Accepted: 13 December 2023

DOI: 10.1111/1471-0528.17747

BJOG An International Journal of Obstetrics and Gynaecology

RESEARCH ARTICLE

Impact of maternal bariatric surgery on offspring perinatal cardiac function: A prospective study

Olga Patey[1] | **Margarita Bartsota**[1] | **Tanya Maric**[2,3] | **Deesha Patel**[2,3] | **Makrina Savvidou**[2,3,4] | **Julene S. Carvalho**[1,5]

[1]Brompton Centre for Fetal Cardiology, Royal Brompton Hospital NHS Foundation Trust, London, UK

[2]Academic Department of Obstetrics and Gynaecology, Chelsea & Westminster Hospital, London, UK

[3]Department of Metabolism, Digestion and Reproduction, Imperial College, London, UK

[4]Fetal Medicine Unit, Chelsea & Westminster Hospital, London, UK

[5]Cardiovascular Clinical Academic Group, Molecular and Clinical Sciences Research Institute, St George's University of London, London, UK

Correspondence
Makrina Savvidou, Fetal Medicine Unit, Chelsea & Westminster Hospital; Academic Department of Obstetrics and Gynaecology, Department of Metabolism, Digestion and Reproduction, Imperial College London, 369 Fulham Road, London SW10 9NH, UK.
Email: m.savvidou@imperial.ac.uk

Funding information
CW+, Grant/Award Number: 1169897

Abstract

Objective: To assess perinatal cardiac function in offspring of women with previous bariatric surgery and examine its association with maternal glucose control.

Design: Prospective study.

Setting: Maternity unit, UK.

Population: Fifty-four fetuses/neonates; 29 of post-bariatric surgery women and 25 of women without surgery.

Methods: Prospective, longitudinal observational study of pregnant women with and without previous bariatric surgery, matched for early pregnancy body mass index. Cardiac function of all offspring was assessed by two-dimensional conventional, spectral tissue Doppler and speckle-tracking echocardiography at 35–37 weeks of gestation and at 5–7 weeks of age. Maternal glycated haemoglobin (HbA1c) was measured at 27–30 weeks of gestation. Maternal demographics and fetal/infant cardiac function indices were compared between the groups. Correlation coefficient (r) is reported.

Main outcome measures: Fetal/infant cardiac function indices.

Results: Compared with no-bariatric neonates, offspring of post-bariatric women were smaller at birth (birthweight centiles: 64.96 ± 36.41 versus 40.17 ± 27.99; $p = 0.007$). There were no significant differences in fetal/infant cardiac function indices and perinatal cardiac changes, between groups. There was a positive correlation between maternal HbA1c and fetal left ventricular (LV) longitudinal strain ($r = 0.33$) and LV longitudinal strain rate ($r = 0.29$), suggesting an inverse relation between HbA1c and fetal LV systolic function, but this was mainly seen in offspring of women with no previous bariatric surgery ($r = 0.56$ and $r = 0.50$, respectively).

Conclusions: Maternal bariatric surgery does not appear to inadvertently affect the offspring cardiac performance. We found an inverse correlation between maternal HbA1c levels and fetal LV systolic function but this was mainly seen in the no-bariatric pregnancies.

KEYWORDS
bariatric surgery, echocardiography, fetal, pregnancy

Makrina Savvidou and Julene S. Carvalho contributed equally as last authors.

1 | INTRODUCTION

Worldwide, the rates of obesity have tripled since 1975. In 2016, almost 40% of women were overweight and 15% were obese.[1] In the recent Mother and Babies Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) report, obesity is noted to be an important contributing factor to adverse pregnancy/maternal outcomes, so an effective way for obese women to achieve normal weight before conception is needed.[2]

Unfortunately, lifestyle interventions and pharmacological therapy have not been successful in achieving durable weight loss.[3,4] Currently, bariatric surgery (gastric band, sleeve gastrectomy and gastric bypass) is considered to be the most promising modality for long-term weight loss and is associated with a reduction in mortality, resolution of diabetes and improvement of cardiovascular profile.[5–8] As a result, the number of women presenting pregnant, having had a previous bariatric surgery, is increasing.[9] It is now well established that pregnancy following bariatric surgery is associated with a reduction in the rates of gestational diabetes mellitus (GDM), hypertensive disorders and macrosomic babies, but an increase in the rates of small-for-gestational-age neonates.[10,11] Studies on the effects of maternal bariatric surgery on the short-term and long-term cardiometabolic health of their offspring have given conflicting results. Some studies suggest that bariatric surgery improves the offspring cardiometabolic profile, including better (normal) weight, better lipid profile, greater insulin sensitivity and differential gene methylation, whereas other studies have shown that children of post-bariatric mothers have higher weight, weight gain, adiposity parameters and diastolic blood pressure, but no difference in endothelial function, compared with children of women without surgery.[12–17] Nevertheless, there is strong evidence that maternal obesity affects the metabolic and cardiac function of their offspring[18–21] and may contribute to their increased risk of cardiovascular disease later in life.[22–24] Several animal studies have shown impaired fetal cardiac function among obese mothers.[18] Some human studies have also demonstrated that fetuses of obese women have signs of cardiac dysfunction from as early as 14 weeks of gestation,[19,20] and altered autonomic nervous system activity.[21] Although the exact mechanisms are unknown, obesity-mediated maternal hyperglycaemia, leading to fetal hyperinsulinaemia[25] and upregulation of the inflammatory mediators of the myocardium have been implicated.[26]

The aim of the current study was to examine the perinatal cardiac function, in both the last trimester of pregnancy and early infancy, of offspring of women with previous bariatric surgery compared with offspring of women without surgery, and to investigate its association with maternal glucose control. As pre-pregnancy maternal bariatric surgery is associated with an improvement in maternal insulin resistance,[27] and considering the link between maternal hyperglycaemia and fetal cardiac dysfunction,[26] we hypothesised that offspring of post-bariatric women will demonstrate better perinatal cardiac function.

2 | METHODS

2.1 | Study population

This study was part of a large prospective longitudinal study aiming to investigate the effect of maternal obesity, and bariatric surgery in particular, on pregnancy outcomes. The study design has been previously described.[27] In brief, women with previous bariatric surgery were matched for early pregnancy body mass index (BMI) with pregnant women with no such surgery. Women were seen; their weight (kg), height (cm), BMI (kg/m^2) and blood pressure were measured; blood and urine samples were collected and fetal growth ultrasound scans were performed longitudinally during pregnancy at 11–14, 20–24, 30–32 and 35–37 weeks of gestation. From 20 to 24 weeks onwards, the estimated fetal weight was calculated, based on measurements of fetal head, abdominal circumference and femur length.[28] For women with previous bariatric surgery, the date of surgery and their weight before surgery were recorded. Based on this information, the time from surgery to conception, total weight loss (%) [((pre-surgery weight–early pregnancy weight)/pre-surgery weight) × 100] and excess weight loss (%) [((pre-surgery excess weight–early pregnancy excess weight)/pre-surgery excess weight) × 100] were calculated. At 27–30 weeks all women underwent screening for GDM. All no-bariatric and the majority of post-bariatric women ($n = 20$) underwent a 75-g, 2-hour full oral glucose tolerance test as a diagnostic test for GDM, which was defined according to National Institute for Health and Care Excellence guidelines.[29] A small number of post-bariatric women ($n = 9$), recruited after December 2017, had fasting glucose levels measured and capillary blood glucose monitoring for 2 weeks, as studies have suggested that the oral glucose tolerance test may not be a reliable method to diagnose GDM in this group of women.[30] At the same time, 27–30 weeks of gestation, maternal levels of glycated haemoglobin (HbA1c), which can reflect the overall glucose control over a period of weeks/months, and haemoglobin were measured in all participants (G8 Glycohemoglobin Analyser, Tosoh Corporation; intra-assay variability 0.6%, inter-assay variability: 0.56%).

Information on pregnancy outcome was obtained from the hospital's perinatal database. Birthweight centiles were calculated based on birthweight and gestational age at delivery.[31] Offspring were seen again at 5–7 weeks of age, had their weight measured and infant weight centile calculated.[32] All women gave written informed consent, and the study was approved by the Local REC (No: 14/LO/0592).

2.2 | Fetal and neonatal echocardiography

For the purposes of this study, cardiac function of the offspring was assessed by two-dimensional (2D) echocardiography at 35–37 weeks of gestation and at 5–7 weeks of age. All echocardiograms were performed by experienced fetal and paediatric cardiologists.[33]

Fetal and postnatal studies included B-mode, M-mode, spectral pulsed-wave (PW) Doppler, spectral tissue Doppler imaging (PW-TDI) and speckle tracking imaging echocardiography (STE). Three investigators (JSC, MB, OP) performed all fetal and neonatal ultrasound examinations using an ARIETTA V70 (Hitachi Ltd, Tokyo, Japan). Fetal M-mode, B-mode and PW Doppler measurements were made with the convex array transducer C251 (5–1 MHz), while the Sector Single Crystal probes S31 (9–2 MHz) and S42 were used for the neonatal and paediatric heart examination. Cross-sectional images for STE analysis was recorded as raw data using the same ultrasound transducer (adult linear transducer S12 5–1 MHz) in both fetal and neonatal groups.

M-mode ultrasound was used for assessment of cardiac systolic function (shortening fraction estimation) and longitudinal annular plane systolic excursion of tricuspid and mitral valves and interventricular septum (TAPSE, MAPSE and SAPSE, respectively). B-mode imaging was performed for obtaining measurements of valve dimensions, ventricular chambers, and both left ventricular (LV) and right ventricular (RV) sphericity indices calculated by dividing ventricular end-diastolic dimension by end-diastolic length for each ventricle.[34,35] PW Doppler technique was used to obtain Doppler signals from the inflow and outflow tracts for evaluation of diastolic and systolic function, respectively. LV and RV stroke volume (SV), cardiac output (CO) and cardiac index (CI) were calculated as follows: SV = outflow valve area × Velocity Time Integral, CO = SV × Heart Rate, and CI = CO/body weight. PW-TDI technique was applied to measure systolic and diastolic myocardial velocities and time intervals with calculation of LV and RV myocardial performance index. STE was used to derive myocardial deformation parameters such as longitudinal strain and systolic strain rate with frame rate greater than 100 frames per second. All STE measurements were performed in a single beat according to the standardised protocol of the study and with regards to previously described fetal echo techniques.[34–36] Several digital clips were obtained and then transferred as raw data to the Tissue Tracking software dedicated for 2D (DAS-RS1; Hitachi Ltd, Japan) for further analysis, which was performed by one investigator (OP). The time-interval values were adjusted by cardiac cycle length considering differences in heart rate. Other fetal and neonatal indices were normalised by dividing corresponding measurements by the ventricular length or end-diastolic dimension according to study methodology with regards to previous recommendations.[34,36–39]

Finally, we investigated any possible associations between maternal glucose control, as assessed by HbA1c, and fetal/infant cardiovascular parameters.

2.3 | Statistical analysis

The Kolmogoroff–Smirnoff test was used to assess normality of the data distribution. Normally and not normally distributed continuous variables were expressed as mean ± standard deviation or as median (interquartile range), respectively. Logarithmic transformation was performed, when necessary. Categorical data are summarised using count and percentages. In order to examine the differences between the study groups, unpaired *t* test/Mann–Whitney *U* test and chi-square tests were used for numerical and categorical data, respectively. Pearson's correlation and multiple linear regression analyses were used to examine the relation between maternal variables and prenatal/postnatal cardiac parameters in the groups, where appropriate. Correlation coefficient (*r*) and 95% confidence intervals are given, when appropriate.

There is no previous study on the cardiac function of offspring of women with previous bariatric surgery, so we based our sample calculation on previous studies in fetuses of diabetic pregnancies.[34] Power analysis indicated that 20 pregnant women in each group (no-bariatric and post-bariatric) would have a power over 80% with $\alpha = 0.05$ (two tails) to detect a mean difference of 0.46 in the relative interventricular septum thickness; a difference reported between fetuses of normal and diabetic mothers.[34] The statistical software package SPSS Statistics 23.0 (SPSS Inc., Chicago, IL, USA) was used for data analyses. Differences were considered as significant only at $p < 0.01$ (Bonferroni correction for type 1 error or false-positive results of multiple measurements).

3 | RESULTS

The study period was May 2016 to August 2019. The study included 29 fetuses of post-bariatric pregnant women (4 with gastric band, 8 with sleeve gastrectomy and 17 with gastric bypass) and 25 fetuses of women without surgery but similar maternal booking BMI. One woman from the post-bariatric group and one from the no-bariatric group did not attend for the postnatal echocardiogram, leaving 28 post-bariatric and 24 no-bariatric infants for assessment. Descriptive maternal, pregnancy and offspring characteristics of the study population are given in Table 1.

3.1 | Maternal and pregnancy characteristics

Women with previous bariatric surgery were older compared with the no-surgery group but there were no other differences in the maternal demographics. The maternal BMI of women at booking and at 36 weeks of gestation, when fetal echocardiography was performed, was similar in the groups. In the post-bariatric group, the mean surgery to conception interval was 60.9 ± 36.7 months and women lost, on average, 11.8 ± 8.0 BMI units, had a total weight loss of 27.35 ± 19.80% and excess body weight loss of 54.85 ± 38.81%, from pre-surgery to early pregnancy. None of the participants had pre-existing diabetes and only one woman in the post-bariatric group developed GDM requiring metformin in the late third trimester.

TABLE 1 Maternal, pregnancy and offspring characteristics of the study participants.

Maternal and neonatal characteristics	No-bariatric cohort, $n=25$	Post-bariatric cohort, $n=29$	p value
Maternal age (years)	29.52 ± 4.82	34.69 ± 4.21	**<0.001**
Maternal race, *n* (%)			
White	19 (76.0)	21 (72.4)	0.76
Other	6 (24.0)	8 (27.6)	
Parity, *n* (%)			
Nulliparous	17 (68.0)	16 (55.2)	0.33
Parous	8 (32.0)	13 (44.8)	
Smoking, *n* (%)			
No	24 (96.0)	27 (93.1)	0.64
Yes	1 (4.0)	2 (6.9)	
Method of conception, *n* (%)			
Spontaneous	24 (96.0)	27 (93.1)	0.64
Assisted	1 (4.0)	2 (6.9)	
Maternal BMI at booking (kg/m^2)	36.56 ± 6.72	33.69 ± 6.84	0.12
Maternal HbA1c at OGTT (mmol/mol)	32.16 ± 4.96	32.28 ± 3.28	0.91
Maternal haemoglobin at OGTT (g/L)	114.20 ± 10.63	111.28 ± 12.11	0.35
Gestational diabetes mellitus, *n* (%)			
No	25 (100.0)	28 (96.6)	0.34
Yes	0 (0)	1 (3.4)	
Maternal BMI at 36 weeks (kg/m^2)	40.07 ± 6.27	37.71 ± 6.96	0.19
Gestational age at fetal echocardiography (weeks)	36.12 ± 0.67	36.18 ± 0.63	0.71
Estimated fetal weight at 36 weeks (centile)	57.88 ± 28.03	40.53 ± 28.14	0.02
Gestational age at delivery (weeks)	39.82 ± 1.54	39.32 ± 1.27	0.99
Mode of delivery, *n* (%)			
Vaginal	13 (52.0)	16 (55.2)	0.81
Caesarean section	12 (48.0)	13 (44.8)	
Birthweight (g)	3628.72 ± 667.22	3218.24 ± 505.09	0.01
Birthweight (centile)	64.96 ± 36.41	40.17 ± 27.99	**0.007**
Small for gestational age, *n* (%)	5 (20%)	6 (29%)	0.95
Neonatal systolic blood pressure (mmHg)	79.50 (66.62–90.50)	70.00 (30.00–84.00)	0.13
Neonatal diastolic blood pressure (mmHg)	40.64 ± 8.94	35.43 ± 8.04	0.05
Type of feeding at hospital discharge, *n* (%)			
Breast milk	15 (60.0)	19 (65.5)	0.67
Mixed or formula milk	10 (40.0)	10 (34.5)	
Infant characteristics	**No-bariatric cohort, $n=24$**	**Post-bariatric cohort, $n=28$**	***p* value**
Age (weeks)	5.72 ± 1.39	6.11 ± 1.83	0.39
Weight (kg)	4.89 ± 0.75	4.49 ± 0.85	0.07
Weight (centiles)	62.53 ± 27.9	44.48 ± 31.58	0.03

Note: Data are given as mean ± SD, median (interquartile range) or *n* (%), as indicated. Significant *p* values are denoted in bold.
Abbreviations: BMI, body mass index; HbA1c, glycated haemoglobin; OGTT, oral glucose tolerance test.

3.2 | Fetal and infant parameters

Compared with the no-bariatric group, fetuses of post-bariatric women tended to be smaller at the 36-week ultrasound assessment, birth and 5–7 weeks of age (Table 1). There were no major structural cardiac abnormalities in any of the fetuses. In five fetuses (four from the no-bariatric group and one from the post-bariatric group), a small muscular ventricular septal defect was suspected, which was confirmed in two of the no-bariatric infants at the time of the postnatal scan.

The prenatal and postnatal cardiac parameters of the two groups are given (unadjusted values) in Table 2. On both fetal and infant echocardiograms, valve diameters and

TABLE 2 Fetal and infant parameters (unadjusted values) of cardiovascular function in the study groups.

Parameter	No-bariatric fetuses, $n = 25$	Post-bariatric fetuses, $n = 29$	p value[a]	No-bariatric infants, $n = 24$	Post-bariatric infants, $n = 28$	p value[a]
Cardiac geometry						
LV Sphericity index	0.53 ± 0.08	0.55 ± 0.07	0.60	0.64 ± 0.05	0.62 ± 0.07	0.31
RV Sphericity index	0.63 ± 0.10	0.65 ± 0.10	0.49	0.53 ± 0.06	0.53 ± 0.07	0.75
IVS (mm)	3.60 ± 0.57	3.60 ± 0.57	0.97	3.68 ± 0.65	3.90 ± 0.87	0.32
IVS (*Z* scores)	0.77 ± 2.78	0.75 ± 3.06	0.97	−0.39 ± 0.79	−0.11 ± 1.07	0.27
Systolic function						
Heart rate (bpm)	141.32 ± 12.28	138.48 ± 7.94	0.31	149.95 ± 15.30	146.46 ± 11.79	0.35
LV S′ (normalised by LV length) (m/s/mm)	0.22 ± 0.06	0.22 ± 0.06	0.90	0.17 ± 0.03	0.19 ± 0.02	0.12
RV S′ (normalised by RV length) (m/s/mm)	0.26 ± 0.07	0.25 ± 0.06	0.56	0.28 ± 0.04	0.30 ± 0.05	0.24
IVS S′ (normalised by LV length) (m/s/mm)	0.17 ± 0.04	0.18 ± 0.03	0.42	0.17 ± 0.03	0.18 ± 0.03	0.16
MAPSE (mm)	6.33 ± 1.14	6.06 ± 1.15	0.40	7.47 ± 1.04	8.04 ± 1.25	0.08
MAPSE (normalised by LV length)	0.24 ± 0.04	0.23 ± 0.05	0.53	0.22 ± 0.02	0.24 ± 0.03	0.11
TAPSE (mm)	8.45 ± 1.80	7.89 ± 1.34	0.19	12.14 ± 1.89	13.11 ± 2.25	0.11
TAPSE (normalised by RV length)	0.55 ± 0.16	0.50 ± 0.1	0.18	0.80 ± 0.16	0.85 ± 0.15	0.27
SAPSE (mm)	3.53 ± 0.71	3.99 ± 1.25	0.11	3.61 (3.14–4.24)	4.07 (3.29–7.22)	0.04
SAPSE (normalised by LV length)	0.13 ± 0.03	0.16 ± 0.05	0.08	0.10 (0.09–0.12)	0.12 (0.11–0.20)	0.01
Diastolic function						
RV-E/A′	0.78 (0.66–0.96)	0.79 (0.69–0.96)	1	1.08 ± 0.31	1.10 ± 0.28	0.82
RV-E/E′	5.91 ± 1.24	5.94 ± 1.42	0.93	4.54 ± 0.96	4.61 ± 1.74	0.91
MV-E/A	0.80 ± 0.14	0.74 ± 0.15	0.20	1.17 ± 0.25	1.15 ± 0.24	0.78
TV-E/A	0.77 ± 0.1	0.73 ± 0.08	0.20	0.84 ± 0.22	0.84 ± 0.26	0.93
LV-E/A'	1.08 ± 0.31	1.04 ± 0.33	0.62	1.26 ± 0.35	1.16 ± 0.36	0.32
LV-E/E'	5.81 ± 1.54	5.68 ± 1.62	0.76	9.17 ± 2.59	9.49 ± 3.78	0.83
IVS-E/A'	0.94 (0.81–1.18)	0.81 (0.71–0.90)	0.07	1.03 ± 0.32	1.02 ± 0.34	0.93
Myocardial function						
LV Longitudinal strain (%)	−11.02 ± 3.52	−11.29 ± 3.90	0.79	−15.43 ± 3.21	−14.51 ± 3.22	0.31
LV Longitudinal strain (normalised by LV length) (%/mm)	−0.42 ± 0.15	−0.44 ± 0.16	0.78	−0.47 ± 0.11	−0.44 ± 0.10	0.29
LV Longitudinal strain rate (1/s)	−0.93 ± 0.27	−0.94 ± 0.42	0.93	−1.22 ± 0.22	−1.06 ± 0.23	0.01
LV Longitudinal strain rate (normalised by LV length) (1/s/mm)	−0.04 ± 0.01	−0.04 ± 0.02	0.88	−0.037 ± 0.007	−0.032 ± 0.008	0.03
RV Longitudinal strain (%)	−12.42 ± 3.71	−10.91 ± 2.92	0.11	−15.91 ± 5.02	−16.79 ± 3.59	0.48
RV Longitudinal strain (normalised by RV length) (%/mm)	−0.80 ± 0.29	−0.70 ± 0.18	0.15	−1.05 ± 0.36	−1.09 ± 0.21	0.57
RV Longitudinal strain rate (1/s)	−0.96 ± 0.24	−0.95 ± 0.18	0.08	−1.40 ± 0.35	−1.34 ± 0.28	0.52
RV Longitudinal strain rate (normalised by RV length) (1/s/mm)	−0.06 ± 0.02	−0.05 ± 0.01	0.11	−0.09 ± 0.02	−0.08 ± 0.18	0.48

(Continues)

TABLE 2 (Continued)

Parameter	No-bariatric fetuses, $n=25$	Post-bariatric fetuses, $n=29$	p value[a]	No-bariatric infants, $n=24$	Post-bariatric infants, $n=28$	p value[a]
Global ventricular performance						
LV-MPI′	0.50 ± 0.08	0.55 ± 0.10	0.04	0.41 ± 0.05	0.41 ± 0.06	0.82
RV-MPI′	0.48 ± 0.09	0.49 ± 0.11	0.69	0.35 ± 0.07	0.37 ± 0.09	0.57
LV-CO (mL/min)	564.88 ± 177.06	504.68 ± 131.53	0.16	992.02 ± 228.66	1054.70 ± 347.67	0.45
LV-CI (mL/min/kg)	197.19 ± 55.43	188.56 ± 52.21	0.56	203.37 ± 43.87	242.35 ± 86.65	0.05
RVCO (mL/min)	753.21 ± 168.08	680.70 ± 157.96	0.11	1117.11 ± 343.45	1212.73 ± 545.73	0.46
RVCI (mL/min/kg)	264.99 ± 60.59	255.17 ± 69.82	0.59	231.23 ± 74.17	284.60 ± 156.94	0.13
CCO (mL/min)	1325.65 ± 289.10	1185.39 ± 239.11	0.06	2109.14 ± 492.11	2177.61 ± 864.89	0.73
CCI (mL/min/kg)	464.42 ± 92.67	443.72 ± 104.12	0.46	434.61 ± 101.93	527.37 ± 229.86	0.07

Note: Data are given as mean ± SD and median (interquartile range). Values are normalised by ventricular length or cardiac cycle length as appropriate. The wall thickness values are normalised by end-diastolic ventricular dimensions.

Abbreviations: A, atrial contraction diastolic peak velocity derived by pulsed wave Doppler; A′, atrial contraction diastolic peak tissue velocity derived by TDI; CCO/CCI, combined CO/CI; CI, cardiac index; CO, cardiac output; E, early diastolic peak velocity derived by pulsed wave Doppler; E′, early diastolic peak tissue velocity derived by TDI; IVS, interventricular septum; MAPSE/TAPSE/SAPSE, mitral/tricuspid/septal annular plane systolic excursion; MPI′, myocardial performance index; RV/LV, right/left ventricular.

[a]Comparisons were made between no-bariatric and post-bariatric fetuses and infants.

PW Doppler velocities were within the normal range. There were no significant differences between the no-bariatric and post-bariatric fetuses or infants. In particular, there were no differences in the STE parameters between the groups, and using multiple regression, we found that bariatric surgery was not a significant determinant of any of the STE parameters, after adjusting for possible confounders including maternal age, ethnicity, smoking, method of conception, BMI, gestational age and estimated fetal weight at the time of the fetal echocardiography, or age and infant weight, at the time of the postnatal assessment.

Offspring from both groups demonstrated similar cardiovascular transitional changes, from fetal to neonatal circulation, with improvement in indices of LV function, as assessed by myocardial function parameters (data not provided but available on request).

3.3 | Correlation between maternal indices and fetal/infant cardiovascular parameters

We investigated the correlation between maternal glucose control, as assessed by measurement of HbA1c, and fetal/infant cardiovascular parameters. In the fetal cohort, overall, we found a positive correlation between maternal HbA1c and fetal LV longitudinal strain ($r=0.33$), LV longitudinal strain normalised by LV length ($r=0.34$), LV longitudinal strain rate ($r=0.29$) and LV longitudinal strain rate normalised by LV length ($r=0.30$), indicating an inverse correlation between maternal glucaemic levels and fetal LV systolic function, which, nevertheless, remained within the normal range. When we examined the groups separately, we found positive correlations between maternal HbA1c and fetal LV longitudinal strain ($r=0.56$), LV longitudinal strain normalised by LV length ($r=0.56$), LV longitudinal strain rate ($r=0.50$) (Figure 1) and LV longitudinal strain rate normalised by LV length ($r=0.52$) in fetuses of women with no previous surgery but no correlations in fetuses of post-bariatric women (r values of 0.06, 0.08, 0.16 and 0.18, respectively).

In the infants, there was no correlation between maternal glucose control, as assessed by HbA1c, and any of the STE indices in the whole group or any of the subgroups.

4 | DISCUSSION

4.1 | Main findings

In the current study, we have shown that, reassuringly, the prenatal and postnatal cardiac function of offspring of women with previous bariatric surgery is similar to that in offspring of women with no history of weight loss surgery, suggesting that maternal bariatric surgery is unlikely to inadvertently affect the cardiovascular performance of their children, at least in the late third trimester of pregnancy and early infancy. Despite having undergone bariatric surgery, the majority of women in the post-bariatric group remained overweight/obese and the values of fetal cardiovascular parameters reported here are similar to the values previously published in obese pregnant women,[18] adding external validity to our results.

4.2 | Strengths and limitations

This was a longitudinal study from fetal to postnatal life and therefore we were able to assess perinatal changes. All cardiac assessments were performed by expert fetal cardiologists using advanced echocardiographic methods. We examined the fetal cardiac function in late pregnancy, at the time when the fetal heart is under more stress compared

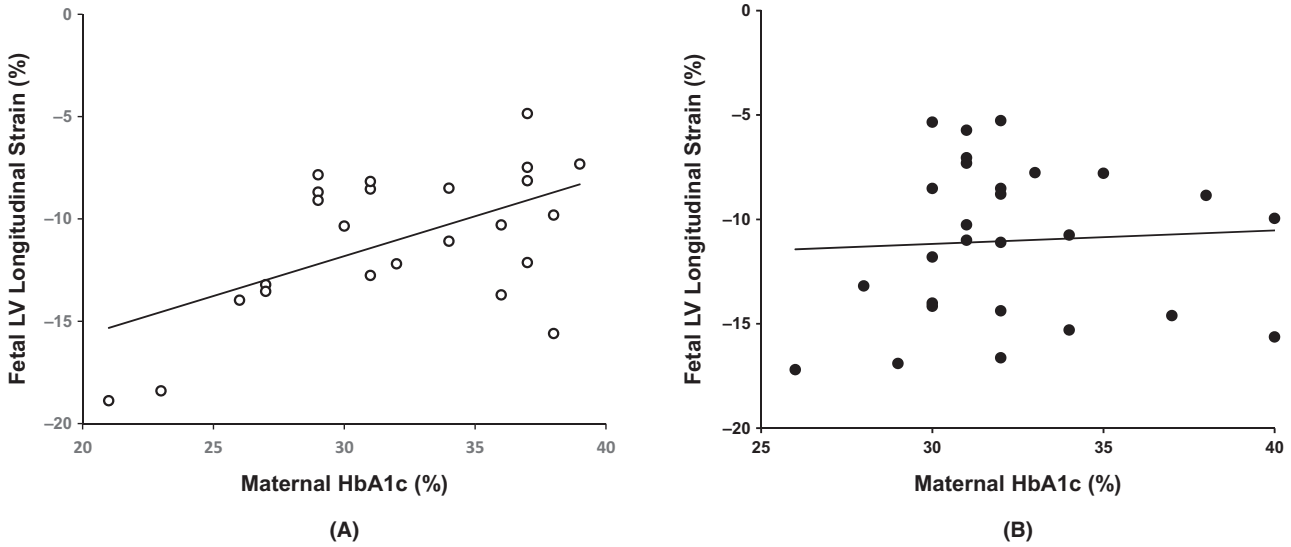

FIGURE 1 Scatterplots illustrating the correlation (regression line) between maternal glycated haemoglobin (HbA1c) and fetal left ventricular (LV) strain in the no-bariatric (A) ($r = 0.56$; 95% CI 0.20–0.78) and post-bariatric (B) ($r = 0.06$; 95% CI: −0.32 to 0.43) groups.

with earlier gestational ages. Additionally, we assessed the infant's cardiac function at 6 weeks of life, when the heart has already adapted to the postnatal environment and circulation, so avoiding transient perinatal changes. Our sample size was calculated to detect a difference in the relative interventricular septum thickness, similar to the one seen in diabetic compared with uncomplicated pregnancies.[34] However, because of the small number of cases, our study may not have had enough power to detect differences in all cardiac indices and correlations assessed or the effect of the different types of maternal weight loss surgery on the offspring heart performance. Despite having undergone a weight loss surgery, most women in this group continued to be overweight/obese and our findings may not be applicable to women who achieve a normal BMI, as a result of the surgery. As we assessed the cardiac function at 6 weeks of age, we cannot comment on the offspring cardiovascular health later in life and, therefore, long-term follow-up studies will be required. Although HbA1c levels reflect the average glucose levels over the preceding 3 months, more detailed assessment of the maternal glucose homeostasis throughout pregnancy may be required to confirm our findings.

4.3 | Interpretation

Maternal metabolic environment appears to have an effect on fetal cardiac function.[18–24] Although, reassuringly, we did not find a difference between the cardiac performance of offspring of women with previous bariatric surgery and those without, we have shown an inverse correlation between maternal glucose control, as assessed by HbA1c, and fetal cardiac systolic function; although this was maintained within the normal range. In animal models, and in the context of overt diabetes, maternal hyperglycaemia has been associated with increased cardiac growth, as a result of elevated collagen synthesis, suppressed fibronectin synthesis, profibrosis, apoptosis, together with altered expression of cardiac genes involved in contractile, electrical, endocrine and metabolic function of the heart.[40,41] Human studies have also shown that fetuses of women with established pre-gestational diabetes demonstrate altered cardiac geometry, myocardial deformation and ventricular function,[34] and these changes appear to persist in infancy,[42] when abnormal cardiovascular structure and function, as assessed by carotid intima-media thickness, carotid-femoral pulse wave velocity and aortic augmentation index[43] are also seen.

Our study has demonstrated a 'negative' impact of maternal glucose homeostasis on fetal cardiac performance, even in cases of 'normal' maternal glucose control, as demonstrated by the normal HbA1c values, suggesting that the 'negative' effect is not restricted only to cases of overt diabetes, as previously described.[40–43] This is comparable to the associations, described in other studies, between increasing (but still normal) maternal glucose levels, across a continuum, and increasing birthweight, cord C-peptide and cord insulin levels.[44] Of note, in our study, the inverse correlation between maternal glucose control and fetal cardiac systolic function was seen only in the no-bariatric group. It appears that in the post-bariatric group there may be a disruption of the maternal–fetal metabolic signalling, similar to the lack of correlation between maternal and neonatal insulin resistance described in this population.[27] The reasons for this dissociation are unknown but could be related to hormonal and metabolic changes induced by the bariatric surgery and include Bile flow alteration, Reduction in stomach size, Anatomical gut rearrangement and altered flow of nutrients, Vagal stimulation and Enteric gut hormone modulation (the BRAVE effect),[45] which could lead to changes in the maternal metabolome, gut microbiome and metabolic signature of the neonate.[46] Currently, we are uncertain whether the

'independence' of the fetal unit from the maternal unit, seen in the post-bariatric pregnancies, could play a role in fetal development and adaptation and, as such, influence the future metabolic health of these children. We did not find an association between maternal glucose control and the infant's cardiac function, suggesting that either maternal glucose homeostasis during pregnancy does not play a role or that other environmental factors, such as type of feeding, may be involved in determining the future cardiovascular performance of the offspring.[47] At least a third of our neonates were on mixed or formula feed at the time of hospital discharge (Table 1), and probably more at the time of the postnatal echocardiography assessment.

We and others have previously shown that offspring of women with previous bariatric surgery are smaller and thinner during pregnancy[48,49] and at delivery, as assessed by skin-fold measurements and dual-energy-X-ray absorptiometry scanning.[50] Although in the current study, the rate of small babies in our groups was not significantly different, probably due to the small sample size, we have found post-bariatric offspring to have lower weight at birth and in early infancy (5–7 weeks of age), compared with those of women without surgery. Currently, there is no consensus on the effect of maternal bariatric surgery on the long-term prevalence of obesity in the offspring, as some studies have shown a reduction, whereas others have shown an increase in obesity rates.[12–15] More studies are needed to investigate whether maternal bariatric surgery itself, low birthweight, postnatal weight gain or diet has greater impact on the offspring's weight later in life.

5 | CONCLUSIONS

In summary, the study has shown that the cardiac performance of the offspring of women with previous bariatric surgery, assessed in late pregnancy and early infancy, is not altered. In no-bariatric pregnancies, we also found an inverse correlation between maternal glucose control and fetal cardiac systolic function but this association was not seen in the post-bariatric cohort. The extent to which these differences impact the future metabolic health of the offspring remains to be determined.

AUTHOR CONTRIBUTIONS

The study was conceived and planned by MS, MB and JSC. The study was carried out by OP, MB, TM, DP and JSC. Analysis of the data was performed by OP, MB, MS and JSC. The manuscript was written by MS and JSC and all authors approved the paper.

ACKNOWLEDGEMENTS

The authors would like to thank Miriam Bourke and Allessandra Rocco for their assistance in the research clinic and all the women taking part in the study. The authors would also like to thank the statistician, Dr Sebastian Nastuta, for his statistical advice and input.

FUNDING INFORMATION

The study was supported by CW+ (CWPLUS Registered Charity No 1169897). The funding sources had no role in the study design, interpretation of data, writing of the report and the decision to submit the article for publication.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

Data are available from the authors upon request.

ETHICS APPROVAL

The study was approved by the Local REC (No: 14/LO/0592—date of approval: 3 June 2014) and all women gave written, informed consent.

ORCID

Tanya Maric https://orcid.org/0000-0002-4878-5092
Makrina Savvidou https://orcid.org/0000-0002-0125-2299

REFERENCES

1. World Health Organization. Obesity and overweight [cited 2023 Dec 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
2. Knight M, Bunch K, Tuffnell D, Patel R, Shakespeare J, Kotnis R, et al. Saving lives, improving mothers' care—lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2017–19. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2021.
3. Apovian CM, Aronne LJ, Bessesen DH, Bessesen DH, McDonnell ME, Murad MH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metabol. 2015;100:342–62.
4. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292:1724–37.
5. Buchwald H, Estok R, Fahrbach K, Banel D, Jensen MD, Pories WJ, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med. 2009;122:248–256.e5.
6. Cardoso L, Rodrigues D, Gomes L, Carrilho F. Short- and long-term mortality after bariatric surgery: a systematic review and meta-analysis. Diabetes Obes Metab. 2017;19:1223–32.
7. Aggarwal R, Harling L, Efthimiou E, Darzi A, Athanasiou T, Ashrafian H. The effects of bariatric surgery on cardiac structure and function: a systematic review of cardiac imaging outcomes. Obes Surg. 2016;26:1030–40.
8. Owen JG, Yazdi F, Reisin E. Bariatric surgery and hypertension. Am J Hypertens. 2017;31:11–7.
9. Booth HP, Khan O, Fildes A, Prevost AT, Reddy M, Charlton J, et al. Changing epidemiology of bariatric surgery in the UK: cohort study using primary care electronic health records. Obes Surg. 2016;26:1900–5.
10. Johansson K, Cnattingius S, Näslund I, Roos N, Trolle Lagerros Y, Granath F, et al. Outcomes of pregnancy after bariatric surgery. N Engl J Med. 2015;372:814–24.
11. Stephansson O, Johansson K, Näslund I, Neovius M. Bariatric surgery and preterm birth. N Engl J Med. 2016;375:805–6.
12. Barisione M, Carlini F, Gradaschi R, Camerini G, Adami GF. Body weight at developmental age in siblings born to mothers before and after surgically induced weight loss. Surg Obes Relat Dis. 2012;8:387–91.
13. Berglind D, Müller P, Willmer M, Sinha I, Tynelius P, Näslund E, et al. Differential methylation in inflammation and type 2 diabetes genes

in siblings born before and after maternal bariatric surgery. Obesity. 2016;24:250–61.
14. Willmer M, Berglind D, Sørensen TIA, Näslund E, Tynelius P, Rasmussen F. Surgically induced interpregnancy weight loss and prevalence of overweight and obesity in offspring. PLoS One. 2013;8:e82247.
15. Van De Maele K, Devlieger R, De Schepper J, Gies I. Endothelial function and its determinants in children born after maternal bariatric surgery. Pediatr Res. 2022;91:699–704.
16. Van De Maele K, Bogaerts A, De Schepper J, Provyn S, Ceulemans D, Guelinckx I, et al. Adiposity, psychomotor and behaviour outcomes of children born after maternal bariatric surgery. Pediatr Obes. 2021;16:e12749.
17. Smith J, Cianflone K, Biron S, Hould FS, Lebel S, Marceau S, et al. Effects of maternal surgical weight loss in mothers on intergenerational transmission of obesity. J Clin Endocrinol Metab. 2009;94:4275–83.
18. Fernandez-Twinn DS, Blackmore HL, Siggens L, Giussani DA, Cross CM, Foo R, et al. The programming of cardiac hypertrophy in the offspring by maternal obesity is associated with hyperinsulinemia, AKT, ERK, and mTOR activation. Endocrinology. 2012;153:5961–71.
19. Ece I, Uner A, Balli S, Kibar AE, Oflaz MB, Kurdoglu M. The effects of pre-pregnancy obesity on fetal cardiac functions. Pediatr Cardiol. 2014;35:838–43.
20. Ingul CB, Lorås L, Tegnander E, Eik-Nes SH, Brantberg A. Maternal obesity affects fetal myocardial function as early as in the first trimester. Ultrasound Obstet Gynecol. 2016;47:433–42.
21. Mat Husin H, Schleger F, Bauer I, Fehlert E, Kiefer-Schmidt I, Weiss M, et al. Maternal weight, weight gain, and metabolism are associated with changes in fetal heart rate and variability. Obesity. 2020;28:114–21.
22. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. Rev Obstet Gynecol. 2008;1:170–8.
23. Ehrenthal DB, Maiden K, Rao A, West DW, Gidding SS, Bartoshesky L, et al. Independent relation of maternal prenatal factors to early childhood obesity in the offspring. Obstet Gynecol. 2013;121:115–21.
24. Reynolds RM, Allan KM, Raja EA, Bhattacharya S, McNeill G, Hannaford PC, et al. Maternal obesity during pregnancy and premature mortality from cardiovascular event in adult offspring: follow-up of 1 323 275 person years. BMJ. 2013;347:f4539.
25. Catalano PM, Presley L, Minium J, Hauguel-de Mouzon S. Fetuses of obese mothers develop insulin resistance in utero. Diabetes Care. 2009;32:1076–80.
26. Vrachnis N, Antonakopoulos N, Iliodromiti Z, Dafopoulos K, Siristatidis C, Pappa KI, et al. Impact of maternal diabetes on epigenetic modifications leading to diseases in the offspring. Exp Diabetes Res. 2012;2012:538474.
27. Maric T, Kanu C, Johnson MR, Savvidou MD. Maternal, neonatal insulin resistance and neonatal anthropometrics in pregnancies following bariatric surgery. Metabolism. 2019;97:25–31.
28. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body and femur measurements—a prospective study. Am J Obstet Gynecol. 1985;151:333–7.
29. National Institute for Health and Clinical Excellence. Diabetes in pregnancy: management from preconception to the postnatal period. NICE; 2015. [Available from: Recommendations | Diabetes in pregnancy: management from preconception to the postnatal period | Guidance | NICE] [cited 2021 Feb 12].
30. Adam S, Ammori B, Soran H, Syed AA. Pregnancy after bariatric surgery: screening for gestational diabetes. BMJ. 2017;356:j533.
31. Nicolaides KH, Wright D, Syngelaki A, Wright A, Akolekar R. Fetal Medicine Foundation fetal and neonatal population weight charts. Ultrasound Obstet Gynecol. 2018;52:44–51.
32. World Health Organization. Child growth standards [cited 2022 Jan 6]. Available from: http://www.who.int/childgrowth/standards/en/
33. Patey O, Gatzoulis MA, Thilaganathan B, Carvalho JS. Perinatal changes in fetal ventricular geometry, myocardial performance, and cardiac function in normal term pregnancies. J Am Soc Echocardiogr. 2017;30:485–92.
34. Patey O, Carvalho JS, Thilaganathan B. Perinatal changes in fetal cardiac geometry and function in diabetic pregnancy at term. Ultrasound Obstet Gynecol. 2019;54:634–42.
35. Brooks PA, Khoo NS, Mackie AS, Hornberger LK. Right ventricular function in fetal hypoplastic left heart syndrome. J Am Soc Echocardiogr. 2012;25:1068–74.
36. Patey O, Carvalho JS, Thilaganathan B. Perinatal changes in cardiac geometry and function in growth-restricted fetuses at term. Ultrasound Obstet Gynecol. 2019;53:655–62.
37. Lorch SM, Ludomirsky A, Singh GK. Maturational and growth-related changes in left ventricular longitudinal strain and strain rate measured by two-dimensional speckle tracking echocardiography in healthy pediatric population. J Am Soc Echocardiogr. 2008;21:1207–15.
38. Cruz-Lemini M, Crispi F, Valenzuela-Alcaraz B, Figueras F, Sitges M, Gomez O, et al. Value of annular M-mode displacement vs tissue Doppler velocities to assess cardiac function in intrauterine growth restriction. Ultrasound Obstet Gynecol. 2013;42:175–81.
39. Patey O. Re: Differential effect of assisted reproductive technology and small-for-gestational age on fetal cardiac remodeling. B. Valenzuela-Alcaraz, F. Crispi, M. Cruz-Lemini, B. Bijnens, L. Garcia-Otero, M. Sitges, J. Balasch and E. Gratacos. Ultrasound Obstet Gynecol. 2017;50:17–8.
40. Lehtoranta L, Vuolteenaho O, Jukka Lain V, Koskinen A, Soukka H, Kytö V, et al. Maternal hyperglycemia leads to fetal cardiac hyperplasia and dysfunction in a rat model. Am J Physiol Endocrinol Metab. 2013;305:E611–9.
41. Lin X, Yang P, Reece EA, Yang P. Pregestational type 2 diabetes mellitus induces cardiac hypertrophy in the murine embryo through cardiac remodelling and fibrosis. Am J Obstet Gynecol. 2017;217:216.e1–216.e13.
42. Aguilera J, Semmler J, Anzoategui S, Zhang H, Nicolaides KH, Charakida M. Cardiac function in gestational diabetes mellitus: a longitudinal study from fetal life to infancy. BJOG. 2021;128:272–9.
43. Yuan WL, Lin J, Kramer MS, Godfrey KM, Gluckman PD, Chong YS, et al. Maternal glycemia during pregnancy and child carotid intima media thickness, pulse wave velocity, and augmentation index. J Clin Endocrinol Metab. 2020;105:dgaa211.
44. HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: associations with neonatal anthropometrics. Diabetes. 2009;58:453–9.
45. Ashrafian H, Bueter M, Ahmed K, Suliman A, Bloom SR, Darzi A, et al. Metabolic surgery: an evolution through bariatric animal models. Obes Rev. 2010;11:907–20.
46. West KA, Kanu C, Maric T, McDonald JAK, Nicholson JK, Li JV, et al. Longitudinal metabolic and gut bacterial profiling of pregnant women with previous bariatric surgery. Gut. 2020;69:1452–9.
47. El-Khuffash A, Lewandowski AJ, Jain A, Hamvas A, Singh GK, Levy PT. Cardiac performance in the first year of age among preterm infants fed maternal breast Milk. JAMA Netw Open. 2021;4:e2121206.
48. Maric T, Kanu C, Muller DC, Tzoulaki I, Johnson MR, Savvidou MD. Fetal growth and fetoplacental circulation in pregnancies following bariatric surgery: a prospective study. BJOG. 2020;127:839–46.
49. Maric T, Kanu C, Mandalia S, Johnson MR, Savvidou MD. Fetal fractional limb volumes in pregnancies following bariatric surgery. Acta Obstet Gynecol Scand. 2021;100:272–8.
50. Carlsen EM, Renault KM, Møller BK, Nørgaard K, Beck Jensen JE, Lauenborg J, et al. Newborn body composition after maternal bariatric surgery. PLoS One. 2020;15:e0231579.

How to cite this article: Patey O, Bartsota M, Maric T, Patel D, Savvidou M, Carvalho JS. Impact of maternal bariatric surgery on offspring perinatal cardiac function: A prospective study. BJOG. 2023;00:1–9. https://doi.org/10.1111/1471-0528.17747