Management of Pregnant Women with Hypertrophic Cardiomyopathy

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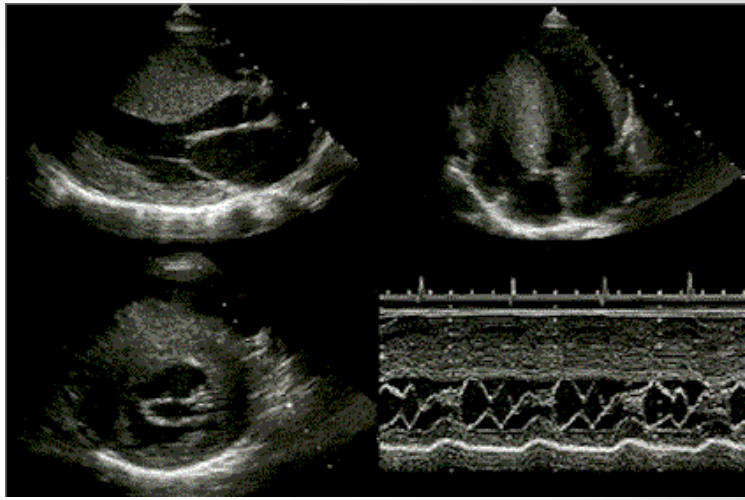
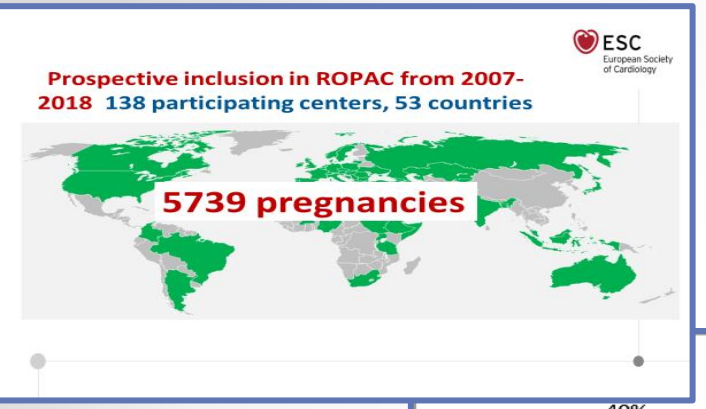
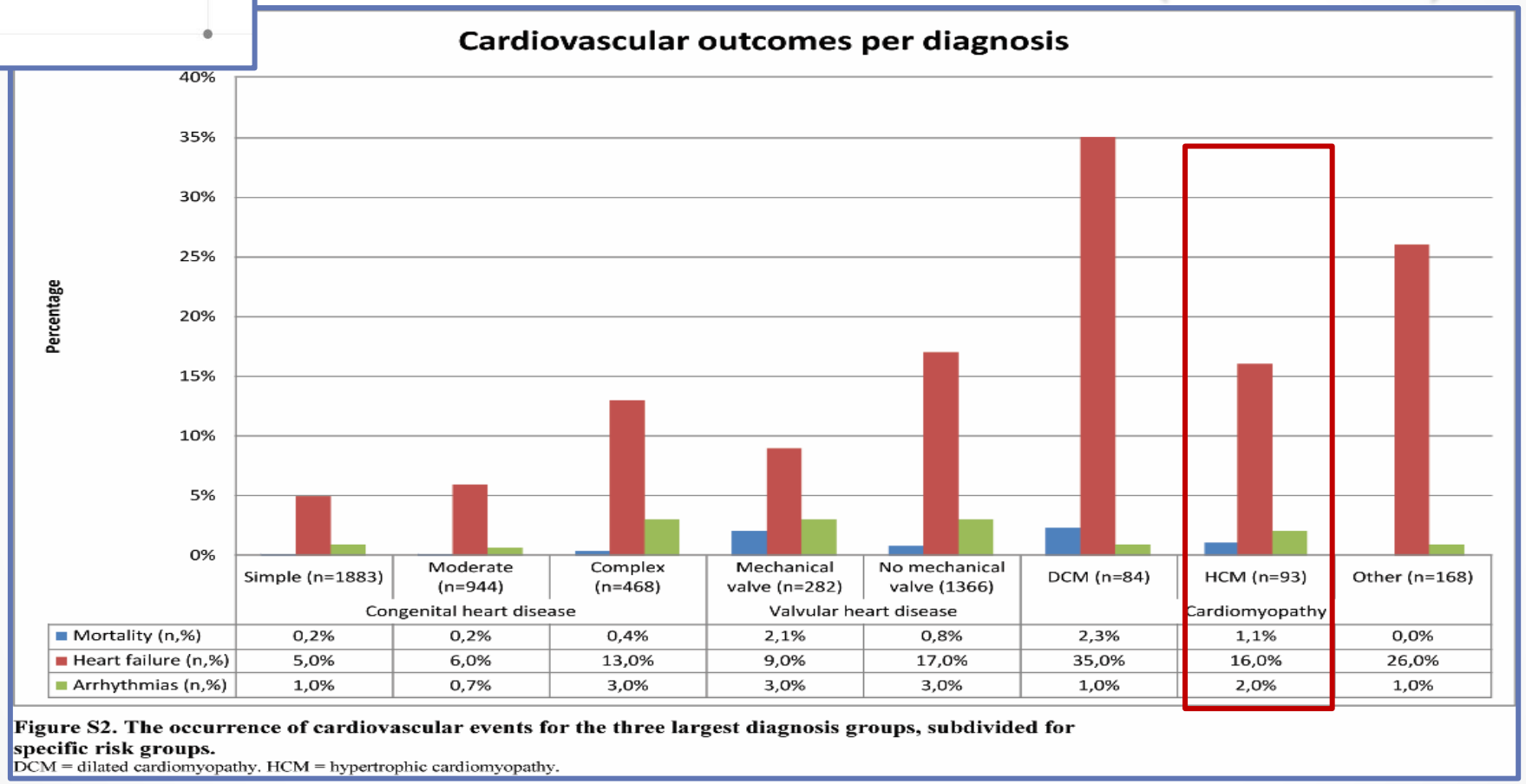
HCM and pregnancy



- Is the most common genetic cardiac disease (2% in general population)
- 30% to 60% have an identifiable pathogenic or likely pathogenic genetic variant (MYH7 & MYBPC3)
- The observed incidence of HCM in pregnancy is <1:1000
- Pregnancy-associated cardiovascular changes may exacerbate the risks of sudden cardiac death, arrhythmia, heart failure
- The risk of the fetus of inheriting the disease is ~50%

CV outcomes from Registry of Pregnancy and Cardiac disease (ROPAC)





	Simple (n=1883)	Moderate (n=944)	Complex (n=468)	Mechanical valve (n=282)	No mechanical valve (1366)	DCM (n=84)	HCM (n=93)	Other (n=168)
	Congenital heart disease			Valvular heart disease			Cardiomyopathy	
Mortality (n,%)	0,2%	0,2%	0,4%	2,1%	0,8%	2,3%	1,1%	0,0%
Heart failure (n,%)	5,0%	6,0%	13,0%	9,0%	17,0%	35,0%	16,0%	26,0%
Arrhythmias (n,%)	1,0%	0,7%	3,0%	3,0%	3,0%	1,0%	2,0%	1,0%

Figure S2. The occurrence of cardiovascular events for the three largest diagnosis groups, subdivided for specific risk groups.
DCM = dilated cardiomyopathy. HCM = hypertrophic cardiomyopathy.

Roos-Hesselink J et al. Eur Heart J. 2019 Mar 25. pii: ehz136. doi: 10.1093

The impact of pregnancy-related changes on symptom occurrence in women with HCM

- Negative hemodynamic effects :
  - ↓ in PVR
  - ↑ in CO ~50%
  - Tachycardia
- Positive effects that offsets the adverse effect of the fall in PVR on the LVOT gradient:
  - ↑ Blood volume
  - ↑ LV size
- At the time of delivery , the auto-transfusion from the uterus into the systemic circulation and stress related tachycardia that may lead to clinical deterioration

2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC)

Risk class	Risk of pregnancy	Application to HCM
I	No detectable increased risk of maternal mortality and no/mild risk of morbidity	-
II	Small increased risk of maternal mortality or moderate increase in morbidity	Most women with HCM: mild to moderate LVOTO; asymptomatic with or without medication, well-controlled arrhythmia, normal systolic LV function or mild LV dysfunction
III	Significantly increased risk of maternal mortality or severe morbidity	Severe LVOTO, symptoms or arrhythmias despite optimal medication, moderate systolic LV dysfunction
IV	Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated	Severe systolic LV dysfunction, severe symptomatic LVOTO

2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2733–2779.

Regitz-Zagrosek V., Roos-Hesselink J.W., Bauersachs J., et. al.: 2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy. Eur Heart J 2018; 39: pp. 3165-3241.

Clinical course and prognosis

Symptoms

- Dyspnea
- Fatigue
- Chest pain
- Syncope

→ **worsen, especially in pts who were already symptomatic**

- The rates of cardiovascular complications significantly vary between reports (2 - 48%)

- Most of the reports are retrospective or include small case series and may suffer from selection bias including more severe cases

Data on HCM and pregnancy

4 contemporary series 2002-2017

- Autore et al 2002: 100 women,199 pregnancies
- Thaman et al: (questionnaire): 127 women, 271 pregnancies
- Avila et al 2007: 23 pregnant and 12 nonpregnant HCM patients
- Tanaka et al 2014 : 27 pregnancies in HCM patients
- Schinkel et al. 2014 review of the existing literature: 237 women with HCM and 408 pregnancies

Autore C et al J Am Coll Cardiol. 2002 Nov 20;40(10):1864-9
Avila W S et al . Arg Bras Cardio 2007 Apr;88(4):480-5
Tanaka H et al. Circ J .2014;78(10):2501-6
Schinkel A F. Sep-Oct 2014;22(5):217-22

Pregnancy in women with HCM: data from the European Society of Cardiology initiated Registry of Pregnancy and Cardiac disease (ROPAC)

- Pregnancies of 60 women with HCM (2007 -2014)
- Definition of HCM: LVWT of ≥15mm on echo, CMR or CT

  HOCM – LVOT peak grad ≥ 30 at rest or provoked ≥ 50 mmHg
- The primary endpoint was a major adverse cardiovascular event (MACE), collected up to 1 week after delivery:
  - maternal death
  - heart failure
  - thromboembolic events
  - supraventricular or ventricular tachyarrhythmia
- Follow-up at 6 months was available in 49 /60 (81.7%) pregnancies

Goland S et al. European Heart Journal 2017

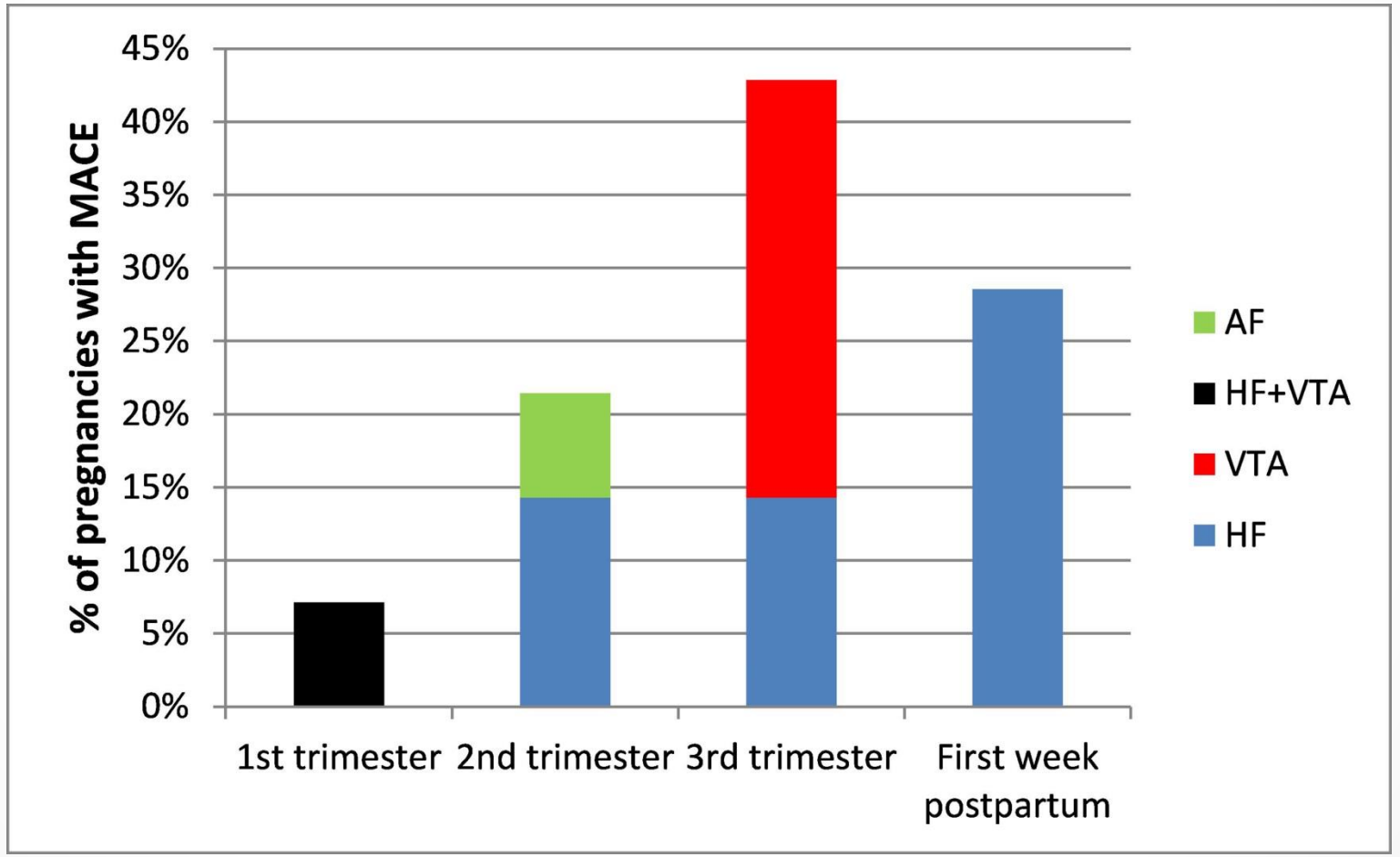
Clinical characteristics

- Mean age was 30.4 (±6.0) years; 50.0% were nulliparous
- 42 % with obstructive HCM
- 13.3% had a prior intervention
  - 3 patients had undergone septal myectomy,1 an alcohol septal ablation, 1 surgical MV repair
- In 4 patients an ICD was implanted
- During pregnancy 48.3% patients were treated :
  - 40.0% BB
  - 8.3% CCB
  - 6.7 % diuretics
  - 5% antiarrhythmic medications

Major adverse cardiovascular events

- No maternal mortality occurred in our cohort.
- **23% patients at least had one MACE :**
- 15% Heart Failure
- 12% Arrhythmias (6 ventricular and 1 AF).
- Mostly MACE occurred during the 3rd trimester and postpartum.

Timing and type of first MAE during pregnancy in women with HCM



Univariable analysis of predictors of MACE in women with HCM

Predictors of MACE	With MACE		Without MACE		OR	95% CI	*P*-value
	n = 14 (23.3%)		*n* = 46 (76.7%)				
Nulliparity	8	(57.1%)	22	(47.8%)	1.46	(0.44–4.86)	0.54
Hypertension before pregnancy	4	(30.8%)	4	(8.9%)	4.56	(0.96–21.7)	0.057
Mitral regurgitation	5	(35.7%)	16	(35.6%)	1.01	(0.29–3.52)	0.99
RVSP>30 mmHg	3	(21.4%)	2	(4.5%)	5.73	(0.85–38.6)	0.07
Septum thickness (Q1–Q3)	18	(17–27)	18.5	(13–25)	1.03	(0.95–1.12)	0.48
LV posterior wall thickness (Q1–Q3)	14	(11–16)	12	(10–14)	1.15	(0.94–1.42)	0.18

CI, confidence interval; NYHA, New York Heart Association functional class; OR, odds ratio; Q1–Q3, 1st to 3rd quartile; RVSP, right ventricular systolic pressure.

NYHA functional class of ≥ II and signs of HF before pregnancy, were associated with MACE.

Obstetric and fetal outcome of pregnancy with HCM

	All women with HCM *n* = 60		Women with MACE *n* = 14 (23.3%)		Women without MACE *n* = 46 (76.7%)		*P*-value
(Pre-)eclampsia or HELLP	3	5.0%	2	14.3%	1	2.2%	0.13
Pregnancy-induced hypertension	0	0.0%	0	0.0%	0	0.0%	na
Postpartum haemorrhage	1	1.7%	1	7.1%	0	0.0%	0.23
Caesarean section	36	60.0%	12	85.7%	24	52.2%	0.031
Emergency CS for a cardiac reason	3	5.0%	3	21.4%	0	0.0%	0.011
Miscarriage <24 weeks	1	1.7%	0	0.0%	1	2.2%	1.00
Foetal death ≥24 weeks	2	3.3%	1	7.1%	1	2.2%	0.42
Termination of pregnancy	0	0.0%	0	0.0%	0	0.0%	na
Small-for-gestational age	9	16.1%	2	14.3%	7	16.7%	1.00
Preterm birth (<37 weeks)	14	24.6%	4	30.8%	10	22.7%	0.72
Low Apgar (<7)	6	11.1%	1	7.7%	5	12.2%	1.00
Pregnancy duration, weeks (Q1–Q3)	38.3	(36.9–39.1)	37.4	(34.6–38.3)	38.6	(36.9–39.9)	0.037
Birthweight, g (Q1–Q3)	3000	(2500–3280)	2900	(2555–3228)	3045	(2488–3389)	0.56
Neonatal death, ≤1 week	0	0.0%	0	0.0%	0	0.0%	na

CS, Caesarean section; HELLP, haemolysis elevated liver enzymes and low platelets; MACE, major adverse cardiac event; na, not applicable; Q1–Q3, 1st to 3rd quartile.
[a]Two patients with heart failure also developed a ventricular arrhythmia.

Comparison with outcomes from previous studies

Heart Failure and LVOT obstruction

- Heart Failure 15% (ROPAC)
- Mainly during the 3rd trimester, but there was no difference in outcome between women with HOCM and non-obstructive HCM.

- Heart Failure 30%
- Mainly during the 3rd trimester, LVOT obstruction had no influence on maternal outcome

Avila WS et al Arq Bras Cardiol 2007;88:480–485

- Heart Failure 30%
- HF symptoms tended to worsen more often in those with HOCM (25% vs. 11%, P=NS)

Autore C et al. Am Coll Cardiol 2002;40:1864–1869.

Comparison with outcomes with previous studies

Mortality

- ROPAC – No mortality at 6 months
- Mortality 0%-2% was obtained from few retrospective studies
  - *Avila WS, et al. Clin Cardiol 2003;26:135–142.*
  - *Siu S et al. Circulation 2001;104:515–521.*
  - *Autore C, et al J Am Coll Cardiol 2002;40:1864–1869.*
- Mortality rate of 0.5% from a recent review (pooled analysis of 408 pregnancies)
  - *Schinkel AF. Cardiol Rev 2014;22:217–222.*

Predictors of maternal complications based on 5 published studies on HCM and pregnancy

- NYHA class of ≥ II
- Signs of HF before pregnancy
- Cardiac medication before pregnancy
- CARPREG or ZAHARA score ≥ 1
- Severe LVOT obstruction

Management of pregnant women with HCM pre-pregnancy evaluation

A detailed evaluation prior to conception

- Family history
- Physical examination, ECG, TTE
- Serum BNP or NT-pro BNP levels
- Stress echo testing and if needed cardiopulmonary exercise test
- 48 hours ambulatory EKG monitoring
- CMR if needed
- Genetic counseling before planned conception for the mother and father
- The potential risk of complications should be discussed with the woman and her family

Management of pregnant women with HCM

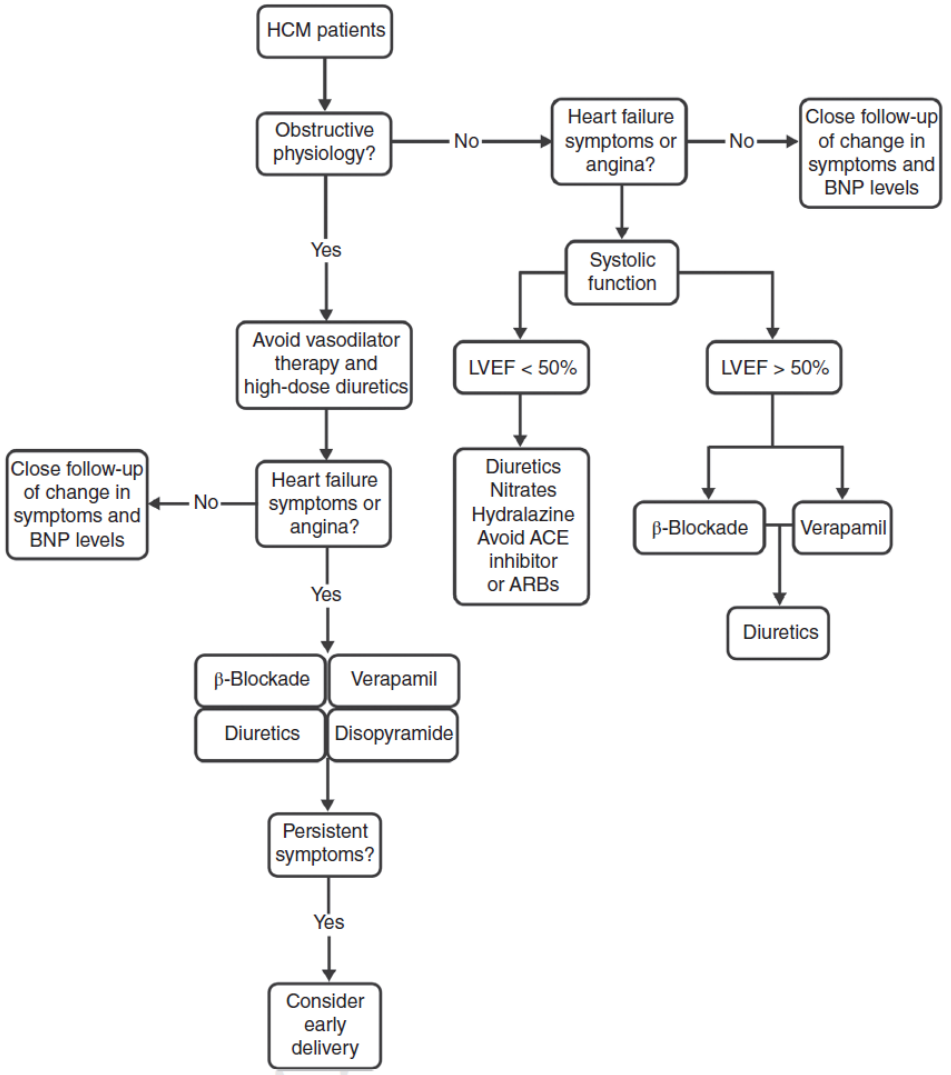
pre-pregnancy evaluation

- In the asymptomatic patient/mild disease: no prophylactic treatment
- Patients with moderate or severe symptoms of heart failure (NYHA III and IV) should be advised against pregnancy.
- Such patients should attempt pregnancy only after a significant symptomatic improvement (to NYHA functional class I or II) on medical therapy achieved with drugs safe for the fetus, (β-adrenergic blocking agents, calcium channel blockers, disopyramide), or surgical/interventional treatment
- ICD implantation should also be considered in patients with HCM with a high risk of sudden cardiac death.

Management during pregnancy

- Follow-up each trimester (low-risk) or monthly/bimonthly (increased risk)
- Clinical assessment, echocardiography
- In the asymptomatic patient/mild disease, no prophylactic treatment is necessary
- Continue beta-blocker or start when symptomatic
- Treat any tachyarrhythmia with medication/cardioversion as needed
- Patients who meet criteria for placement of ICD, should have it done prior to conception

Management of pregnant women with HCM during pregnancy



Management during delivery

- **Vaginal delivery appropriate**
- Blood pressure and rhythm monitoring
- Monitor preload using echo when necessary
- Cautious use of epidural or spinal anesthesia
- Replace fluid loss, avoiding overhydration
- Oxytocin only as slow iv infusion
- Clinical observation for at least 24 h post-delivery

2018 ESC Guidelines for the management of cardiovascular diseases during pregnancy

In patients with HCM, the same risk stratifications as for non-pregnant women are recommended.[313]	I	C
In patients with HCM, it is recommended that beta-blockers are continued in women who used them before pregnancy.[313]	I	C
In patients with HCM, beta-blockers should be started in women who develop symptoms due to outflow tract obstruction or arrhythmia during pregnancy.	IIa	C
In HCM, cardioversion should be considered for persistent atrial fibrillation.[306]	IIa	C

2020 AHA/ACC Guideline for the Diagnosis and Treatment

1	C-LD	3. In most pregnant women with HCM, vaginal delivery is recommended as the first-choice delivery option (4,6).
1	B-NR	4. In affected families with HCM, preconceptional and prenatal reproductive and genetic counseling should be offered (4–7).
1	C-EO	5. For pregnant women with HCM, care should be coordinated between their cardiologist and an obstetrician. For patients with HCM who are deemed high risk, consultation is advised with an expert in maternal-fetal medicine.
2a	C-LD	6. For women with clinically stable HCM who wish to become pregnant, it is reasonable to advise that pregnancy is generally safe as part of a shared discussion regarding potential maternal and fetal risks, and initiation of guideline-directed therapy (8–11).
2a	C-LD	7. In pregnant women with HCM, cardioversion for new or recurrent AF, particularly if symptomatic, is reasonable (7,12).
2a	C-LD	8. In pregnant women with HCM, general or epidural anesthesia is reasonable, with precautions to avoid hypotension (9).
2a	C-EO	9. In pregnant women with HCM, it is reasonable to perform serial echocardiography, particularly during the second or third trimester when hemodynamic load is highest, or if clinical symptoms develop (8).
2b	C-EO	10. In pregnant women with HCM, fetal echocardiography may be considered for diagnosis of fetal HCM in the context of prenatal counseling.

Ommen S R et al , 2020 JACC 2020

Conclusions

- Most women with HCM tolerated pregnancy well with very low mortality
- Cardiovascular complications are not uncommon and influenced fetal outcome and delivery
- Functional status and signs of HF prior to pregnancy are important risk factors for cardiac complications
- Pre-pregnancy counseling including genetic, monitoring and optimal care are important to prevent complications in women with HCM

Thank you

Case

- A 38-year-old pregnant woman presented to the high-risk pregnancy clinic
- Past medical history of familial HCM and also a family history of SD
- At the age of 36 she underwent placement of an AICD
- At 13 weeks of her first pregnancy she was in a good functional capacity
- Echocardiography demonstrated LV hypertrophy, LVEF of 50%
- LV function remained preserved during the 2nd and 3rd trimester
- Her obstetric follow up was unremarkable, at 35 weeks she presented with premature contractions and heart failure and NSVT (metoprolol was initiated)
- No LVEF changes compared with her previous imaging tests
- The same clinical scenario of HF and NSVT 14 hours after delivery