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Hemodynamic adaptation to pregnancy in women with structural heart disease

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ABSTRACT

Background: Many women with structural heart disease reach reproductive age and contemplate motherhood. Pregnancy induces and requires major hemodynamic changes. Pregnant women with structural heart disease may have a reduced cardiac reserve. There are no longitudinal data on cardiovascular adaptation throughout pregnancy in women with structural heart disease.

Methods: Thirty-five women with structural heart disease were included in a prospective observational trial. Maternal hemodynamics were assessed before conception, during pregnancy and 6 months postpartum by transthoracic echocardiography. Uteroplacental perfusion was analyzed by obstetric Dopplers. Longitudinal evolution over time was analyzed as well as the long term influence of pregnancy on cardiac function.

Results: Cardiac output (CO), stroke volume (SV), left ventricular mass (LV mass) and E/E′ ratio significantly increased and ejection fraction (EF) and fractional shortening (FS) decreased during pregnancy. There was a statistically significant difference in EF, FS and E/E′ ratio before and after pregnancy.

Conclusions: The characteristic pattern of hemodynamic adaptation to pregnancy is attenuated in women with structural heart disease. The pregnancy related volume load induces progression of diastolic dysfunction. Our data suggest a persistent reduction in systolic and diastolic cardiac functions after pregnancy in women with structural heart disease.

1. Introduction

Normal pregnancy induces and requires a major cardiac adaptation. An initial arterial vasodilatation, early in pregnancy, triggers a rapid increase in blood volume, cardiac output and ventricular mass [1,2]. Most of these changes are reversed 6 months after pregnancy [3].

Advances in medical and surgical care of patients with structural heart disease have led to improved survival and outcome, especially in women with congenital and valvular heart disease. Many of these women reach reproductive age and experience their quality of life to be sufficient to consider pregnancy and motherhood. However, they are at increased risk for cardiac and obstetric complications [4–6]. The hemodynamic changes can put a strain on their circulatory system and may induce cardiac complications such as heart failure or arrhythmia. Alternatively, their reduced cardiac reserve could prevent adequate adaptation, possibly leading to hypertensive disorders of pregnancy, fetal growth restriction or adverse fetal outcome.

Timely counseling and specialized follow up by a dedicated team of cardiologists, obstetricians and anesthesiologists, with knowledge of the implications of structural heart defects as well as adaptive requirements of pregnancy, are therefore advised [7,8].

While cardiac (mal)adaptation to pregnancy has mostly been studied in healthy women, women with hypertensive disorders or with growth restricted fetuses, there is hardly any longitudinal data on women with structural heart disease [9]. As such most information comes from extrapolation of other patient groups [10–17].

Also, little is known on the degree of reversibility of hemodynamic adaptation and its effects on cardiac function after pregnancy [18,19].

We therefore aimed to prospectively study longitudinal hemodynamic adaptation to pregnancy in women with structural heart disease and asses the influence of this cardiac adaptation on postpartum cardiac function.

2. Methods

The prospective single center observational study was conducted from 2007 until 2010 in a joint collaboration by the departments of Cardiology and Obstetrics at the Erasmus MC. Women with inherited or acquired structural heart disease visiting the

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outpatient clinic of cardiology and/or obstetrics for preconceptional counseling or pregnancy during the study period were invited to participate. Women received an individualized, standard management by a multidisciplinary team consisting of dedicated cardiologists, obstetricians and anesthesiologists according to international guidelines.

Maternal and uteroplacental hemodynamics were assessed by transthoracic echocardiography and obstetric Dopplers. Maternal and pregnancy outcomes were assessed. Cardiac measurements were performed before pregnancy, in each trimester of pregnancy and six months postpartum. Obstetric Doppler measurements of the uterine and umbilical artery were performed in the second and third trimesters. Preconceptional hemodynamics were investigated at inclusion or retrieved from a recent previous echocardiographic exam. Pre and post pregnancy measurements were performed irrespective of the menstrual cycle, method of anticonception and breast feeding status. The study was approved by the medical ethical committee of the Erasmus MC University Medical Centre of Rotterdam and all participants gave written informed consent. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

2.1. General outcomes

Demographics, cardiac diagnoses, obstetric outcomes and both maternal and obstetric complications were prospectively recorded. Post-partum hemorrhage (PPH) was defined as blood loss above 500 ml after vaginal delivery and 1000 ml after cesarean section [20].

Birthweight centiles, corrected for gestational age, maternal race, parity and fetal sex were derived from the Dutch national reference curves [21]. A birthweight less than the 10th percentile, was considered as small for gestational age (SGA).

Hypertension (HT) during pregnancy was classified as either pre-existent (occurring before 20 weeks of gestation), gestational hypertension (de novo hypertension without proteinuria occurring after 20 weeks of gestation) or pre-eclampsia (hypertension in combination with proteinuria) [22].

Preterm delivery was defined as a delivery occurring before 37 weeks of gestation. Pregnancy loss was defined as a miscarriage before and intrauterine death from 20 weeks of gestation.

2.1.1. Echography

Transthoracic echocardiography was performed using commercially available devices with sector transducers (SONOS 7500, Philips Medical Systems, Best, The Netherlands or iE33, Philips Medical Systems, Best, The Netherlands), according to the guidelines of the American Society of Echocardiography and, when necessary, adapted to the structural abnormality [23].

Diastolic and systolic volumes were computed from the left ventricular end systolic and end diastolic diameters (LVESD, LVEDD) using the Teicholz formula and fractional shortening (FS) and ejection fraction (EF) were calculated accordingly [24]. Left ventricular mass (LVmass) was calculated using the Devereux formula [25]. Left ventricular outflow tract diameter was obtained from the parasternal long access view and left ventricular outflow tract velocity time integral from the apical five chamber view. Stroke volume (SV) was calculated by multiplying left ventricular outflow area with left ventricular velocity time integral, cardiac output (CO) by multiplying stroke volume with heart rate. Diastolic function was assessed by pulsed wave Doppler of the mitral inflow (E/A ratio) and tissue Doppler of the septal mitral annulus (E/E′ ratio).

Obstetric Dopplers were obtained with commercially available ultrasound devices with curved array transducers (iU22, Philips Ultrasound Bothell, WA, USA and Voluson 730 Expert G.E, Medical systems, Zimpf, Austria).

Pulsatility index of the umbilical artery (Umb PI) and mean pulsatility index of both uterine arteries (Uter PI) were obtained by color directed pulsed wave Doppler.

2.2. Statistical analysis

Continuous variables are displayed as means with a standard deviation (SD) and range, discrete variables are displayed as counts and proportions.

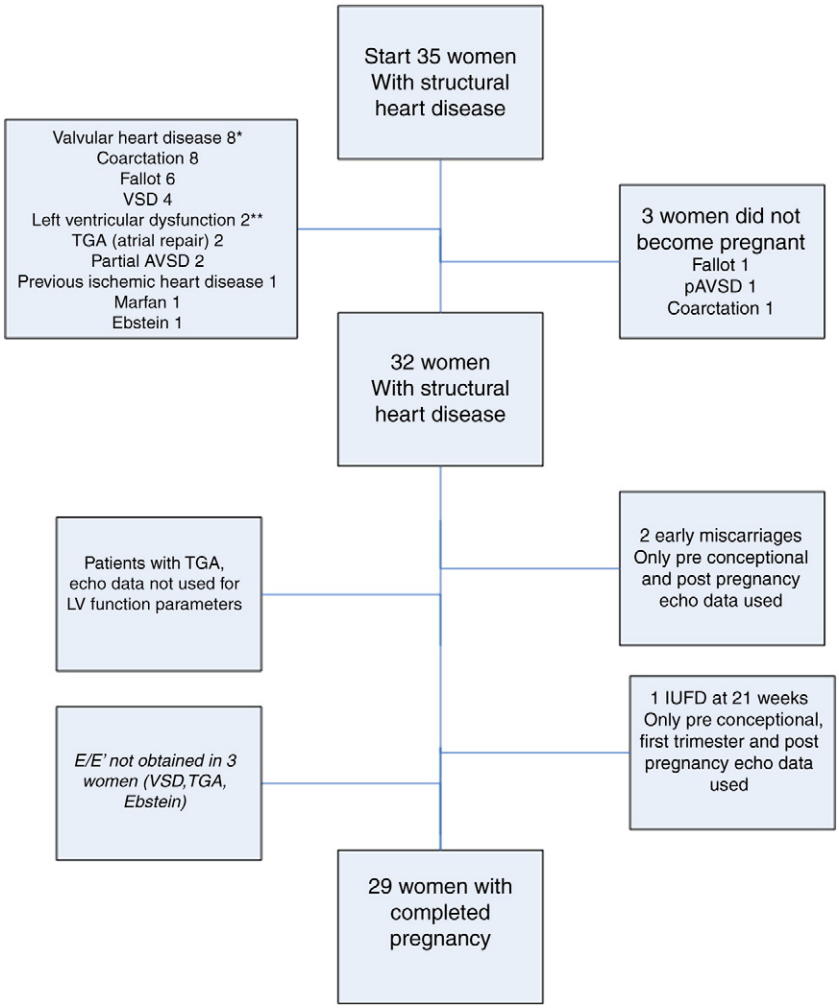

Fig. 1. Organogram of the study population with details on cardiac diagnosis. * Five women with mechanical aortic and/or mitral valve. ** One woman after previous chemotherapy and one woman with a dilated cardiomyopathy.

Table 1
Detailed information on type of structural heart disease, previous interventions, preconceptional cardiac condition and WHO group of the study population. Abbreviations in order of appearance: WHO: WHO group, RHD: rheumatic heart disease, AVR: aortic valve replacement, MVR: mitral valve replacement, //: subsequent intervention, TV: tricuspid valve, AF: atrial fibrillation, AS: aortic valve stenosis, bicus AV: bicuspid aortic valve, MS: mitral valve stenosis, LV: left ventricle, MV: mitral valve, ACS: acute coronary syndrome, Ao asc: aorta ascendens, PS: pulmonary valve stenosis, MI: mitral valve insufficiency, LA: left atrium, DM: diabetes mellitus, RF: renal failure, Coarct: aortic coarctation, HT: hypertension, APVD: anomalous pulmonary venous drainage, ASD I: atrium septum defect type 1, Le–Ri shunt: left to right shunt, RV: right ventricle, TI: tricuspid valve insufficiency, VSD: ventricular septum defect, PODB: persistent open ductus of Botalli, PA: pulmonary artery, PV: pulmonary valve, TOF: tetralogy of Fallot, RA: right atrium, RV: right ventricle, PI: pulmonary valve insufficiency, AI: aortic valve insufficiency, ASD II: atrium septum defect type 2, DCM: dilated cardiomyopathy, CM: cardiomyopathy, TGA: transposition of the great arteries: pAVSD: partial atrioventricular septum defect, AMI: acute myocardial infarction, PTCA: percutaneous transluminal coronary angioplasty, RCA: right coronary artery, LAD: left anterior descendens coronary artery, RCX: ramus circumflexus.

Diagnosis	Interventions prior to pregnancy	Condition prior to pregnancy	WHO
RHD	St Judes AVR (2×), St Judes MVR//TV plasty (2×)	AF	3
RHD	St Judes MVR//St Judes AVR	AF	3
AS (bicus AV)	St Judes AVR	Aortic root dilatation 48 mm	3
MS (congenital)	St-Judes MVR	Good LV and MV function after previous valve thrombosis with ACS	3
AS (bicus AV)	Homograft	Ao asc 43 mm	2
PS	balloon dilatation	Mild PS	1
MI	No	Severe MI, dilated LA with DM and RF	1
Coarct, bicus AV	Patch//valvulotomy//Ross//stent recoarctation//Bentall	No rest coarct, no HT	3
Coarct, bicus AV	End to end anastomosis	Mild AS, no rest coarct, Ao asc 40 mm, no HT	2
Coarct, APVD	Subclavian flap	Mild rest coarct, no HT	2
Coarct, ASD I	End to end anastomosis//balloon dilatation	Mild rest coarct, HT, Le-Ri shunt over ASD and elevated RV filling pressures	3
Coarct, bicus AV, cervical arch	End to end anastomosis	Mild rest coarct, no HT, Ao asc 44 mm	3
Coarct	End to end anastomosis	No rest coarct, no HT, moderate MI and TI	2
Coarct	End to end anastomosis	Mild rest coarct, HT	2
Coarct, bicus AV	End to end anastomosis//balloon dilatation	Mild rest coarct, HT, Ao asc 37 mm	2
Coarct, VSD, PODB	Subclavian flap, PA banding, closure PODB//PA debanding, PV plasty (2×), balloon dilatation recoarctation	Mild rest coarct, mild PS, no HT	2
VSD, subvalvular aortic membrane	Closure VSD (2×), resection subvalvular aortic membrane	Ao asc 41 mm	2
TOF	Closure VSD, transannular patch	Dilated RA and RV, mild PS and severe PI	3
TOF, atresia left PA	Closure VSD and PODB, transannular patch	Mild PS	2
TOF	Closure VSD, transannular patch//homograft for severe PI	Moderate PI	2
TOF, atresia PA	Waterston//Rastelli//plasty for PS, closure VSD	Severe AI and moderate PI	3
TOF	Closure VSD, transannular patch//homograft	Mild PI	2
TOF	Blalock-Taussig//closure VSD, infundibulectomy 2×//balloon dilatation PV	Moderate PI	2
VSD	No	Mild Le-Ri shunt	2
VSD, ASD II	No	Mild Le-Ri shunt	2
VSD, double orifice MV	PA banding//PA debanding, closure VSD//MV plasty	Mild MI and PS	2
DCM (familial)	No	Mild LV impairment	2
CM (chemotherapy)	No	Dilated LV, mild LV impairment, mild MI	2
TGA	Senning	Mild RV impairment	3
TGA	Mustard	Mild RV impairment	3
pAVSD	Closure ASD, VSD, MV plasty	Moderate MI	2
pAVSD	Closure ASD (2×), VSD (2×), MV plasty (2×) and TV plasty	Moderate MI, dilated LA	2
AMI (inferioposterior)	PTCA RCA, stent LAD and RCX//PTCA LAD for restenosis	Mild LV impairment	3
Marfan syndrome	No	Aorta 39 mm	2
Ebstein anomaly	RV and TV plasty (Chauvaud), partial cavopulmonary shunt	AF, severe TI, RV impairment	3

To investigate the longitudinal evolution over time of the individual cardiac and obstetric Doppler parameters and to account for the correlation in the measurements taken from the same patients, a repeated measurement analysis using linear mixed effect models was performed [26]. As the evolution of each parameter during pregnancy may not be linear, we used in our model specification second degree polynomials for both the fixed and random effects parts. The models' assumptions were validated using residual plots. The analysis was performed in the R statistical software (version 2.14.0, 2011-10-31) using package nlme (version 3.1-102). The significance level was set at 5% and no multiple testing corrections were applied.

Differences between pre-and post-pregnancy values were analyzed with an F-test. To assess whether the evolution during pregnancy predicted this pre–post pregnancy difference, the area under the longitudinal trajectory during pregnancy using linear mixed effect models was computed and subsequently the association between this area and pre–post pregnancy difference was tested.

To investigate the association between fetal growth and cardiac adaptation, these areas were also correlated with adjusted birthweight centiles and evolution in uterine artery flow.

To assess the influence of the severity of cardiac condition and the occurrence of pregnancy complications on the longitudinal evolution of the parameters, the population was divided in two groups. For the severity of cardiac condition, the division was based on the WHO cardiac function classification (WHO classes 1–2 versus WHO classes 3–4) [27]. For the occurrence of pregnancy complications, only those associated with maladaptation to hemodynamic changes were taken into account. As such the population was divided based on the occurrence of hypertension and/or small for gestational age fetuses (HT/SGA).

The same types of analysis as for the whole population were performed, allowing for differences in the average longitudinal evolutions per risk group. Likelihood ratio tests for differences in average longitudinal evolutions between both groups were calculated as well as differences between the pre–post pregnancy values. The effect of the severity of cardiac condition on adjusted birthweight centiles and occurrence of complications was analyzed with a Wilcoxon test and Fisher's exact test respectively.

3. Results

Thirty-five women with structural heart disease were invited to participate into the study. Thirty-two of them became pregnant and 29 reached a gestational age beyond the limits of viability (24 weeks). One woman had a spontaneous first trimester miscarriage, one woman miscarried after a septic episode following a first trimester reduction of a spontaneous triplet to a singleton pregnancy and one woman had an intrauterine death with signs of severe placental insufficiency at 20 weeks gestation.

Table 2
Details of maternal and obstetric complications and outcomes.

Complications	N	%	WHO 1–2 (n)	WHO 3–4 (n)	Remarks
Cardiac			21	11	
Valve thrombosis	1	3%	–	1	Aortic valve thrombosis leading to heart failure
Heart failure	1	3%	–	1	
Non-cardiac					
Kidney transplant	1	3%	1	–	Kidney failure during pregnancy in diabetic women with pre-existent kidney dysfunction necessitating postpartum dialysis and transplant
Sepsis	1	3%	1		After early reduction of a triplet pregnancy
Suicide attempt	1	3%	–	1	
Post partum depression	2	6%	1	1	
Pyelonefritis	1	3%	1		
Obstetric					
Pre-existent hypertension	3	9%	2	1	
Gestational hypertension	3	9%	3	–	
Pre-eclampsia	1	3%	1	–	
Preterm delivery	3	9%	1	2	$34^{3/7}$, $35^{1/7}$, $35^{6/7}$ weeks
Postpartum hemorrhage	8	25%	5	3	
Cesarean section	7	22%	6	1	
early miscarriage	2	6%	1	1	
Fetal-neonatal					
Intrauterine death	1	3%	–	1	At 21 weeks
Major congenital abnormality	1	3%	1	–	Trisomy 21 with duodenal atresia
NICU admission	3	9%	1	2	
SGA	6	18%	2	4	

Pregnancy outcomes	**Mean**	**SD**	**WHO 1–2 (mean)**	**WHO 3–4 (mean)**	**Median**	**Min**	**Max**
Gestational age (weeks)	39	2	39.175	38.011	39	$34^{3/7}$	$41^{6/7}$
Birthweight (g)	3156	587	3319	2792	3255	1810	4100
Apgar 5 minute	9	1	9.40	9.56	10	8*	10

* Excluding the intrauterine death at 21 weeks.

Fig. 1 represents an organogram of the study population. Table 1 offers details on diagnosis, previous cardiac interventions, the cardiac condition before pregnancy as well as the WHO risk group classification for each women individually. Of the 32 included women, 85% had a congenital structural heart defect and 82% had a prior cardiac intervention. Fifty-six percent of women were nulliparous at inclusion. Mean age at delivery was 32 years (SD: 4.3 years, Range: 24 to 41 years) and mean BMI was 25 (SD: 3.9, Range: 18 to 34).

Major maternal (both cardiac and non-cardiac) and/or obstetric (miscarriage, fetal death, gestational hypertension, pre-eclampsia, SGA, PPH and major congenital abnormality) complications occurred in 62.5% of pregnancies. There was no significant difference in complication rate between the low risk (WHO 1–2) and high risk (WHO 3–4) groups.

Three women had pre-existent atrial fibrillation and 3 other women reported transient episodes of palpitations. There were no new arrhythmic complications during the study period. One woman developed a thrombosis of her prosthetic aortic valve (St-Judes) at 32 weeks, leading to heart failure and requiring postpartum valve replacement.

Details of maternal and obstetric complications as well as obstetric outcomes are represented in Table 2.

The longitudinal profiles over time of the echocardiographic and uteroplacental parameters, starting before pregnancy until six months postpartum, are presented in Fig. 2 and estimated regression coefficients in Table 3.

A statistically significant linear evolution was observed towards a larger LVESD ($P=0.001$) and smaller FS ($P=0.001$) and EF ($P\leq0.001$).

E/E′ ratio ($P=0.008$), SV ($P=0.045$), CO ($P=0.028$), LVmass ($P=0.005$) as well as uterine and umbilical artery PI ($P\leq0.001$, $P\leq0.001$ respectively) showed a statistically significant parabolic evolution (quadratic effect) with increase during pregnancy for the cardiac parameters and decrease for the obstetric Doppler indices.

There was a statistically significant increase in LVESD ($P=0.001$) and E/E′ ratio ($P=0.006$) and decrease in FS ($P=0.001$) and EF ($P=0.001$) after pregnancy as compared to before pregnancy, however evolution during pregnancy was not predictive for this difference. Neither was it related to evolution in uterine artery flow nor with adjusted birthweight.

The influence of severity of cardiac structural defect based on WHO class on longitudinal evolution of the parameters is illustrated in Fig. 3. There were no significant differences in average evolution over time between groups except for heart rate (LRT 9.78, $P=0.021$). Severity of structural heart defects only influenced heart rate on pre–post pregnancy difference. Adjusted birthweight centiles were significantly higher in the low risk group (WHO1–2) (median = 38: IQR 35.6) as compared to the high risk group (WHO3–4) (median = 14: IQR 24) ($P=0.04$).

Thirteen women presented with pregnancy complications associated with hemodynamic maladaptation (HT/SGA). There were no significant differences in average longitudinal evolution of the parameters between patients with and without HT/SGA. The corresponding fitted average longitudinal evolutions are illustrated in Fig. 4. There was a significant pre–post pregnancy difference for the LVEDD (mean diff = −2.97 mm, $P=0.031$) between patients with and without HT/SGA.

4. Discussion

Our results offer an insight on both hemodynamic adaptation to pregnancy and long term influence of pregnancy on cardiac function in a population of women with structural heart disease. They show an attenuated cardiovascular adaptation with reduction in systolic function and progression of diastolic dysfunction during pregnancy, which persist 6 months after pregnancy.

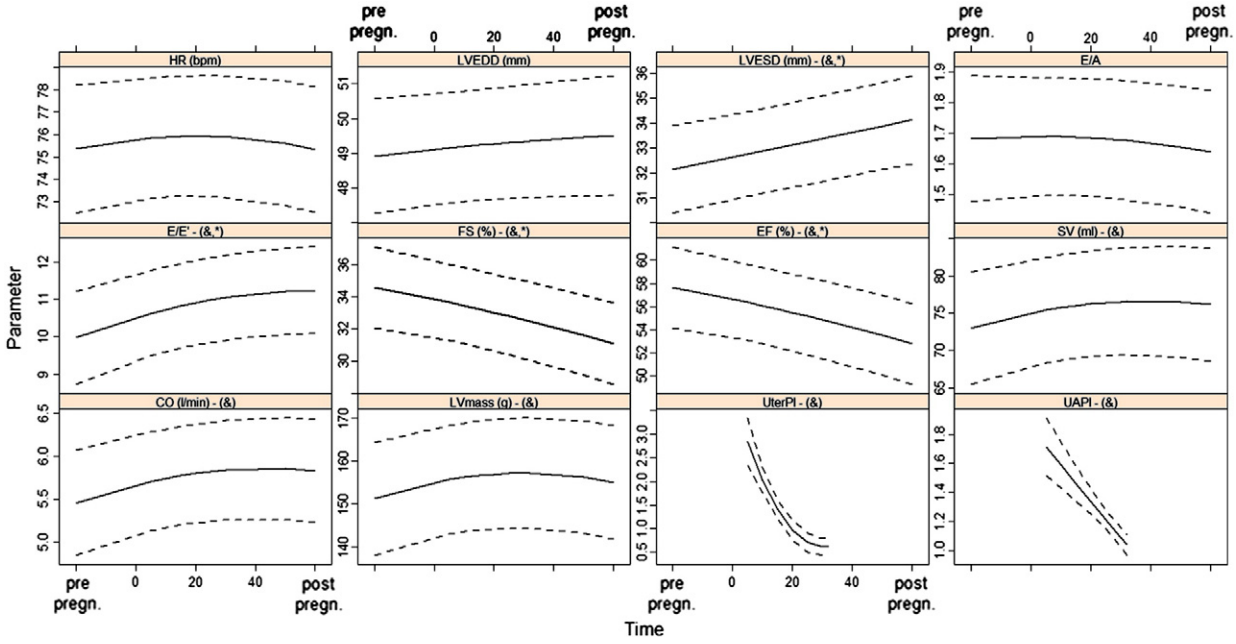

Fig. 2. Fitted longitudinal profiles of each parameters for the whole population. The dashed lines denote 95% point-wise confidence intervals. The symbol '&' denotes parameters for which there was a significant time effect, and the symbol '*' parameters for which there was a significant difference between pre- and post pregnancy measurements.

We observed the characteristic significant increase in SV and CO, with steep rise in the first half and a more gradual plateau-like phase in the second half of pregnancy.

However, the magnitude of increase seems lower than in previously described normal pregnant populations and more comparable to the pattern observed in pregnancies complicated by growth restriction and pregnancies at high altitude [10,11,13–15,28].

Table 3
Estimated regression coefficients per parameter for the whole population.

Parameter	Coef	Value	Std. error	t-Value	P-Value
HR	Intercept	75.78	1.39	54.48	<0.001
	Time	0.01	0.02	0.76	0.447
	Time^2	−0.00	0.00	−2.02	0.046
LVEDD	Intercept	49.11	0.82	59.93	<0.001
	Time	0.01	0.01	0.91	O.366
	Time^2	−0.00	0.00	−0.43	0.667
LVESD	Intercept	32.63	0.88	37.02	<0.001
	Time	0.02	0.01	2.50	0.014
	Time^2	0.00	0.00	0.08	0.939
E/A	Intercept	1.69	0.10	16.98	<0.001
	Time	0.00	0.00	0.06	0.954
	Time^2	−0.00	0.00	−1.22	0.225
E/E′	Intercept	10.52	0.60	17.63	<0.001
	Time	0.02	0.01	3.10	0.003
	Time^2	−0.00	0.00	−2.96	0.004
FS	Intercept	33.84	1.23	27.56	<0.001
	Time	−0.04	0.02	−2.15	0.034
	Time^2	−0.00	0.00	−0.76	0.452
EF	Intercept	56.61	1.71	33.08	<0.001
	Time	−0.05	0.02	−2.22	0.029
	Time^2	−0.00	0.00	−0.74	0.460
SV	Intercept	75.03	3.68	20.38	<0.001
	Time	0.08	0.05	1.75	0.084
	Time^2	−0.00	0.00	−2.55	0.013
CO	Intercept	5.67	0.30	18.95	<0.001
	Time	0.01	0.00	2.17	0.034
	Time^2	−0.00	0.00	−2.73	0.008
LVmass	Intercept	155.01	6.55	23.65	<0.001
	Time	0.14	0.08	1.84	0.069
	Time^2	−0.00	0.00	−3.25	0.002
UterPI	Intercept	3.81	0.45	8.48	<0.001
	Time	−0.21	0.04	−4.83	<0.001
	Time^2	0.00	0.00	3.69	0.001
UAPI	Intercept	1.84	0.13	14.71	<0.001
	Time	−0.03	0.00	−5.68	<0.001

The pre-pregnancy LVmass was already elevated in our population, comparable to third trimester levels for normal healthy women [17]. While somewhat attenuated, we still observed a statistically significant increase in LVmass during pregnancy.

Our data also showed a gradual decline in FS and EF due to an increase in LVESD, similar to normal pregnancy [17]. While the absolute values persisted within normal ranges, the decline continued until six months postpartum leading to a statistically significant difference between pre- and post-pregnancy measurements.

These findings suggest a negative influence of pregnancy on systolic function in women with structural cardiac disease. Our data are in contrast to Uebing's findings who could not observe a deleterious effect pregnancy on left ventricular function [19]. One could question the accuracy of EF and FS derived from the Teicholz formula in reflecting systolic function in pregnant women with structural heart disease. As most other echocardiographic volume estimations equally have intrinsic limitations, we believe that MRI analysis of systolic function is necessary to confirm our findings.

Normally the E/A ratio decreases with gestational age, as the importance of atrial contribution to ventricular filling increases along with HR towards the end of pregnancy [13,17,29]. We observed a relatively constant E/A ratio and HR within normal ranges throughout pregnancy in our population.

However, E/E′ ratio, which was already elevated before pregnancy in our population, showed a further significant increase with gestational age. While the pattern is similar to normal pregnancy the absolute values were far above both normal and pre-eclamptic pregnancy values, clearly in the pathological range [11–13].

Our findings suggest a progressive diastolic dysfunction in women with structural heart disease with advancing gestational age. In normal pregnancy, increased load is compensated by myocardial hypertrophy. Due to elevated baseline levels, the capacity for further expansion in LVmass seems reduced in our population. Increments in load therefore lead to elevation of filling pressures, as reflected by the E/E′ ratio.

The significant difference in pre–post-pregnancy E/E′ ratio, indicates a persistent negative influence of pregnancy on diastolic function in women with structural heart disease 6 months postpartum.

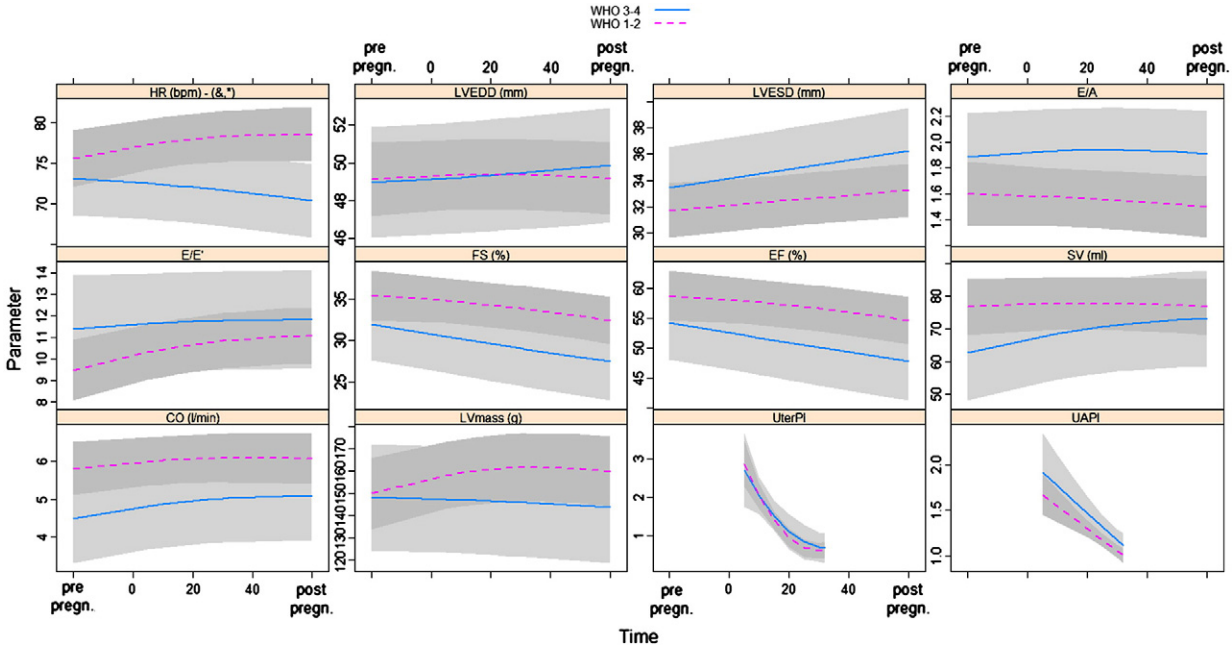

Fig. 3. Fitted longitudinal profiles for each parameter divided according to the severity of the cardiac condition. The dark gray area surrounding the dashed red line and lighter gray area surrounding the full blue line denote the 95% pointwise confidence intervals for the WHO1–2 group and WHO3–4 group respectively. The symbol '&' denotes parameters for which there was a significant difference in the average evolutions in time, and the symbol '*' parameters for which there was a significant difference between pre and post pregnancy measurements between groups.

Future studies should consider a longer postpartum follow-up to evaluate the transient or permanent nature of these changes.

To our knowledge this is the first study assessing diastolic function during and after pregnancy in women with structural heart disease.

Our observations also highlight the importance of tissue Doppler in the longitudinal assessment of diastolic dysfunction during pregnancy. As important volume- and loading shifts occur along with gestational age, changes are best evaluated by a combined assessment of the pulsed wave mitral inflow Doppler and load independent tissue Doppler of the mitral annulus.

Not surprisingly, all these findings suggest a mildly reduced cardiac potential for adaptation to the normal requisites of pregnancy in women with structural heart disease. The maladaptation is partly comparable to that observed in women with growth restriction and gestational hypertension, however diastolic dysfunction is more severe [11,30].

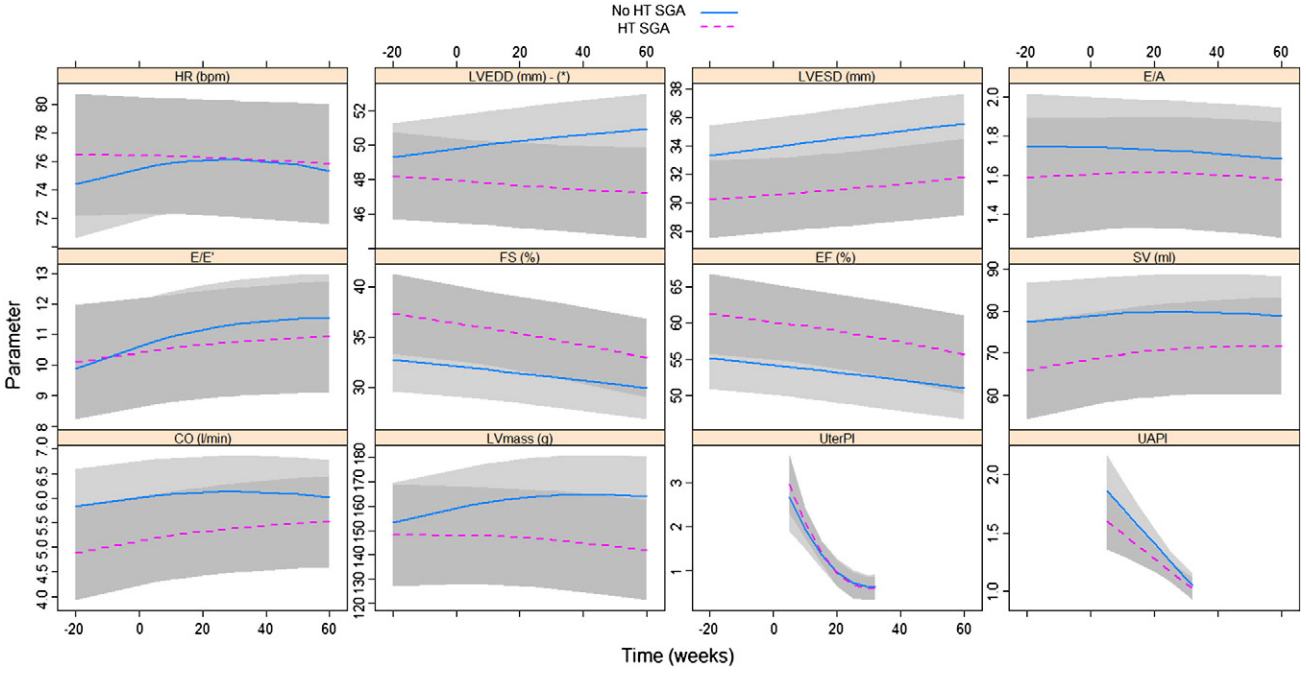

Fig. 4. Fitted longitudinal profiles for each parameter divided according to the occurrence of hypertension and/or small for gestational age fetus. The dark gray area surrounding the dashed red line and lighter gray area surrounding the full blue line denote the 95% pointwise confidence intervals for the group with and the group without hypertension and/or small for gestational age fetus respectively. The symbol '*' parameters for which there was a significant difference between pre and post pregnancy measurements.

When assessing the influence of severity of cardiac disease on cardiac adaptation we observed a similar pattern betweenWHO1–2 and WHO3–4 groups. While the trend seems visually more pronounced for the severe group (WHO 3–4) in Fig. 3, it failed to show statistical significance except for heart rate. Considering the known association between fetal growth restriction and hemodynamic maladaptation, the difference in adjusted birthweight centiles nevertheless emphasizes the impression of a reduced cardiac adaptive potential in high risk groups (Fig. 3) and thus requires further investigation in a larger population.

A similar effect is observed for the influence of HT/SGA in Fig. 4. This suggests that the reduced cardiac reserve is probably intrinsic to the structural heart disease rather than caused by the relatively high prevalence of hypertensive complications and SGA in our population (40%).

While the incidence of cardiac complications was relatively low in our population, the overall complication rate was high (62.5%). Previous research has demonstrated that women with heart disease are also at increased risk for non-cardiac and obstetric pathology [4–6]. Most hypertensive complications occurred in women with known risk factors such as aortic stenosis and coarctation [4]. As expected, SGA infants occurred mostly in women with atrial repair of transposition of the great arteries and pulmonary stenosis spectra [31,32]. Of note is the occurrence of post-partum depression in 2 women and a suicide attempt during pregnancy in a third woman. One could imagine that the burden of cardiac disease adds to the normal psychological challenge which accompanies pregnancy and early motherhood.

A higher incidence of depression or psychiatric disturbances has not been described in women with structural heart disease. It merits attention in further prospective trials as both cardiac disease and suicide are the main causes of maternal mortality in the western world [33].

Data on hemodynamic adaptation in pregnancy in women with structural heart disease are scarce and have not been described in a longitudinal matter. Therefore comparison with other studies is very difficult. Lesniak et al. analyzed the evolution of echocardiographic parameters of various valvular conditions during pregnancy, describing slightly different patterns according to the specific valvular pathology [9].

The strength of our study lies in its prospective nature and longitudinal assessment of hemodynamic adaptation during pregnancy as well as in the observation of the influence of pregnancy on long term cardiac outcome.

The main weaknesses of our study are the relatively limited number of patients, the heterogeneity of structural heart diseases and the absence of a control group. Future prospective research should be multicentric in order to allow pathology specific pattern analysis. Where evolutions during pregnancy were compared with previously published populations of pregnant women, a matched control group would certainly be preferable, ideally with inclusion of preconceptional measurements.

In conclusion our results show an attenuated cardiovascular adaptation to pregnancy in women with structural heart disease. Our data indicate a reduction in systolic function and progression diastolic dysfunction during pregnancy, which persist 6 months after pregnancy.

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