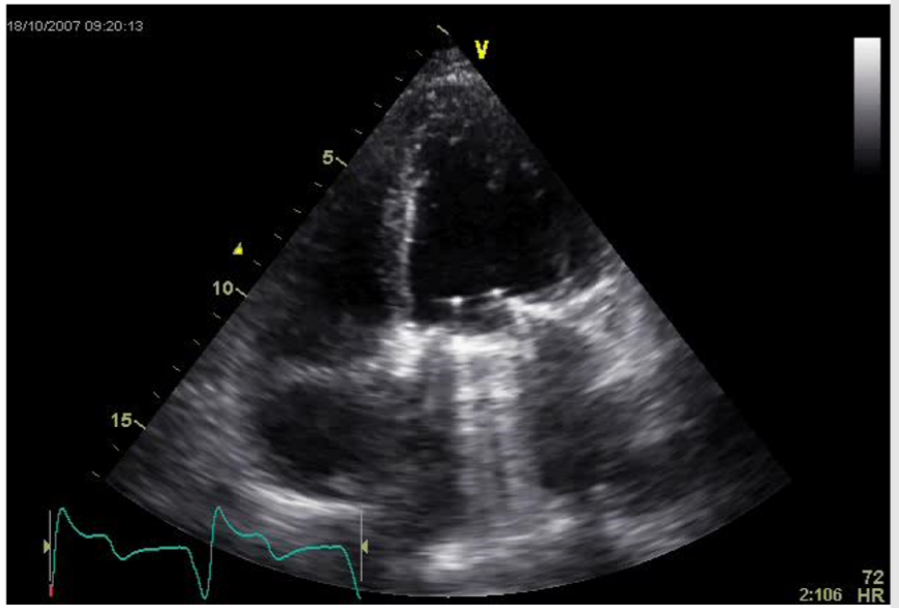
(plasma volume↑ and GFR ↑)

↓

Influences choice and monitoring of anticoagulation

Indications for anticoagulation during pregnancy

f1699



Atrial fibrillation

Impaired ventricular function

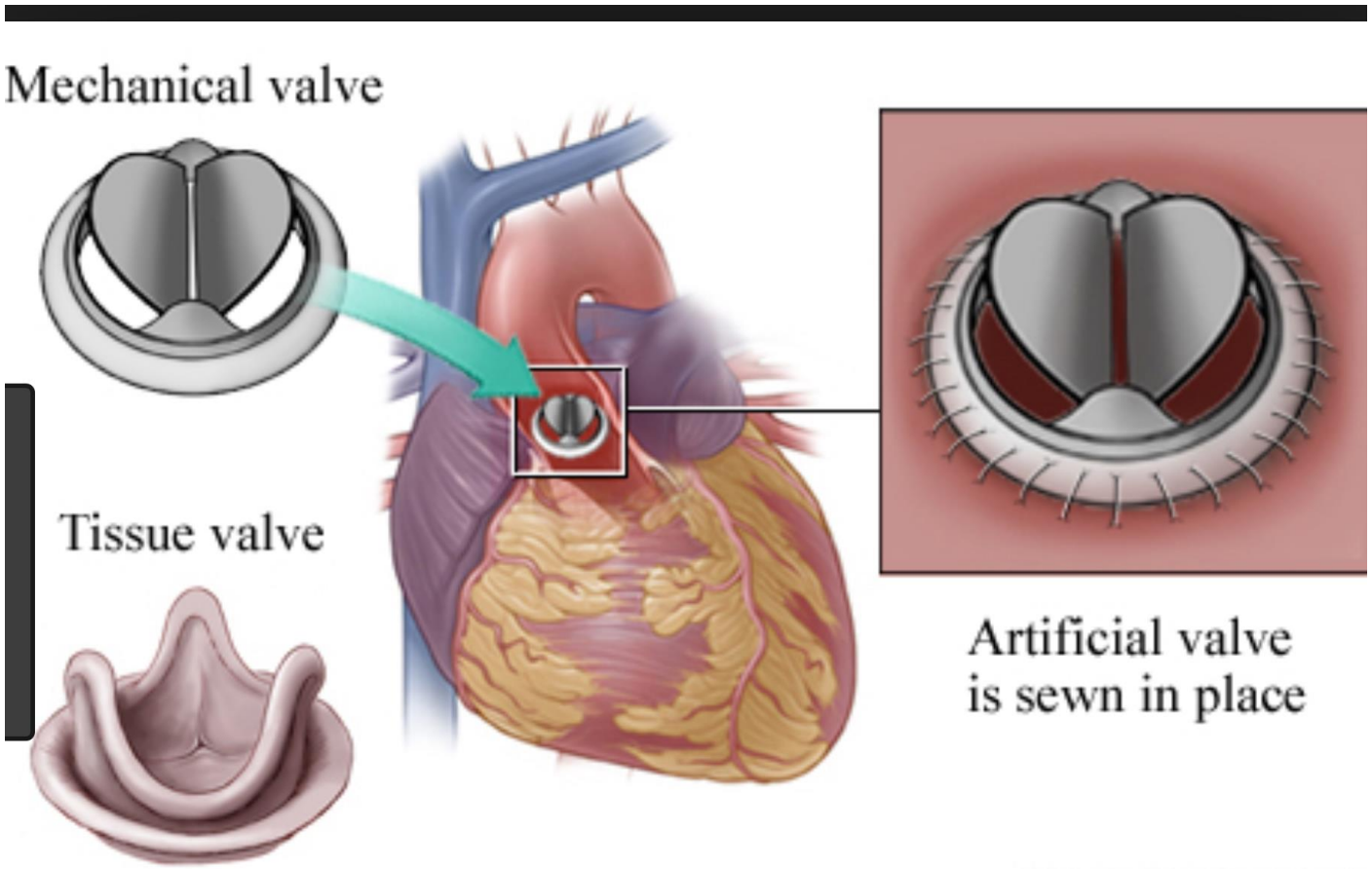
Pulmonary hypertension

Cyanotic heart disease, Fontan circulation

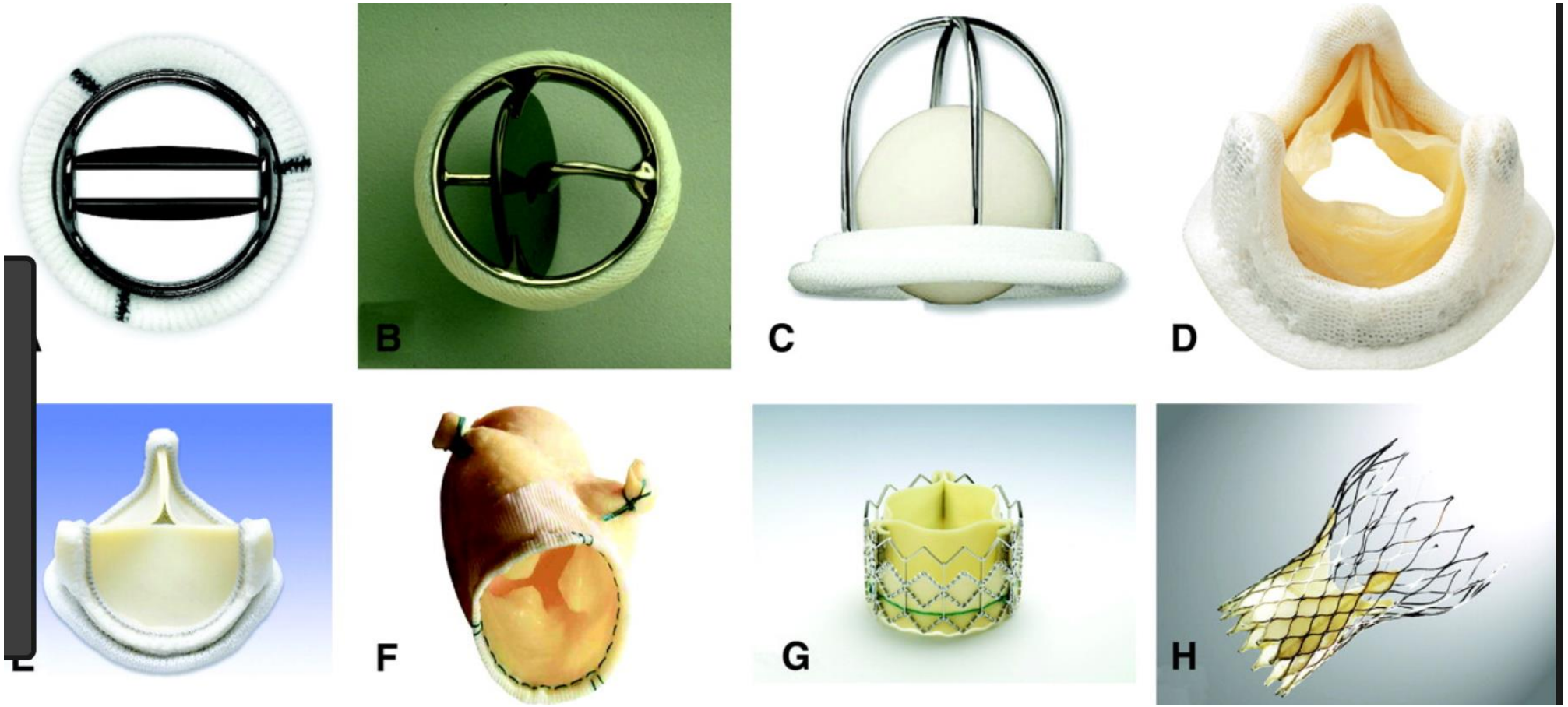
Venous thrombosis, pulmonary emboli

Valvular heart disease

Prosthetic heart valves



Types of prosthetic valves



Prosthetic valve thrombosis

- **Malfunction of valve** : leads to Dyspnea, pulmonary edema, cardiogenic shock

- **Embolic events**: Stroke, limb ischemia, mesenteric ischemia, myocardial infarction

Table 6 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

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

Valvular heart disease

Mechanical valve prostheses

controversy: LMWH / UFH or vit K antagonists?

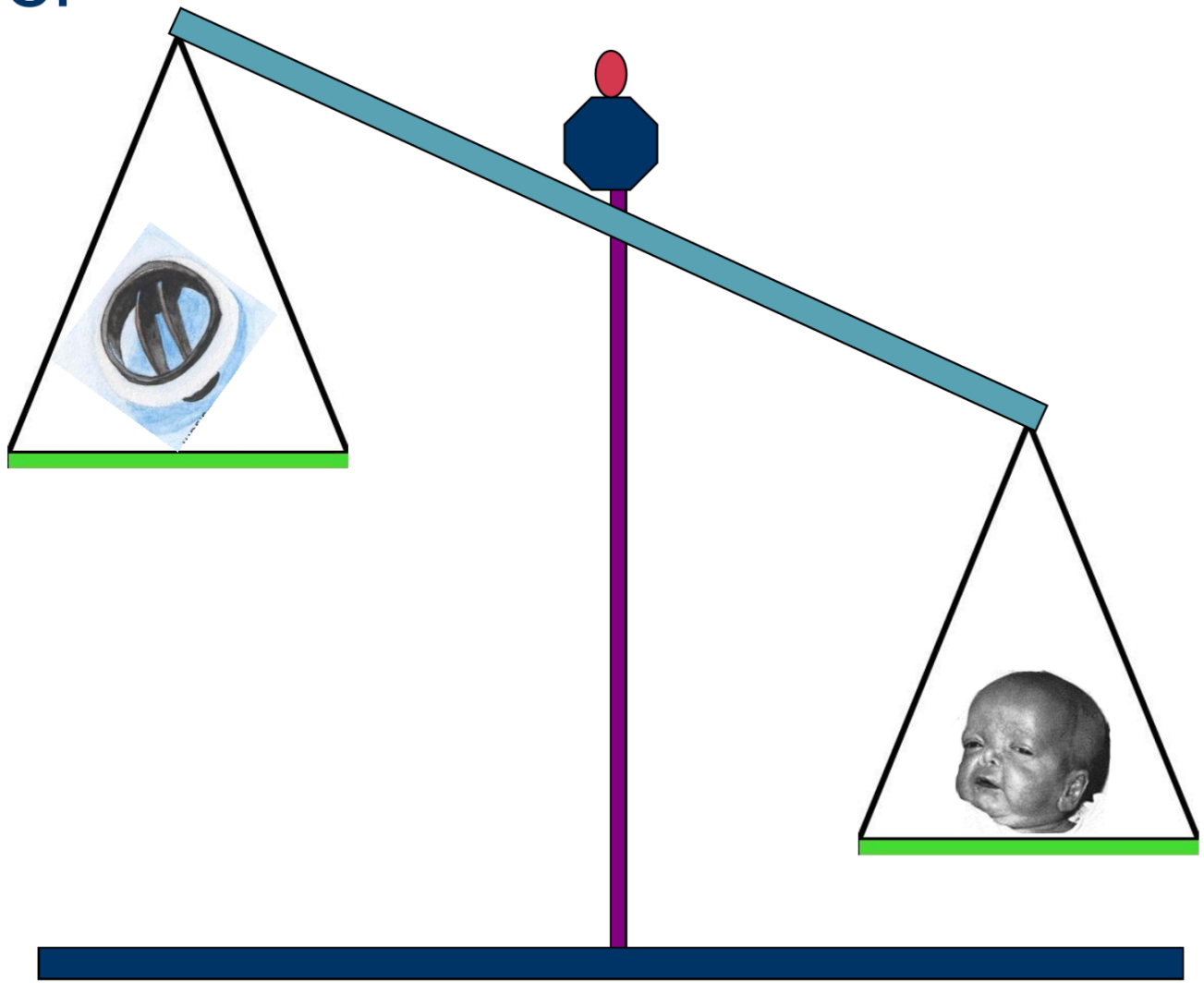
- How toxic are vitamin K antagonists for the foetus?

- How effective are LMWH / UFH to prevent mechanical valve thrombosis?

mother

Vit K antagonist

baby



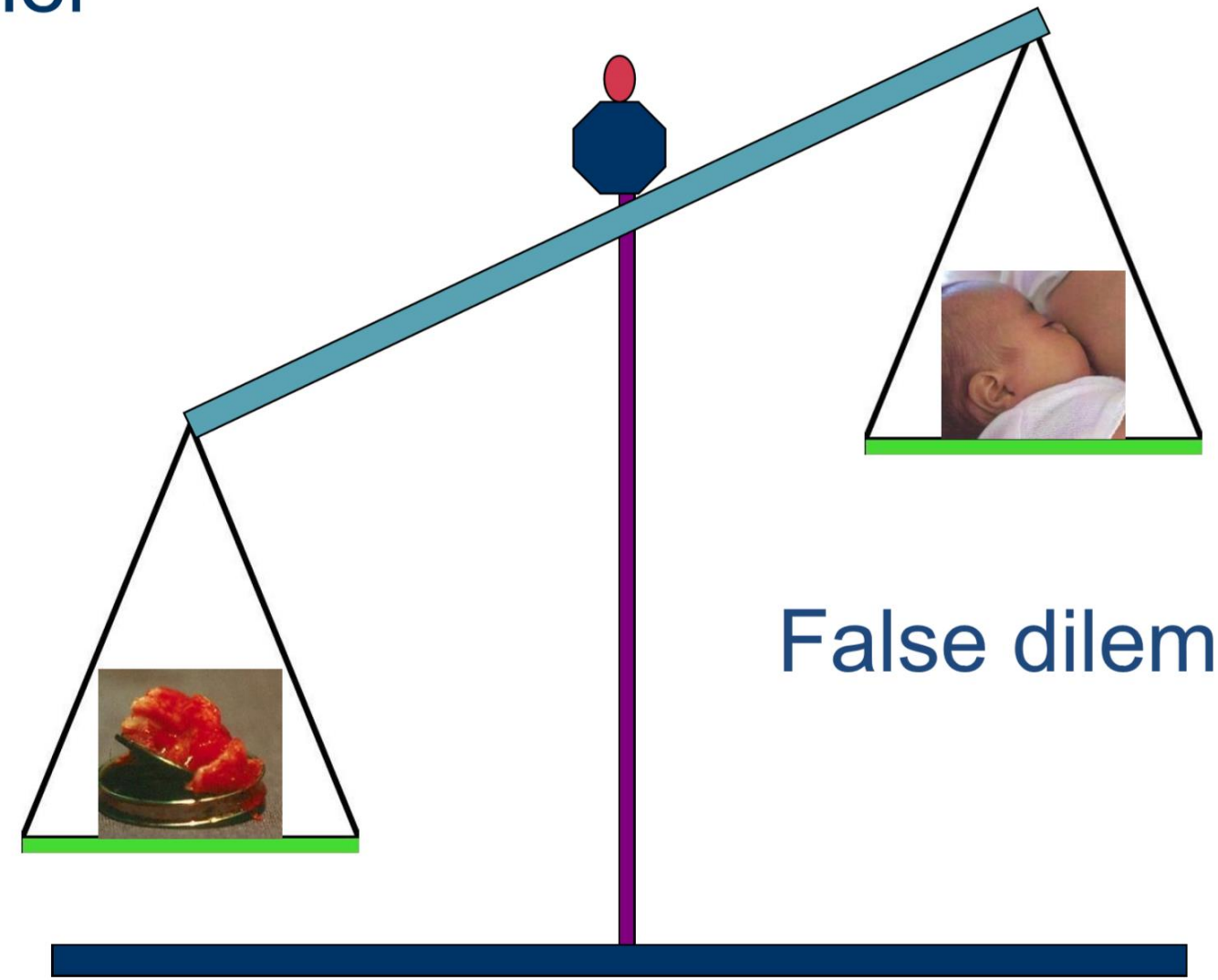
Safe pregnancy

but risk of embryopathy

mother

LMWH / UHF

baby



False dilemma

risk of valve thrombosis

but baby is safe

Valve thrombosis

mother

baby

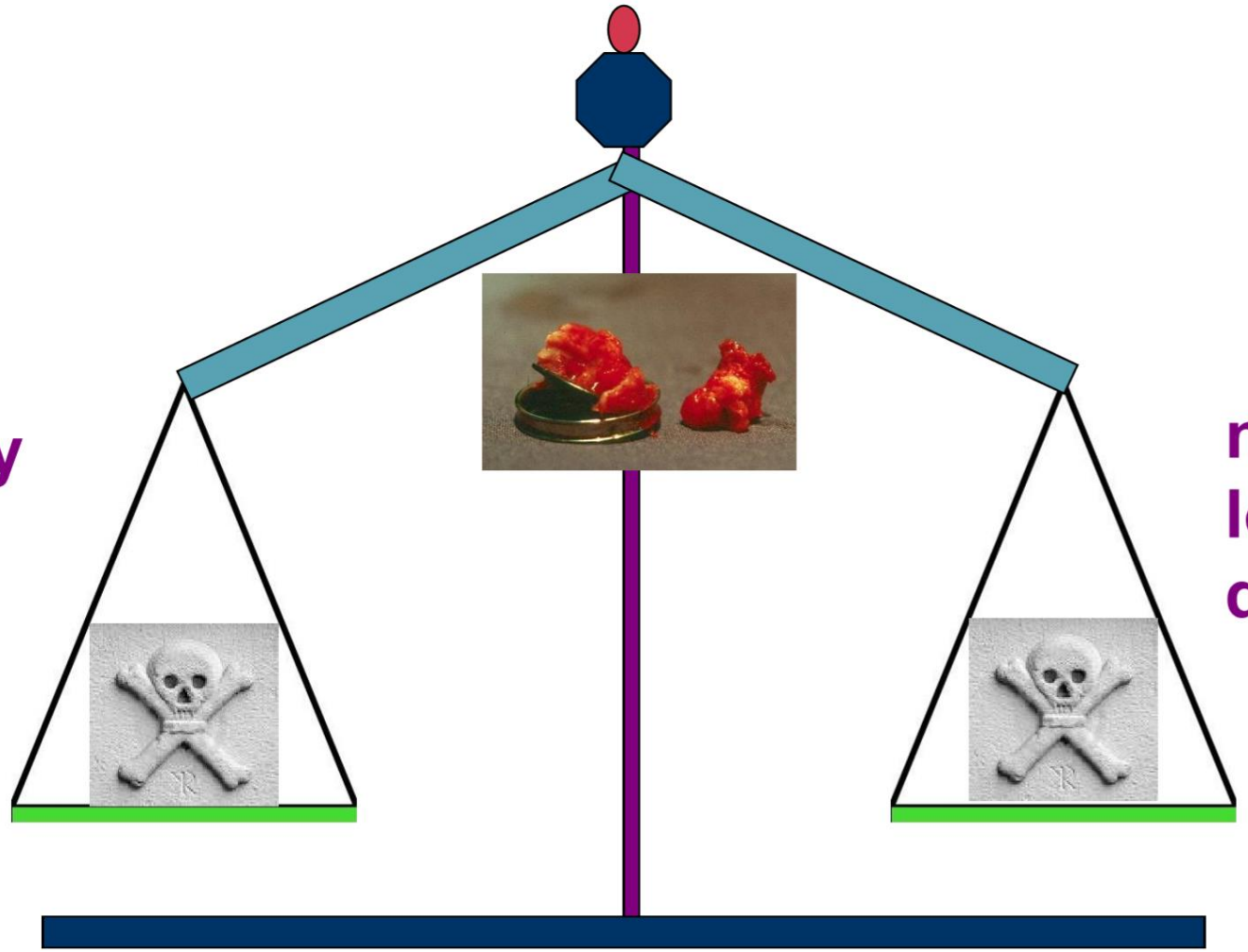
†

†

†

surgery

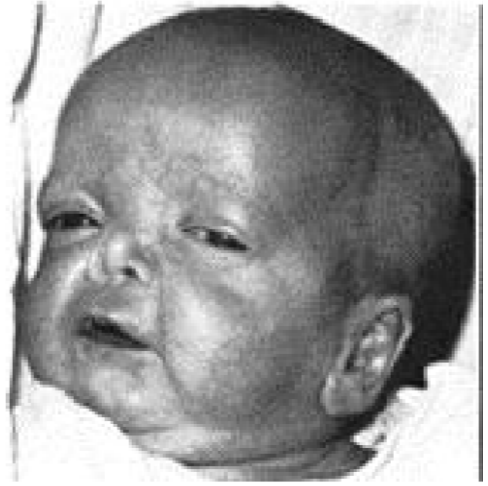
neuro-logical damage



No risk-free options, no easy choices

How toxic are vitamin K antagonists for the foetus?

- embryopathy: mainly nasal hypoplasia
sometimes severe abnormalities



0% if avoided from week 6-12

- vitamin K ant throughout pregnancy:

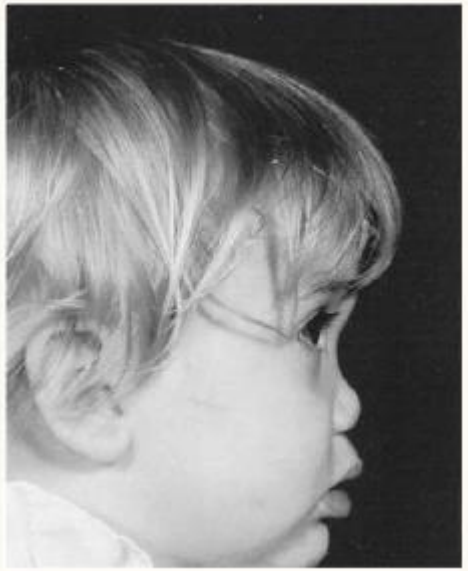
Chan (review, 549 pregn): 6.4%
v Driel (review, 394 pregn): 6.0%

older studies, high dose

Table 5. Adverse effects of warfarin in the fetus

Warfarin embryopathy (6 - 12 weeks)

- Nasal hypoplasia
- Stippled epiphyses
- Saddle-nose deformity
- Mental retardation
- Optic atrophy
- Frontal bossing
- Hypertelorism
- High-arched palate
- Short neck
- Short stature



Fetal effects (all trimesters and delivery)

- Ocular abnormalities – blindness
- Neurological abnormalities – microcephaly, mental retardation, low intelligent quotients
- Fetal loss
- Bleeding

Warfarin

- Risk of embryopathy up to 10 percent
- Risk is increased with exposure after 5 weeks (6- 12 weeks)
- Miscarriage 30% (before 20 weeks) and fetal death 10% (after 20 weeks)
- Dose dependent effect on embryopathy and fetal death (5 mg)

European Heart Journal (2017) **38**, 1509–1516
doi:10.1093/eurheartj/ehx032

META-ANALYSIS

Anticoagulation for pregnant women with mechanical heart valves: a systematic review and meta-analysis

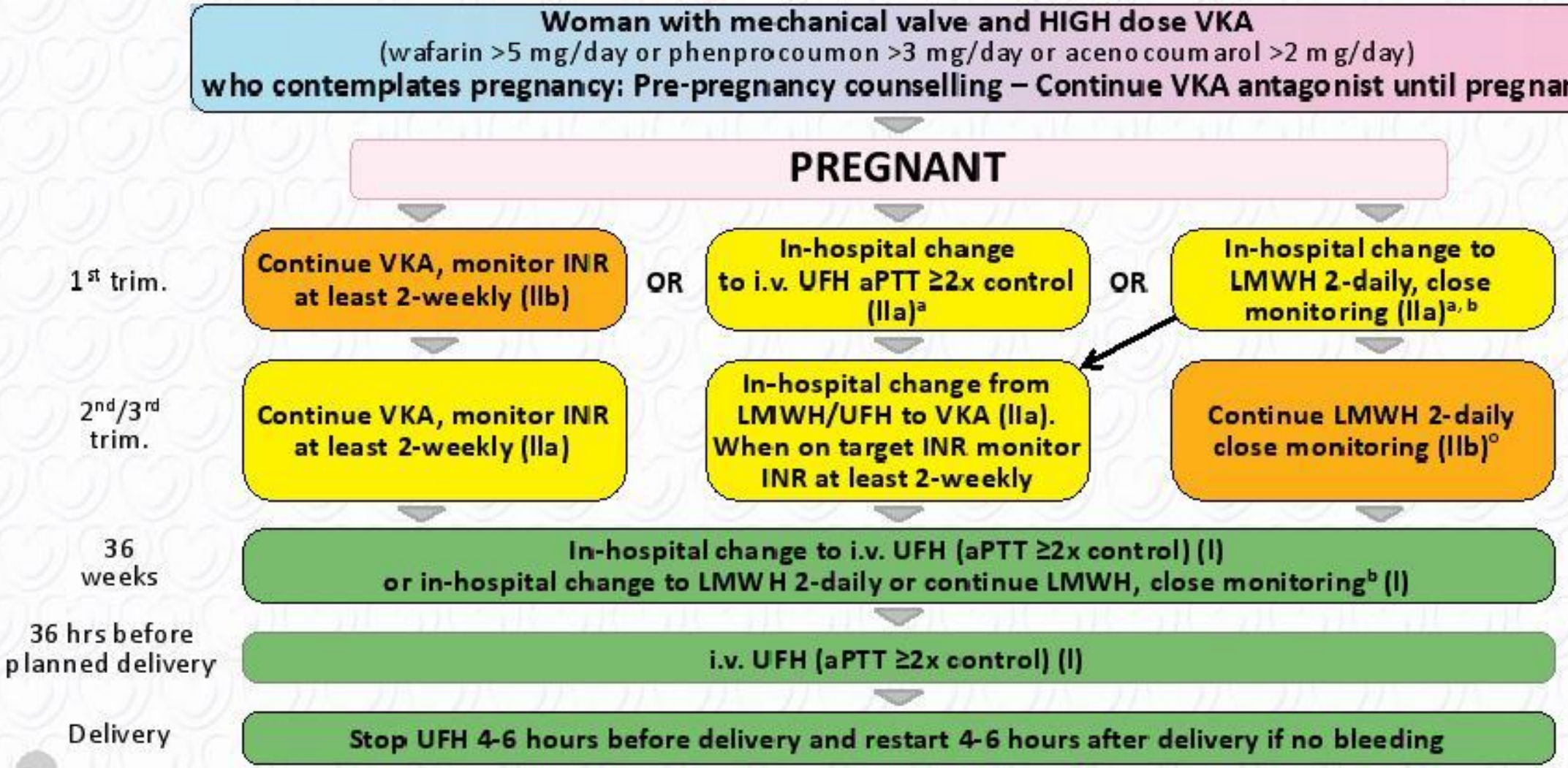
Rohan D'Souza[1,2]*, Jackie Ostro[3], Prakesh S. Shah[2,4], Candice K. Silversides[5], Ann Malinowski[1], Kellie E. Murphy[1,2], Mathew Sermer[1], and Nadine Shehata[2,6]

Mode of anticoagulation	Vit K antagonist	Sequential LMWH and VKA	LMWH alone
Maternal mortality	0.9%	2.0%	2.9%
Thromboembolic events	2.7%	5.8%	8.7%
Live birthes	64.5%	79.9%	92%
Anticoagulation related fetal/ neonatal adverse events	2.0%	1.4%	0%

Table 2. Factors affecting choice of anticoagulant

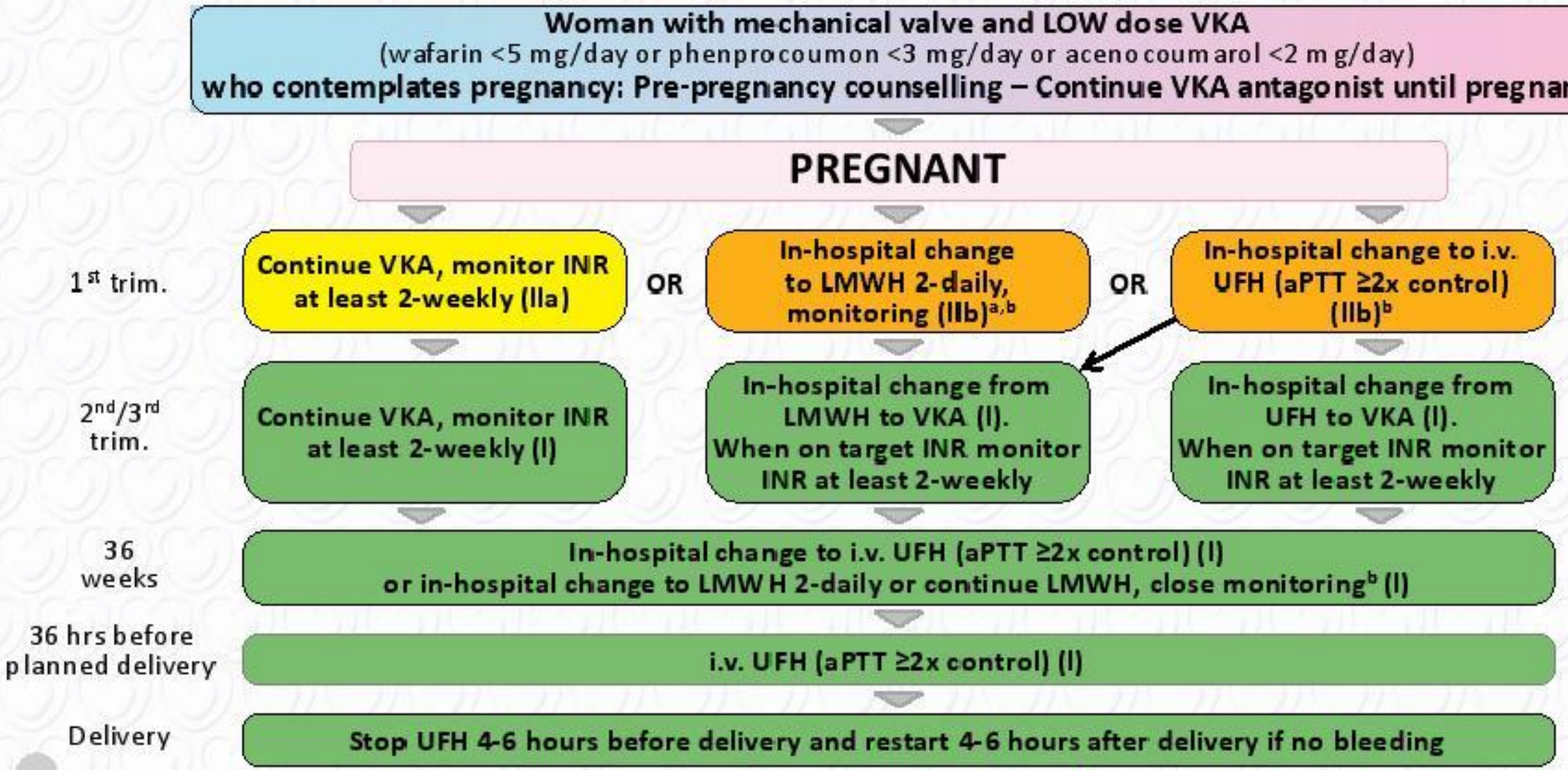
Risk factors for thromboembolism
Valve type
Valve position
History of thromboembolism
Economic factors
Availability of the anticoagulants
Cost of the anticoagulants
Access to laboratory testing
Access to specialist care
Maternal preferences
Fetal and maternal adverse outcomes

Figure 2 Flowchart on anticoagulation in mechanical valves and high-dose VKA



2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy
European Heart Journal (2018) 00, 1–83- doi:10.1093/eurheartj/ehy 340

Figure 3 Flowchart on anticoagulation in mechanical valves and low-dose VKA



www.escardio.org/guidelines

Figure 4 Flowchart on anticoagulation in mechanical valves and target international normalized ratio for mechanical prostheses

Prosthesis Thrombogenicity	Risk factors [a]	
	None	≥1
Low [b]	2.5	3.0
Medium [c]	3.0	3.5
High [d]	3.5	4.0

Table 11 Management of prosthetic heart valves (1)

ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended that the valve prosthesis for a woman contemplating pregnancy is chosen in consultation with a pregnancy heart team.	I	C
It is recommended to manage pregnancy in women with mechanical valves in a centre with a pregnancy heart team.	I	C
If delivery starts while on a VKA or in less than 2 weeks after discontinuation of a VKA, caesarean section is recommended.	I	C
It is recommended to discontinue VKAs and start adjusted-dose intravenous UFH (aPTT ≥2x control) or adjusted-dose LMWH[c] at the 36th week of gestation.	I	C
In pregnant women on LMWH or UFH, it is recommended to perform weekly anti-Xa level monitoring or aPTT monitoring with dose adjustment (within 36 h).	I	C

Table 11 Management of prosthetic heart valves (2)

Recommendations	Class	Level
In pregnant women on a VKA, it is recommended to perform INR monitoring weekly or every 2 weeks.	I	C
In pregnant women with LMWH, it is recommended to target anti-Xa levels 4–6 h post-dose at 0.8–1.2 U/l (aortic valve prosthesis) or 1.0–1.2 IU/mL (mitral and right-sided valve prostheses).	I	C
It is recommended to replace LMWH with intravenous UFH (aPTT ≥2x control) at least 36 h before planned delivery. UFH should be continued until 4–6 h before planned delivery and restarted 4–6 h after delivery if there are no bleeding complications.	I	C
It is recommended to anticipate the timing of delivery to ensure safe and effective peripartum anticoagulation.	I	C
Immediate echocardiography is recommended in women with mechanical valves presenting with dyspnoea and/or an embolic event.	I	C

Table 11 Management of prosthetic heart valves (3)

Recommendations	Class	Level
It is recommended to implement changes in the anticoagulation regimen during pregnancy in hospital.	I	C
During the second and third trimesters until the 36th week, VKAs are recommended in women needing a low dose.[d]	I	C
A bioprosthesis should be considered in young women contemplating pregnancy.	IIa	C
During the second and third trimesters until the 36th week, VKAs should be considered in women needing a high dose.[e]	IIa	C
Continuation of VKAs 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

Table 11 Management of prosthetic heart valves (4)

ESC European Society of Cardiology

Recommendations	Class	Level
Discontinuation of VKAs between weeks 6 and 12, and replacement with adjusted-dose intravenous UFH (aPTT ≥2x control) or adjusted-dose LMWH[c] twice daily (see separate recommendations), should be considered in patients with a warfarin dose >5 mg/day (or phenprocoumon >3 mg/day or acenocoumarol >2 mg/day).	IIa	C
During the second and third trimesters, LMWH[c] with anti-Xa level monitoring and dose adjustment (see separate recommendations) may be considered in women who need a high dose of VKA[e] after patient information and consent.	IIb	C
In pregnant women with LMWH, in addition to monitoring peak anti-Xa levels, monitoring pre-dose levels targeted at ≥0.6 IU/mL may be considered.	IIb	C
LMWH is not recommended when weekly anti-Xa level monitoring and dose-adjustment is not available.	III	C

Monitoring of LMWH

- higher targets (1.0 to 1.2 units/mL) for mechanical valves in the mitral position and lower targets (0.8 to 1.0 units/mL) for mechanical aortic valve replacements.
- Peak anti-Xa levels should be <1.5 units/mL to avoid excessive anticoagulation and increased risk of bleeding.
- We also suggest monitoring anti-Xa trough levels (target ≥0.6 units/mL

Recommendations	COR	LOE
LMWH should not be administered to pregnant patients with mechanical prostheses unless anti-Xa levels are monitored 4 to 6 hours after administration	III: Harm	B

Table 4. Interpretation of anti-Xa levels in patients on LMWH

Target anti-Xa levels
1.0 - 1.2 anti-Xa U/mL
Low anti-Xa level
Inadequate dosing
Delayed specimen draw
Dose of LMWH omitted
Weight gain
Gestation (volume of distribution of LMWH changes)
High anti-Xa level
Excessive dosing
Weight loss
Renal dysfunction
Reduced creatinine clearance (end of third trimester)

Pregnant woman with one of theses conditions

- Old or small mechanical mitral valve
- Atrial fibrillation or flutter
- Previous thromboembolic complications
- Multiple mechanical heart valves

continuing vitamin K antagonist (VKA; eg, warfarin) with close international normalized ratio (INR) monitoring throughout pregnancy (along with low-dose aspirin) until 36 weeks

Approach for planned delivery

- At approximately 36 weeks, VKA (eg, warfarin) should be switched to dose-adjusted subcutaneous (SC) low molecular weight heparin (LMWH) administered at least twice per day
- Dose-adjusted continuous infusion of unfractionated heparin should only be offered if LMWH is unavailable.
- The last dose of dose-adjusted SC LMWH is administered 24 hours before planned induction of labor or cesarean delivery (regional anesthesia/analgesia , risk of bleeding)

Post partum resuming anticoagulation

- We suggest starting an infusion of UFH at a usual dose with no bolus and gradually increasing the dose to achieve therapeutic anticoagulation over 24 to 48 hours if a vaginal delivery and 48 to 72 hours if a cesarean delivery
- warfarin should not be reintroduced until day 5 to 7.

Novel anticoagulants

- Direct oral anticoagulants (DOACs, also known as non-vitamin K oral anticoagulants [NOACs]) including direct thrombin inhibitors (eg, dabigatran) and direct factor Xa inhibitors (eg, rivaroxaban, apixaban, and edoxaban) **should not** be considered alternatives to therapy with warfarin or heparin in patients with mechanical heart valves (during or outside of pregnancy).

Case senario

- 26 years old pregnant woman with previous history of mitral valve surgery with metallic prosthetic valve and pregnancy of 12 weeks present with acute dyspnea….