Impact of gestational risk factors on maternal cardiovascular system

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Background: Scarce evidence is available on the potential cardiovascular abnormalities associated with some common gestational complications. We aimed to analyze the potential maternal cardiac alterations related to gestational complications, including body mass index (BMI) >25 kg/m^2, gaining excessive weight, or developing antenatal depression.

Methods: The design of this study was a secondary analysis of a randomized controlled trial. Echocardiography was performed to assess cardiovascular indicators of maternal hemodynamic, cardiac remodeling and left ventricular (LV) function in 59 sedentary pregnant women at 20 and 34 weeks of gestation.

Results: Starting pregnancy with a BMI >25 kg/m^2, gaining excessive weight, and developing antenatal depression had no cardiovascular impact on maternal health (P value >0.002). Depressed women were more likely to exceed weight gain recommendations than non-depressed women (P value <0.002).

Conclusions: The evaluated gestational complications seem not to induce cardiovascular alterations in hemodynamic, remodeling and LV function indicators. However, developing antenatal depression increases the risk of an excessive weight gain. This finding is potentially important because excessive weight gain during pregnancy associates with a higher risk of cardiovascular diseases (CVD) later in life.

Keywords: Pregnancy; weight; depression; cardiovascular disease (CVD); echocardiography

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Introduction

The maternal cardiovascular system undergoes profound changes to support the increasing demands of fetal growth and development during pregnancy (1). Some studies showed that some maternal obstetric complications can lead to abnormal changes that may ultimately increase the maternal and fetal risk of cardiovascular disease (CVD) (2-6). Along this line, gestational hypertension impairs maternal left ventricular (LV) geometry toward concentric hypertrophy in hypertensive women and is also associated with depressed systolic and diastolic LV function, left atrial (LA) dysfunction, increased total vascular resistance and adverse pregnancy outcomes (3,4). Similarly, gestational diabetes mellitus (GDM) induces diastolic dysfunction during pregnancy (5,6), and the consequent risk of coronary heart

disease in GDM patients is approximately 70% higher than in patients without GDM (7).

It is estimated that an increasing number of women develop CVD during pregnancy, raising the risk to 0.2–4% of all pregnancies in western countries (8,9), largely due to the increasing presence of maternal cardiovascular risk factors (10). In the general population, a high body mass index (BMI) is linked to heart failure, including abnormal LV function and structure (11,12). Although weight gain is expected during pregnancy, mothers who start their pregnancy being overweight or even obese have an increased risk of many maternal and fetal complications such as excessive weight gain, which can lead to other long-term maternal health consequences including CVD (13), or antenatal depression, which enhances the risk of pre-eclampsia (14).

Despite these concerns, the adverse effects of these common complications on the maternal cardiovascular system remain uncertain. Thus, the knowledge of the risks associated with CVD during pregnancy and their management is important for advising women before and during pregnancy. The main objective of this study was to assess the potential maternal cardiac alterations associated with starting pregnancy with a BMI >25 kg/m^2, gaining excessive weight, and developing antenatal depression, based on echocardiographic indicators of maternal hemodynamics, cardiac remodeling and LV function. We hence hypothesized that these complications may alter the maternal cardiovascular system during pregnancy.

Methods

Study characteristics

The present study was a secondary analysis of a randomized controlled trial (clinicaltrials.gov identifier NCT01723098) performed from February 2009 to March 2013 (15). Informed consent was obtained from all enrolled participants. The study was approved by the Research Ethics Committee of the Hospital Universitario de Fuenlabrada (Madrid, Spain; approval number 240/09) and was in accordance with the ethical guidelines of the Declaration of Helsinki (modified in 2008).

Only those healthy pregnant women (n=121) who were randomly allocated to the standard care program group in the aforementioned trial were included in the present study. They met the following inclusion criteria: (I) having no obstetric or medical complications (based on the American college of obstetricians and gynecologists guidelines (ACOG) (16); (II) time of pregnancy <16 weeks; (III) not exercising regularly for more than 30 min (3 d·week^{-1}); (IV) able to communicate in Spanish; (V) followed throughout pregnancy and giving birth at the Hospital Universitario de Fuenlabrada. Participants received regular general counseling regarding healthy habits (nutritional and physical activity) by their obstetricians and midwives.

Data collection

Personal data were obtained from participants during their first prenatal visit (9–11 weeks of gestation) through a structured questionnaire at the beginning of the study and before group allocation. Pregnancy outcomes were also collected and obtained from the medical records at delivery. Maternal pre-pregnancy BMI, maternal gestational weight gain and the diagnoses of GDM were collected from medical records. Pregnant women were divided into two groups, depending on whether they were at risk or not for each obstetric complication:

(I) Pre-pregnancy maternal BMI (risk = BMI ≥25 kg/m^2; non-risk BMI <25 kg/m^2);

(II) Maternal gestational weight gain classified as "excessive-risk" or "adequate non-risk" based on the Institute of Medicine (IOM) guidelines (13): "underweight" women (pre-gestational BMI ≤18.5 kg/m^2) weight gain: risk 18 kg; non-risk ≤18 kg; "normal weight" (pre-gestational BMI 18.5–24.9 kg/m^2) weight gain: risk >16 kg; non-risk ≤16 kg; "overweight" women (pre-gestational BMI 25–29 kg/m^2) weight gain: risk >11.5 kg; non-risk ≤11.5 kg; and "obese" women (pre-gestational BMI ≥30 kg/m^2) weight gain: risk >9 kg; non-risk ≤9 kg;

(III) Antenatal depression was assessed by the center for epidemiological studies depression (CESD) scale: risk (depressed women) = CESD score ≥16; non-risk (non-depressed women) = CESD score <16.

Primary outcomes

Two echocardiographic assessments were performed by the same experienced cardiologist at mid and late pregnancy (20 and 34 weeks, respectively), with patients lying on their left side. An ultrasound system (Vivid-i; GE Healthcare, Waukesha, WI) with a 2.5 MHz transducer was used in accord with the guidelines of the American Society of Echocardiography (17) to collect hemodynamic, structural and functional cardiovascular variables as described in our

Table 1 Maternal characteristics at the beginning of the study

Variables	Pregnant women (n=59)
Age (years)	31±4
Previous pregnancies (%)	
0	60
1	37
≥2	7
Smoking during pregnancy (%)	15
Gestational diabetes mellitus (%)	9

Data are mean ± SD or percentage.

previous study (15) and outlined below:

(I) Hemodynamic variables: systolic and diastolic blood pressure (SBP/DBP), heart rate (HR), stroke volume (SV), cardiac output (CO), and total vascular resistance (TVR);

(II) Cardiac remodeling variables: LA area and volume, LV diastolic diameter (LVDD), LV systolic diameter (LVSD), interventricular septal thickness (IVST), posterior wall thickness (PWT), posterior wall thickness at systole (PWTs), relative wall thickness (RWT), LV mass (LVM), LV mass index (LVMI), wall stress (cESS); LV geometry pattern: normal pattern, concentric remodeling, eccentric remodeling, and concentric hypertrophy;

(III) LV function variables: LV ejection fraction (LVEF), fractional shortening (FS), early filling velocity (E), atrial filling velocity (A), deceleration time of E wave (DT), and isovolumetric relaxation time (IVRT).

Secondary outcomes

Secondary outcomes included duration (dilation, delivery and childbirth time) and type (normal, instrumental, cesarean) of labor, occurrence of pre-term delivery (≤259 days), newborns' gestational age, weight, height and head circumference at birth, Apgar score at 1 and 5 min, and pH of the umbilical cord.

Statistical analysis

Statistical analyses were performed with the Stata Statistical Software Package (version 13, Stata Corp, College Station, TX) and IBM SPSS 22 package (SPSS, Inc., Chicago, IL) for Mac. The intention-to-treat principle was used considering baseline values as posttest values when posttest data were missing.

A two-factor ANOVA repeated measures analysis [group (non-obstetric complication, obstetric complication group) by time (at 20 and 34 weeks)] was used to assess the effect of obstetric complications on study outcomes (or its equivalent non-parametric test in the case of non-parametrical distribution). Moreover, differences between the frequencies of women by obstetric complication group (pre-pregnancy maternal BMI, weight gain or antenatal depression) in each categorical variable at 20 and 34 weeks were assessed by the Chi-square test (χ^2) (or Fisher's test if all expected cell frequencies are not equal to or greater than 5). Unpaired Student's *t*-test (or its equivalent non-parametric test) was used to compare the pregnancy outcome net change (post–pre outcome values) by each obstetric complication group.

Finally, univariate Kaplan-Meier analysis of dilation, delivery and childbirth duration, respectively, by obstetric complication group was calculated. The log rank test was used to compare the curves. Data are shown as mean ± standard deviation (SD) or n/percentage, where appropriate. To minimize the risk of statistical error type I, all the analyses were corrected for multiple comparisons using the stringent Bonferroni method, in which the threshold P value is obtained by dividing 0.05 by the number of comparisons [threshold P value set at ≤0.002 (i.e., 0.05 divided by the number of outcomes in these analyses (n=27)].

Results

Maternal characteristics at the beginning of the study are presented in *Table 1*. A total of 59 participants completed the study, including primary and/or secondary outcomes.

Primary outcomes

Analyses based on pre-gestational BMI

The results of repeated measures two-factor ANOVA revealed a significant time effect from 20 to 34 weeks of gestation (P<0.002) for several primary outcomes related to changes in maternal hemodynamics (decrease in SV), cardiac remodeling (increase in LVM), and LV function (decrease in early filling velocity and E/A ratio) (*Table 2*). Twenty-six women (77%) with BMI <25 kg/m^2 presented a normal cardiac pattern, 4 (12%) presented concentric remodeling, and 2 (6%) presented eccentric hypertrophy. Similarly, 20 (59%) women with BMI ≥25 kg/m^2 presented a normal cardiac pattern, 7 (21%) presented concentric

Table 2 Outcomes variables by group (pre-gestational BMI <25 kg·m^{-2} *vs.* ≥25 kg·m^{-2}) at second (20 weeks) and third (34 weeks) trimesters

Outcomes	Group (kg·m^{-2})	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
Hemodynamic							
SBP (mmHg)	BMI <25	25	106±8	109±15	0.014	0.493	0.359
	BMI ≥25	19	114±10	113±9	—	—	—
DBP (mmHg)	BMI <25	24	61±7	64±12	0.025	0.424	0.612
	BMI ≥25	19	67±8	68±9	—	—	—
HR (beats·min^{-1})	BMI <25	29	79±9	80±11	0.156	0.028	0.201
	BMI ≥25	23	81±12	86±13	—	—	—
SV (mL·beat^{-1})	BMI <25	31	56±13	54±12	0.885	0.001*	0.355
	BMI ≥25	23	57±12	53±12	—	—	—
CO (mL·min^{-1})	BMI <25	30	4,442±1,064	4,243±984	0.544	0.128	0.565
	BMI ≥25	23	4,554±1,066	4,463±1,047	—	—	—
CO index (mL·min^{-1}·m^{-2})	BMI <25	28	2,674±610	2,490±574	0.309	0.011	0.714
	BMI ≥25	21	2,485±562	2,347±637	—	—	
TVR (dynes·s·cm^{-5})	BMI <25	28	1,467±377	1,577±491	0.724	0.171	0.457
	BMI ≥25	23	1,542±364	1,576±386	—	—	—
Cardiac remodeling							
LA area (mm)	BMI <25	34	18±3	17±3	0.789	0.111	0.583
	BMI ≥25	25	18±3	17±3	—	—	—
LA volume (mm^3)	BMI <25	34	50±11	49±13	0.667	0.071	0.215
	BMI ≥25	25	51±17	46±11	—	—	—
LVDD (mm)	BMI <25	34	45±15	45±1	0.041	0.265	0.110
	BMI ≥25	24	47±1	48±1	—	—	—
LVSD (mm)	BMI <25	34	27±3	27±4	0.039	0.330	0.831
	BMI ≥25	24	28±3	29±3	—	—	—
IVST (mm)	BMI <25	34	8±1	9±2	0.797	0.019	0.597
	BMI ≥25	25	8±2	9±1	—	—	—
PWT (mm)	BMI <25	34	8±2	9±2	0.918	0.021	0.276
	BMI ≥25	25	8±2	9±2	—	—	—
PWTs (mm)	BMI <25	33	14±3	15±3	0.864	0.148	0.451
	BMI ≥25	25	15±2	15±2	—	—	—
RWT (mm)	BMI <25	34	4±1	4±1	0.276	0.125	0.074
	BMI ≥25	24	4±1	4±1	—	—	—
LVM (g)	BMI <25	34	115±26	127±38	0.133	0.001*	0.740
	BMI ≥25	24	129±38	139±33	—	—	—
LVMI (g·m^{-2})	BMI <25	32	68±17	74±22	0.699	0.004	0.880
	BMI ≥25	22	67±15	72±13	—	—	—
cESS (kdynes·cm^{-2})	BMI <25	30	98±27	98±29	0.134	0.698	0.784
	BMI ≥25	22	109±24	106±25	—	—	—
LV function							
LVEF (%)	BMI <25	32	71±5	70±7	0.798	0.878	0.169
	BMI ≥25	23	70±7	70±6	—	—	—
FS (%)	BMI <25	34	41±4	40±6	0.542	0.894	0.241
	BMI ≥25	24	39±6	40±4	—	—	—

Table 2 (*continued*)

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Outcomes	Group (kg·m^{-2})	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
E (m·s^{-1})	BMI <25	32	96±18	89±19	0.011	0.001*	0.657
	BMI ≥25	23	86±18	77±13	—	—	—
A (m·s^{-1})	BMI <25	32	54±11	60±15	0.108	0.046	0.217
	BMI ≥25	23	61±15	63±12	—	—	—
E/A	BMI <25	32	1.8±0.5	1.5±0.4	0.002	<0.001*	0.264
	BMI ≥25	23	1.4±0.4	1.2±0.3	—	—	—
DT (ms)	BMI <25	32	148±37	146±37	0.029	0.083	0.144
	BMI ≥25	22	134±41	118±40	—	—	—
IVRT (ms)	BMI <25	30	75±12	79±17	0.296	0.105	0.801
	BMI ≥25	17	70±18	75±20	—	—	—

Threshold P value set at 0.002 [i.e., 0.05 divided by the number of outcomes in these analyses (n=27)]. *, P<0.002. A, atrial filling velocity; cESS, wall stress; CO, cardiac output; CO, index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT, isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LV, left ventricular; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

remodeling, 1 (3%) presented concentric hypertrophy, and 4 (12%) presented eccentric hypertrophy remodeling (P=0.43). No significant differences were found in any of the remaining pregnancy outcomes' net change by group (*Figure 1*).

Analyses based on gestational weight gain

Analyses based on maternal gestational weight gain showed a significant time effect from 20 to 34 weeks of gestation, related to changes in hemodynamics (decrease in SV), cardiac remodeling (increase in LVM), and LV function (decrease in early filling velocity and E/A ratio) (P<0.002) (*Table 3*). No effects were found in group-time interaction for hemodynamics and cardiac remodeling [women in risk (71% normal pattern, 6% concentric remodeling, 3% concentric hypertrophy and 11% eccentric hypertrophy) *vs.* women in non-risk (74% normal pattern, 9% concentric remodeling and 9% eccentric hypertrophy), P=0.89] or LV function (*Table 3*, all P≥0.002). No significant differences were found in any of the remaining pregnancy outcomes' net change by group (*Figure 2*).

Analyses based on antenatal depression (first trimester)

Results from depressed pregnant women in the first trimester of pregnancy showed a significant time effect in LV function (decrease in E/A ratio; P=0.002). No differences were found in hemodynamic or cardiac remodeling variables [women in risk (60% normal pattern, 11% concentric remodeling, 2% concentric hypertrophy and 11% eccentric hypertrophy) versus women in non-risk (80% normal pattern, 7% concentric remodeling and 7% eccentric hypertrophy), P=0.67] (*Table 4*), or in any of the remaining pregnancy outcomes' net change by group (*Figure 3*).

Analyses based on antenatal depression (third trimester)

Significant time effects were found in cardiac remodeling and LV function between depressed and non-depressed women at the third trimester of pregnancy, presenting as an increase in LVM and a decrease in E/A ratio, respectively (P≤0.001) (*Table 5*). Thirty-one non-risk women (72%) presented a normal cardiac pattern, 5 (12%) a concentric remodeling and 3 (7%) an eccentric hypertrophy. Similarly, 28 (65%) at risk women presented a normal cardiac pattern, 5 (12%) a concentric remodeling, 1 (2%) a concentric hypertrophy and 5 (12%) an eccentric hypertrophy remodeling (P=0.82). Moreover, depressed pregnant women were more likely to exceed weight gain recommendations than non-depressed women (P<0.002). Finally, no significant differences were found in any of the remaining pregnancy outcomes' net change by group (*Figure 4*).

Secondary outcomes

No differences were found in pregnancy outcomes between women with or without obstetric complications regarding excessive weight, antenatal depression or pre-gestational BMI

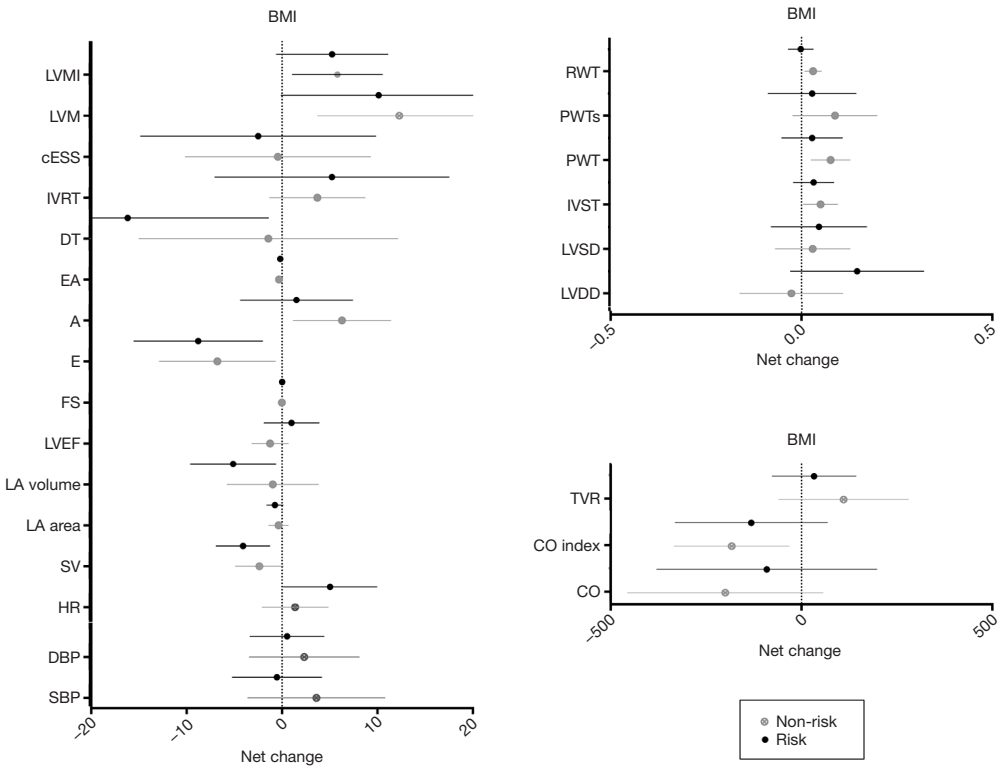

Figure 1 Cardiovascular indicators based on pre-gestational BMI. Risk = BMI ≥25 kg/m^2; non-risk BMI <25 kg/m^2. A, atrial filling velocity; BMI, body mass index; cESS, wall stress; CO, cardiac output; CO index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

(*Tables 2-5*, *Figures 1-4*). Also, the delivery duration curves were similar as revealed by log rank test between all groups of risk and non-risk women [P>0.05; BMI risk women [median (range) of dilation phase duration 510 min (range, 120–1,200 min); expulsion phase duration 136 min (range, 5–209 min); childbirth phase duration 6 min (range, 3–30 min)] *vs.* BMI non-risk women [dilation 360 min (range, 30–1,260 min); expulsion 83 min (range, 8–226 min); childbirth time 5 min (range, 3–15 min)]; excessive weight gain non-risk women [dilation 480 min (range, 120–1,260 min); expulsion 129 min (range, 5–209 min); dilation 5 min (range, 3–30 min)] *vs.* excessive weight gain risk women [dilation 345 min (range, 30–1,080 min); expulsion 101 min (range, 8–226 min); childbirth 5 min (range, 3–15 min)]; antenatal depression (first trimester) non-risk women [dilation 435 min (range, 30–1,260 min); expulsion 87 min (range, 5–226 min); childbirth 5 min (range, 3–30 min)] *vs.* antenatal depression (first trimester) risk women [dilation 540 min (range, 120–1,080 min); expulsion 133 min (range, 11–198 min); childbirth 5 min (range, 3–10 min)]; antenatal depression (third trimester) risk women [dilation 480 min (range, 30–1,260 min); expulsion 136 min (range, 8–226 min); childbirth 5 min (range, 3–30 min)] *vs.* antenatal depression (third trimester) non-risk women [dilation 300 min (range, 180–1,080 min); expulsion 49 min (range, 5–205 min); childbirth 5 min (range, 5–10 min)].

Discussion

Contrary to our original hypothesis, we found that excessive weight gain, developing antenatal depression or starting pregnancy with a BMI >25 kg/m^2 has no impact on echocardiographic indicators of maternal hemodynamics, cardiac remodeling or LV function during the period of pregnancy assessed. Similar and significant cardiovascular changes were found between pregnant women with and

Table 3 Outcomes variables by group (excessive weight gain *vs.* adequate weight gain) at second (20 weeks) and third (34 weeks) trimesters

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
Hemodynamic							
SBP (mmHg)	Excessive weight gain	18	111±7	110±10	0.712	0.532	0.322
	Adequate weight gain	26	108±11	112±15	—	—	—
DBP (mmHg)	Excessive weight gain	18	64±6	65±7	0.903	0.401	0.944
	Adequate weight gain	25	64±9	66±13	—	—	—
HR (beats·min^{-1})	Excessive weight gain	20	81±12	87±14	0.101	0.022	0.205
	Adequate weight gain	31	78±10	80±11	—	—	—
SV (mL·beat^{-1})	Excessive weight gain	32	54±13	50±11	0.116	0.001*	0.541
	Adequate weight gain	21	59±12	56±12	—	—	
CO (mL·min^{-1})	Excessive weight gain	20	4,463±1,228	4,412±1,093	0.963	0.168	0.387
	Adequate weight gain	32	4,534±959	4,314±976	—	—	—
CO index (mL·min^{-1}·m^{-2})	Excessive weight gain	18	2,519±645	2,397±513	0.587	0.016	0.573
	Adequate weight gain	30	2,648±570	2,454±662	—	—	—
TVR (dynes·s·cm^{-5})	Excessive weight gain	20	1,560±436	1,567±401	0.645	0.225	0.276
	Adequate weight gain	30	1,552±323	1,576±480	—	—	—
Cardiac remodeling							
LA area (mm)	Excessive weight gain	23	18±3	17±2	0.612	0.147	0.834
	Adequate weight gain	35	18±3	17±3	—	—	—
LA volume (mm^3)	Excessive weight gain	23	52±16	48±12	0.758	0.095	0.684
	Adequate weight gain	35	50±12	48±12	—	—	—
LVDD (mm)	Excessive weight gain	23	46±5	46±5	0.635	0.454	0.719
	Adequate weight gain	34	45±5	46±6	—	—	—
LVSD (mm)	Excessive weight gain	23	27±3	28±4	0.681	0.218	0.146
	Adequate weight gain	34	28±3	27±4	—	—	—
IVST (mm)	Excessive weight gain	23	9±1	9±1	0.036	0.007	0.207
	Adequate weight gain	35	8±1	8±2	—	—	—
PWT (mm)	Excessive weight gain	35	8±2	9±2	0.964	0.012	0.647
	Adequate weight gain	23	8±2	9±2	—	—	—
PWTs (mm)	Excessive weight gain	23	15±2	15±2	0.183	0.129	0.963
	Adequate weight gain	34	14±3	15±3	—	—	—
RWT (mm)	Excessive weight gain	23	4±1	4±1	0.563	0.044	0.248
	Adequate weight gain	34	4±1	4±1	—	—	—
LVM (g)	Excessive weight gain	23	125±31	139±30	0.309	0.001*	0.488
	Adequate weight gain	34	118±34	128±40	—	—	—
LVMI (g·m^{-2})	Excessive weight gain	21	68±18	74±13	0.951	0.002	0.357
	Adequate weight gain	32	66±13	73±23	—	—	—
cESS (kdynes·cm^{-2})	Excessive weight gain	21	98±21	97±26	0.391	0.736	0.966
	Adequate weight gain	30	104±28	102±27	—	—	—
LV function							
LVEF (%)	Excessive weight gain	21	72±6	70±6	0.574	0.414	0.054
	Adequate gain	33	70±6	71±6	—	—	—
FS (%)	Excessive weight gain	23	41±6	39±6	0.956	0.704	0.111
	Adequate weight gain	34	39±5	40±5	—	—	—

Table 3 (*continued*)

Table 3 (*continued*)

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
E ($m \cdot s^{-1}$)	Excessive weight gain	21	86±22	78±15	0.029	0.001*	0.906
	Adequate weight gain	33	96±15	88±19	—	—	—
A ($m \cdot s^{-1}$)	Excessive weight gain	21	59±15	61±12	0.635	0.044	0.523
	Adequate weight gain	33	56±12	61±15	—	—	—
E/A	Excessive weight gain	21	1.5±0.5	1.3±0.3	0.043	<0.001*	0.618
	Adequate weight gain	33	1.7±0.5	1.4±0.5	—	—	—
DT (ms)	Excessive weight gain	21	134±35	123±39	0.108	0.116	0.530
	Adequate weight gain	33	147±41	142±40	—	—	—
IVRT (ms)	Excessive weight gain	19	68±17	76±21	0.117	0.075	0.329
	Adequate weight gain	28	77±12	79±15	—	—	—

Threshold P value set at 0.002 [i.e., 0.05 divided by the number of outcomes in these analyses (n=27)]. *, P<0.002. A, atrial filling velocity; cESS, wall stress; CO, cardiac output; CO, index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT, isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LV, left ventricular; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

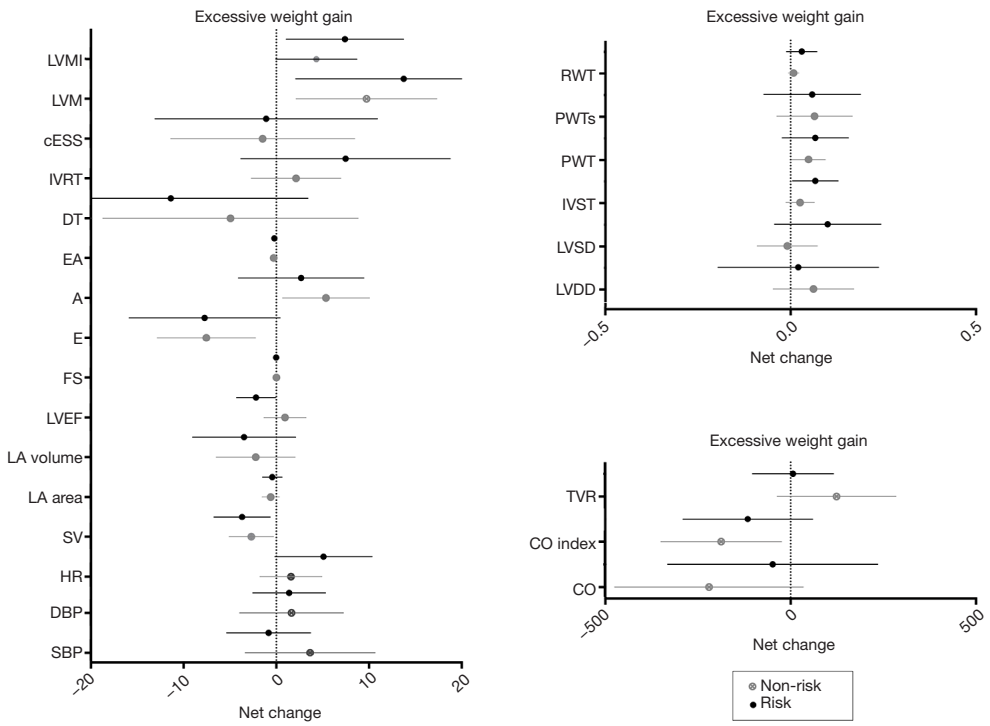

Figure 2 Cardiovascular indicators based on gestational weight gain. "Underweight" women: risk = weight gain >18 kg; non-risk ≤18 kg; "normal weight": risk= weight gain >16 kg; non-risk ≤16 kg; "overweight" women: risk = weight gain >11.5 kg; non-risk ≤11.5 kg; "obese" women: risk = weight gain >9 kg; non-risk ≤9 kg. A, atrial filling velocity; BMI, body mass index; cESS, wall stress; CO, cardiac output; CO index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

Table 4 Outcomes variables by group (depressive *vs.* non-depressive at 1st trimester) at second (20 weeks) and third (34 weeks) trimester

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
Hemodynamic							
SBP (mmHg)	Non-depressive	34	109±8	112±14	0.571	0.911	0.292
	Depressive	10	110±14	108±9	—	—	—
DBP (mmHg)	Non-depressive	33	64±8	66±11	0.727	0.622	0.656
	Depressive	10	64±10	64±8	—	—	—
HR (beats·min^{-1})	Non-depressive	41	79±9	83±12	0.855	0.469	0.078
	Depressive	11	81±16	80±13	—	—	—
SV (mL·beat^{-1})	Non-depressive	42	57±12	53±12	0.069	0.068	0.069
	Depressive	12	56±14	56±12	—	—	—
CO (mL·min^{-1})	Non-depressive	42	4,447±1,037	4,302±879	0.567	0.168	0.898
	Depressive	11	4,654±1,162	4,478±879	—	—	—
CO index (mL·min^{-1}·m^{-2})	Non-depressive	40	2,611±575	2,439±638	—	—	—
	Depressive	9	2,512±693	2,368±410	0.717	0.061	0.769
TVR (dynes·s·cm^{-5})	Non-depressive	40	1,508±375	1,590±477	0.577	0.378	0.580
	Depressive	11	1,473±366	1,494±283	—	—	—
Cardiac remodeling							
LA area (mm)	Non-depressive	44	18±3	17±3	0.839	0.180	0.985
	Depressive	15	18±3	17±2	—	—	—
LA volume (mm^3)	Non-depressive	44	51±13	48±12	0.708	0.130	0.838
	Depressive	15	50±14	47±11	—	—	—
LVDD (mm)	Non-depressive	43	46±4	47±5	0.275	0.342	0.645
	Depressive	15	44±7	45±6	—	—	—
LVSD (mm)	Non-depressive	43	28±3	28±4	0.042	0.335	0.789
	Depressive	15	26±3	27±4	—	—	—
IVST (mm)	Non-depressive	44	8±1	0.84±0.16	0.079	0.138	0.138
	Depressive	15	9±1	9±1	—	—	—
PWT (mm)	Non-depressive	44	8±2	9±2	0.100	0.049	0.673
	Depressive	15	9±2	9±2	—	—	—
PWTs (mm)	Non-depressive	44	14±3	15±3	0.638	0.161	0.894
	Depressive	14	14±2	15±2	—	—	—
RWT (mm)	Non-depressive	43	3±1	4±1	0.022	0.285	0.255
	Depressive	15	4±1	4±1	—	—	—
LVM (g)	Non-depressive	43	118±29	131±36	0.424	0.008	0.453
	Depressive	15	128±41	136±38	—	—	—
LVMI (g·m^{-2})	Non-depressive	41	67±16	73±20	0.957	0.019	0.618
	Depressive	13	69±16	73±16	—	—	—
cESS (kdynes·cm^{-2})	Non-depressive	40	104±28	104±29	0.293	0.539	0.554
	Depressive	12	98±21	93±20	—	—	—
LV function							
LVEF (%)	Non-depressive	42	70±6	69±6	0.009	0.876	0.752
	Depressive	15	74±4	74±4	—	—	—
FS (%)	Non-depressive	43	39±6	39±5	0.102	0.974	0.845
	Depressive	15	41±5	41±6	—	—	—

Table 4 (*continued*)

Table 4 (*continued*)

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
E ($m \cdot s^{-1}$)	Non-depressive	42	93±17	84±19	0.984	0.017	0.374
	Depressive	13	90±23	86±16	—	—	—
A ($m \cdot s^{-1}$)	Non-depressive	42	56±12	62±14	0.821	0.210	0.210
	Depressive	13	60±18	60±13	—	—	—
E/A	Non-depressive	42	1.7±0.4	1.4±0.4	0.826	0.002*	0.118
	Depressive	13	1.5±0.7	1.4±0.5	—	—	—
DT (ms)	Non-depressive	41	144±35	135±38	0.664	0.291	0.686
	Depressive	13	137±50	133±49	—	—	—
IVRT (ms)	Non-depressive	36	71±15	76±19	0.210	0.315	0.474
	Depressive	11	79±11	80±12	—	—	—

Threshold P value set at 0.002 [i.e., 0.05 divided by the number of outcomes in these analyses (n=27)]. *, P<0.002. A, atrial filling velocity; cESS, wall stress; CO, cardiac output; CO, index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LV, left ventricular; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

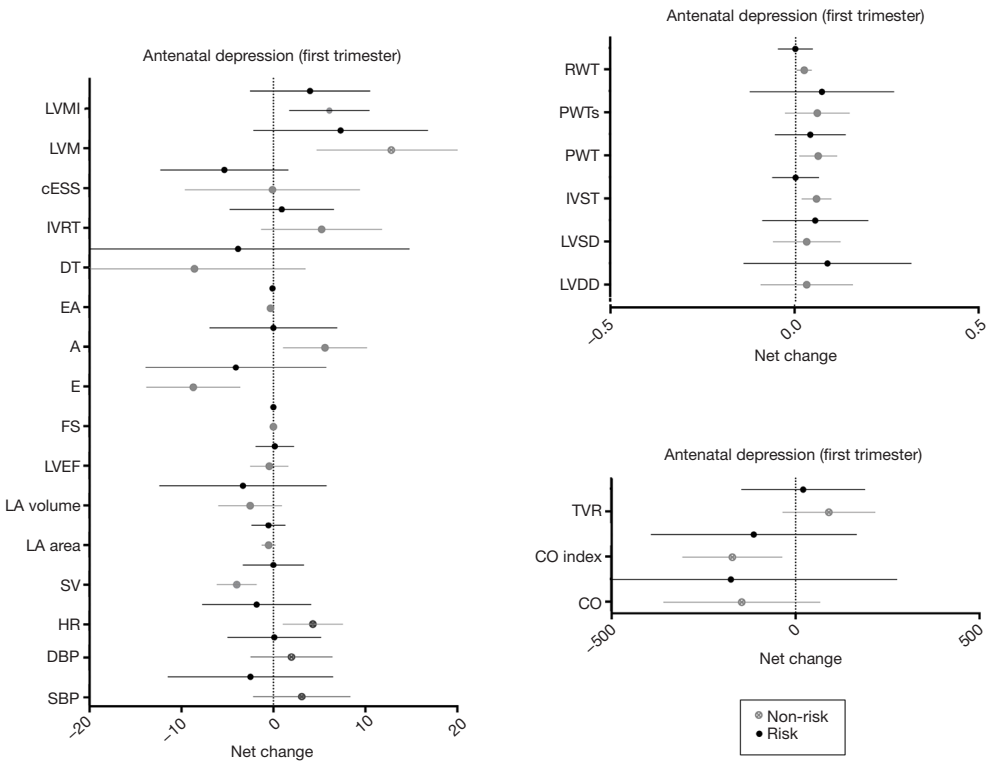

Figure 3 Cardiovascular indicators based on antenatal depression (first trimester). Risk (depressed women) = CESD score ≥16; non-risk (non-depressed women) = CESD score <16. A, atrial filling velocity; BMI, body mass index; cESS, wall stress; CO, cardiac output; CO index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

Table 5 Outcomes variables by group (depressive *vs.* non-depressive at third trimester) at second (20 weeks) and third (34 weeks) trimester

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
Hemodynamic							
SBP (mmHg)	Non-depressive	31	109±9	113±14	0.412	0.942	0.096
	Depressive	13	110±11	107±8	—	—	—
DBP (mmHg)	Non-depressive	31	64±8	65±12	0.788	0.547	0.695
	Depressive	12	65±9	65±7	—	—	—
HR (beats·min^{-1})	Non-depressive	39	79±10	82±12	0.535	0.140	0.515
	Depressive	12	82±14	83±15	—	—	—
SV (mL·beat^{-1})	Non-depressive	38	56±13	53±12	0.247	0.009	0.320
	Depressive	16	59±13	57±11	—	—	—
CO (mL·min^{-1})	Non-depressive	38	4,389±1,073	4,236±1,004	0.228	0.148	0.997
	Depressive	15	4,749±999	4,598±1,005	—	—	—
CO index (mL·min^{-1}·m^{-2})	Non-depressive	35	2,558±640	2,380±648	0.412	0.026	0.716
	Depressive	14	2,680±457	2,551±456	—	—	—
TVR (dynes·s·cm^{-5})	Non-depressive	37	1,377±354	1,631±481	0.209	0.378	0.348
	Depressive	14	1,435±354	1,432±289	—	—	—
Cardiac remodeling							
LA area (mm)	Non-depressive	43	18±3	17±3	0.149	0.314	0.425
	Depressive	16	17±2	17±2	—	—	—
LA volume (mm^3)	Non-depressive	43	52±14	49±12	0.210	0.265	0.452
	Depressive	16	47±11	46±11	—	—	—
LVDD (mm)	Non-depressive	42	45±5	46±5	0.312	0.922	0.143
	Depressive	16	47±4	47±5	—	—	—
LVSD (mm)	Non-depressive	42	27±3	28±4	0.414	0.186	0.296
	Depressive	16	28±3	29±3	—	—	—
IVST (mm)	Non-depressive	43	8±2	8±2	0.452	0.003	0.098
	Depressive	16	8±1	9±2	—	—	—
PWT (mm)	Non-depressive	43	8±2	9±2	0.382	0.008	0.294
	Depressive	16	8±2	9±2	—	—	—
PWTs (mm)	Non-depressive	42	14±3	15±3	0.931	0.049	0.198
	Depressive	16	14±3	16±2	—	—	—
RWT (mm)	Non-depressive	42	37±8	37±8	0.831	0.009	0.034
	Depressive	16	35±8	40±10	—	—	—
LVM (g)	Non-depressive	42	118±33	128±37	0.209	0.001*	0.578
	Depressive	16	128±31	142±32	—	—	—
LVMI (g·m^{-2})	Non-depressive	39	67±16	72±20	0.400	0.005	0.760
	Depressive	15	70±15	77±16	—	—	—
cESS (kdynes·cm^{-2})	Non-depressive	36	101±25	104±15	0.730	0.365	0.137
	Depressive	16	105±30	95±32	—	—	—
LV function							
LVEF (%)	Non-depressive	39	70±6	70±6	0.522	0.286	0.090
	Depressive	16	72±6	70±6	—	—	—
FS (%)	Non-depressive	42	39±5	40±5	0.953	0.255	0.019
	Depressive	16	41±5	38±6	—	—	—

Table 5 (*continued*)

Table 5 (*continued*)

Outcomes	Group	N	20 weeks of gestation	34 weeks of gestation	P value (group)	P value (time)	P value (interaction)
E ($m \cdot s^{-1}$)	Non-depressive	39	92±15	83±16	0.711	0.007	0.417
	Depressive	16	92±25	87±23	—	—	—
A ($m \cdot s^{-1}$)	Non-depressive	39	56±12	61±12	0.315	0.073	0.606
	Depressive	16	60±15	63±17	—	—	—
E/A	Non-depressive	39	1.6±0.5	1.4±0.4	0.627	<0.001*	0.312
	Depressive	16	1.5±0.6	1.4±0.4	—	—	—
DT (ms)	Non-depressive	38	143±38	136±38	0.724	0.163	0.898
	Depressive	16	140±44	132±47	—	—	—
IVRT (ms)	Non-depressive	32	74±16	79±19	0.310	0.206	0.479
	Depressive	15	71±11	73±14	—	—	—

Threshold P value set at 0.002 [i.e., 0.05 divided by the number of outcomes in these analyses (n=27)]. *, P<0.002. A, atrial filling velocity; cESS, wall stress; CO, cardiac output; CO, index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LV, left ventricular; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

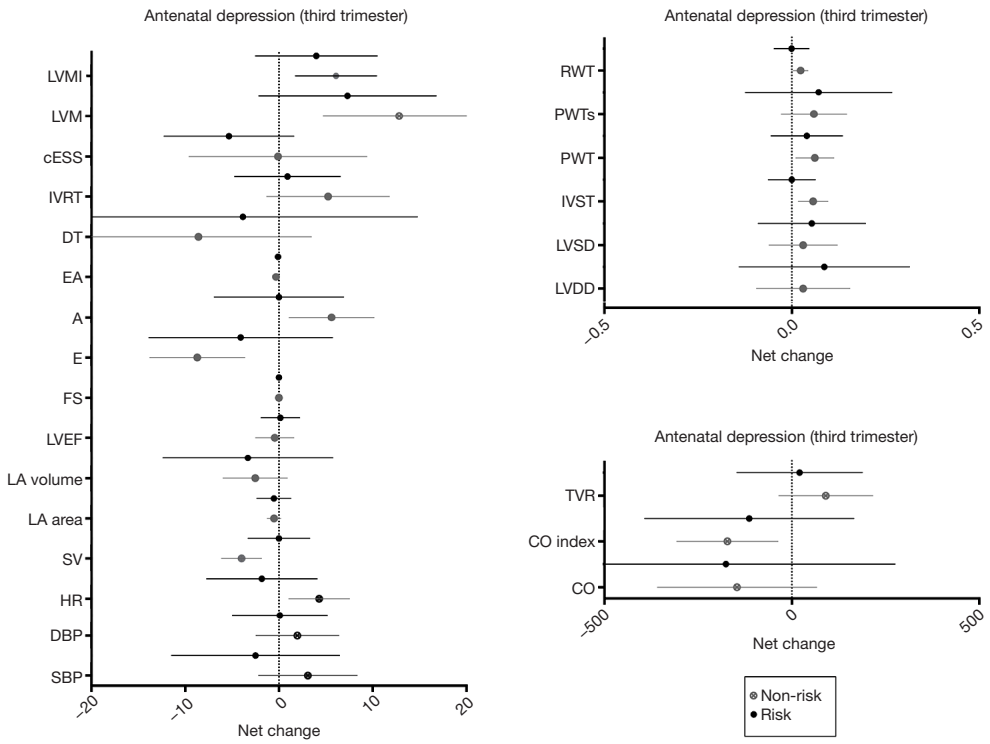

Figure 4 Cardiovascular indicators based on antenatal depression (third trimester). Risk (depressed women) = CESD score ≥16; non-risk (non-depressed women) = CESD score <16. A, atrial filling velocity; BMI, body mass index; cESS, wall stress; CO, cardiac output; CO index, cardiac output index; DBP, diastolic blood pressure; DT, deceleration time of E wave; E, early filling velocity; FS, fractional shortening; HR, heart rate; IVRT: isovolumetric relaxation time; IVST, interventricular septal thickness; LA, left atrial; LVDD, LV diastolic diameter; LVEF, LV ejection fraction; LVM, LV mass; LVMI, LV mass index; LVSD, LV systolic diameter; PWT, posterior wall thickness; PWTs, posterior wall thickness at systole; RWT, relative wall thickness; SBP, systolic blood pressure; SV, stroke volume; TVR, total vascular resistance.

without these complications over time (from 20 to 34 weeks of gestation). These cardiovascular changes are considered physiological in pregnant women (18-22). Previous studies showed that these three complications can lead to an increased risk for CVD later in life (13,14,23-25).

Excessive weight gain can lead to higher postpartum weight retention and higher weight status in subsequent pregnancies that increase the risk for maternal CVD, cancer, type II diabetes and obesity (13,23,24). In turn, developing antenatal depression in early pregnancy is linked to the risk of subsequent pre-eclampsia (OR =3.1; 95% CI: 1.4–6.9) (14). A prospective study found that pre-eclampsia increases the risk of death from CVD, particularly in women who developed this complication by 34 weeks of gestation [hazard ratio =9.54 (95% CI: 4.50–20.26)] (25).

Having a high BMI is a recognized risk factor for CVD in the general population. It is reported that men present a 5% increased risk of clinical heart failure with every 1 kg/m^2 increase in BMI, and in women this risk is even higher, approximating 7% (11). Elevated BMI seems to alter LV morphology and diastolic function (11,12). A recent prospective study with a median participant follow-up of 37 years reported that women with higher pre-gestational BMI had a higher risk of death from CVD than those with normal BMI. The most frequent causes of death were coronary heart disease (12.3%) and stroke (6%) (26).

Despite the evidence for the long-term consequences on cardiovascular health, the present study shows that the brief period of time established to evaluate potential complications appears to be too short to alter maternal cardiovascular health. By contrast, other complications such as gestational hypertension and GDM alter LV structure and function in only a few weeks (3,7). As described, cardiovascular response to acute stress is an important risk predictor of health outcomes. This risk depends on the duration and strength of stressor exposure (27). Notably, gestational hypertension occurs at 20 weeks of gestation (28) and GDM appears in the early second trimester in patients at high risk (16–18 weeks) and around 24–28 weeks in normal-risk women (29). However, antenatal depression tends to be more frequent during the second and third trimester of pregnancy (30,31). Similarly, a recent study of 172 pregnant women reported that 45% of them had excessive weight gain in the second half of pregnancy, and 55% exceeded weight gain recommendations in the first half of pregnancy (32). The absence of cardiovascular alterations in women who exceed normal weight gain, and in women with antenatal depression, may be due to their appearance later than GDM and hypertension. Importantly, the present study shows that depressed women are more likely to exceed weight gain recommendations, which is consistent with other studies (33,34). This result highlights the importance of finding alternative treatments to control and reduce depression symptoms to prevent excessive weight gain and its consequent negative health effects for the mother and the fetus (13).

No effect of the aforementioned complications was found for newborn outcomes in our study. However, adverse health effects for newborns have been described because of these complications (13,35,36). With regard to high pre-gestational BMI and excessive weight gain, the common related adverse effects on newborns are preterm birth, cesarean section and macrosomia (13,35). A recent systematic review reported that the increased risk of premature birth and low birth weight associated with antenatal depression remains controversial (36). Thus, further studies are needed to determine whether adverse effects increase the risks for prematurity and low birth weight.

The main limitations of the present study were the small sample size since it was divided into complicated and non-complicated groups, and the high dropout rate of pregnant women, which call for new strategies to enhance patient adherence to the study. Nevertheless, this is the first study to examine the influence of the aforementioned common complications, during this period of pregnancy, on maternal health by echocardiography assessment with a wide range of cardiovascular variables. Future research should be directed towards examining the effect of common obstetrics complications for both understanding their impact on the maternal and fetal cardiovascular system in the long and short-term, and for initiating alternative treatments to control them.

In conclusion, becoming pregnant with a BMI higher than 25, gaining excessive weight during pregnancy or developing antenatal depression does not seem to generate short-term negative consequences on maternal cardiovascular health. However, developing antenatal depression increases the risk for excessive weight gain. The rising incidence of these gestational complications highlights the need for further research in this field.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was approved by the Research Ethics Committee of the Hospital Universitario de Fuenlabrada (Madrid, Spain; approval number 240/09) and was in accordance with the ethical guidelines of the Declaration of Helsinki (modified in 2008) and written informed consent was obtained from all patients.

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