Pregnancy in Women with Hypertrophic Cardiomyopathy (data from ROPAC)

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Background

- Hypertrophic Cardiomyopathy (HCM) is the most common genetic cardiac disease with prevalence of 2% in general population
- It is associated with an increased risk of sudden cardiac death, arrhythmia and heart failure
- Pregnancy-associated cardiovascular changes may exacerbate these risks
- The risk of the fetus of inheriting the disease is ~50%

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

Background

- Generally women tolerate pregnancy well
- 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

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

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Aim

- To provide information on the outcome of pregnancy in a cohort of pregnant women with HCM recruited to the observational, contemporary, worldwide Registry of Pregnancy and Cardiac disease (ROPAC).
- To identify women at high-risk of an adverse outcome.

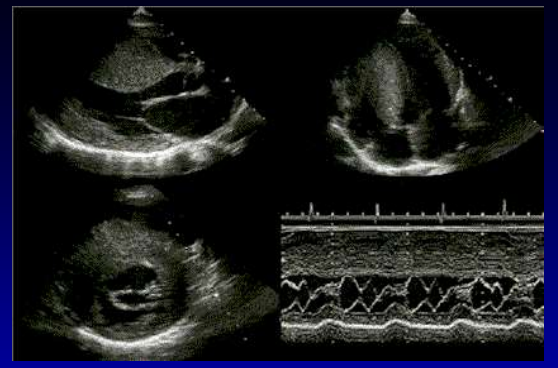
Methods

- ROPAC is prospective worldwide registry which includes consecutive pregnant women with structural heart disease
- Data were prospectively collected, and centers could also retrospectively include all consecutive patients up to 6 months before study entry.
- Pregnancies of women with HCM included 2007 - 2014 were selected

Methods

- The primary endpoint was a major adverse cardiovascular event (MACE), collected up to 1 week after delivery, including :
- maternal death
- heart failure
- thromboembolic events
- supraventricular or ventricular tachyarrhythmia
- Follow-up at 6 months was available in 49 /60 (81.7%) pregnancies

HCM definition



- The presence of increased LV wall thickness that is not solely explained by abnormal loading conditions
- The diagnosis HCM was confirmed if one or more LV myocardial segments showed a thickness of ≥15mm on echocardiography, CMR or CT.
- Obstructive HCM was defined as ‘an instantaneous peak Doppler LV outflow tract pressure gradient ≥ 30mm Hg at rest or Valsalva maneuver, standing or exercise

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.

Clinical characteristics

- 60 women from ROPAC from 28 centers in 19 countries
- Mean age was 30.4 (±6.0) years
- 30 (50.0%) were nulliparous
- All pregnancies were singleton
- 25 (41.7%) with obstructive hypertrophic cardiomyopathy

Goland S et al JACC 2017

Clinical characteristics

- 8 patients (13.3%) had a prior intervention
  - 3 patients had undergone septal myectomy
  - 1 an alcohol septal ablation
  - 1 surgical repair of the MV
- In 4 patients (6.7%) an implantable cardioverter-defibrillator (ICD) was implanted
- During pregnancy 48.3% patients were treated :
  - 40.0% BB
  - 8.3% CCB
  - 6.7 % diuretics and 5% antiarrhythmics

Results

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.

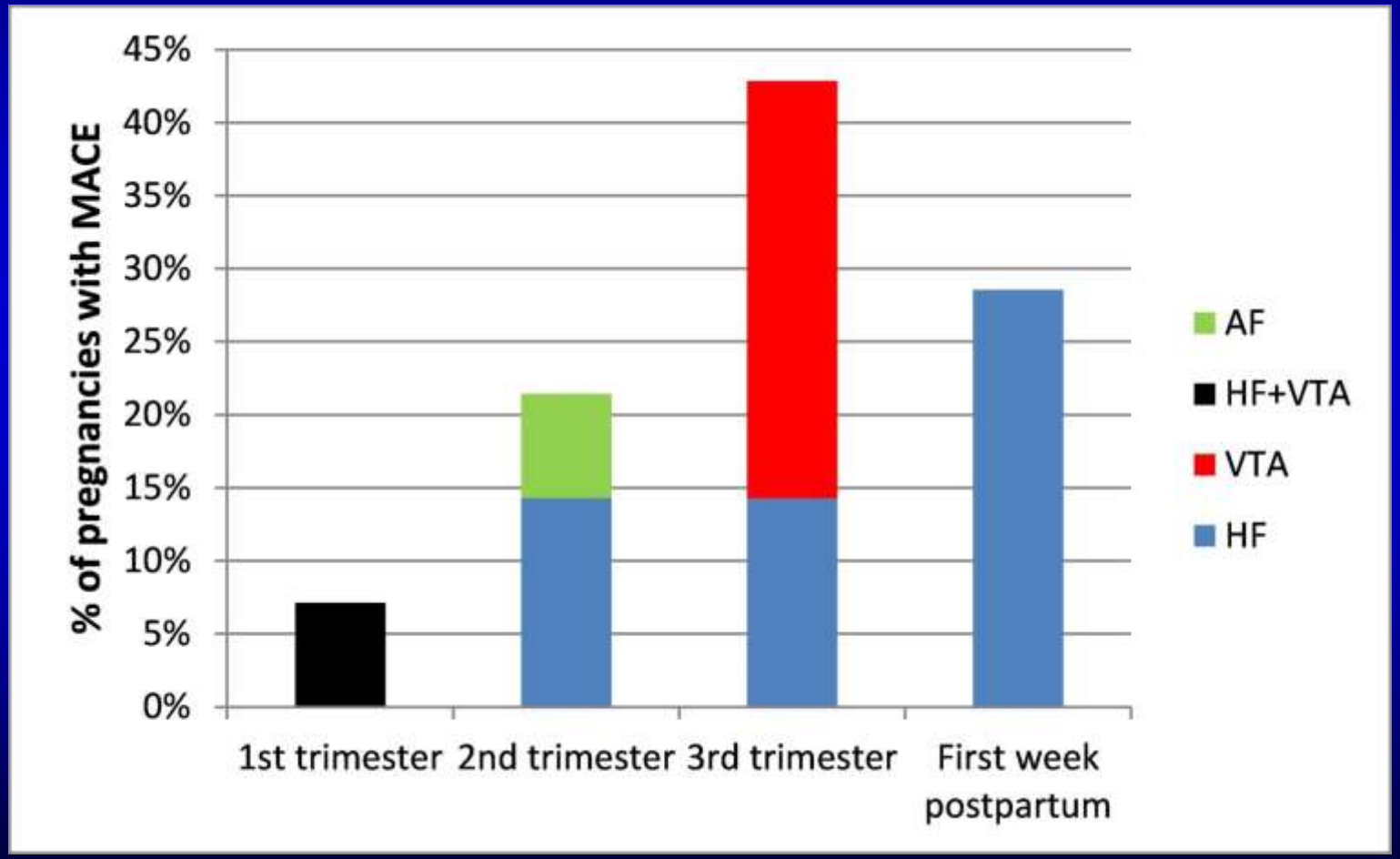
Univariable analysis of predictors of MACE in women with HCM

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

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
NYHA class >1	9	(64.3%)	8	(18.6%)	8.55	(2.26–32.4)	0.002
Signs of heart failure	4	(28.6%)	1	(2.3%)	17.2	(1.73–171)	0.015
Obstructive cardiomyopathy	4	(28.6%)	21	(45.7%)	0.48	(0.13–1.74)	0.26
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.

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



Obstetric and fetal outcome of pregnancy with HCM

	All women with HCM		Women with MACE		Women without MACE		
	n = 60		*n* = 14 (23.3%)		*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.

Outcome in women with obstructive and non-obstructive HCM

	Women with obstructive HCM $n = 25$ (41.7%)		Women with non-obstructive HCM $n = 35$ (58.3%)		*P*-value
MACE[a]					
Maternal mortality	0	0%	0	0%	na
Heart failure	2	8.0%	7	20.0%	0.28
Supraventricular tachyarrhythmia	1	4.0%	0	0%	0.42
Ventricular tachyarrhythmia	1	4.0%	5	14.3%	0.39
Thrombo-embolic complication	0	0%	0	0%	na
Hospital admission	8	32.0%	13	38.2%	0.62
Cardiac hospital admission	4	16.0%	8	22.9%	0.51
(Pre-)eclampsia or HELLP	0	0.0%	3	8.6%	0.26
Postpartum haemorrhage	0	0.0%	1	2.9%	1.00
Caesarean section	14	56.0%	22	62.9%	0.59
Emergency CS for a cardiac reason	2	8.0%	1	2.9%	0.57
Miscarriage <24 weeks	0	0.0%	1	2.9%	1.00
Foetal death ≥24 weeks	1	4.0%	1	2.9%	1.00
Small-for-gestational age	4	16.7%	5	15.6%	1.00
Preterm birth (<37 weeks)	4	16.7%	10	30.3%	0.24
Low apgar (<7)	5	21.7%	1	3.2%	0.073
Pregnancy duration, weeks (Q1–Q3)	38.6	(37.0–39.1)	38.1	(36.4–39.6)	0.70
Birthweight, g (Q1–Q3)	3014	(2568–3258)	3000	(2420–3450)	0.80

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 with previous studies
Heart Failure

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

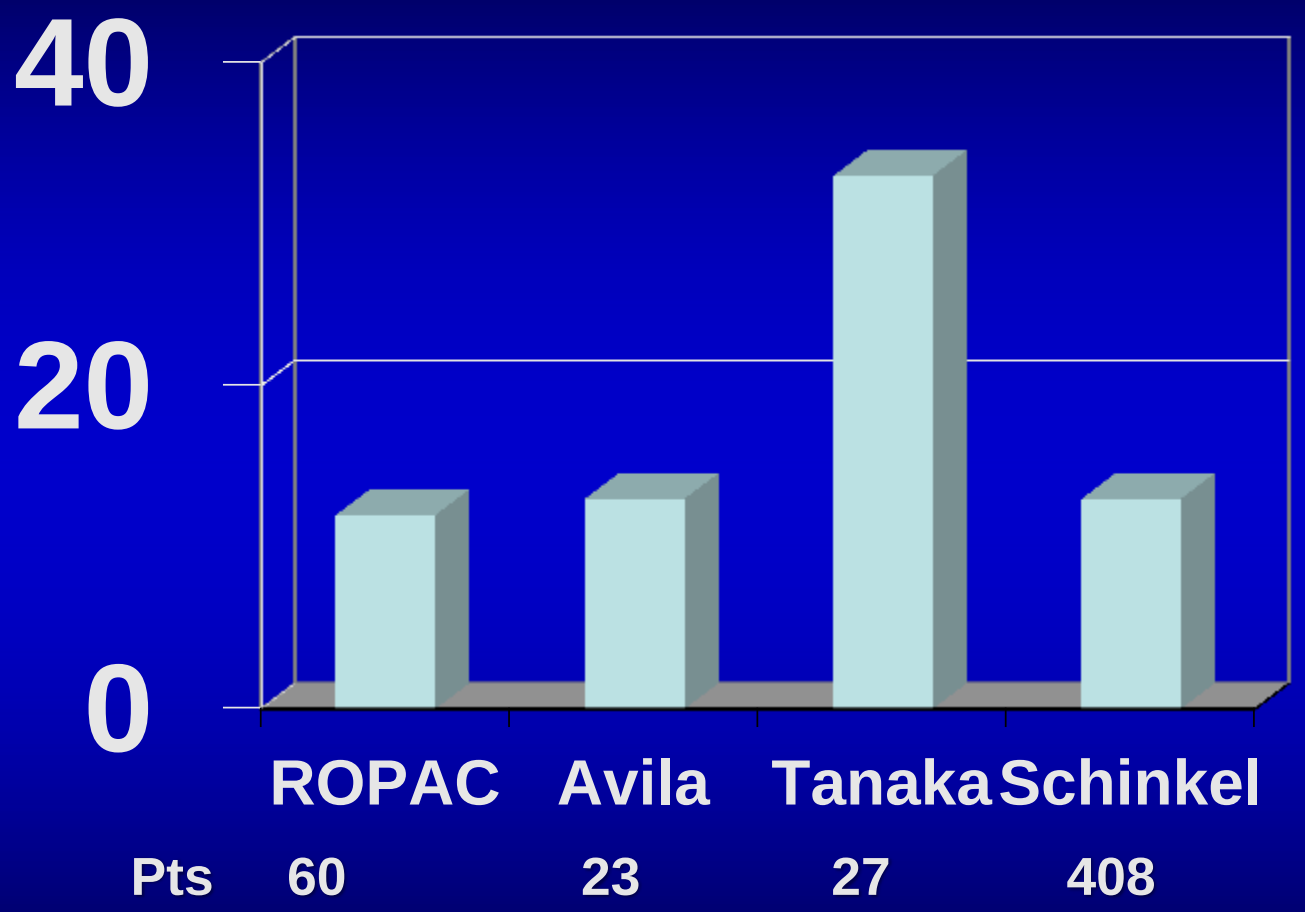
Heart Failure 30%

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

Arrhythmias



Tanaka R et al Circ J 2014;78:2501–2506.
Avila WS, et al. Clin Cardiol 2003;26:135–142.
Schinkel AF. Cardiol Rev 2014;22:217–222.

Comparison with outcomes with previous studies
Mortality

- ROPAC – No mortality
- 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 recent review (pooled analysis of 408 pregnancies)

Schinkel AF. Cardiol Rev 2014;22:217–222.

Conclusions

- Considerable progress has been made in the evaluation, risk assessment, and management in patients with HCM.
- **Most women with HCM tolerated pregnancy well and there was no mortality.**
- **However, cardiovascular complications were not uncommon and influenced fetal outcome and delivery.**
- **Functional status and signs of heart failure prior to pregnancy are important risk factors for cardiac complications .**
- **Pre-pregnancy counseling, monitoring and optimal care are mandatory to prevent complications in women with HCM.**

Thank you!