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*Published in:*
European Heart Journal

*DOI:*
10.1093/eurheartj/ehx189

ESC European Society of Cardiology

European Heart Journal (2017) **38**, 2683–2690
doi:10.1093/eurheartj/ehx189

**CLINICAL RESEARCH**
*Heart failure/cardiomyopathy*

# 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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*Received 24 November 2016; revised 27 February 2017; editorial decision 23 March 2017; accepted 27 April 2017; online publish-ahead-of-print 10 May 2017*

**See page 2691 for the editorial comment on this article (doi: 10.1093/eurheartj/ehx304)**

**Aims** We report the maternal and foetal outcomes at birth and after 6 months in a cohort of pregnant women with hypertrophic cardiomyopathy (HCM). Although most women with HCM tolerate pregnancy well, there is an increased risk of obstetric and cardiovascular complications.

**Methods and results** All pregnant women with HCM entered into the prospective worldwide Registry of Pregnancy and Cardiac disease (ROPAC) were included in this analysis. The primary endpoint was a major adverse cardiovascular event (MACE), which included death, heart failure (HF), thrombo-embolic event, and arrhythmia. Baseline and outcome data were analysed and compared for patients with MACE vs. without MACE and for patients with obstructive HCM vs. non-obstructive HCM. Sixty pregnant women (mean age 30.4 ± 6.0 years) with HCM (41.7% obstructive) were included. No maternal mortality occurred in this cohort. In 14 (23%) patients at least one MACE occurred: 9 (15.0%) HF and 7 (12%) an arrhythmia (6 ventricular and 1 atrial fibrillation). MACE occurred most commonly during the 3rd trimester and postpartum period. In total, 3 (5.0%) women experienced foetal loss. Women with MACE had a higher rate of emergency Caesarean delivery for cardiac reasons (21.4% vs. 0%, $P = 0.01$). No significant differences in pregnancy outcome were found between women with obstructive and non-obstructive HCM. NYHA functional class of ≥II and signs of HF before pregnancy, were associated with MACE.

**Conclusion** Although most women with HCM tolerated pregnancy well, cardiovascular complications were not uncommon and predicted by pre-pregnancy status facilitating pre-pregnancy counselling and targeted antenatal care.

**Keywords** Pregnancy • Hypertrophic • Cardiomyopathy • Outcome

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# Introduction

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiac disease and has a prevalence of 2% in the general population. The widespread use of echocardiography and genetic screening for HCM has led to a growing number of young women diagnosed with HCM where most of them desire pregnancy. HCM in the non-pregnant state is associated with an increased risk of sudden cardiac death, arrhythmia, and heart failure and the pregnancy-associated changes in the cardiovascular system may exacerbate these risks, although their impact on maternal haemodynamics is not well understood. During pregnancy, there is an initial fall in peripheral vascular resistance occurring predominantly during the 1st and 2nd trimesters. This results in an increase in cardiac output of around 50% due to the combination of a greater stroke volume and higher heart rate.[1,2] The increase in blood volume and consequently of left ventricular size offsets the adverse effect of the fall in peripheral vascular resistance on the LVOT gradient. In addition, enhanced LV contractility and higher heart rate with a shortened diastolic filling time, could exacerbate or precipitate heart failure and may not be well tolerated. Moreover, at the time of delivery, the auto-transfusion from the contracting uterus into the systemic circulation and stress related tachycardia during delivery and early postpartum, may lead to clinical deterioration. Despite these potential complications, it appears that most women with HCM tolerate pregnancy well. Previous studies report widely differing rates of cardiovascular complications, varying between 2 and 48%. However, most of the reports are retrospective or include small case series and may suffer from selection bias including more severe cases.[3–8]

This prospective study aims 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). Such information may be helpful in pre-pregnancy counselling of women with HCM and identifying women at high-risk of an adverse outcome.

# Methods

ROPAC is an ongoing prospective and worldwide registry initiated in 2007 by the European Society of Cardiology working groups on valvular heart disease and on congenital heart disease.[9] All consecutive pregnant women with structural heart disease, aortic pathology or pulmonary hypertension were included; non-structural heart diseases such as lone arrhythmic disease were excluded. Data were prospectively collected, and centres could also retrospectively include all consecutive patients up to 6 months before study entry. For this interim analysis, pregnancies in women with hypertrophic cardiomyopathy who were included in the study from 2007 up to 2014 were selected.

## Data

The patient characteristics collected at baseline (before pregnancy) included age, ECG rhythm, diagnosis, risk factors for cardiovascular disease (smoking, diabetes, hypertension), previous interventions, medication, parity, obstetric history and facultative echocardiographic parameters. Follow-up was available for all patients up to 1 week after delivery; in addition follow-up at 6 months was available for part of the cohort. Patient characteristics and events were reported by the individual sites and did not undergo centralized adjudication. However, all events were predefined in the case report form.

## Definitions

HCM was defined 'by the presence of increased left ventricular wall thickness that is not solely explained by abnormal loading conditions'.[10] The diagnosis HCM was confirmed if one or more left ventricular (LV) myocardial segments showed a thickness of ≥15 mm on echocardiography, cardiac resonance imaging or computed tomography. Obstructive HCM was defined as 'an instantaneous peak Doppler LV outflow tract pressure gradient ≥30 mm Hg at rest or during physiological provocation such as Valsalva maneuver, standing and exercise' (2014 ESC guidelines[10]). These diagnostic features were confirmed in each patient by the local cardiologist. LVOT gradient was not collected as separate variable, and therefore could not be analysed.

The *primary endpoint* was a major adverse cardiovascular event (MACE), collected up to 1 week after delivery, including maternal death, heart failure (HF), thrombo-embolic events, and supraventricular or ventricular tachyarrhythmia. *Heart failure* was defined according to ACC/AHA guidelines as a clinical syndrome that is characterized by specific symptoms (dyspnea and fatigue) and signs (of fluid retention, such as oedema, or rales) on physical examination as judged by the treating cardiologist.[11,12] The heart failure episode was only registered when signs or symptoms of HF were present which required new treatment, change of treatment or hospital admission. A *ventricular tachyarrhythmia* (VTA) was defined as three or more consecutive ventricular beats with a mean rate of more than 100 beats per minute; however, only clinically relevant VTA (when the patient had physical complaints, needed treatment for VTA or when the patient had more than 100 consecutive beats) was included. Other endpoints of interest were hospitalization for a cardiac reason, a Caesarean delivery for a cardiac reason, birth weight, small for gestational age (birth weight <10th percentile), miscarriage (<24 weeks), foetal death (≥24 weeks), neonatal death, termination of pregnancy, and preterm birth (<37 weeks).

Baseline and outcome data were analysed for the total group; patients with and without MACE were compared and those with obstructive HCM compared with those with non-obstructive HCM.

## Statistical analysis

Continuous variables are presented as mean and standard deviation, or as median and quartiles where appropriate. Differences were assessed with Student's *t*-test. Categorical variables are presented as percentages and differences were assessed using $\chi^2$ tests. Predictors of MACE were identified by performing univariable logistic regression analyses. The number of events ($n = 15$) did not allow for multivariable regression analysis. Statistical tests were considered significant if a p-value was less than 0.05 (two-sided). All analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY).

# Results

Sixty pregnancies in women with hypertrophic cardiomyopathy were included, from 28 centres in 19 countries; the majority were from countries with an advanced economy (n= 49, 81.7%). Mean age was 30.4 (±6.0) years and 30 (50.0%) were nulliparous. All pregnancies were singleton. Baseline characteristics are presented in *Table 1*. Twenty-five patients (41.7%) were reported to have an obstructive hypertrophic cardiomyopathy. Eight patients (13.3%) had had a prior intervention (3 patients had undergone septal myectomy, 1 patient

**Table 1 Baseline characteristics of women with hypertrophic cardiomyopathy with and without MACE**

| | All women with HCM *n* = 60 | | Women with obstructive HCM *n* = 25 (41.7%) | | Women with non-obstructive HCM *n* = 35 (58.3%) | | *P*-value |
|---|---|---|---|---|---|---|---|
| Age, years | 30.4 | (±6.0) | 30.4 | (±5.4) | 30.3 | (±6.5) | 0.98 |
| Nullipara | 30 | 50.0% | 10 | 40.0% | 20 | 57.1% | 0.19 |
| Living in an emerging country | 11 | 18.3% | 4 | 16.0% | 7 | 20.0% | 0.75 |
| Hypertension | 8 | 13.8% | 1 | 4.0% | 7 | 21.2% | 0.12 |
| Diabetes | 2 | 3.3% | 1 | 4.0% | 1 | 2.9% | 1.00 |
| Current smoking | 3 | 5.8% | 1 | 4.5% | 2 | 6.7% | 1.00 |
| NYHA class | | | | | | | 0.44 |
| NYHA I | 40 | 66.7% | 16 | 72.7% | 24 | 68.6% | |
| NYHA II | 16 | 26.7% | 5 | 22.7% | 11 | 31.4% | |
| NYHA III | 1 | 1.7% | 1 | 4.5% | 0 | 0.0% | |
| NYHA IV | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | |
| Signs of heart failure at baseline | 5 | 8.6% | 2 | 8.7% | 3 | 8.6% | 1.00 |
| Episode of atrial fibrillation at baseline | 1 | 1.7% | 0 | 0.0% | 1 | 2.9% | 1.00 |
| Intervention or ICD | 11 | 18.3% | 8 | 32.0% | 3 | 8.6% | 0.039 |
| Cardiac medication | 33 | 55.0% | 16 | 64.0% | 17 | 48.6% | 0.23 |
| Betablocker | 29 | 48.3% | 15 | 60.0% | 14 | 40.0% | 0.13 |
| Calcium antagonist | 2 | 3.3% | 0 | 0.0% | 2 | 5.7% | 0.51 |
| Antiarrhythmic | 1 | 1.7% | 1 | 4.0% | 0 | 0.0% | 0.42 |
| Diuretic | 2 | 3.3% | 1 | 4.0% | 1 | 2.9% | 1.00 |
| ACE inhibitor | 2 | 3.3% | 0 | 0.0% | 2 | 5.7% | 0.51 |
| Obstructive cardiomyopathy | 25 | 41.7% | | | | | |
| Mitral regurgitation (mild to moderate) | 21 | 35.6% | 9 | 36.0% | 12 | 35.3% | 0.96 |
| RVSP >30 mmHg | 5 | 8.6% | 2 | 8.3% | 3 | 8.8% | 1.00 |
| Median IVS, mm (Q1–Q3) *(missing in: 17 cases)* | 18 | (14–25) | 19 | (16–27.5) | 18 | (13–25.5) | 0.65 |
| Median LVPW, mm (Q1–Q3) *(missing in: 19 cases)* | 12 | (10–14) | 12 | (11–15.5) | 12.5 | (10–14) | 0.45 |

HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; IVS, intraventricular septum; LVPW, left ventricle posterial wall; NYHA, New York Heart Association functional class; RVSP, right ventricular systolic pressure; Q1–Q3, 1st to 3rd quartile.

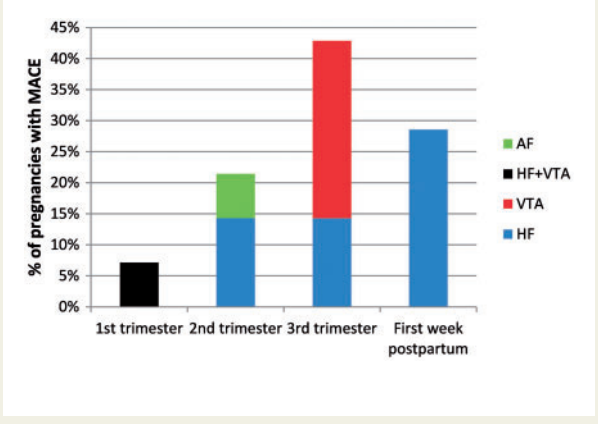


**Figure 1** Timing and type of first major adverse cardiac event during pregnancy in women with hypertrophic cardiomyopathy. Cummulative percentage of pregnancies complicated by MACE was 23.3%. No maternal mortality or thrombo-embolic events occurred. AF, atrial fibrillation; HF, heart failure; MACE, major adverse cardiac event; VTA, ventricular tachyarrhythmia.

had had an alcohol septal ablation, 1 patient surgical repair of the mitral valve had been performed, and in 3 patients there had been an unspecified intervention). In 4 patients (6.7%) an implantable cardioverter-defibrillator (ICD) was implanted.

During pregnancy, 29 patients were treated with cardiac medication (48.3%); 24 were taking a beta-blocker (40.0%), five a calcium-antagonist (8.3%), four diuretics (6.7%), and three antiarrhythmic medications (5.0%).

## Maternal outcome

No maternal mortality occurred in this cohort. In 14 patients, at least one MACE occurred (23.3%, *Figure 1*); 9 developed HF (15.0%), 6 patients had a ventricular tachyarrhythmia (10%), and 1 patient had atrial fibrillation (1.7%). Two patients had two major adverse cardiac events: one developed both HF and ventricular tachycardia at 5 weeks of gestation and one developed HF at gestational age 23 weeks followed by a ventricular arrhythmia at 32 weeks. The timing of the first MACE was mainly in the 3rd trimester ($n = 6$) or postpartum ($n = 4$) (*Figure 1*).

In *Table 2*, the management of patients who suffered a MACE during pregnancy is presented. Before the event, four patients were

**Table 2 Description of MACE and medical management**

| Patient | MACE | Timing event | Timing second event | Medication before pregnancy | Medication changes before event | Medication changes after event | Intervention |
|---|---|---|---|---|---|---|---|
| 1 | HF + VTA | 23 + 2 | 32 + 0 | | | Betablocker + antiarrhythmic started | |
| 2 | HF + VTA | 5 + 6 | 5 + 6 | Betablocker and calcium antagonist | Betablocker and calcium antagonist stopped | | |
| 3 | VTA | 35 + 0 | | Betablocker stopped | | | |
| 4 | VTA | 38 + 3 | | | | | |
| 5 | VTA | 40 + 1 | | | Betablocker started | Betablocker continued | |
| 6 | HF | 2 days pp | | Betablocker started, ACE-i stopped | | Betablocker continued | |
| 7 | HF | 1 day pp | | Betablocker | Betablocker stopped | | |
| 8 | HF | 1 day pp | | | | Betablocker and diuretic started | |
| 9 | HF | 27 + 3 | | Betablocker | Calcium antagonist started | Betablocker changed and diuretics started | |
| 10 | HF | 32 + 6 | | ACE-i stopped | Calcium antagonist started | Betablocker started | |
| 11 | VTA | 34 + 5 | | | | Betablocker started | ICD implanted 2 days pp |
| 12 | HF | 24 + 5 | | | | Betablocker started | |
| 13 | HF | 7 days pp | | Betablocker | Betablocker stopped | | |
| 14 | AF | 23 + 6 | | Betablocker and diuretic | | Betablocker and diuretic increased | |

ACE-i, angiotensin converting enzyme receptor inhibitor; AF, atrial fibrillation; HF, heart failure; ICD, implantable cardioverter defibrillator; MACE, major adverse cardiovascular event; pp, postpartum; VTA, ventricular tachyarrhythmia.

**Table 3 Univariable analysis of predictors of MACE during pregnancy in women with hypertrophic cardiomyopathy**

| 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.

taking a beta-blocker and in another four patients, a beta-blocker had been stopped. After the event, 9 of 14 started or continued a beta-blocker, in some in addition to diuretics or antiarrhythmic medication. One patient with a ventricular tachyarrhythmia in the 3rd trimester had an ICD implantation 2 days postpartum.

Results of the univariable analysis for MACE are shown in *Table 3*. NYHA functional class of ≥2 and signs of HF before pregnancy were significantly associated with MACE. The number of events was too small to allow for multivariable analysis.

## Obstetric and foetal outcome

*Table 4* shows the obstetric and foetal outcome for the total HCM group and for women with MACE vs. those without MACE. Three

**Table 4 Obstetric and foetal outcome of pregnancy in the presence of hypertrophic cardiomyopathy, in women with and women without MACE**

| | 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.

**Table 5 Outcome in women with obstructive and non-obstructive HCM**

| | Women with obstructive HCM | | Women with non-obstructive HCM | | |
|---|---|---|---|---|---|
| | *n* = 25 (41.7%) | | *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.

foetal losses occurred; 1 miscarriage and 2 foetal deaths after 24 weeks. The miscarriage occurred at 23 weeks and the growth-restricted foetus was suspected of a mitochondrial cardiomyopathy. In the patient who had developed HF and a ventricular tachyarrhythmia at 5 weeks, intrauterine foetal death occurred at 29 weeks of gestation. One patient with pre-existing permanent atrial fibrillation, was treated with disopyramide, digoxin and unfractionated heparin and had an intrauterine foetal death at 27 weeks.

Pregnancy duration in women with MACE was significantly shorter than in women without MACE. An emergency Caesarean delivery for a cardiac reason was performed in three of the 14 women with MACE: in 2 after HF (of whom one also had a ventricular tachyarrhythmia) and in 1 after atrial fibrillation.

Five neonates (8.3%) were diagnosed with an inherited hypertrophic cardiomyopathy: 3 babies of women with non-obstructive HCM (8.6%) (in 1 of these 3, foetal loss at 23 weeks occurred), and 2 of the women with obstructive HCM (8.0%).

## Obstructive and non-obstructive HCM

No significant differences in pregnancy outcome were found between women with obstructive and non-obstructive HCM. The data are presented in *Table 5*.

## Follow-up

Follow-up at 6 months was available in 49 of the 60 pregnancies (81.7%) and no maternal mortality occurred during follow-up. One patient, with non-obstructive HCM and good LV function prior to pregnancy, was found to have severe LV dysfunction with apical thrombus formation—along with signs and symptoms of overt HF—at 4 months after delivery with a gradual recovery of LV function after heart failure medication was started.

# Discussion

The results of our study demonstrate a favourable maternal and foetal outcome in the majority of women with HCM who tolerated pregnancy well without maternal mortality. At the same time, however, 23% of the patient still developed important MACE including HF and arrhythmias. In addition, women with cardiac complications had a shorter duration of pregnancy and higher rates of emergency caesarean delivery. Functional status and signs of HF prior to pregnancy were associated with these complications.

## Mortality in pregnant women with HCM

The results of this study support data obtained from few retrospective studies reporting low mortality rate (0%-2%) related to pregnancy in women with HCM.[5,13,14]. In the study by Autore *et al.*[5], 2 women (out of 100) with very high-risk profiles died during pregnancy. One had a septum thickness of more than 30 mm, a very high LVOT gradient and a poor functional class and the other had an extremely strong familial history of sudden death and had experienced prolonged runs of VT prior to death. A recent review presented the pooled analysis of 408 pregnancies including these two cases, which were the only deaths in the series, giving a maternal mortality rate of 0.5%.[15] It seems likely, if current recommendations[10] had been followed, that both of these deaths would have been prevented. Indeed, in our contemporaneous data, there was no maternal mortality, although at least 7 patients had a septal thickness of more than 30 mm.

## MACE in pregnant women with HCM

A number of complications such as HF, arrhythmias, syncope, and thrombo-embolic complications have been described in women with HCM during pregnancy. The rates of these vary from 15% to 48% depending on the study design and patient population.[5,7,8,15,16] In our contemporary registry, almost a quarter of pregnant women with HCM developed either HF or arrhythmia and most of these complications occurred during the 3rd trimester or postpartum, consistent with the reported literature.

## Heart failure and timing of occurrence

In our registry, 15% of women experienced HF, mainly during the 3rd trimester, but there was no difference in pregnancy outcome between women with obstructive and non-obstructive HCM. These data are consistent with two other studies where the presence of LVOT obstruction had no influence on maternal outcome.[6,7] Avila *et al.*[7] compared 12 non-pregnant and 23 pregnant women with HCM, and found that similar to our findings, 30% of pregnant women experienced HF mainly during the 3rd trimester. However, in the retrospective study by Autore *et al.*[5] HF symptoms tended to worsen more often in those with LVOT obstruction (25% vs. 11%), this difference however, was not statistically significant.

## Arrhythmia

In our study we found that 11.7% of patients developed arrhythmia, 10% ventricular tachyarrhythmia, and 1.7% atrial fibrillation (1.7%). Avilla *et al.*[7] reported an arrhythmia rate of only 13% among 23 pregnant women with HCM, a rate lower than found in non-pregnant women with HCM and episodes of palpitations and arrhythmia during pregnancy in women with HCM which were similar to those experienced before their pregnancy.[6,7] In contrast, in a retrospective review of 27 pregnancies in 23 women with HCM, Tanaka *et al.*[8] reported a cardiovascular event rate of 48%; the vast majority involved an arrhythmia and occurred during the 3rd trimester. In a series of 8 high risk women with HCM who had an implantable cardioverter defibrillator (ICD), 2 patients had VT (1 sustained and 1 non-sustained), and 2 had SVT.[17] Supporting our findings, Schinkel *et al.* in his recent review of the existing literature reported ventricular arrhythmias in 5% and supraventricular arrhythmias in 7% of the patients.[18] More information is needed in order to define the effect of pregnancy on the incidence and severity of arrhythmias in women with HCM.

## Predictors of complications in pregnant women with HCM

Several studies reported that symptomatic women deteriorated more often during pregnancy than asymptomatic women with HCM.[6–8] In a large retrospective study (using questionnaires), Thaman *et al.* described 271 pregnancies in 127 women with HCM and found that the majority (90%) of women with symptoms during pregnancy had been symptomatic before.[8] Similarly, Autore *et al.*[5] found that those who had symptoms prior to pregnancy were more likely to deteriorate then those who did not (42% vs. 4%). Tanaka *et al.*[8] identified the use of cardiac medication prior to pregnancy as a predictor of maternal complications in a retrospective study of 27 pregnancies in 23 women with HCM. In line with ESC risk stratification guidelines,[10] the results of our contemporary registry show that NYHA functional class of ≥2 and signs of HF prior to pregnancy are associated with the occurrence of MACE.

## Obstetric and foetal outcome

In this registry, the most frequently observed foetal morbidity was premature birth (26%), followed by being small for gestational age (8%) and developing foetal bradycardia (3%). Another study described termination of pregnancy in 4 out of 27 pregnancies, all due to cardiovascular complications.[8] Pregnancy duration in this study in women with MACE was significantly shorter than in women without MACE and emergency Caesarean delivery for cardiac reasons was performed in 3 women, all of whom had a MACE. In a review of a large number of published cases Schinkel reported a 25% Caesarean section rate for predominantly obstetric indications and a 15% rate of spontaneous abortion 5% therapeutic abortions and a 2% stillbirth rate.[18] As in the current series, foetal mortality in all available reports is comparable with the general population[18] although it seems to occur mostly in women with cardiac complications, emphasizing the need for appropriate follow-up and management of women after a MACE, including close foetal monitoring.

# Conclusions

Over the last decades, considerable progress has been made in the diagnostic evaluation, risk assessment, and clinical management in patients with HCM. Results of this contemporaneous, multicentre, prospective, worldwide registry showed that most women with HCM tolerated pregnancy well and there was no mortality. However, cardiovascular complications such as heart failure and arrhythmias were not uncommon and influenced foetal outcome and delivery. Functional status and signs of heart failure prior to pregnancy are important risk factors for cardiac complications in pregnant women with HCM. Pre-pregnancy counselling, close monitoring, and optimal care are mandatory to prevent complications in women with HCM.

# Limitations

Our study has a number of limitations mostly related to missing information such as the LVOT gradient and its changes during pregnancy. However, obstructive HCM was defined as the presence of an LVOT gradient >30 mmHg, so we could characterize the group of women with obstructive HCM. In addition, there was incomplete information regarding family history, syncope and arrhythmias prior to pregnancy. In addition, a small number of women (13.8%) had a history of hypertension, which can cause LV hypertrophy leading to over diagnosis of HCM in some cases, unfortunately, the information on genetic testing is lacking in our registry. Despite these limitations, this prospective registry included a large number of women with HCM, managed according to contemporary guidelines, providing important information related to the maternal and foetal outcome in women with HCM.

## Acknowledgements

We would like to thank all ROPAC investigators, who are listed in the online supplement. Our gratitude goes to the EORP team for their contribution, in particular: Thierry Ferreira (Head of Department EORP), Elin Folkesson Lefrancq (Project Officer), and Viviane Missiamenou (Data Manager). To join the Registry: http://www.escardio.org/guidelines-surveys/eorp/surveys/pregnancy/Pages/welcome.aspx.

## Funding

Since the start of EORP, the following companies have supported the programme: Abbott Vascular Int. (2011–2014), Amgen Cardiovascular (2009–2018), AstraZeneca (2014–2017), Bayer (2009–2018), Boehringer Ingelheim (2009–2016), Boston Scientific (2009–2012), The Bristol Myers Squibb and Pfizer Alliance (2011–2016), The Alliance Daiichi Sankyo Europe GmbH and Eli Lilly and Company (2011–2017), Edwards (2016–2019), Gedeon Richter Plc. (2014–2017), Menarini Int. Op. (2009–2012), MSD-Merck & Co. (2011–2014), Novartis Pharma AG (2014–2017), ResMed (2014–2016), Sanofi (2009–2011), SERVIER (2010–2018). The companies that support EORP were not involved in any part of the study or this report.

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**CARDIOVASCULAR FLASHLIGHT**

doi:10.1093/eurheartj/ehw545
*Online publish-ahead-of-print 7 December 2016*

# Myocardial crystallization arising from a mitral annulus calcification

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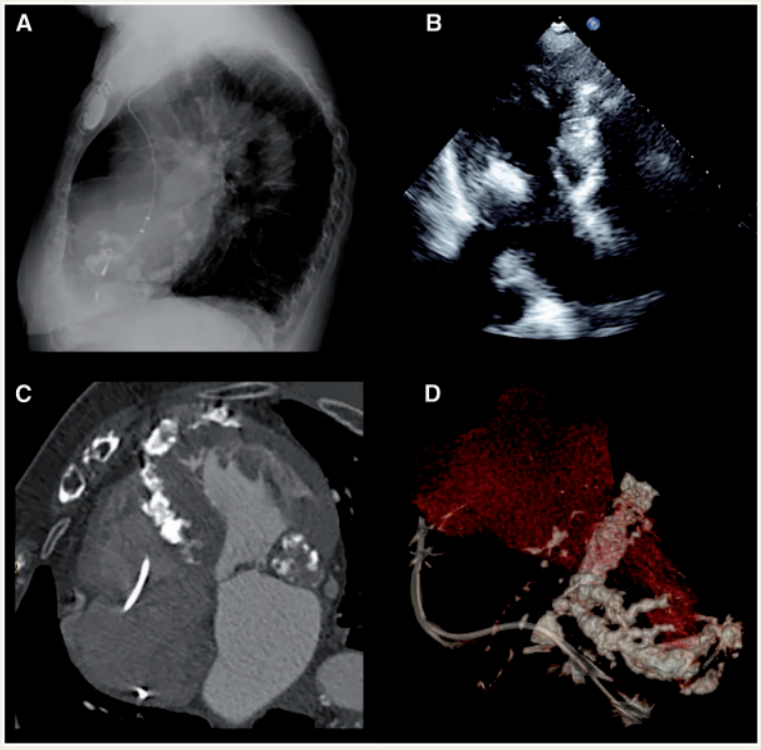
Mitral annulus calcification is a common degenerative disorder in the elderly, being more prevalent in patients with renal failure and in women. Caseous calcification is a rare variant characterized by a putty-like material surrounded by a calcified envelope. This disease is considerated a benign lesion; however, due to its active chronic inflammatory process, calcification can expand to adjacent structures.




We report a case of an 89-years-old female who presented to the emergency department with a progressive exertional shortness of breath. She had a previous history of chronic kidney disease, atrioventricular block treated with a pacemaker implantation and a severe mitral annulus calcification. Chest radiograph confirmed the mitral annulus calcification and showed an unspecific pattern of cardiac calcifications (*Panel 1A*). The echocardiogram documented a restrictive pattern and a caseous variant of mitral annulus calcification (*Panel 1B*; Supplementary material online, *Video 1*). In term to define these findings, a contrast enhanced cardiac CT was performed evidencing a severe continuous linear caseous calcification arising from the mitral annulus expanding to the contiguous ventricular myocardium till the apex (*Panels 1C* and *1D*; Supplementary material online, *Video 2*).

As shown in our patient, conduction system calcification can lead to heart blocks and massive myocardial infiltration can develop heart failure with a restrictive physiology. In addition, renal failure is a recognized risk factor for heart structures calcifications. This is a rare condition that we should take in consideration when we assess patients with symptoms of heart failure and history of mitral annulus calcification.

Supplementary material is available *at European Heart Journal* online.