A Dilemma for Women: Love of Multiple Children or Deterioration of Diastolic Functions

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August 17, 2020

Abstract

Echocardiography is the most widely used diagnostic tool for detecting the cardiac functional changes. Pregnancy is a dynamic process that affects cardiovascular system. Recent studies showed that increased parity may cause irreversible changes in cardiovascular system. In this study, we aimed to evaluate echocardiographic changes on women, especially grand multiparous (up to 9 parities) and great grand multiparous (more than 10 parities) women after all their pregnancies finished. This is a cross-sectional study and contains 195 women patients. Women with one delivery history was defined as primiparous (PP), 2 to 5 deliveries were defined as multiparous (MP), 5 to 9 deliveries were defined as grand multiparous (GMP) and more than 9 deliveries were defined as great grand multiparous (GGMP). The mean age was 50.6±16.3 and mean parity was 6.5±4.2. Spearman correlation analysis showed that diastolic dysfunction has positive correlations with parity, age, hypertension, and diabetes mellitus. ROC analysis showed that the best cut-off value of the parity number for predicting left ventricular diastolic dysfunction was 6.5, with 66.3% sensitivity and 66.7% specificity. In present study, we showed that diastolic dysfunction statistically increases as the number of pregnancies increases. Additionally, cut of value of parity for diastolic dysfunction was 6.5 which is higher than other studies.

Introduction

Echocardiography is the most widely used diagnostic tool for detecting the cardiac functional changes[1]. New updates for calculating the cardiac ventricular functions are still continuing [2]. Systolic and diastolic functions of the heart can be affected by many variables [3, 4]. Especially systemic chronic diseases (diabetes mellitus, hypertension, hyperlipidemia...) deteriorate these functions. However, in healthy population, some situations as pregnancy may change cardiovascular mechanism.

Pregnancy is a dynamic process that affects cardiovascular system. During pregnancy maternal cardiac output, preload and maternal blood volume increase and systemic vascular resistance decreases [5]. These changes are necessary for the continuation of pregnancy and the health of the fetus. Most of the changes occur during pregnancy however, these changes return to normal after pregnancy [6].

Recent studies showed that increased parity may cause irreversible changes in cardiovascular system [7, 8]. Left ventricular diastolic functions deteriorate during pregnancy and this is associated with increased cardiovascular mortality [9-11]. Diastolic function and other cardiovascular changes tend to return to normal however as the parity increases, diastolic parameters are affected and these reversible changes may become permanent [6, 12].

In this study, we aimed to evaluate echocardiographic changes on women, especially grand multiparous (up to 9 parities) and great grand multiparous (more than 10 parities) women after all their pregnancies finished.

Methods

This is a cross-sectional study and contains 195 women patients. All patients with a history of one or more delivery and above 18 years-of-age were included in this study. Patients under 18 years-of-age, history of coronary artery disease, heart failure, structural heart diseases, rhythm disorders, renal or hepatic disorders and women who are currently pregnant were excluded from the study. However, patients with a history of hypertension and diabetes mellitus that may affect left ventricular diastolic functions were included to study. Binary and multinominal logistic regression analyses were done for two of these situations

Women with one delivery history was defined as primiparous (PP), 2 to 5 deliveries were defined as multiparous (MP), 5 to 9 deliveries were defined as grand multiparous (GMP) and more than 9 deliveries were defined as great grand multiparous (GGMP).

Echocardiographic (Vivid 7 system with 3S echocardiography probe, GE Vingmed Ultrasound AS, Horten, Norway) evaluation was done by trained cardiology specialists. The evaluated parameters were peak early filling velocity during atrial systole (E), peak filling velocity during atrial systole (A), left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter, left ventricular end-diastolic diameter, lateral e' velocity, lateral s' velocity, septal e' velocity, septal s' velocity, tricuspid S velocity. E / A was calculated as the ratio of E to A. E / e' ratio was calculated as the ratio of E velocity to mean e' (as average of lateral e' wave and septal e' wave).

Septal e' [?] 8 cm / sec, lateral e' [?]10 cm / sec was evaluated as normal diastolic function. Diastolic dysfunction was determined to be septal e '<8 cm / sec, lateral e'<10 cm / sec. Stage 1 diastolic dysfunction was defined as; mitral E and A wave velocity ratio (E / A) < 0.8, the ratio of E to the mean early diastolic mitral annular velocity (E/e') [?] 8. Stage 2 diastolic dysfunction was determined as E / A to be between 0.8-1.5 and E / e' ratio between 9 and 12. Stage 3 diastolic dysfunction was determined as E / A ratio being [?] 2 and E / mean e' ratio was [?] 13. All these parameters were obtained American Society of Echocardiography and European Association of Cardiovascular Imaging (ASE/EACVI) guidelines recommendations[13].

Hypertension was defined as systolic pressure greater than 140 mm Hg or diastolic pressure greater than 90 mm Hg or a history of hypertension with the use of antihypertensive medication. Diabetes mellitus was defined as a fasting blood glucose level of 126 mg/dl, a random glucose measurement of 200 mg/dl, hemoglobin A1c >6.5%, or a previous diagnosis with any use of anti-diabetic medication.

Datas were presented as mean ± standard deviation (SD) for continuous variables and as numbers and proportions for categorical variables. Distribution of the data for normality was tested by the Shapiro–Wilk test and homogeneity of group variances were tested by the Levene test. The t-test or Chi-square test was used for comparisons of continuous and categorical variables, respectively. For the parameters which are not normally distributed, Mann Whitney U test was used. More than two independent groups with normal distribution were compared with the ANOVA test. Binary logistic regression analysis was used to identify the associations of diastolic dysfunction presence to other variables. Multinominal regression analysis was used to evaluate the associations of diastolic dysfunction grades to other variables. The data analyses were performed with SPSS 23.0 (IBM SPSS Ver. 23.0, IBM Corp, Armonk NY, USA). A p-value of <0.05 was considered significant.

Results

Study population consists of 195 women with a history of at least one delivery. PM women constituted 8.2% (n=16), MP women constituted 37.4% (n=73), GMP women constituted 23.6% (n=46) and GGMP women constituted 30.8% (n=60) of the study population. The mean age was 50.6±16.3 and mean parity was 6.5±4.2. The characteristics of the study population were given in Table I.

The E velocity (p=0.017), A velocity (p=0.000), lateral e' velocity (p=0.000), lateral s' (p=0.027), septal e' (p=0.000), septal s' (p=0.000) and EF (p=0.000) values were significantly different among all parity groups. The results were shown in Table II. Binary comparison of the study groups evaluating the echocardiographic parameters can be seen in Table III.

Diastolic dysfunction classification was done according to the echocardiographic parameters. For the PM group, 87.5% (n=14) had normal diastolic function, 6.25% (n=1) had grade 1 diastolic dysfunction and 6.25% (n=1) had grade 2 diastolic dysfunction. For the MP women; 71.2% (n=52) had normal diastolic function, 12.4% (n=9) had grade 1 diastolic dysfunction and 16.4% (n=12) had grade 2 diastolic dysfunction. For the GMP women; 56.5% (n=26) had normal diastolic function, 10.9% (n=5) had grade 1 diastolic dysfunction and 32.6% (n=15) had grade 2 diastolic dysfunction. For the GGMP women; 28.6% (n=17) had normal diastolic function, 33.2% (n=20) had grade 1 diastolic dysfunction and 38.2% (n=23) had grade 2 diastolic dysfunction (Table IV). There were no women with grade 3 diastolic dysfunction among the study population.

Spearman correlation analysis showed that diastolic dysfunction has positive correlations with parity, age, hypertension, and diabetes mellitus (Table V).

Table VI and Table VII report the findings of the binary and multinomial logistic regressions. Explanatory variables in both models are age, number of parity, hypertension and diabetes mellitus. The difference among the models stems from how the dependent variable is handled. In the binary logistic regression, dependent variables are grouped into two categories: diastolic dysfunction existence or the patient has normal diastolic function. On the other hand, multinomial logistic regression in this study separates the patients into three groups: patients without diastolic dysfunction, patients with grade 1 and grade 2 diastolic dysfunction. Both models show that only number of parity and age are statistically significant.

ROC analysis showed that the best cut-off value of the parity number for predicting left ventricular diastolic dysfunction was 6.5, with 66.3% sensitivity and 66.7% specificity (Figure 1).

Discussion

In present study, we showed that diastolic dysfunction statistically increases as the number of pregnancies increases. Additionally, cut of value of parity for diastolic dysfunction was 6.5 which is higher than other studies [6, 12].

Previous studies showed that cardiovascular mortality increases along with increased parity [7]. Changes in the renin-angiotensin-aldosterone system explain this mechanism [14]. Estrogen secreted by placenta increases the release of angiotensinogen. Angiotensinogen produces angiotensin-2 that activates the RAS system. RAS system induces sodium and water retention. As a result, increased afterload is observed along with pregnancy. Also decreased relaxin levels affect cardiovascular mortality during pregnancy [15]. However, these changes continue only with pregnancy and their effects after pregnancy are still not clear.

We also found that diastolic function deteriorates as the parity increases. Aggarwal et al, performed the first known study on this issue and they found the same results[16]. Other studies similarly showed that diastolic dysfunction increases with the parity [6, 12]. However; they performed these studies up to 7 pregnancies (grand multiparity). In our study, women that have a history of 9 and more pregnancies (great grand multiparity) were also included. The present study has the highest number of parity in the literature.

There is lack of evidence about relationship between the parity and the severity of diastolic dysfunction. Kim et al. found that 2.5 and above parity number significantly increases the diastolic dysfunction[6]. Other study performed by Keskin et al. showed that pregnancies of 4 and above significantly increase the diastolic dysfunction [12]. In our study, the cut-off value for diastolic dysfunction severity according to the ROC curve analysis was 6.5 pregnancies. This difference attributed to the number of pregnancies included in this study is higher than other studies before.

Aortic stiffness is a prognostic risk factor for cardiovascular mortality. In the present study, binary logistic regression analysis showed that presence of hypertension and diabetes mellitus did not make a significant difference in terms of diastolic dysfunction; however number of pregnancies and age did make a significant difference. This can be attributed to increasing of aortic stiffness. In our study, we showed the same results as the previous studies in the literature [17-20].

In the present study, significant decrease in ejection fraction was observed as the number of pregnancies

increases. However, this decrease did not reach the systolic dysfunction range (greater than %50). Although Kim et al. found same results as ours; other studies did not show this correlation [6, 12, 16]. This result attributed to be exposed of long time diastolic dysfunction as our study population has higher pregnancy numbers.

LIMITATIONS

This study has limitations that should be considered. First of all, our study population consists of limited number of patients. Second, our findings do not represent healthy population, because our study only studied patients that referred to the cardiology clinic with cardiac complaints. Third, we performed this study in a lower socio-economic area that it affects cardiovascular status independently. Finally, due to lack of facility, we did not perform cardiac magnetic resonance measurements or measure brain natriuretic peptides that show more proper information about diastolic dysfunction.

Author contributions

Concept/design: MO

Data analysis/interpretation: MO, OTY, MSK

Drafting article: MO, OTY, MSK

Critical revision of article: MO, MAA

Statistics: MO, MAA

Data collection: MO

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Table I. Characteristics of the study population

	Primiparous 1 delivery n=16	Multiparous 1 < to 5 deliveries n=73	Grand multiparous 5 < to 9 deliveries n=46	Great grand multiparous 9 < deliveries n=60	p
Age, years (±SD)	30.8±9.0	39.4±8.8	52.8±11.9	67.7±9.5	0.000
Parity number, n	1.0±0.0	2.9±1.0	7.5±1.2	11.7±1.8	0.000
Diabetes mellitus, n (%)	2, 12.5%	3, 4.1%	8, 17.4%	19, 31.7%	0.000
Hypertension, n (%)	4, 25.0%	19, 26.0%	32, 69.6%	55, 91.6%	0.000
Sistolic BP, mmHg	105.6±15.9	115.6±19.4	132.4±22.0	137.5±23.1	0.000
Diastolic BP, mmHg	67.1±9.6	75.5±12.0	83.0±11.3	83.2±12.9	0.000

Abb. BP, blood pressure; SD, standard deviation.

Table II. Echocardiographic parameters of the study groups

Variables	PP	MP	GMP	GGMP	p
E, cm/s	87.7±15.4	89.1±26.2	102.4±19.8	90.7±25.3	**0.017**
A, cm/s	66.6±11.8	78.2±20.4	101.6±21.4	101.6±20.1	**0.000**
Lateral e', cm/sn	14.0±3.3	12.7±3.4	10.6±3.0	8.6±2.7	**0.000**
Lateral s', cm/sn	10.1±0.9	10.3±2.0	9.7±2.1	9.3±2.4	**0.027**
Septal e', cm/sn	10.5±2.3	9.5±2.4	7.4±2.1	6.2±1.7	**0.000**
Septal s', cm/sn	8.1±1.1	8.2±1.5	8.1±2.0	7.0±1.8	**0.000**
EDD, mm	44.7±2.4	44.4±3.5	44.8±4.4	44.5±6.0	0.964
ESD, mm	28.7±2.3	27.4±3.8	27.1±4.9	27.2±6.5	0.733
EF, %	62.3±3.1	62.4±3.0	58.9±5.4	56.2±6.7	**0.000**

Table III. Binary comparison of parity groups according to parameters

	PP vs MP	PP vs GMP	PP vs GGMP	MP vs GMP	MP vs GGMP	GMP vs GGMP
E	0.844	0.009	0.779	**0.004**	0.714	0.011
A	0.025	**0.000**	**0.000**	**0.000**	**0.000**	**0.987**
Lateral e'	0.147	**0.000**	**0.000**	**0.001**	**0.000**	**0.000**
Lateral s'	0.623	0.442	**0.026**	0.084	**0.005**	0.350
Septal e'	0.138	**0.000**	**0.000**	**0.000**	**0.000**	**0.001**
Septal s'	0.830	0.907	**0.018**	0.645	**0.000**	**0.003**
EF	0.892	**0.019**	**0.000**	**0.000**	**0.000**	**0.027**

Table IV. Diastolic function classification among study population

	PP (n=16)	MP(n=73)	GMP(n=46)	GGMP(n=60)
Normal diastolic function	14	52	26	17
DD Grade 1	1	9	5	20
DD Grade 2	1	12	15	23

Table V. Spearman correlation analysis between the diastolic dysfunction presence and number of parity, age, hypertension and diabetes mellitus

	Number of parity	Age	Hypertension	Diabetes Mellitus
r	0.404	0.614	0.448	0.331
p	**0.000**	**0.000**	**0.000**	**0.000**

Table VI. Binary logistic regression analysis for the presence of diastolic dysfunction

	Odds Ratio	95% CI	P
Number of parity	0.805	0.692-0.938	**0.005**
Age	1.166	1.103-1.234	**0.000**

	Odds Ratio	95% CI	P
Hypertension	0.968	0.359-2.611	0.949
Diabetes Mellitus	0.520	0.176-1.536	0.237

Table VII. Multinomial logistic regression analysis for diastolic dysfunction grade

Diastolic Dysfunction Grades		Odds ratio	95%	p
Grade 1	Number of parity	0.760	0.625-0.925	**0.006**
	Age	1.198	1.118-1.283	**0.000**
	Hypertension	0.885	0.217-3.614	0.865
	Diabetes Mellitus	0.525	0.152-1.815	0.309
Grade 2	Number of parity	0.829	0.705-0.976	**0.024**
	Age	1.150	1.084-1.220	**0.000**
	Hypertension	1.006	0.334-3.032	0.991
	Diabetes mellitus	0.516	0.164-1.621	0.257

Figure I. Receiver-operating curve (ROC) analysis. ROC analysis revealed that the best cut-off value of the parity number for predicting left ventricular diastolic dysfunction was 6.5, with 66.3% sensitivity and 66.7% specificity (Area Under the Curve: 0.734; 95% CI 0.663 to 0.805; p<0.000).