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ORIGINAL ARTICLE CARDIAC SURGERY

Preconception consultation using treadmill exercise stress echocardiography for pregnant women with the left-sided heart valve stenosis: A preliminary report

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ABSTRACT

OBJECTIVE: Pregnancy can increase gradients across the heart valves and consequently deteriorates maternal and fetoneonatal conditions. Hence, pregnancy during heart valve diseases can be challenging and we need to risk stratify patients before conception. We tried to assess the role of preconception consultation using treadmill stress echocardiography (TSE) testing for identifying pregnancy outcomes in women with mitral valve stenosis (MS) or aortic valve stenosis (AS).

METHODS: Pregnant patients with a diagnosis of MS or AS were evaluated from January 2015 to December 2018. First group included patients undergoing the TSE testing and they were permitted to get pregnant if they met pre-defined criteria. Second group comprised women who did not undergo TSE testing. Maternal and fetoneonatal outcomes were also recorded.

RESULTS: A total of 29 and 18 patients with MS and AS, respectively, were recruited. Among MS patients, individuals without TSE had more functional deterioration (11.1% vs. 35%) and more fetoneonatal events (FNE) (22.2% vs. 55%) compared with those undergoing TSE. The rates of maternal events and mitral valvuloplasty during pregnancy were significantly higher in patients without TSE compared with those undergoing TSE (p=0.015 and p=0.042, respectively). Among AS patients, maternal and FNE were higher in patients without TSE compared with those undergoing TSE, but those were comparable.

CONCLUSION: Pregnant patients with the left-sided valvular stenosis who received preconception TSE testing had better outcomes compared with those who did not undergo preconception consultation. This underscores the utility of stress echocardiography in the risk stratification of pregnancies.

Keywords: Aortic valve; mitral valve; pregnancy; stress echocardiography; valvular stenosis.

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The development of cardiovascular cares and the implementation of practical guidelines have led to an increase in the number of women with heart diseases who desire pregnancy [1]. Valvular heart disease (VHD) is a common clinical entity during pregnancy. The risk stratification of women with VHD is challenging in our daily practice so that the preconception evaluation by risk stratification tools has been recommended in the practical guidelines, including the American College of Cardiology/American Heart Association (ACC/AHA) and

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the European Society of Cardiology (ESC) [2, 3]. The modified World Health Organization (mWHO) tool for risk stratification has recommended against pregnancy in patients with a diagnosis of mitral stenosis (MS) [4], while we visit pregnant women who were diagnosed with MS during pregnancy. The prevalence of rheumatismal etiologies in developing countries is more than that in developed countries; nonetheless, the immigration has greatly influenced the frequency of rheumatismal cases in developed countries [5]. On the other hand, in developed nations, the main etiology of VHD is congenital heart diseases such as aortic valve stenosis (AS) [5, 6].

The expansion of plasma volume during pregnancy can enhance valvular gradients resulting in the deterioration of patient's condition, particularly in individuals with valvular stenosis and consequently deteriorate patient's condition [7]. The stress echocardiography has been found to be of paramount role in the evaluation of patients with VHD [8] so that the recent ACC/AHA guideline recommends using the stress echocardiography for the risk stratification of patients with VHD [9]. In this study, we sought to determine the role of preconception consultation on maternal and fetal outcomes in women with a diagnosis of MS or AS and to evaluate the utility of treadmill stress echocardiography (TSE) test for identifying maternal tolerance and the risk of complications.

Highlight key points

- Mitral and AS pose high risk to pregnant patients.
- Preconception TSE improves risk stratification.
- Patients with preconception TSE has fewer mitral valvuloplasty during pregnancy.
- Maternal/neonatal events reduce in those with preconception consultation using TSE.

MATERIALS AND METHODS

Study Patients and Protocols

In a retrospective study, all pregnant patients with MS or AS who visited our maternal cardiology clinic were recruited into the study from January 2015 to December 2018. Based on practical guidelines, the severe MS was defined as the mitral valve area <1.5 cm^2 measured by transthoracic echocardiography (TTE) in the setting of rheumatismal changes. Patients with AS caused by bicuspid aortic valve or in the setting of rheumatismal changes were also included in the study. The detection of AS was based on following criteria: Valve area <1.5 cm^2, peak gradient >36 mm Hg, or peak velocity >3 m/s measured by Doppler TTE. The study protocol was approved by the Institutional Review Board. The study protocol was approved by the Institutional Review Board (identification number: 98084; date: March 1 2020).

Exclusion criteria included patients with symptomatic left-sided heart valve stenosis, those with critical AS proposing functional class of IV, and asymptomatic individuals with pulmonary arterial hypertension at rest detected by echocardiography. Patients desired to become pregnant and pregnant individuals visiting our clinic were recruited after evaluation by a multidisciplinary team (Fig. 1). First group included patients with preconception visit undergoing the TSE. These patients were permitted to get pregnant if they met pre-defined criteria (Fig. 2). The second group included women who visited maternal cardiology clinic after 12 weeks and they did not undergo TSE test; however, based on the recommended classifications by risk tools and the practical guidelines, they were permitted to continue pregnancy. All patients received medical therapies based on clinical status and symptoms during pregnancy, and all drugs were adjusted based on their clinical conditions.

Exercise Stress Echocardiography

Patients underwent TSE test with the implementation of the standard Bruce protocol. During the TSE test, the comprehensive evaluation of valvular hemodynamics was performed at rest and at peak exercise point. The test was terminated when patients requested or they had symptoms, including chest pain, dyspnea, blood pressure reduction >20 mm Hg, and electrocardiographic changes. The metabolic equivalents (METs) were calculated based on the formula as 3.5 mL O_2/kg body weight/min [10]. After exercise, peak-stress TTE was performed with the implementation of practical recommendations [11]. At the peak point, changes in heart rate, blood pressure, left ventricular ejection fraction (LVEF), valvular hemodynamic, pulmonary artery pressure, ST-T changes, myocardial reserve, and TSE-induced arrhythmia were recorded and those were compared with baseline values.

Maternal and Fetal Outcomes

Maternal peripartum events (MPE) included adverse events during pregnancy and 6 months postpartum period. The MPE comprised heart failure requiring hospitalization, arrhythmia, syncope, thromboembolic events, and invasive cardiac interventions (i.e., percutaneous

Table 1. Baseline characteristics of patients in study groups by MS

	With TSE % (n=9)	Without TSE % (n=20)	p
Maternal age at conception, year	31.3±3.4	32.6±5.5	0.522
Age group			0.491
18–35 year	77.8	65	
<18 or >35 year	22.2	35	
Education			0.706
Under high school diploma	33.3	25	
High school diploma	33.3	50	
University graduated	33.3	25	
Gravidity			0.469
1	33.3	30	
2–3	66.7	55	
>3	0	15	
Parity			0.467
0	55.6	45	
1–2	44.4	40	
≥3	0	15	
Abortion history			0.285
0	77.8	80	
1	11.1	20	
≥2	11.1	0	
NYHA at first visit			0.147
Class I	33.3	50	
Class II	55.6	20	
Class III	11.1	30	
Prior cesarean section	33.3	45	0.555
Prior PTMC	33.3	15	0.260
TTE findings at first visit			
AI	33.3	20	0.438
TR	22.2	60	0.060
Concomitant MR	11.1	30	0.271
LVEF, %	50±5.6	48.7±6.8	0.636

Values presented as mean±SD or number (percentage); TSE: Treadmill exercise stress echocardiography; NYHA: New York heart association functional class; PTMC: Percutaneous transluminal mitral valve commissurotomy; TTE: Transthoracic echocardiography; AI: Aortic insufficiency; TR: Tricuspid regurgitation; MR: Mitral regurgitation; LVEF: Left ventricular ejection fraction; MS: Mitral stenosis.

Table 2. Baseline characteristics of patients in study groups by AS

	With TSE n=7	Without TSE n=11	p
Maternal age at conception, year	28 (24, 32)	30 (27, 32)	0.425
Age group (%)			0.412
18–35 year	100	90.9	
<18 or >35 year	0	1 (9.1	
Education (%)			0.684
Under high school diploma	0	9.1	
High school diploma	42.9	45.5	
University graduated	57.1	45.5	
Gravidity (%)			0.629
1	57.1	45.5	
2–3	42.9	54.5	
Parity (%)			0.171
0	85.7	54.5	
1–2	14.3	45.5	
Abortion history (%)			0.605
0	71.4	81.8	
1	28.6	18.2	
NYHA at first visit (%)			0.474
Class II	71.4	54.5	
Class III	28.6	45.5	
Prior cesarean section	14.3	27.3	
Prior cardiac surgery	42.9	36.4	
TTE findings at first visit (%)			
AI	42.9	45.5	0.911
CoA	0	9.1	0.412
BAV	42.9	27.3	0.494

Values presented as median (interquartile range) or number (percentage); AS: Aortic stenosis; TSE: Treadmill exercise stress echocardiography; NYHA: New York heart association functional class; TTE: Transthoracic echocardiography; AI: Aortic insufficiency; CoA: Coarctation of aorta; BAV: Bicuspid aortic valve.

transluminal mitral valve commissurotomy [PTMC] or valvular open surgery). Fetoneonatal events (FNE) consisted of preterm birth, small for gestational age, intrauterine growth retardation, and respiratory distress disorder. All pregnant patients routinely visited clinic around the end of trimesters except for those without TSE test that was visited firstly after 12 weeks.

Statistical Analysis

Continuous variables were reported as mean±SD or median (interquartile range) based on the normality of distribution. Categorical variables were reported as number (percentage). The Chi-squared test or Fisher's exact test was used as appropriate. Based on the normality of data distribution, continuous variables were compared between groups using the t-test or Mann–Whitney U-test as appropriate. Two-sided P-values were reported. All statistical analyses were performed using the STATA software (StataCorp, TX, USA).

TABLE 3. Treadmill exercise stress echocardiographic findings among patients with MS and AS

	Values
MS	
METs	9.6±1.7
Baseline HR, bpm	76.6±11.9
Peak HR, bpm	162.4±29.2
Baseline SBP, mm Hg	117.9±11.2
Peak SBP, mm Hg	145.9±19
Baseline DBP, mm Hg	72.2±12.3
Peak DBP, mm Hg	84.4±8.4
Baseline LVEF, %	52.2±5
Peak LVEF, %	62.7±6.2
Baseline MG, mm Hg	5.5±1.3
Peak MG, mm Hg	17.7±9.8
Baseline PAP, mm Hg	35±6.1
Peak PAP, mm Hg	54.3±7.7
TSE-induced ST-T changes	0
Myocardial reserve	9 (100)
TSE-induced arrhythmia	1 (11.1)
AS	
METs	10.4±1.8
Baseline HR, bpm	94.7±13
Peak HR, bpm	181.8±11.3
Baseline SBP, mm Hg	102.8±16.5
Peak SBP, mm Hg	132.7±19.7
Baseline DBP, mm Hg	64.4±11.1
Peak DBP, mm Hg	81.3±6.7
Baseline LVEF, %	55
Peak LVEF, %	65.7±4.5
Baseline MG, mm Hg	34.7±10
Peak MG, mm Hg	61.4±22.3
TSE-induced ST-T changes	0
Myocardial reserve	7 (100)
TSE-induced arrhythmia	1 (14.3)

Values presented as mean±SD or number (percentage); AS: Aortic stenosis; TSE: Treadmill exercise stress echocardiography; MS: Mitral stenosis; METs: Metabolic equivalents; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PAP: Pulmonary arterial pressure; MG: Mean gradient; LVEF: Left ventricular ejection fraction.

TABLE 4. Maternal and Neonatal events in left-sided heart valve stenosis

	With TSE	Without TSE	p
MS			
Total number of patients	9	20	
FNE	22.2	55	0.101
MPE	0	45	0.015
NICU admission	11	25	0.393
ICU admission >48 hours	22.2	10	0.371
PTMC during pregnancy	0	35	0.042
NYHA deterioration	11.1	35	0.136
AS			
Total number of patients	7	11	
FNE	0	9.1	0.412
MPE	0	18.2	0.231
NICU admission	14.3	18.2	0.829
ICU admission >48 h	0	18.2	0.231
NYHA deterioration	0	10	0.388

Values presented as number (percentage); TSE: Treadmill exercise stress echocardiography; MS: Mitral stenosis; FNE: Fetal neonatal events; MPE: Maternal peripartum events; NICU: Neonatal intensive care unit; ICU: Intensive care unit; PTMC: Percutaneous transluminal mitral valve commissurotomy; NYHA: New York heart association functional class; AS: Aortic stenosis.

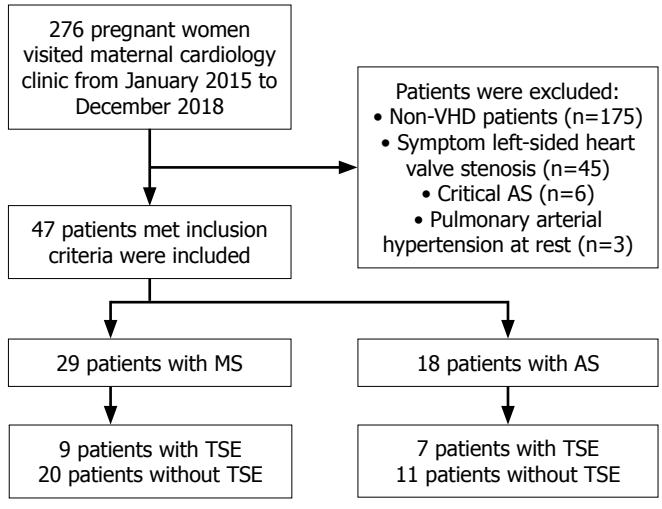

FIGURE 1. The flow diagram for population selection.

AS: Aortic valve stenosis; MS: Mitral valve stenosis; TSE: Treadmill exercise stress echocardiography; VHD: Valvular heart disease.

RESULTS

During the study period, a total of 29 and 18 patients with MS and AS, respectively, were recruited. There was a trend toward patients without TSE test to have more tricuspid valve regurgitation compared to those with TSE test (6% vs. 22.2%; p=0.060). Other baseline characteristics were comparable between those with or without TSE test (Table 1). Among patients with AS, there was a trend toward patients undergoing TSE to be more nulliparous (85.7% vs. 54.5%; p=0.171). Other baseline characteristics were comparable between patients with or without TSE test (Table 2).

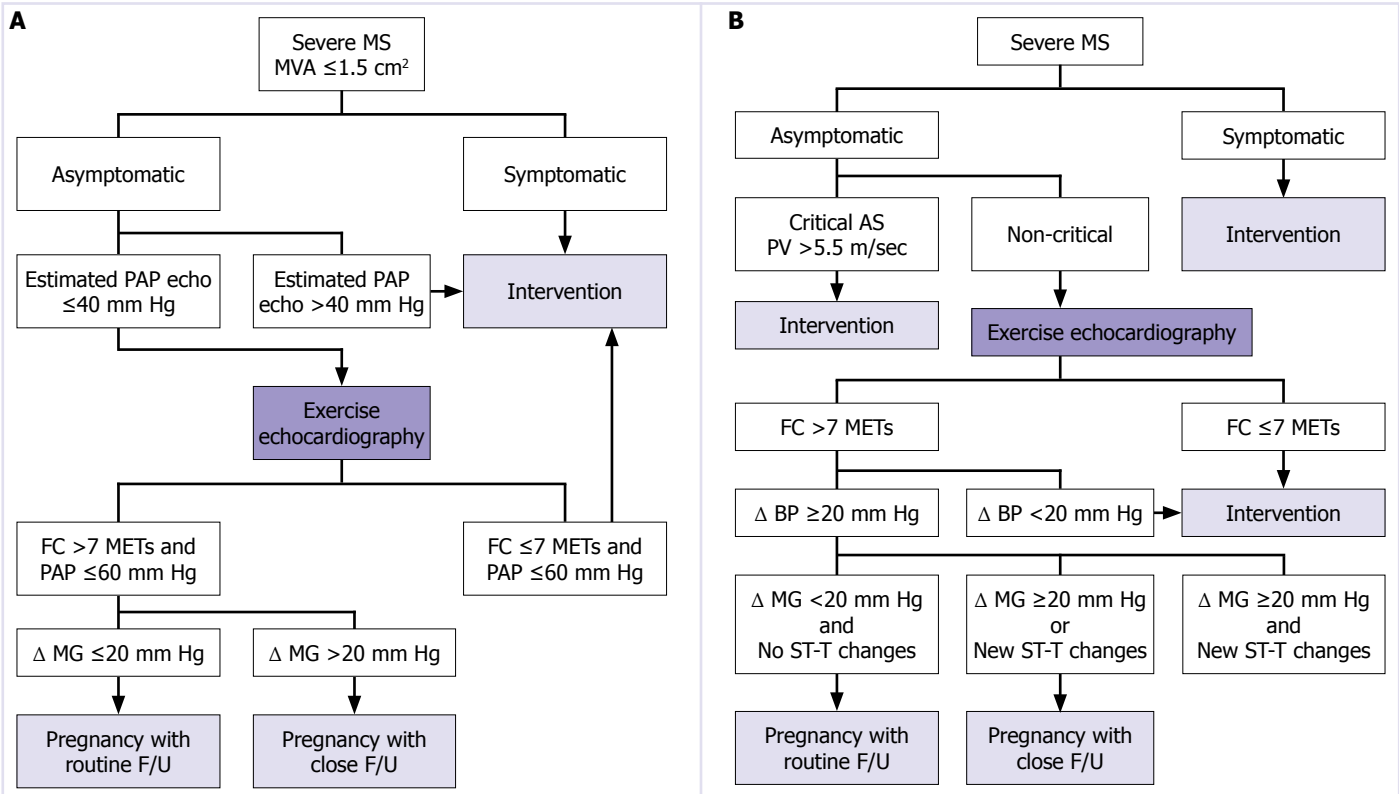

Figure 2. Protocols for preconception consultation using treadmill exercise echocardiographic testing among patients with **(A)** MS and **(B)** AS.

AS: Aortic valve stenosis; BP: Blood pressure; FC: Functional class; F/U: Follow-up; METs: Metabolic equivalents; MG: Mean gradient; MS: Mitral valve stenosis; PAP: Pulmonary arterial pressure; PV: Peak instantaneous velocity; TSE: Treadmill exercise stress echocardiography; VHD: Valvular heart disease.

The amount of METs in patients with MS and AS was 9.6±1.7 and 10.4±1.8, respectively. All patients undergoing TSE test had myocardial reserve at peak, and around 10% increase in LVEF was observed at peak exercise among patients with MS and AS. The results of TSE test for patients with MS or AS are shown in Table 3. Among patients with MS, patients without TSE test have more functional class deterioration (11.1% vs. 35%) and the FNE (22.2% vs. 55%) compared to those in patients with TSE test. The frequency of MPE was significantly higher in patients without TSE test compared to patients with TSE test (0 vs. 45%, p=0.015). In addition, patients without TSE had a higher frequency of PTMC during pregnancy compared to those with TSE test (35% vs. 0, p=0.042). Among patients with AS, all events were higher in patients without TSE compared to those with TSE; however, all were comparable between groups (Table 4). Among patients without TSE test, the mean of time interval between first visit and the MPE and/or PTMC was found to be 12 weeks and 10 weeks for patients with MS and AS, respectively.

DISCUSSION

In this preliminary study, we showed that pregnant women with the left-sided valvular stenosis can benefit from preconception counseling with the implementation of TSE test. Patients with MS undergoing pre-conception TSE test had lower rates of MPE and PTMC during pregnancy compared to those without preconception counseling. Moreover, no maternal events were detected among AS patients during 6 months postpartum. These findings might propose the potential role of preconception counseling in the reduction of maternal and neonatal events among such vulnerable population, and the paramount implication of stress test for the risk stratification of patients with MS or AS.

Patients with severe symptomatic MS or AS may require invasive therapeutic modalities before pregnancy and develop more complications [12–14]. However, VHD, even severe involvements, can be asymptomatic and patients are unable to have a true perception of their condition. The exercise stress test is a useful assessment

of functional capacity and the hemodynamic changes of cardiac pathologies. According to the guidelines [15, 16], the exercise test can be used as a prognostic tool among non-pregnant asymptomatic patients with VHD and congenital heart diseases. In addition, in the latest ESC guidelines for the management of pregnant patients with cardiovascular diseases [3], pre-pregnancy exercise test and exercise echocardiography have been recommended for the evaluation of patients with MS or AS to reduce pregnancy-related complications.

Ohuchi et al. [17] examined the exercise capacity of women with congenital heart disease and showed that cardiopulmonary exercise test can predict pregnancy outcomes. They also found that peak heart rate ≥150 beats/min and/or peak VO_2 ≥25 ml * kg (-1) * min (-1) were cutoff points to predict a safe pregnancy. In a multicenter study, Lui et al. [18] demonstrated that heart rate response during cardiopulmonary exercise test was associated with adverse events in pregnant patients with congenital heart disease. The exercise-induced increase in transvalvular gradient can be useful for risk stratification of patients with asymptomatic AS [19]. It has been suggested that symptomatic severe AS or asymptomatic AS with impaired left ventricular function or a pathological exercise test are required to undergo heart valve surgery before pregnancy [20, 21]. Therefore, the risk stratification of asymptomatic AS patients would help with the improvement of pregnancy outcome. In addition, among patients with primary MS, Gentry et al. [22] showed that an impaired exercise capacity and post-stress right ventricular systolic pressure were associated with worse outcomes. Moreover, the systolic pulmonary arterial pressure >60 mm Hg during exercise indicates a hemodynamically significant MS, at a higher risk of hemodynamic worsening, which may require PTMC [23]. Therefore, stress echocardiographic test can be of great value to provide prognostic guidance, particularly among women who desire pregnancy [24, 25]. In our study, we found that patients with MS or AS who underwent preconception TSE test had fewer maternal and fetoneonatal adverse events compared to those without preconception counseling. The practical guidelines have recommended using TSE test and TTE for pregnant women with heart diseases, but we think that the combined implementation of preconception TTE and TSE test can provide invaluable tool to identify individuals at a higher risk of complications. Moreover, even with the implementation of the mWHO risk tool, the underestimation or the overestimation of risks during pregnancy can be observed in our daily practices, which underscore the need for further tools to improve risk prediction. Proper risk estimation tools can help us to identify MS patients who can benefit from PTMC before pregnancy, or to replace aortic valve before conception in patients with asymptomatic severe AS. Therefore, the implementation of TSE test as preconception counseling in patients with the left-sided valvular stenosis can be a useful tool for improving outcomes of patients and prevent from valvular intervention or surgical modalities.

Study Limitations

The present study has some limitations need to be addressed in future studies. First, the sample size of patients undergoing the TSE test was relatively small, and we were unable to assess the diagnostic accuracy of exercise test components for identifying adverse events. Second, we have established a protocol to prevent pregnancy in patients with an impaired TSE test; therefore, the control group was recruited from patients without preconception visit who did not undergo exercise test. On the other hand, due to ethical issues, we could not let patients with an abnormal exercise test to become pregnant. Given our findings in this preliminary report, we think that future studies should evaluate exercise echocardiography in a large-scale population to determine the utility of stress testing in risk stratification of pregnancy in patients with the left-sided valvular stenosis.

Conclusions

Patients with the left-sided valvular stenosis undergoing preconception TSE test had fewer maternal and fetoneonatal adverse events compared to those without preconception evaluation. This study underscores the utility of stress echocardiography in the risk stratification of high-risk pregnancies to improve peripartum outcomes.

Ethics Committee Approval: The Shahid Rajaie Hospital Clinical Research Ethics Committee granted approval for this study (date: 01.03.2020, number: 98084).

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