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Association between the number of pregnancies and cardiac target organ damages: a cross-sectional analysis of data from the Korean women's chest pain registry (KoROSE)

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Abstract

Background Pregnancy increases long-term cardiovascular risk after childbirth, but the mechanisms are unclear. This study was performed to investigate the association between the number of pregnancies and several cardiac target organ damage (TOD) in middle-aged and elderly women.

Methods Using the database of the nation-wide registry, a total of 1,137 women (mean age 63.0 ± 10.9 years) with stable chest pain undergoing invasive coronary angiography (CAG) were analyzed. Information on the number of pregnancies was obtained through a questionnaire. Obstructive coronary artery disease (CAD), left ventricular (LV) mass index (LVMI) and LV septal annular (e') velocity were assessed as indicators of cardiac TOD.

Results Women with higher number of pregnancies (≥ 3) were older (66.3 ± 9.6 vs. 57.4 ± 10.7 years; $P < 0.001$), had more cardiovascular risk factors, and took more cardiovascular medications than those with lower number of pregnancies (< 3). In multivariable analyses, higher number of pregnancies (≥ 3) was associated with obstructive CAD (odds ratio [OR], 1.62; 95% confidence interval [CI], 1.21–2.17; $P = 0.001$), a higher LVMI (> 95 g/m^2) (OR, 1.46; 95% CI, 1.08–1.98; $P = 0.013$) and a lower septal e' velocity (< 7 cm/s) (OR, 1.55; 95% CI, 1.12–2.14; $P = 0.007$) even after controlling for potential confounders. As the number of pregnancies increased, the prevalence of CAD and LVMI increased, and the septal e' velocity gradually decreased ($P < 0.001$ for each).

Conclusions In women with chest pain undergoing invasive CAG, higher number of pregnancies was associated with multiple cardiac TOD. Parity information should be checked when assessing a woman's cardiovascular risk.

Keywords Coronary angiography, Diastolic function, Left ventricular mass, Parity, Pregnancy, Target organ damage

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Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality for both men and women worldwide [1]. As women have a longer lifespan than men, and the prevalence of CVD is increasing more rapidly after menopause [2], the importance of CVD in women is gradually emerging. According to European data, 55% of women and 43% of men die from CVD [3]. The most effective way to lower cardiovascular risk is to detect high-risk individuals early and provide intensified preventive strategy [4]. Until now, traditional risk factors such as hypertension, diabetes mellitus, dyslipidemia, obesity and smoking have mainly been used as data in screening high-risk subjects [5]. However, these traditional risk factors do not fully represent an individual's cardiovascular risk. In fact, despite having had myocardial infarction, there was a substantial proportion of patients without traditional risk factors [6]. In this regard, it is necessary to pay attention to non-traditional cardiovascular risk factors.

Pregnancy is one of the women-specific cardiovascular risk factors. Pregnancy places a functional and structural burden on the cardiovascular system and increase cardiovascular risk through multiple pathways [7, 8]. Additionally, pregnancy-related complications such as preterm delivery, hypertensive disorders of pregnancy and gestational diabetes mellitus, are another important cardiovascular risk factors [9–11]. There are several epidemiologic studies showing a positive association between the number pregnancies and the incidence of CVD [12–17]. The results of a meta-analysis also support this finding [18].

The presence of cardiac target organ damage (TOD) predicts future cardiovascular events, so their early detection and treatment is clinically important [19]. Using the nation-wide chest pain registry, KoRean wOmen'S chest pain rEgistry (KoROSE), our group has shown the association between parity and specific cardiac TOD, including obstructive coronary artery disease (CAD) [20] and left ventricular (LV) diastolic dysfunction [21]. However, these studies focused on only one cardiac TOD. To date, there are no research results that have addressed the relationship between the number of pregnancies and multiple cardiac TODs in the same patient. Also, as the number of patients enrolled in the KoROSE increased over time, it was necessary to reassess the correlation between parity and cardiac TOD using a larger number of study patients. We hypothesized that increased number of pregnancies is associated with multiple cardiac TOD, which leads to poor cardiovascular outcomes. Using the KoROSE, this study was performed to investigate the associations of the number of pregnancies with cardiac TOD parameters including findings of invasive coronary angiography (CAG), LV mass index (LVMI) and indicators of LV diastolic function of Korean middle-aged and elderly women. We focused these cardiac TOD parameters because they are closely related to cardiovascular prognosis [22–25] and readily available data from the KoROSE.

Methods

Study population

For the analysis of this study, we used database of the KoROSE [20, 21]. From March 2011, women who underwent invasive CAG for the evaluation of CAD have been prospectively enrolled in the KoROSE. Patient registration in the KoROSE is still in progress. The KoROSE was constructed to observe the clinical features and prognoses of Korean women with stable chest pain syndrome. Patients with acute coronary syndrome were excluded. Enrolled patients complained of chest pain, but were in a stable condition. Whether to perform invasive CAG was decided by the attending physician based on the characteristics of chest pain, the patient's cardiovascular risk, and the results of non-invasive imaging tests or exercise stress tests. A total of 2,253 women were enrolled in the KoROSE, and among them, 1,137 women with accurate parity information were analyzed. The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices. Study protocol was reviewed and approved by the institutional review board (IRB) of Boramae Medical Center (Seoul, Republic of Korea). Approval number of the IRB was 06-2011-222. Written informed consent was obtained from each subject before the registry enrollment.

Data collection

Body mass index was calculated as weight (kg) divided by the square of height (m^2). Blood pressure was measured on the right upper arm by a trained nurse using an oscillometric device. Hypertension was defined based on previous diagnosis, current use of antihypertensive medications or systolic/diastolic blood pressure ≥ 140/90 mmHg [26]. Diabetes mellitus was defined based on previous diagnosis, current use of antidiabetic medications, glycated hemoglobin ≥ 6.5% or fasting plasma glucose ≥ 126 mg/dL [27]. Dyslipidemia was defined based on previous diagnosis or low-density lipoprotein cholesterol ≥ 160 mg/dL [28]. Obesity was defined as body mass index ≥ 25 kg/m^2 [29]. After an overnight fast, blood was aspirated from the antecubital vein to obtain blood levels of the following parameters: white blood cell count, hemoglobin, creatinine, total cholesterol, low-density lipoprotein cholesterol, triglycerides, high-density lipoprotein cholesterol, glucose, glycated hemoglobin and C-reactive protein. Glomerular filtration rate was calculated using the Modification of Diet in Renal Disease (MDRD) study equation [30].

Transthoracic echocardiography

Transthoracic echocardiography was performed according to the current guidelines [31, 32]. LV ejection fraction was obtained using M-mode tracing, 2D-guided linear measurements or biplane disk summation. During the end-diastolic period, internal dimension (LVIDd) as well as septal wall (IVSd) and posterior wall (LVPWd) thickness of the LV was obtained using M-mode in parasternal long- or short-axis views. Relative wall thickness (RWT) was defined as 2×LVPWd/LVIDd. RWT > 0.42 was used as the criterion for concentric remodeling or hypertrophy. LV mass was obtained using the following Cube formula: LV mass=(0.8)(1.04)×[(LVIDd+LVPWd+IVSd)^3–IVSd^3]+0.6. LVMI was calculated as LV mass indexed to the body surface area. LV hypertrophy was defined as LVMI > 95 g/m^2. In apical four-chamber view, the movement of the LV septal annulus was measured with the tissue Doppler imaging technique to determine e' velocity. E and A waves of mitral inflow were also measured using a pulse wave Doppler. Septal e' velocity < 7 cm/s and E/e' >15 were considered diastolic dysfunction.

Invasive CAG

Invasive CAG was performed via the radial or femoral artery according to current guidelines [33, 34]. Obstructive CAD was defined as luminal stenosis ≥ 50% of epicardial coronary arteries. CAD extents were classified as 1-, 2- or 3-vessel disease depending on the number of vessels with ≥ 50% stenosis.

Statistical analysis

Numbers are expressed as mean ± SD or n (%). For univariable comparisons, study patients were stratified into 2 groups according to median value of the number of pregnancies (≥3 *vs.* <3). Student's t-test and chi-square test were used for the comparisons of continuous and categorized variables, respectively, between the two groups. The association between CAD prevalence and the number of pregnancies was estimated with chi-square test of linear by linear association. Comparisons of mean value of LVMI and septal e' were assessed using one-way analysis of variances (ANOVA). The adjusted risks of higher number of pregnancies (≥3) for target organ damages were obtained using multiple binary logistic regression analysis. Three different multivariable analyses were performed with higher number of pregnancy (≥3) as common independent variable, and obstructive CAD, LVMI > 95 g/m^2, and septal e′ velocity < 7 cm/s as dependent variables in each multivariable model. Following clinical covariates were adjusted during the multivariable analysis: age, body mass index, hypertension, diabetes mellitus and dyslipidemia. Major cardiovascular risk factors, including age, diabetes mellitus, hypertension, dyslipidemia, and smoking, were controlled for through 1:1 propensity score matching (nearest neighbor method within a 0.2 caliper size) between patients with a pregnancy number of ≥3 and <3. Multivariable analysis was also performed using the matched dataset to demonstrate an independent association between a higher number of pregnancies (≥3) and cardiac TOD. SPSS statistical package version 20 (IBM Corp, Armonk, NY USA) and R (version 4.2.3; R Foundation for Statistical Computing, Vienna, Austria) were used for the statistical analysis. A *P* value of < 0.05 was considered statistically significant.

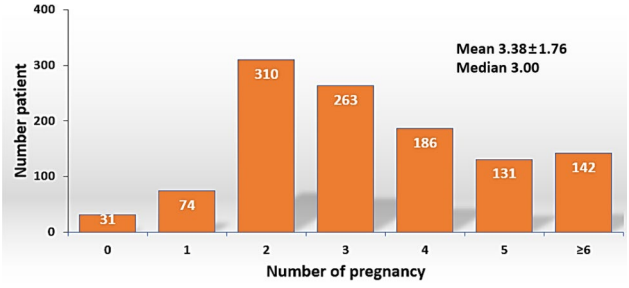

Fig. 1 Distribution of number of pregnancies

Results

The mean and median values of the number of pregnancies among the study patients were 3.38 ± 1.76 and 3.00, respectively (Fig. 1). Patients were stratified into two groups according to the number of pregnancies: higher (≥3, n = 722) and lower (<3, n = 415) numbers of pregnancies.

Clinical characteristics according to the number of pregnancies

The clinical characteristics of the study patients according to the number of pregnancies are shown in Table 1. Patients with higher number of pregnancies were older (66.3 ± 9.6 vs. 57.4 ± 10.7 years, $P < 0.001$) and had more cardiovascular risk factors including hypertension and diabetes mellitus than those with lower number of pregnancies. The laboratory findings did not show any significant differences between the patients with higher and lower pregnancy numbers.

Cardiac TOD parameters according to the number of pregnancies

Comparisons of cardiac TOD parameters between patients with the higher and lower numbers of pregnancies are shown in Table 2. Patients with higher number of pregnancies had lower LV ejection fraction, higher LVMI, lower septal e′ velocity, higher E/e′ and more extensive obstructive CAD, compared to those with lower number of pregnancies ($P < 0.05$ for each). As the number of pregnancies increased, the prevalence rate of obstructive

Table 1 Clinical characteristics according to pregnancy number

Characteristic	Pregnancy number ≥ 3 (n = 722)	Pregnancy number < 3 (n = 415)	*P*
Age, years	66.3 ± 9.6	57.4 ± 10.7	< 0.001
Weight, kg	59.4 ± 9.1	60.0 ± 9.6	0.245
Height, cm	153 ± 5	155 ± 5	< 0.001
Body mass index, kg/m^2	25.0 ± 3.6	24.8 ± 3.7	0.240
Systolic blood pressure, mmHg	129 ± 17	128 ± 18	0.552
Diastolic blood pressure, mmHg	76.8 ± 10.9	76.9 ± 11.7	0.977
Heart rate, per minute	74.7 ± 13.4	76.0 ± 14.0	0.247
Cardiovascular risk factors			
Hypertension	419 (58.0)	184 (44.3)	< 0.001
Diabetes mellitus	215 (30.0)	99 (24.1)	0.035
Dyslipidemia	163 (22.6)	114 (27.5)	0.064
Current smoking	20 (2.8)	14 (3.4)	0.565
Obesity (body mass index ≥ 25 kg/m^2)	326 (46.5)	169 (42.6)	0.208
Major laboratory findings			
White blood cell count, per μL	6945 ± 2592	6920 ± 3005	0.885
Hemoglobin, g/dL	12.6 ± 1.3	12.8 ± 1.2	0.209
GFR, mL/min/1.73m^2	85.2 ± 32.8	87.3 ± 28.7	0.315
Total cholesterol, mg/dL	176 ± 44	181 ± 45	0.111
LDL cholesterol, mg/dL	104 ± 36	107 ± 38	0.314
Triglyceride, mg/dL	123 ± 103	119 ± 59	0.470
HDL cholesterol, mg/dL	49.7 ± 13.2	50.9 ± 13.1	0.217
Glucose, mg/dL	126 ± 60	119 ± 61	0.070
Glycated hemoglobin, %	6.34 ± 1.18	6.28 ± 1.20	0.631
C-reactive protein, mg/dL	0.70 ± 2.51	0.70 ± 2.44	0.993

Numbers are expressed as mean ± SD or n (%). GFR, glomerular filtration rate; LDL, low-density lipoprotein; HDL, high-density lipoprotein

Table 2 Parameters of target organ damage according to pregnancy number

Characteristic	Pregnancy number ≥ 3 (n = 722)	Pregnancy number < 3 (n = 415)	*P*
LV ejection fraction, %	59.4 ± 8.9	60.5 ± 7.9	0.049
LV ejection fraction < 55%	115 (18.0)	43 (12.1)	0.016
RWT	0.39 ± 0.08	0.38 ± 0.07	0.081
RWT > 0.42	175 (28.6)	97 (27.6)	0.739
LV mass index	100.2 ± 30.1	92.4 ± 27.1	< 0.001
LV mass index > 95 g/m^2	292 (50.9)	121 (35.5)	< 0.001
Septal e' velocity, cm/s	5.58 ± 1.86	6.73 ± 2.32	< 0.001
Septal e' velocity < 7 cm/s	448 (74.5)	189 (55.8)	< 0.001
Septal E/e'	11.9 ± 5.2	10.5 ± 4.1	< 0.001
Septal E/e' > 15	87 (17.3)	32 (10.1)	0.004
Obstructive CAD, yes	384 (55.9)	136 (35.4)	< 0.001
CAD extent			0.001
Insignificant	303 (44.1)	248 (64.6)	
One-vessel disease	229 (33.3)	90 (23.4)	
Two-vessel disease	103 (15.0)	32 (8.3)	
Three-vessel disease	52 (7.6)	14 (3.6)	

Numbers are expressed as mean ± SD or n (%). LV, left ventricular; RWT, relative wall thickness; LA, left atrial; CAD, coronary artery disease

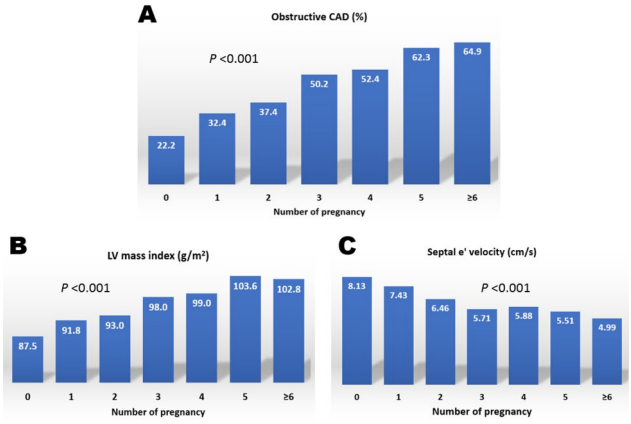

Fig. 2 Associations of number of pregnancies with prevalence of obstructive CAD (**A**), LV mass index (**B**) and LV septal e' velocity (**C**)
CAD, coronary artery disease; LV, left ventricular

Table 3 Adjusted risk of higher number of pregnancy (≥ 3) for obstructive CAD, increased LV mass index and LV diastolic dysfunction

Dependent variable	OR (95% CI)	*P*
Obstructive CAD	1.62 (1.21–2.17)	0.001
LV mass index > 95 g/m^2	1.46 (1.08–1.98)	0.013
Septal e' velocity < 7 cm/s	1.55 (1.12–2.14)	0.007

Following variables were adjusted: age, body mass index, hypertension, diabetes mellitus and dyslipidemia. CAD, coronary artery disease; LV, left ventricular; OR, odds ratio; CI, confidence interval

CAD and LVMI increased, and septal e' velocity decreased proportionally ($P<0.001$ for each) (Fig. 2).

Independent association between the number of pregnancies and cardiac TOD

Adjusted risks of higher number of pregnancies (≥3) for obstructive CAD, increased LVMI and LV diastolic dysfunction are shown in Table 3. In each separate model, higher number of pregnancies was significantly associated with obstructive CAD (odds ratio [OR], 1.62; 95% confidence interval [CI], 1.21–2.17; $P=0.001$), LV hypertrophy (LVMI > 95 g/m^2) (OR, 1.46; 95% CI, 1.08–1.98; $P=0.013$) and LV diastolic dysfunction (e' velocity < 7 cm/s) (OR, 1.55; 95% CI, 1.12–2.14; $P=0.007$) even after controlling for confounding effects of age and other important clinical covariates.

Cardiac TOD in nulliparity

We analyzed the data by dividing the study patients into two groups: patients with a pregnancy number ≥ 1 (n = 1106) vs. <1 (= nulliparity, n = 31). Nulliparity women were younger and had fewer cardiovascular risk factors (**Supplementary Table** S1). Also, nulliparity women had a lower LVMI, more favorable LV diastolic function, and

less obstructive CAD (**Supplementary Table** S2). However, nulliparity was not associated with cardiac TOD in multivariable analysis (**Supplementary Table** S3).

Propensity score matching analysis

We corrected for differences in major cardiovascular risk factors between patients with more than 3 and less than 3 pregnancies through 1:1 propensity score matching analysis (**Supplementary Table** S4). Multivariable analysis showed that a greater number of pregnancies (≥3) were associated with obstructive CAD and LV diastolic dysfunction but not with LVMI. Although LVMI was not statistically significant, there was a numerical trend, which is consistent with the results of unmatched analysis (**Supplementary Table** S5).

Discussion

Main findings

The main finding of this study is that higher number of pregnancies (≥3) was associated with higher prevalence of obstructive CAD, greater LVMI and lower septal e′ velocity than lower number of pregnancies (<3) in Korean middle-aged and elderly women undergoing invasive CAG. This associations were significant even after controlling for potential cofounders. To the best of our knowledge, this is the first study showing the association between parity and multiple cardiac TOD in the same patient.

Previous studies on the association between the number of pregnancies and cardiovascular risk

Many epidemiologic studies have shown that the number of pregnancies is positively associated with cardiovascular risk. Parikh et al. analyzed data of large number of women (n=1,332,062) from the Swedish population registry, and demonstrated that the number of pregnancies was associated with incident maternal CVD in a J-shaped fashion [12]. In another study of 2,357 women who were followed up for 28 years through the Framingham Heart Study, the incidence rate of coronary heart disease was 1.6 times higher in women with number of pregnancies≥6 compared to women who had never been pregnant [13]. Lawlor et al. also reported that each additional child increased the age-adjusted risk of coronary heart disease by 30% for women with at least 2 children [14]. A study that examined 16,515 women in Sweden showed that women with grand multiparous women (≥5 children) had an increased risk of CVD by 1.6-fold compared to those with 2 children [17]. In a meta-analysis of 3,089,929 women from 10 cohort studies, it has been shown that ever parity increased the CVD risk by 14% compared to nulliparity [18].

Few studies have analyzed the mechanisms for which increased number of pregnancies has poor cardiovascular prognosis. Previously, our group has shown the associations of increased number of pregnancies with higher prevalence of obstructive CAD [20] and LV diastolic dysfunction [21] using the KoROSE database. However, those studies analyzed a smaller number of study patients [20] and focused on only one TOD [20, 21]. We showed the association between parity and multiple cardiac TODs, which provides stronger evidence for increased cardiovascular risk in women with higher number of pregnancies.

Mechanisms

There are several hypotheses that explain the association between higher number of pregnancies and increased maternal cardiovascular risk. It has been reported that a single birth is associated with an average weight gain of 2–3 kg, which increases the risk of overweight or obesity even years after childbirth [35]. Long-term metabolic abnormalities such as dyslipidemia and hyperglycemia due to pregnancy are other problems that increases maternal cardiovascular risk [36, 37]. Also, the incidence of pregnancy complications will increase as the number of pregnancies increases.

Pregnancy associated complications such as gestational hypertension, pre-eclampsia, gestational diabetes, low birth weight, preterm birth and miscarriages are all associated with maternal cardiovascular risk [9–11]. Obstructive CAD, LV mass and LV diastolic function are closely associated with the development of future cardiovascular events [22–25]. There are few data on the relationship between these strong prognostic factors and the number of pregnancies. Our study suggests that obstructive CAD, LV hypertrophy and LV diastolic dysfunction are mediators that explains, at least in part, the association between the number of pregnancies and the occurrence of cardiovascular events.

Clinical implications

For women, it is important to understand risk factors associated with pregnancy and to incorporate them into practical preventive therapy in order to reduce the cardiovascular risk. However, women-specific risk factors are under recognized [38]. As the number of pregnancies is easily identified with a simple question, obtaining this information should be a routine in cardiovascular examinations in women. Combining the results of previous studies and ours, when the number of pregnancies is three or more, the cardiovascular risk increases compared to women with fewer or no pregnancies. Therefore, it is better to pay more attention and actively examine subclinical TOD for women with higher number of pregnancies. According to the results of this study, although there are various indicators of cardiac TOD, it would be desirable to examine them with interest in CAD, LV

hypertrophy, and LV diastolic dysfunction. Of course, the association between other cardiac TOD indicators and the number of pregnancies should be elucidated through additional studies. Better understanding of the association between higher number of pregnancies and cardiac TOD could be explored in additional studies to identify the areas of modifiable risk in women in order to reduce their cardiovascular risk.

Several studies have suggested that the relationship between the number of pregnancies and the risk of cardiovascular disease in women follows a J- or U-shaped curve [12, 39, 40]. These findings indicate that women with one or two pregnancies had a lower cardiovascular risk compared to those who had never been pregnant, suggesting that a few pregnancies may have a protective effect on cardiovascular health. Taken together, it becomes apparent that while having a high number of pregnancies (3 or more) elevates cardiovascular risk, having one or two pregnancies may be neutral or even beneficial for women's cardiovascular system.

Study limitations

There are several limitations of this study. First, this cross-sectional study could not determine the causal relationship between the number of pregnancies and cardiac TOD parameters. Secondly, only the confounding effects of several important clinical covariates were adjusted in multivariable analyses. Our results may have been influenced by other variables such as socioeconomic status, lifestyle, environmental factors, and pregnancy associated complications, which are not included in the registry database. Thirdly, while the cardiovascular risk in the nulliparity group may be a significant concern, the impact of nulliparity on TOD could not be effectively analyzed in our study due to the limited sample size. To properly assess this, future research should conduct a comparative analysis with a larger cohort of nulliparous women. Lastly, since our study results were obtained from Koreans who had undergone invasive CAG, caution is required when applying to other groups.

Conclusions

In Korean women undergoing invasive CAG, increased number of pregnancies was associated with higher prevalence of obstructive CAD, increased LVMI and LV diastolic dysfunction. Efforts should be made to reduce cardiovascular risk by paying more attention to women with a higher number of pregnancies. Also, obtaining a pregnancy history should be an integral part of women's cardiovascular risk assessment. Further well-designed prospective studies are needed to support our findings and to clarify causal relationships between parity and cardiac TOD.

Abbreviations

ANOVA	analysis of variance
CAD	coronary artery disease
CAG	coronary angiography
CVD	cardiovascular disease
IRB	institutional review board
IVSd	interventricular septal wall thickness during diastole
KoROSE	KoRean wOmen's chest pain rEgistry
LV	left ventricular
LVIDd	left ventricular internal dimension during diastole
LVMI	left ventricular mass index
MDRD	Modification of Diet in Renal Disease
RWT	relative wall thickness
TOD	target organ damage

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-023-02514-w.

Supplementary Table S1. Clinical characteristics according to pregnancy number.

Supplementary Table S2. Parameters of target organ damage according to pregnancy number.

Supplementary Table S3. Adjusted risk of nulliparity for obstructive CAD, increased LV mass index and LV diastolic dysfunction.

Supplementary Table S4. Clinical characteristics according to pregnancy number before and after propensity score matching.

Supplementary Table S5. The risk of higher number of pregnancy (≥3) for obstructive CAD, increased LV mass index and LV diastolic dysfunction in propensity score matched set.

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Author contributions

H-LK and M-AK designed the research. H-LK wrote the manuscript. H-JK, MK, S-MP, HJY, YSB, SMP, MSS and KSH were involved in literature searches and manuscript editing. M-AK revised the manuscript and had all responsibility of this study. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki Ethical Principles and Good Clinical Practices. Study protocol was reviewed and approved by the institutional review board (IRB) of Boramae Medical Center (Seoul, Republic of Korea). Approval number of the IRB was 06-2011-222. Written informed consent was obtained from each subject before the registry enrollment.

Consent for publication

Not applicable.

Competing interests

The authors declare that there is no conflict of interest.

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References

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart Disease and Stroke Statistics-2020 update: a Report from the American Heart Association. Circulation. 2020;141(9):e139–e596.
2. Wenger NK. Coronary heart disease: an older woman's major health risk. BMJ. 1997;315(7115):1085–90.
3. Stramba-Badiale M, Fox KM, Priori SG, Collins P, Daly C, Graham I, et al. Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology. Eur Heart J. 2006;27(8):994–1005.
4. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the primary Prevention of Cardiovascular Disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140(11):e596–e646.
5. Visseren FLJ, Mach F, Smulders YM, Carballo D, Koskinas KC, Bäck M, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42(34):3227–337.
6. Canto JG, Kiefe CI, Rogers WJ, Peterson ED, Frederick PD, French WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. JAMA. 2011;306(19):2120–7.
7. Henry D, Gonzalez JM, Harris IS, Sparks TN, Killion M, Thiet MP, et al. Maternal arrhythmia and perinatal outcomes. J Perinatol. 2016;36(10):823–7.
8. Mahendru AA, Everett TR, Wilkinson IB, Lees CC, McEniery CM. A longitudinal study of maternal cardiovascular function from preconception to the postpartum period. J Hypertens. 2014;32(4):849–56.
9. Jasper R, Skelding K. Cardiovascular disease risk unmasked by pregnancy complications. Eur J Intern Med. 2018;57:1–6.
10. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular Disease in Women: clinical perspectives. Circ Res. 2016;118(8):1273–93.
11. Cho L, Davis M, Elgendy I, Epps K, Lindley KJ, Mehta PK, et al. Summary of updated recommendations for primary Prevention of Cardiovascular Disease in Women: JACC State-of-the-art review. J Am Coll Cardiol. 2020;75(20):2602–18.
12. Parikh NI, Cnattingius S, Dickman PW, Mittleman MA, Ludvigsson JF, Ingelsson E. Parity and risk of later-life maternal cardiovascular disease. Am Heart J. 2010;159(2):215–21. e6.
13. Ness RB, Harris T, Cobb J, Flegal KM, Kelsey JL, Balanger A, et al. Number of pregnancies and the subsequent risk of cardiovascular disease. N Engl J Med. 1993;328(21):1528–33.
14. Lawlor DA, Emberson JR, Ebrahim S, Whincup PH, Wannamethee SG, Walker M, et al. Is the association between parity and coronary heart disease due to biological effects of pregnancy or adverse lifestyle risk factors associated with child-rearing? Findings from the British Women's Heart and Health Study and the british Regional Heart Study. Circulation. 2003;107(9):1260–4.
15. Catov JM, Newman AB, Sutton-Tyrrell K, Harris TB, Tylavsky F, Visser M, et al. Parity and cardiovascular disease risk among older women: how do pregnancy complications mediate the association? Ann Epidemiol. 2008;18(12):873–9.
16. Green A, Beral V, Moser K. Mortality in women in relation to their childbearing history. BMJ. 1988;297(6645):391–5.
17. Klingberg S, Brekke HK, Winkvist A, Engström G, Hedblad B, Drake I. Parity, weight change, and maternal risk of cardiovascular events. Am J Obstet Gynecol. 2017;216(2):172. e1-.e15.
18. Li W, Ruan W, Lu Z, Wang D. Parity and risk of maternal cardiovascular disease: a dose-response meta-analysis of cohort studies. Eur J Prev Cardiol. 2019;26(6):592–602.
19. Devereux RB, Alderman MH. Role of preclinical cardiovascular disease in the evolution from risk factor exposure to development of morbid events. Circulation. 1993;88(4 Pt 1):1444–55.
20. Kim HL, Kim MA, Shim WJ, Park SM, Kim YH, Na JO, et al. Reproductive factors Predicting Angiographic Obstructive Coronary Artery Disease: the KoRean wOmen'S chest Pain rEgistry (KoROSE). J Womens Health (Larchmt). 2016;25(5):443–8.
21. Kim HJ, Kim MA, Kim HL, Shim WJ, Park SM, Kim M, et al. Effects of multiparity on left ventricular diastolic dysfunction in women: cross-sectional study of the KoRean wOmen'S chest pain rEgistry (KoROSE). BMJ Open. 2018;8(12):e026968.
22. Hoang K, Zhao Y, Gardin JM, Carnethon M, Mukamal K, Yanez D, et al. LV Mass as a predictor of CVD events in older adults with and without metabolic syndrome and diabetes. JACC Cardiovasc Imaging. 2015;8(9):1007–15.
23. Desai CS, Bartz TM, Gottdiener JS, Lloyd-Jones DM, Gardin JM. Usefulness of Left Ventricular Mass and geometry for determining 10-Year prediction of Cardiovascular Disease in adults aged > 65 years (from the Cardiovascular Health Study). Am J Cardiol. 2016;118(5):684–90.
24. Nayor M, Cooper LL, Enserro DM, Xanthakis V, Larson MG, Benjamin EJ et al. Left ventricular diastolic dysfunction in the community: impact of Diagnostic Criteria on the Burden, correlates, and prognosis. J Am Heart Assoc. 2018;7(11).
25. Bella JN, Palmieri V, Roman MJ, Liu JE, Welty TK, Lee ET, et al. Mitral ratio of peak early to late diastolic filling velocity as a predictor of mortality in middle-aged and elderly adults: the strong heart study. Circulation. 2002;105(16):1928–33.
26. Kim HC, Ihm SH, Kim GH, Kim JH, Kim KI, Lee HY, et al. 2018 korean Society of Hypertension guidelines for the management of hypertension: part I-epidemiology of hypertension. Clin Hypertens. 2019;25:16.
27. Hur KY, Moon MK, Park JS, Kim SK, Lee SH, Yun JS, et al. 2021 clinical practice guidelines for diabetes Mellitus of the korean Diabetes Association. Diabetes Metab J. 2021;45(4):461–81.
28. Rhee EJ, Kim HC, Kim JH, Lee EY, Kim BJ, Kim EM, et al. 2018 guidelines for the management of dyslipidemia. Korean J Intern Med. 2019;34(4):723–71.
29. Seo MH, Lee WY, Kim SS, Kang JH, Kang JH, Kim KK, et al. 2018 korean Society for the study of obesity Guideline for the management of obesity in Korea. J Obes Metab Syndr. 2019;28(1):40–5.
30. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130(6):461–70.
31. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1–39e14.
32. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by Echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016;29(4):277–314.
33. Bangalore S, Barsness GW, Dangas GD, Kern MJ, Rao SV, Shore-Lesserson L, et al. Evidence-based Practices in the Cardiac Catheterization Laboratory: A Scientific Statement from the American Heart Association. Circulation. 2021;144(5):e107–e19.
34. Pepine CJ, Allen HD, Bashore TM, Brinker JA, Cohn LH, Dillon JC, et al. ACC/AHA guidelines for cardiac catheterization and cardiac catheterization laboratories. American College of Cardiology/American Heart Association Ad Hoc Task Force on Cardiac catheterization. Circulation. 1991;84(5):2213–47.

35. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. Epidemiol Rev. 2000;22(2):261–74.
36. Cohen A, Pieper CF, Brown AJ, Bastian LA. Number of children and risk of metabolic syndrome in women. J Womens Health (Larchmt). 2006;15(6):763–73.
37. Gunderson EP, Lewis CE, Murtaugh MA, Quesenberry CP, Smith West D, Sidney S. Long-term plasma lipid changes associated with a first birth: the coronary artery risk development in young adults study. Am J Epidemiol. 2004;159(11):1028–39.
38. Humphries KH, Izadnegahdar M, Sedlak T, Saw J, Johnston N, Schenck-Gustafsson K, et al. Sex differences in cardiovascular disease - impact on care and outcomes. Front Neuroendocrinol. 2017;46:46–70.
39. Dior UP, Hochner H, Friedlander Y, Calderon-Margalit R, Jaffe D, Burger A, et al. Association between number of children and mortality of mothers: results of a 37-year follow-up study. Ann Epidemiol. 2013;23(1):13–8.
40. Zeng Y, Ni ZM, Liu SY, Gu X, Huang Q, Liu JA, et al. Parity and all-cause mortality in women and men: a dose-response Meta-analysis of Cohort Studies. Sci Rep. 2016;6:19351.

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