

# Chlopenní vady u žen a v těhotenství (ESC 2025)



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## Osnova přednášky

- Liší se srdce a krevní oběh u M a Ž?
- Jaká je vlastně prevalence chlopenních vad v závislosti na pohlaví?
- A proč?
- Jak mění těhotenství krevní oběh matky?
- Co nového přinášejí GL ESC 2025 z hlediska chlopenních vad u žen?

**Liší se ženské srdce od mužského? Ano.**

**Ženské srdce:**

- více podléhá emocím
- je klíčem, který otevírá cestu k celé její osobnosti
- těžko může opravdově milovat více mužů najednou
- ....



The image features a stack of approximately ten books on a wooden desk. The top book is open, showing its pages. The background is a blurred bookshelf filled with books. On the left side, there is a vertical border composed of colorful, irregular mosaic tiles in shades of blue, green, yellow, orange, and pink. In the top right corner, there is a white square containing a pink heart icon with closed eyes and two white hands embracing it from below.

Ženské srdce:

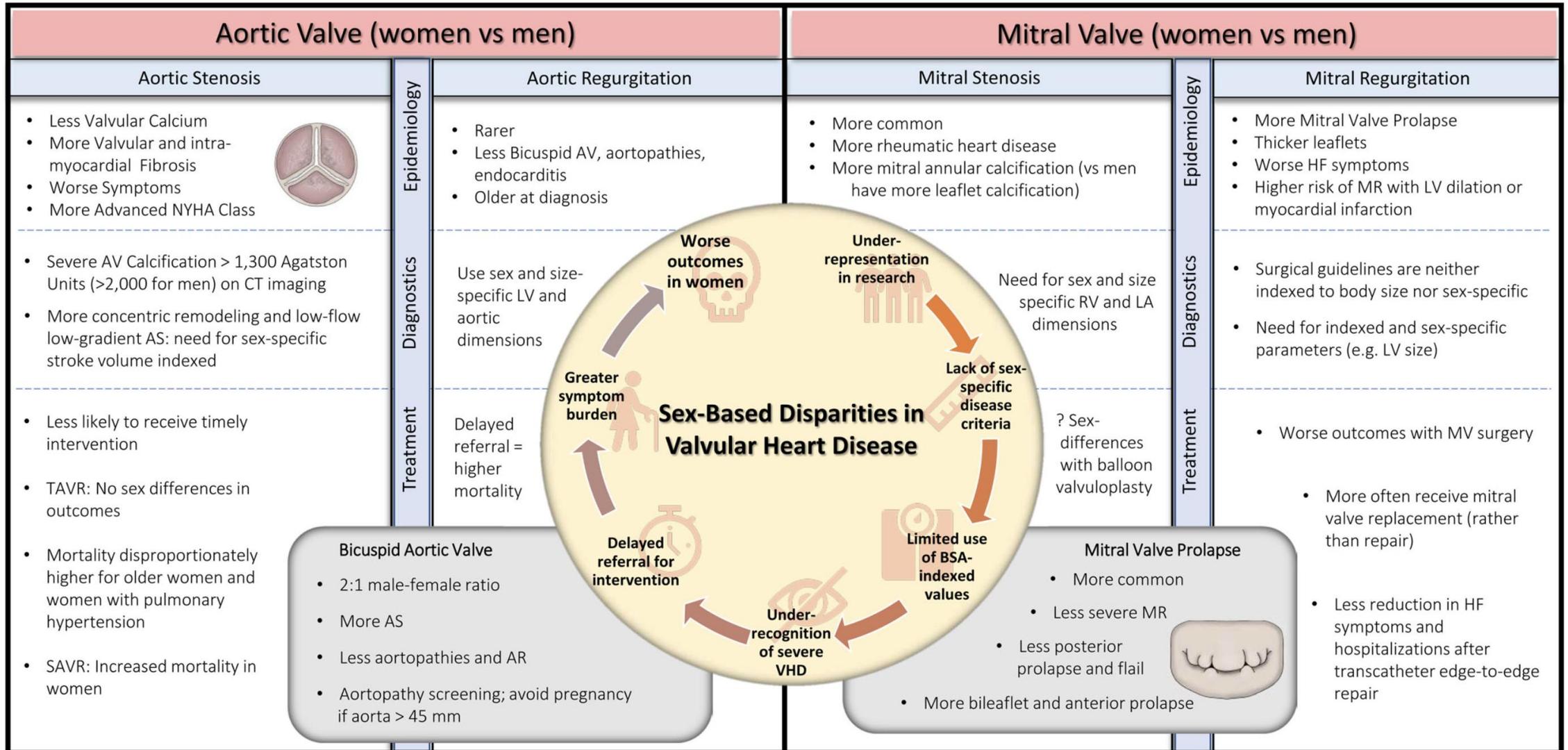
Úroveň důkazů: C

# Krevní oběh a srdce ženy

- podléhá hormonálním měsíčním cyklům i podstatným změnám v těhotenství
- srdce je menší, má vyšší EF, reaguje větším vzestupem TF i CO na zátěž
- tedy jiná manifestace kliniky u podobné vady
- hyperkoagulační stav v graviditě
- naopak možné komplikace antikoagulační léčby (...33% !)
- v těhotenství vyšší krevní objem, vyšší TF i CO – kritické pro stenotické vady, demaskace tiché vady...



# CENTRAL ILLUSTRATION: Sex Differences in Valvular Heart Disease



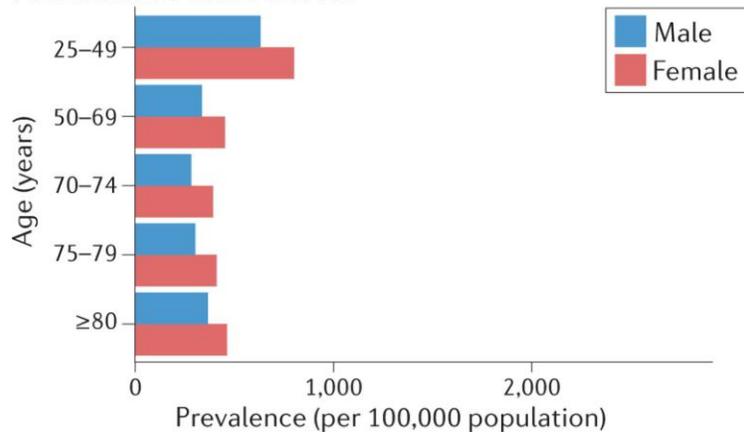
## Sex Differences and Similarities in Valvular Heart Disease

Jacqueline T. DesJardin, Joanna Chikwe, Rebecca T. Hahn, Judy W. Hung, Francesca N. Delling  
 Circulation Research [Volume 130, Number 4, https://doi.org/10.1161/CIRCRESAHA.121.319914](https://doi.org/10.1161/CIRCRESAHA.121.319914)

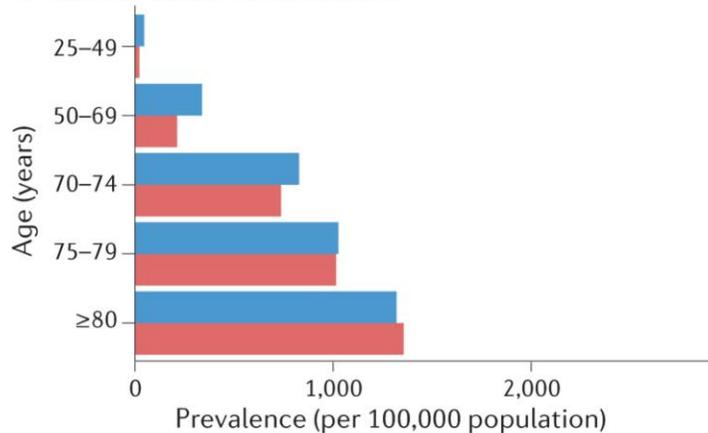
## Prevalence chlopenních vad

- je v součtu u mužů a u žen stejná
- ale liší se proporcionalní zastoupení jednotlivých vad mezi pohlavími
- na základě genetických rozdílů
- pokud se budeme bavit o vadách v těhotenství, tak jde samozřejmě především o vrozené patologie anebo porevmatické vady

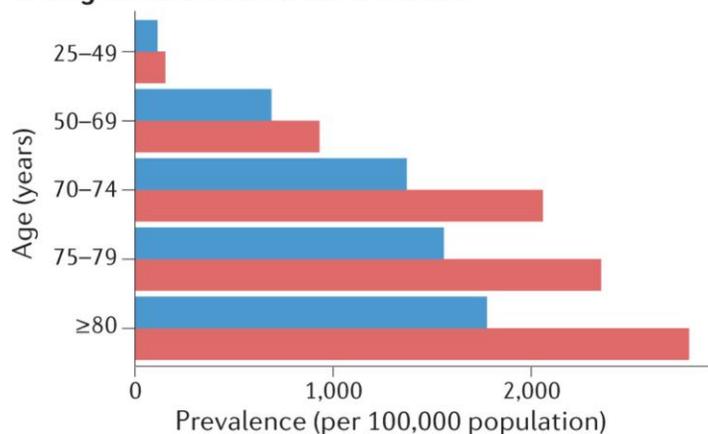
### A Rheumatic heart disease



### B Calcific aortic valve disease



### C Degenerative mitral valve disease



Mitrální stenóza (MS) postihuje ženy až 3x častěji než muže, zejména v důsledku revmatické horečky.

U mužů je celkově vyšší riziko rozvoje AoS, částečně kvůli častějšímu výskytu bikuspidální aortální chlopně (v poměru 2:1 až 4:1). U žen se však AS stává dominantní ve vyšším věku; nad 80 let tvoří ženy většinu pacientů s touto vadou.

Prolaps mitrální chlopně (MVP) je také častější u žen, které mívají difuznější myxomatózní postižení. MR obecně více u žen

(Prevalence střední a těžké TR je statisticky výrazně vyšší u žen. Podle Framingham Heart Study byl poměr výskytu u mužů a žen 1 : 1,6.)

Movahed MR, Bahrami A, Eshraghi R. Gender specific echocardiographic prevalence of valvular stenosis and regurgitations in a large inpatient database of 24,265 patients. *Am J Cardiovasc Dis.* 2025 Feb 15;15(1):21-28. doi: 10.62347/HYOC9461. PMID: 40124090; PMCID: PMC11928885.

Evan J. Wiens, Kristal Kawa, Malek Kass, and Ashish H. Shah. 2024. Impact of biological sex on valvular heart disease, interventions, and outcomes. *Canadian Journal of Physiology and Pharmacology.* **102**(10): 585-593. <https://doi.org/10.1139/cjpp-2023-0390>

Singh JP, Evans JC, Levy D, et al. Prevalence and clinical determinants of mitral, tricuspid, and aortic regurgitation (the Framingham Heart Study). *Am J Cardiol.* 1999;83(6):897-902. doi:10.1016/S0002-9149(98)01064-9

## Proč je incidence chlopenních vad odlišná u M / Ž?

- Genetické faktory hrají zásadní roli v tom, proč se chlopenní vady u mužů a žen vyvíjejí odlišně. Rozdíly nejsou dány pouze pohlavními hormony, ale i specifickou expresí genů na chromozomu X a odlišnými signálními drahami v buňkách chlopni (intersticiální buňky chlopně – VIC)....
- Aterosklerosa je častější u mužů, patogenesa je podobná...

# Pohlavně specifická genová exprese v chlopních

.....u žen a mužů dochází k aktivaci odlišných genových sad při rozvoji fibrózy a kalcifikace. U žen je výrazněji aktivována dráha **NOTCH1**, jejíž mutace jsou přímo spojeny s kalcifikací aortální chlopně, ale její regulace se mezi pohlavími liší.

Acharya A, Hans CP, Huang ET, et al. Notch1 signaling maintains lineage fidelity and inhibits osteogenic differentiation in cardiac valve progenitors. *Development*. 2011;138(19):4221-4232. doi:10.1242/dev.062083

Schlotter F, Halu A, Goto S, et al. Spatiotemporal Multi-Omics Mapping Generates a Molecular Atlas of the Aortic Valve and Reveals Network Dysregulation in Calcific Aortic Valve Disease. *Circulation*. 2018;138(4):377-393. doi:10.1161/CIRCULATIONAHA.117.032291

Hadji F, Boulanger MC, Guay SP, et al. Altered DNA Methylation and Gene Expression Profiles in Male and Female Visceral Adipose Tissue Context of Calcific Aortic Valve Stenosis. *Front Cell Dev Biol*. 2021;9:693510. doi:10.3389/fcell.2021.693510

# Bikuspidální Ao chlopeň

- BAV je nejsilnějším genetickým prediktorem aortální stenózy a její výskyt je silně vázán na mužské pohlaví. Předpokládá se zapojení genů na chromozomu X nebo genů jako **GATA4** (a dalších), které vykazují rozdílnou penetranci u mužů a žen.

Tzemos N, Therrien J, Yip J, et al. Outcomes in adults with bicuspid aortic valves. **JAMA**. 2008;300(11):1317-1325. doi:10.1001/jama.300.11.1317

Garg V, Muth AN, Ransom JF, et al. Mutations in NOTCH1 cause aortic valve disease. **Nature**. 2005;437(7056):270-274. doi:10.1038/nature03940

Michelena HI, Khanna AD, Cassot DM, et al. Sex differences in bicuspid aortic valve disease: Presentation, phenotype, and outcomes. **JACC Cardiovasc Imaging**. 2020;13(10):2180-2191. doi:10.1016/j.jcmg.2020.03.008

- 
- U žen dochází k remodelaci aortální chlopně spíše cestou vazivové přestavby (fibrózy), zatímco u mužů převažuje masivní depozice vápníku (kalcifikace).
  - U žen je častějším komp. mechanismem koncentrická HLK (s větší intersticiální fibrózou), u mužů excentrická HLK.

Clavel MA, Messika-Zeitoun D, Pibarot P, et al. The complex nature of aortic stenosis in women: genetics, biology, and clinical outcomes. *Can J Cardiol.* 2021;37(7):1004-1017.  
doi:10.1016/j.cjca.2021.03.014

Thaden JJ, Nkomo VT, Suri RM, et al. Sex differences in calcific aortic stenosis: Protective role of estrogen? *Circulation.* 2014;130(Suppl 2):A19232. [Link na Circulation AHA](#)

Simard L, Côté N, Dagenais F, et al. Sex-related differences in the pathogenesis, diagnosis, and management of aortic stenosis. *J Am Coll Cardiol.* 2018;71(13):1457-1470.  
doi:10.1016/j.jacc.2018.01.059

# Role estrogenových receptorů a chromozomu X

- Estrogeny modulují genovou expresi prostřednictvím receptorů **ER $\alpha$**  a **ER $\beta$** . U žen tyto receptory v intersticiálních buňkách chlopně tlumí osteogenní diferenciaci - méně kalcia, ale více vazivové tkáně

Parra-Izquierdo I, Castanos-Mollor I, Lopez J, et al. Lipoprotein(a) and valve calcification: a sex-specific genetic relationship in aortic stenosis. **Eur Heart J**. 2019;40(27):2245-2253.

doi:10.1093/eurheartj/ehz102

Masjedi S, Lei Y, Khoo A, et al. Sex-related differences in the valvular interstitial cell response to mechanical stretch and TGF- $\beta$ 1. **Cardiovasc Eng Technol**. 2017;8(4):458-471.

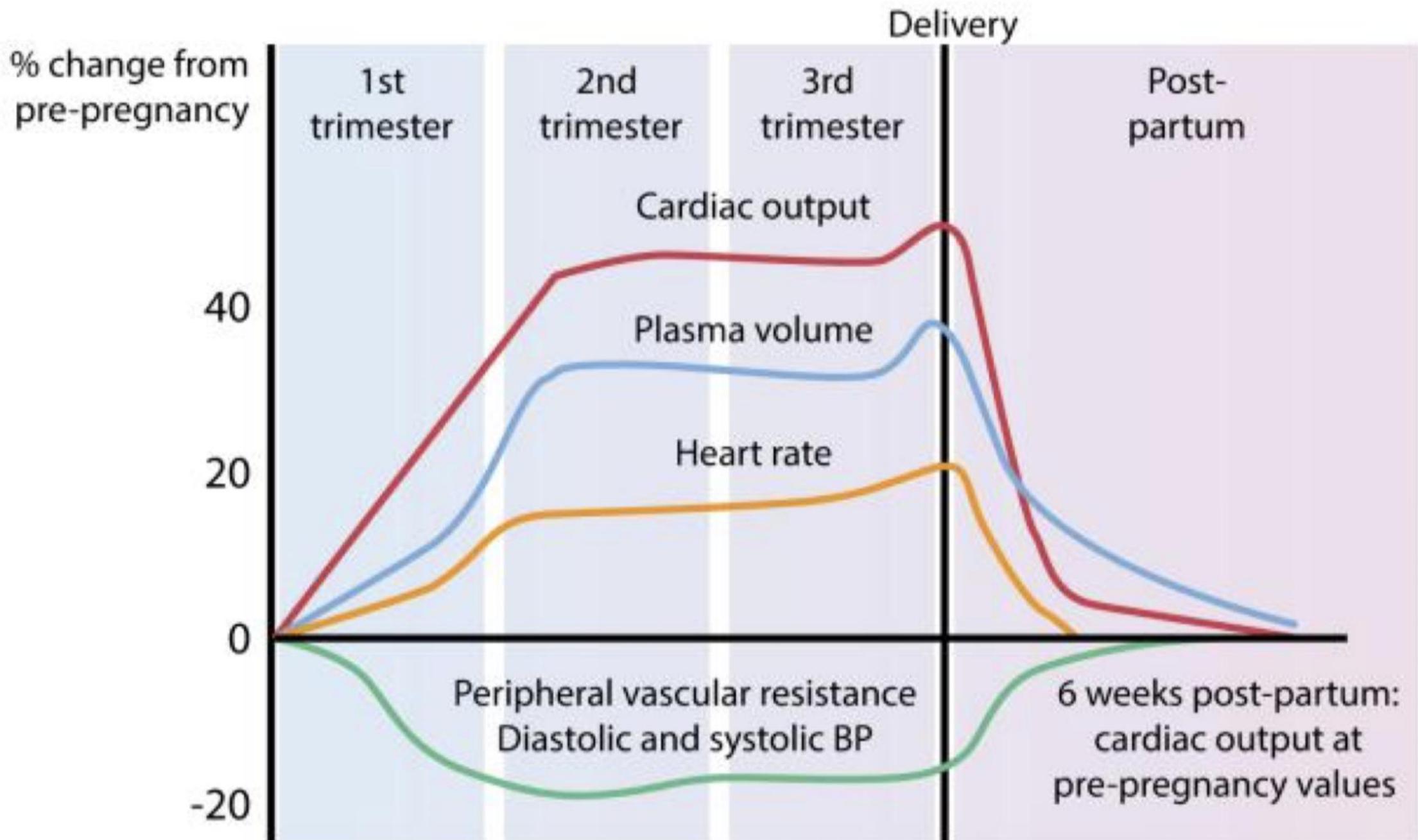
doi:10.1007/s13239-017-0322-z

Kaden JJ, Bickelhaupt S, Weiner SM, et al. Genetic polymorphisms in the calcium receptor gene and calcific aortic stenosis. **J Heart Valve Dis**. 2010;19(2):206-212. PubMed Link

## Plicní hypertenze u MS

- PH je u žen s MS výraznější než u mužů – zřejmě jde o jinou vasoreaktivitu plicního řečiště?

Hart SA, Krasuski RA, Wang A, Kisslo K, Harrison JK, Bashore TM. Pulmonary hypertension and elevated transpulmonary gradient in patients with mitral stenosis. J Heart Valve Dis. 2010;19:708–715.



# Pregnancy Heart Team

## New recommendations (1)



### Recommendations

Class Level

#### Section 4. The Pregnancy Heart Team

Although the concept of the Pregnancy Heart Team was previously part of the general principles, it has now been given its own dedicated section, which covers all aspects from pre-conception to the postpartum period.

A discussion by the Pregnancy Heart Team about the high risk of maternal morbidity and the related high foetal risk is recommended for women with class IV conditions, including a shared decision-making process involving psychological support.

It is recommended that the risk be evaluated...

**Těhotné ženy ve vysokém riziku by měly být pod dozorem „pregnancy týmu“  
Individualizace přístupu a diskuse**

enough	I	C
... prior to pregnancy in PCM, cardiomyopathy, ACHD, and ... according to the underlying disorder and in case ... symptoms.	IIa	B

2025 ESC Guidelines for the management of cardiovascular disease and pregnancy (European Heart Journal; 2025 – doi: 10.1093/eurheartj/ehaf193)

# Pregnancy Heart Team

Extended with specific multidisciplinary teams if indicated



## Pre-conception

- Risk assessment mWHO 2.0
- Genetic counselling
- Lifestyle counselling
- Reproductive technology
- Drug review
- Clinical optimization
- Contraception



## Pregnancy

- Disease-specific
- Regular follow-up and risk assessment
  - Regular foetal assessment
  - Documented delivery plan



## Delivery (plan)

- Timing and mode of delivery
- Foetal and maternal monitoring
- Anaesthesia and pain relief methods
- Drug management and bleeding control
- Device management



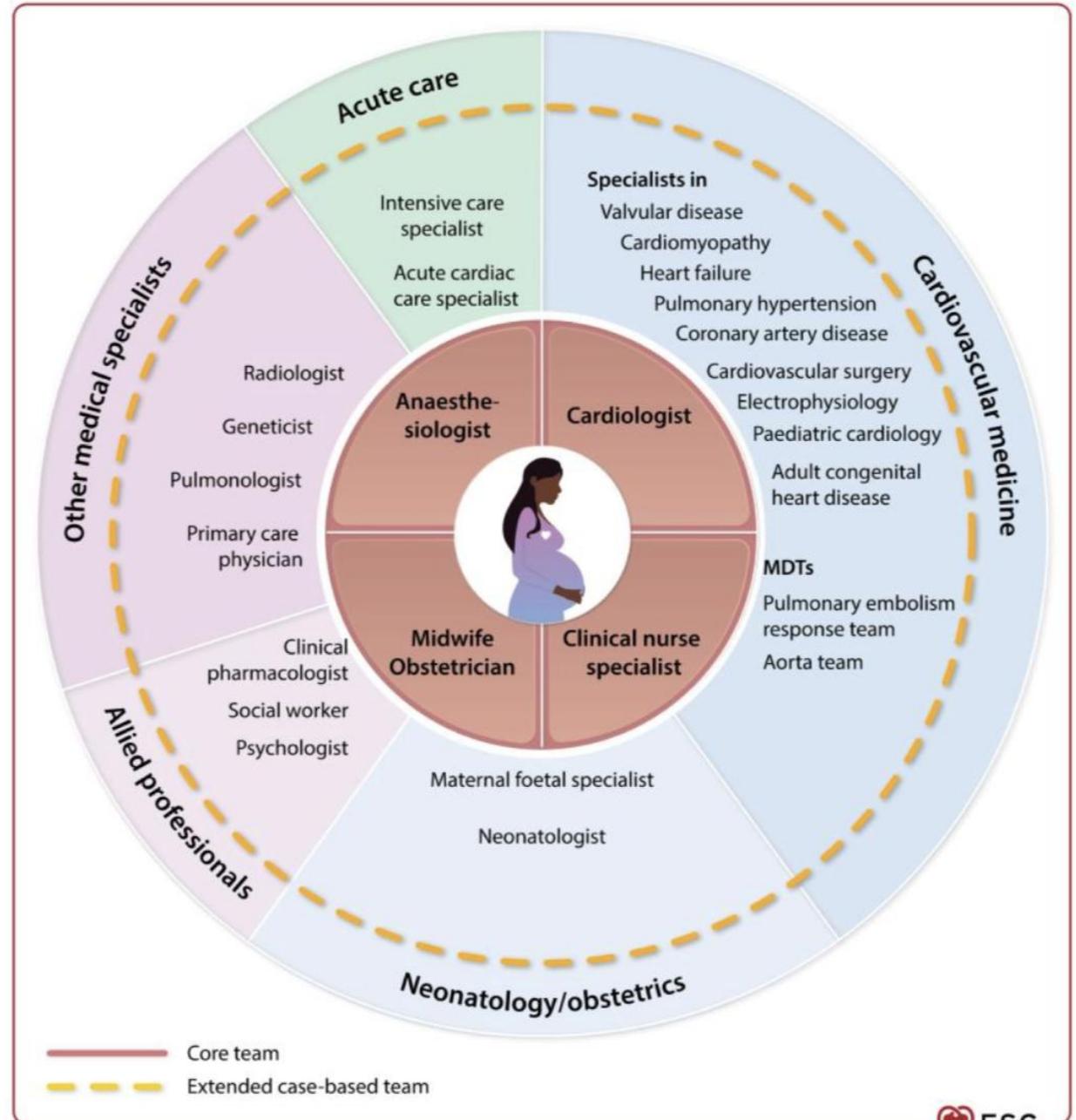
## Post-partum

- Breastfeeding and lactation
- Contraception
- Maternal cardiac follow-up



## Long term

- Identify adverse pregnancy outcome
- Women's Heart Clinic
- Cardiovascular risk factor screening

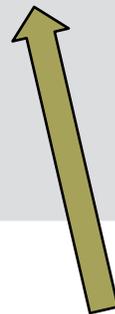
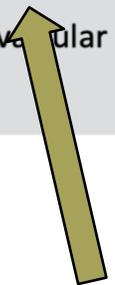
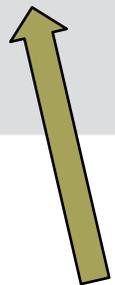


— Core team  
 - - - Extended case-based team

# Modified WHO 2.0 classification of maternal CV risk (1)

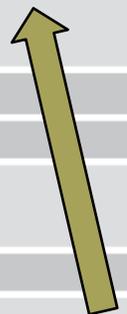
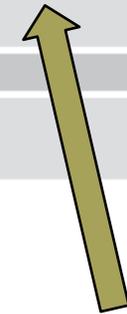
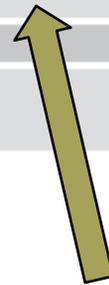
mWHO 2.0 I	mWHO 2.0 II	mWHO 2.0 II–III	mWHO 2.0 III	mWHO 2.0 IV
<b>Ventricular (dys)function + pulmonary hypertension</b>				
		Mild left ventricular impairment: EF >45% Significantly impaired RV (sub-pulmonary) function	Moderate left ventricular impairment: EF 30%–45% Previous PPCM with not more than mild residual left ventricular impairment	Severe left ventricular impairment: EF <30% or NYHA class III/IV Previous PPCM with more than mild left ventricular impairment  PAH
<b>Valvular heart disease</b>				
Small or mild pulmonary stenosis  mitral valve prolapse without significant regurgitation		Native, homograft or tissue valve disease not considered mWHO 2.0 I or IV: mild mitral stenosis, moderate aortic stenosis Moderate valvular regurgitation	Uncomplicated mechanical valve with stable well controlled INRs. Moderate mitral stenosis Severe asymptomatic aortic stenosis Severe left-sided valvular regurgitation	Severe mitral stenosis Severe symptomatic aortic stenosis

**Valvular heart disease**



# Modified WHO 2.0 classification of maternal CV risk (5)

mWHO 2.0 I	mWHO 2.0 II	mWHO 2.0 II–III	mWHO 2.0 III	mWHO 2.0 IV
<b>Risk</b>				
No detectable increased risk of maternal mortality and no/mild increased risk in morbidity	Small increased risk of maternal mortality or moderate increase in morbidity	Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity	Significantly increased risk of maternal mortality or severe morbidity	Extremely high risk of maternal mortality or severe morbidity
<b>Average maternal cardiac event rates</b>				
<i>Van Hagen et al 2016</i>				
9.9%	7.7%	17.7%	28.9%	50.3%
<i>Silversides et al 2018</i>				
3.1%	21.7%	12.8%	21.1%	35.6%



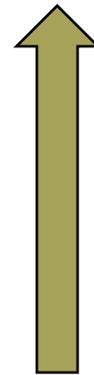
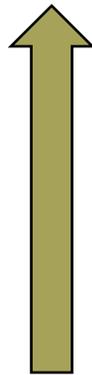
# Modified WHO 2.0 classification of maternal CV risk (6)

mWHO 2.0 I	mWHO 2.0 II	mWHO 2.0 II-III	mWHO 2.0 III	mWHO 2.0 IV
<b>Individualize each maternal risk with the modifiers below (derived from CARPREG II)</b>				
<b>CARPREG II score:1 point</b> - No prior cardiac intervention indicated - Late pregnancy assessment	<b>CARPREG II score :2 points</b> - Ventricular dysfunction - High-risk left-sided valve disease or outflow tract obstruction - Pulmonary hypertension - Coronary artery disease - High-risk aortopathy		<b>CARPREG II score:3 points</b> - Prior cardiac event or arrhythmias - Baseline NYHA III/IV or cyanosis - Mechanical valve	
<b>Involvement of the Pregnancy Heart Team</b>				
No	No		Yes	Yes
<b>Counselling</b>				
Yes: (by regular healthcare professional)	Yes: (by regular healthcare professional)		Yes: expert counselling by Pregnancy Heart Team is required	Yes: expert counselling by Pregnancy Heart Team is required, with clear and thorough discussion of very high pregnancy risk and shared decision-making process for termination if pregnancy occurs
<b>Obstetric and cardiac care during pregnancy</b>				
Local hospital	Local hospital		Shared care with local hospital + Pregnancy Heart Team.	Care led by Pregnancy Heart Team in expert centre
<b>Location of delivery</b>				
Local hospital	Local hospital		Shared care with local hospital + Pregnancy Heart Team. Location depends on CV status and evolution of pregnancy	Expert centre, care led by Pregnancy Heart Team

Yes	Yes	Yes
Yes: expert counselling by Pregnancy Heart Team is required	Yes: expert counselling by Pregnancy Heart Team is required	Yes: expert counselling by Pregnancy Heart Team is required, with clear and thorough discussion of very high pregnancy risk and shared decision-making process for termination if pregnancy occurs
Shared care with local hospital + Pregnancy Heart Team.	Care led by Pregnancy Heart Team in expert centre	Care led by Pregnancy Heart Team
Shared care with local hospital + Pregnancy Heart Team. Location depends on CV status and evolution of pregnancy	Expert centre, care led by Pregnancy Heart Team	Expert centre, care led by Pregnancy Heart Team

# ATB profylaxe IE

2018 Guidelines	Class	Level	2025 Guidelines	Class	Level
<b>Section 4. The Pregnancy Heart Team</b>					
Prophylactic antibiotic therapy to prevent endocarditis during delivery is not recommended.	<b>III</b>	<b>C</b>	Systemic antibiotic prophylaxis may be considered for delivery in women at high risk.	<b>IIb</b>	<b>C</b>



# Aortopatie

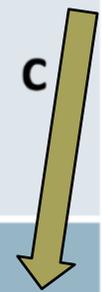
2018 Guidelines	Class	Level	2025 Guidelines	Class	Level
<b>Section 8. Recommendations for aortopathies, cardiac surgery, and pregnancy</b>					
Pregnancy is not recommended in patients with vascular Ehlers–Danlos syndrome.	<b>III</b>	<b>C</b>	It is recommended that women with vascular Ehlers–Danlos syndrome wishing to become pregnant are counselled regarding the very high risk of pregnancy-related adverse events by a multidisciplinary team, considering family history, genetic variant, and previous vascular events.	<b>I</b>	<b>C</b>
Beta-blocker therapy throughout pregnancy should be considered in women with Marfan syndrome and other heritable thoracic aortic diseases.	<b>IIa</b>	<b>C</b>	Beta-blocker therapy throughout pregnancy and in the post-partum period is recommended in women with MFS and other HTADs.	<b>I</b>	<b>C</b>



2018 Guidelines	Class	Level	2025 Guidelines	Class	Level
<b>Section 9. Recommendations for congenital heart disease and pregnancy</b>					
Patients with a systemic right ventricle (Mustard/Senning or congenitally corrected TGA), in NYHA class III/IV, systemic ventricular dysfunction (EF <40%), or severe TR, should be advised against pregnancy.	IIa	C	It is reasonable to advise patients with a systemic right ventricle, in NYHA class III/IV, systemic ventricular dysfunction (EF <40%), or severe TR, wishing to become pregnant, to be counselled by the physician regarding the risks of pregnancy.	IIb	C
Transcatheter aortic valvuloplasty should be considered during pregnancy in patients with severe aortic stenosis and symptoms.	IIa	C	Transcatheter aortic valvuloplasty should be considered during pregnancy in patients with severe aortic stenosis not responding to medical therapy, non-surgical options such as balloon valvuloplasty or TAVI may be considered.	IIb	C
Bioprosthetic aortic valve replacement should be considered in young women contemplating pregnancy.	IIa	C	A bioprosthetic valve is recommended (over a mechanical valve) in young women contemplating pregnancy requiring a valve prosthesis.	I	B

**Lehce rezervovanější přístup k intervenci u symptomatické AoS – raději medikace**

**Jednoznačné doporučení bioprotesy před plánovaným těhotenstvím**



# Aortální stenóza

## Recommendations for patients with aortic stenosis and pregnancy (1) ESC

**Závažnou AoS jednoznačně vyřešit před těhotenstvím**

Recommendation	Class	Level
Intervention is recommended before pregnancy in symptomatic patients with aortic stenosis.	I	C
Intervention should be considered before pregnancy in asymptomatic severe aortic stenosis after counselling on the risks.	IIa	C

**....a to raději dokonce i když je asymptomatická....**



## AoR a MiR

### Recommendations

Diuretics are

regurgitant

Level

C

C

Závažnou regurgitaci se symptomy, LV dysfunkcí nebo dilatací řešit před těhotenstvím

V těhotenství jsou u závažné symptomatické regurgitační vady doporučena diuretika

# Chlopenní chirurgie u těhotných

Valve surgery during pregnancy should only be considered when there is a maternal mortality risk and other treatment options have failed.

Ila

C

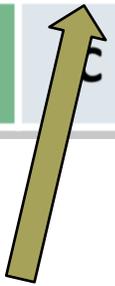
Na chirurgy se obrátit teprve tehdy, když vše ostatní selže... 😊

## Umělé chlopně

- Data from the ROPAC III study, focusing on prosthetic valves, show that the chance of an uncomplicated pregnancy with a live birth in women with a MHV was 54%, compared to 79% in women with a tissue valve.
- MHV: Thrombotic complications occur in 9%–24% and bleeding complications in 20%–30% of the cases in the ROPAC III and a United Kingdom study, respectively

# Umělé chlopně

Recommendations	Class	Level
A bioprosthetic valve is recommended (over a mechanical valve) in young women contemplating pregnancy requiring a valve prosthesis.	I	B
It is recommended that the type of valve surgery or intervention for a woman contemplating pregnancy is chosen in consultation with the Pregnancy Heart Team.	I	C



- mechanická chlopeň u mladých mužů x **bioprotéza u mladých žen**
- Možnost Valve-in-valve procedury...

## Umělé chlopně

Vysoké riziko trombózy: Warfarin ve II a III  
Nízké riziko trombózy: možno zvážit LMWH (+-ASA)

Recommendation	Class	Level
... on therapeutic-dose LMWH, it is recommended to monitor anti-Xa levels and to target levels according to individual clinical situation.	II	C
... during the second and third trimesters until the 36th week of gestation.	III	C
... considered in women with prosthetic heart valves.	III	C
... During the second and third trimesters, regular monitoring and dose adjustment are necessary.	III	C
... LMWH is not recommended.	III	C

MHV: Účinnost LMWH nutno monitorovat anti-Xa hodnotami. Pokud to není možné, aplikace LMWH není doporučena!

# Umělé chlopně

Má se stanovit a zapsat plán AK terapie pro těhotenství u pacientek s mechanickou chlopní (LMWH 1.Tri?)

INR každý týden! (max. á 2T) – stejná rozmezí

Plánovaný porod – vysadit VKA 2 týdny před (LMWH)

Pokud porod urgentní, pak podat koa faktory a porod SC

Pozor – narozený plod je až 10 dní antikoagulovaný!

Recommendations	Class	Level
A bioprosthetic valve is preferred over a mechanical valve in patients who are on long-term anticoagulation.	I	B
For patients with a mechanical valve who are on long-term anticoagulation, the use of a mechanical valve is recommended.	I	C
For patients with a mechanical valve who are on long-term anticoagulation, the use of a mechanical valve is recommended.	I	C
For patients with a mechanical valve who are on long-term anticoagulation, the use of a mechanical valve is recommended.	I	C
For patients with a mechanical valve who are on long-term anticoagulation, the use of a mechanical valve is recommended.	I	C

# Pregnancy

Physiologic Changes: Hypercoagulability - ↑ Blood Volume / Preload - ↑ Cardiac Output - ↑ Heart Rate -  
 ↓ Systemic & Pulmonary Vascular Resistance - ↓ Diastolic Filling Time - ↓ Systemic Blood Pressure - Chamber Dilation

## Stenotic Valve Disease

- Poorly tolerated
- Nodal blocking agents and diuretics first line
- Valvuloplasty considered when medical therapy fails
- If surgery required, preferred during 2<sup>nd</sup> trimester

## Regurgitant Valve Disease

- Well-tolerated due to lower SVR/afterload
- Possible symptoms in late pregnancy or post-partum period

## Prosthetic Valves

- Adverse maternal and fetal outcomes with mechanical valves during pregnancy
- Bioprosthetic valves preferred in women of childbearing age

### Aortic Stenosis

- Bicuspid AV common
- Highest risk during 2<sup>nd</sup> and 3<sup>rd</sup> trimester, labor, immediate post-partum period
- Adverse fetal outcomes

**mWHO Class IV**  
 (Pregnancy Contraindicated)  
 Severe Symptomatic Aortic Stenosis

### Mitral Stenosis

- Risk of arrhythmias (e.g. atrial fibrillation)
- Adverse fetal outcomes

**mWHO Class IV**  
 (Pregnancy Contraindicated)  
 Severe Mitral Stenosis

### Pulmonic Stenosis

- Generally well-tolerated (unlike AS/MS)
- ↑ Cardiac output ↑ gradients
- Monitor for RV failure in severe PS

### Left-Sided Regurgitation

- Surgical repair before pregnancy in severe symptomatic AR/MR
- Avoid pregnancy if severe AR/MR and LVEF < 30%
- Diuretics PRN, afterload reduction
- Avoid surgery during pregnancy

### Pulmonic Regurgitation

- Risk of RV failure in moderate to severe PR with additional risk factors (e.g. PA stenosis, RV hypertrophy or dysfunction, multiple gestation)

### Bioprosthetic

- ? Increased valvular degeneration
- Low-dose aspirin
- No adverse maternal or fetal outcomes if no valve dysfunction or thrombosis

### Mechanical

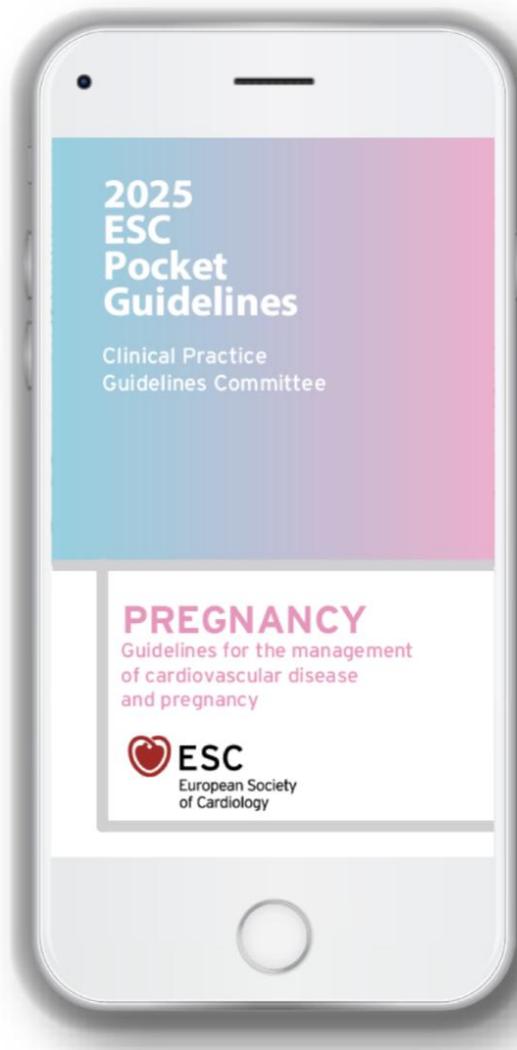
- ↑ Risk of valve thrombosis
- Warfarin associated with dose-dependent fetal birth defects in 1<sup>st</sup> trimester
- 1<sup>st</sup> trimester: Warfarin if ≤ 5 mg daily vs LMWH; 2<sup>nd</sup> trimester: warfarin; 3<sup>rd</sup> trimester: transition to LMWH at 36 weeks
- LMWH Anti-Xa goal 0.8-1.2 U/mL
- Low-dose aspirin

**mWHO Class III**  
 (Significant Morbidity & Mortality)  
 Any Mechanical Valve

#### Sex Differences and Similarities in Valvular Heart Disease

Jacqueline T. DesJardin, Joanna Chikwe, Rebecca T. Hahn, Judy W. Hung, Francesca N. Delling  
 Circulation Research [Volume 130, Number 4, https://doi.org/10.1161/CIRCRESAHA.121.319914](https://doi.org/10.1161/CIRCRESAHA.121.319914)

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