Clinical Significance of Dynamic Left Ventricular Outflow Tract Obstruction During Dobutamine Stress Echocardiography in Women With Suspected Coronary Artery Disease

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Background: Although dobutamine stress echocardiography (DSE) is frequently associated with dynamic left ventricular outflow tract obstruction (DLVOTO), little is known about its clinical significance in women with suspected coronary artery disease (CAD).

Methods and Results: One hundred and two female patients (57±10 years) who underwent DSE as part of the Korean women’s chest pain registry study were included. Doppler echocardiography was performed during DSE to assess the presence of DLVOTO. Patients with DLVOTO (n=52) were older than those without DLVOTO (n=50; P=0.001). Hypertension was more prevalent in patients with DLVOTO (P=0.02). Patients with DLVOTO had smaller LV diameter, but higher LV mass index and relative wall thickness (P<0.05 for all). LV diastolic function (as reflected by late diastolic velocity, deceleration time of early diastolic velocity [E], and ratio of E velocity to early diastolic mitral annular velocity), was worse in patients with DLVOTO (P<0.05 for all). Patients with DLVOTO had shorter exercise time (P=0.02) and lower amount of work (P=0.04) than patients without DLVOTO. DSE-provoked DLVOTO was not related to the presence of CAD in these patients.

Conclusions: In Korean women with suspected CAD, DSE-provoked DLVOTO is correlated with LV concentric remodeling and LV diastolic dysfunction, and may be associated with limited exercise tolerance and symptoms of chest pain. (Circ J 2015; 79: 2255–2262)

Key Words: Diastolic function; Dobutamine stress; Exercise; Left ventricular outflow tract obstruction; Woman

Do utamine stress echocardiography (DSE) is widely used as an alternative stress imaging test for the evaluation of suspected or known coronary artery disease (CAD).1–3 The development of dynamic left ventricular outflow tract obstruction (DLVOTO) in states of hypercontractility is not infrequently observed during DSE. Although several studies investigating DLVOTO during DSE have been conducted, the clinical significance of DSE-provoked DLVOTO remains controversial. Pellikka et al suggested that the development of dynamic intraventricular obstruction leads to hypotension during DSE,4 but this was not found in another study.5 Furthermore, the development of DLVO gradient during DSE was not associated with dobutamine induced-chest pain or shortness of breath.6 In contrast, Barletta et al showed that intraventricular obstruction during DSE was clinically significant in patients without CAD who have unexplained reduced effort tolerance.7 The dynamic LV cavity obliteration or LVOTO seemed to be associated with smaller LV and a greater LV wall thickness in patients who underwent DSE for the evaluation of chest pain and preoperative evaluation for non-cardiac surgery.8 These studies, however, were performed in heterogeneous participants with different reasons for undergoing DSE, and the relationship between DLVOTO and symptoms has not been well investigated. Moreover, DLVOTO during DSE is more prevalent in female subjects,8 and a considerable number of women have effort-induced and unexplained chest symptoms such as angina and shortness of breath with no significant evidence of angiographic CAD.
The Korean Women’s Chest Pain Registry (KoROSE) study is a multicenter Women’s Heart Disease Research Working Group study that was designed to evaluate Korean women with suspected CAD on diagnostic testing, as well as investigate the characteristics of patients with and without CAD. As part of this study, DSE was performed in the participating women and the aim of this study was to assess the clinical significance of DSE-provoked DLVOTO and its relationship to cardiac function and exercise tolerance in women with suspected CAD.

**Methods**

**Subjects**

DSE was performed in 197 of the 880 patients in the KoROSE study between October 2011 and January 2014. Patients were excluded if they had regional wall motion abnormalities for CAD at baseline. Patients were also excluded if they had inducible myocardial ischemia on DSE. Women were eligible for the study if they: (1) had a history of typical/atypical chest pain or ischemic equivalents (e.g., dyspnea); (2) were aged ≥20 years; (3) were capable of undergoing stress tests (exercise treadmill test [ETT] and/or DSE); (4) had no significant structural or valvular heart disease; and (5) had coronary angiography (CAG). Any epicardial arteries with irregularities that reduced the lumen diameter ≥50% were considered to be indicative of CAD. Each center obtained institutional review board approval and participant consent prior to enrollment.

**Conventional Echocardiography**

Conventional 2-dimensional echocardiography was performed prior to DSE. The chamber diameter and wall thickness were measured directly from the 2-D echocardiographic images, and the LV mass was calculated using linear measurements, as recommended by the American Society of Echocardiography. The chamber diameters and LV mass were indexed to body surface area. LV relative wall thickness (RWT) was calculated as 2-fold the thickness of the posterior wall in diastole divided by LV end-diastolic diameter. LV ejection fraction (LVEF) was calculated using the modified Simpson’s method from apical 4- and 2-chamber views. The diameter of the LVOT was measured in the longitudinal plane during systole as the smallest distance between the anterior mitral valve and the interventricular septum, as described previously. Aortic annular cross-sectional area was calculated as follows: \( \pi \times \left( \frac{\text{LVOT diameter}}{2} \right) \). Doppler stroke volume was calculated as annular cross-sectional area multiplied by the time-velocity integral of flow through the LVOT. Cardiac output was calculated as stroke volume multiplied by heart rate (HR) and was indexed to body surface area as cardiac index.

The mitral inflow was obtained on pulsed-wave Doppler echocardiography with the sample volume between the mitral leaflet tips during diastole; early and late diastolic velocities (E velocity and A velocity, respectively) and deceleration time (DT) were also measured. The early diastolic septal mitral annular velocity (e’ velocity) was obtained from the pulse wave velocity of the spectral tissue, and the E/e’ ratio was calculated.

DSE was performed using a standard protocol. Beta-blocker and calcium-channel blocker were withheld on the morning of the stress tests. Patients fasted for >6 h prior to the tests. After the acquisition of baseline images, i.v. dobutamine infusion was started at 10 μg · kg⁻¹ · min⁻¹, and increased to 20, 30, and 40 μg · kg⁻¹ · min⁻¹ at 3-min intervals. Atropine was administered i.v. in 0.5-mg doses, with a maximum dose of 2.0 mg if HR response was inadequate. The infusion was discontinued when the patient reached the target HR of 85% of the age-predicted maximum HR (calculated by subtracting the patient’s age in years from 220).

Standard 2-D echocardiography views were obtained in the parasternal long and short axes, and apical 4- and 2-chamber views at baseline, low dose, peak dose, and recovery. Pulsed wave and continuous wave Doppler interrogations of the LVOT were obtained at baseline and at peak dose from the apical window. The LV was divided into 16 segments as previously described. Normal response was defined as progressive augmentation of wall motion and thickening when compared with the previous stage of dobutamine infusion. Ischemic response was defined as development of new or worsening wall motion abnormalities. Segmental hypokinesis or akinesis at rest and peak infusion were interpreted as signs of infarcted tissue.
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Table 1. Clinical Characteristics

|                      | No DLVOTO (n=50) | DLVOTO (n=52) | P-value |
|----------------------|------------------|---------------|---------|
| Age (years)          | 53.8±8.7         | 60.0±9.3      | 0.001   |
| BMI (kg/m²)          | 24.9±3.2         | 25.9±3.7      | 0.134   |
| SBP (mmHg)           | 120.7±18.0       | 126.4±18.2    | 0.116   |
| DBP (mmHg)           | 66.0±12.0        | 68.8±12.4     | 0.262   |
| HR (beats/min)       | 66.1±9.5         | 65.2±10.0     | 0.658   |
| Hypertension         | 15 (30.0)        | 28 (53.8)     | 0.017   |
| Diabetes mellitus    | 4 (8.0)          | 7 (13.5)      | 0.526   |
| Dyslipidemia         | 9 (18.0)         | 10 (19.2)     | 1.000   |
| Smoking              | 1 (2.0)          | 3 (5.8)       | 0.618   |
| Hemoglobin (g/dl)    | 13.1±0.9         | 13.9±1.1      | 0.986   |
| Serum creatinine (mg/dl) | 0.96±0.14   | 0.98±0.18     | 0.550   |
| Diuretics            | 3 (6.0)          | 1 (1.9)       | 0.358   |
| ACEi or ARB          | 7 (14.0)         | 11 (21.1)     | 0.439   |
| β-blocker            | 5 (10.0)         | 6 (11.5)      | 1.000   |
| CCB                  | 12 (24.0)        | 14 (26.9)     | 0.822   |

Data given as mean±SD or n (%). ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CCB, calcium channel blocker; DBP, diastolic blood pressure; DLVOTO, dynamic left ventricular outflow tract obstruction; HR, heart rate; SBP, systolic blood pressure.

DLVOTO was defined as the presence of systolic flow with a dagger-shaped late peak and a peak pressure gradient ≥50 mmHg in the LVOTr or the midventricular area, not present at baseline, and which disappeared after the recovery phase (Figure 1).

Hypotensive response was defined as a drop of at least 15% in systolic blood pressure (SBP) compared with the baseline SBP.

All interpretations were carried out using digitized images in the echocardiographic core laboratory, and videotaped images were reviewed only for clarification of questionable findings.

ETT

Routine ETT was performed using the standard Bruce protocol. Twelve-lead ECG was recorded prior to exercise, at the end of each exercise stage, at the exercise peak, and at 2-min intervals during recovery. The ETT was continued until the occurrence of marked ST-segment changes, limiting symptoms (angina, dyspnea, or fatigue), or abnormalities in heart rhythm or BP. Throughout testing, 3 standard ECG leads were continuously monitored, and HR and BP were recorded. The ECG criterion for a positive test was ≥1-mm exercise-induced ST-segment deviation at 0.06 after the J point, relative to the PR segment generally occurring in 2 leads. The ECG was interpreted by site investigators.

Duke Treadmill Score (DTS)

The DTS is the most widely used risk score in ETT, and has diagnostic and prognostic value in both women and men. The DTS allows exercise capacity to be estimated by incorporating exercise time and ST-segment changes. DTS was calculated as follows:

\[ \text{DTS} = \text{exercise time} - (5 \times \text{ST deviation}) - (4 \times \text{treadmill angina}) \]

Exercise time was measured in minutes. ST deviation was the largest net deviation, either depression or elevation, in any lead except the aVR lead. Treadmill angina was graded on the following scale: 0, no angina during exercise; 1, non-limiting angina during exercise; and 2, exercise-limiting angina. The distinction between exercise-induced angina and non-anginal chest pain was based on the supervising clinician’s judgment, although particular attention was paid to reproduction of the presenting symptoms and the classic features of typical angina.

Statistical Analysis

SPSS version 14.0 was used for statistical analysis. All results are expressed as mean±SD. Paired sample t-test was used to compare baseline and peak infusion variables. Group comparisons were made using either chi-squared test for dichotomous variables or t-test for continuous variables. Significance of the correlation between stress peak LVOT pressure gradient and clinical and echocardiographic parameters was determined on correlation analysis. Multivariate linear regression analysis was performed to evaluate independent determinants of the stress peak LVOT pressure gradient and presence of DLVOTO. P<0.05 was considered significant.

Results

Clinical Characteristics

A total of 95 patients were excluded from the study for the following reasons: 16 patients had LV regional wall motion abnormalities at baseline; 24 patients had inducible myocardial ischemia during DSE; 11 patients were unable to complete the study due to high BP, significant arrhythmia, or diaphoresis during DSE; 21 patients had no ETT; and 23 patients had no LVOT Doppler data. A total of 102 patients were included in the analysis.

Mean patient age was 57±10 years. DLVOTO was observed in 52 (51%) of the patients, while 50 (49%) of the 102 patients had no DLVOTO. The patients with DLVOTO were older than those with no DLVOTO (P=0.001). Hypertension was more prevalent in the patients with DLVOTO (P=0.017), but the prevalences of diabetes mellitus, dyslipidemia, and smoking were similar between the 2 groups (Table 1).

Baseline Echocardiographic Parameters

The patients with DLVOTO had a smaller LV diameter but had larger LV mass index and higher RWT (P<0.05 for all).
Peak LVOT velocity, peak LVOT pressure gradient and the cardiac index were significantly increased by dobutamine infusion in both groups. The patients with DLVOTO had a more significant increase in the peak LVOT parameters and cardiac index than those without DLVOTO, but there were no significant differences between the 2 groups in peak stress BP or HR (Table 3).

Hypotensive response at peak stress was observed in 9 patients (4 patients with no DLVOTO vs. 5 patients with DLVOTO, P=1.0), and there was no significant difference in stress peak LVOT pressure gradient between patients who did or did not have hypotensive response (51.3±40.9 mmHg vs. 64.9±54.8 mmHg, P=0.531).

Chest discomfort or pain during DSE was reported by 30
There were no differences, however, in the LVOT diameter index between the 2 groups (P=0.701). LV diastolic function (as reflected by A velocity, DT, and E/e’) was worse in patients with DLVOTO (P<0.05 for all; Table 2). There were no differences in baseline peak LVOT velocity, peak LVOT pressure gradient, or cardiac index between patients with and without DLVOTO (Table 2).

DSE
The LV end diastolic and systolic diameter indexes (LVEDD and LVESD indexes, respectively) were reduced, and LVEF was increased by dobutamine infusion in both groups. LVESD index, however, was more reduced and LVEF was more increased in patients with DLVOTO (Table 3).

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### Table 2. Baseline Echocardiographic Parameters

|                      | No DLVOTO (n=50) | DLVOTO (n=52) | P-value |
|----------------------|------------------|----------------|---------|
| LVEDD index (mm/m²)  | 29.6±3.0         | 28.3±2.9       | 0.041   |
| LVESD index (mm/m²)  | 18.0±3.0         | 17.1±2.9       | 0.150   |
| LVEF (%)             | 59.2±3.9         | 60.2±4.4       | 0.248   |
| LV septal wall thickness (mm) | 8.6±1.1         | 9.6±1.4       | <0.001  |
| LV posterior wall thickness (mm) | 8.5±1.1         | 9.3±1.2       | 0.001   |
| LV mass index (g/m²) | 88.8±18.0        | 98.7±21.4      | 0.022   |
| RWT                  | 0.36±0.07        | 0.41±0.06      | <0.001  |
| LAD index (mm/m²)    | 22.0±2.6         | 22.7±2.9       | 0.164   |
| E velocity (cm/s)    | 64.1±14.7        | 59.3±10.8      | 0.067   |
| A velocity (cm/s)    | 59.6±15.4        | 70.1±17.2      | 0.002   |
| E/A                  | 1.1±0.4          | 0.9±0.3        | 0.001   |
| DT (m/s)             | 185±34           | 222±49         | <0.001  |
| e’ velocity (cm/s)   | 7.4±2.0          | 6.0±1.5        | 0.001   |
| E/e’                 | 9.1±2.3          | 10.4±3.1       | 0.014   |
| PA systolic pressure (mmHg) | 29.4±5.2       | 30.0±5.1       | 0.610   |
| LVOT diameter index (mm/m²) | 0.98±0.07      | 0.98±0.07      | 0.910   |
| Peak LVOT velocity (m/s) | 1.27±0.28      | 1.36±0.31      | 0.136   |
| Peak LVOT pressure gradient (mmHg) | 6.9±3.4       | 7.7±3.9        | 0.247   |
| Stroke volume (ml)   | 68.9±17.2        | 71.2±16.3      | 0.516   |
| Cardiac output (L/min) | 4.42±1.15     | 4.44±1.01      | 0.912   |
| Cardiac index (L · min⁻¹ · m⁻²) | 2.77±0.68   | 2.81±0.67      | 0.817   |

Data given as mean±SD. A, late diastolic mitral inflow velocity; DT, deceleration time of E velocity; E, early diastolic mitral inflow velocity; e’, early diastolic mitral annular tissue velocity; LAD, left atrial diameter; LVEDD, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic diameter; PA, pulmonary artery; RWT, relative wall thickness. Other abbreviations as in Table 1.

### Table 3. Blood and Echocardiographic Parameters at Peak Stress

|                      | No DLVOTO (n=50) | DLVOTO (n=52) | P-value |
|----------------------|------------------|----------------|---------|
| SBP (mmHg)           | 134.8±25.7       | 130.3±25.7     | 0.375   |
| DBP (mmHg)           | 65.2±15.5        | 64.3±14.7      | 0.771   |
| HR (beats/min)       | 138.3±13.3       | 134.3±16.1     | 0.180   |
| LVEDD index (mm/m²)  | 25.5±3.3         | 24.7±3.0       | 0.211   |
| LVESD index (mm/m²)  | 13.8±2.9         | 12.3±2.7       | 0.010   |
| LVEF (%)             | 66.4±8.2         | 71.2±6.0       | 0.003   |
| Peak LVOT velocity (m/s) | 2.14±0.31     | 4.50±1.00      | <0.001  |
| Peak LVOT pressure gradient (mmHg) | 18.7±5.0    | 85.3±39.5      | <0.001  |
| Stroke volume (ml)   | 67.0±18.6        | 93.9±36.0      | <0.001  |
| Cardiac output (L/min) | 8.93±2.20       | 12.56±4.61     | <0.001  |
| Cardiac index (L · min⁻¹ · m⁻²) | 5.56±1.21   | 7.96±3.04      | <0.001  |

Data given as mean±SD. Abbreviations as in Tables 1,2.
patients, 24 of whom (80%) had DLVOTO and 6 of whom had no DLVOTO (P<0.001).

**DLVOTO, DTS, and CAD**

Of 102 patients, 19 patients had significant CAD. There were no differences in the baseline or stress peak LVOT pressure gradient (7.0±4.0 mmHg vs. 7.4±3.7 mmHg, P=0.50 and 42.8±38.5 mmHg vs. 54.9±44.8 mmHg, P=0.73, respectively), or the prevalence of DLVOTO (9 of 19 patients vs. 43 of 83 patients, P=0.80) between patients with and without CAD. There were also no significant differences in the DTS of patients with and without CAD (4.5±4.9 vs. 5.1±4.0, P=0.62).

Patients with DLVOTO, however, had lower DTS (P=0.02), shorter exercise time (P=0.02), and lower amount of work (P=0.04) than those without DLVOTO (Table 4). There were no significant differences between patients with and without DLVOTO in the hemodynamic parameters at baseline or at peak exercise. There were also no differences in the prevalence of ST-segment deviation or the number of leads with ST-segment deviation during ETT between patients with and without DLVOTO (Table 4). There was a mild correlation between stress peak LVOT pressure gradient and DTS (r=−0.230, P=0.031) and when adjusted by age (r=−0.211, P=0.049).

**DLVOTO and Echocardiographic Parameters**

Stress peak LVOT pressure gradient was related to LVEDD index, LV mass index, RWT, and LV diastolic parameters such as A velocity, E/A, DT, e’ velocity, and E/e’ (Table 5). RWT (r=0.428, P<0.001) and DT (r=0.328, P=0.001) were particularly significantly related to the stress peak LVOT pressure gradient (Figure 2). Even when adjusted by age, LVEDD index, LV mass index, RWT, A velocity, and DT all remained significantly associated with stress peak LVOT pressure gradient (Table 5).

Of the 102 patients enrolled, 83 had no CAD, and all of the aforementioned findings were consistent in this subset of patients (LVEDD index, r=−0.224, P=0.045; RWT, r=0.490, P<0.001; A velocity, r=0.383, P=0.001; E/A, r=−0.360, P=0.001; DT, r=0.325, P=0.003; e’ velocity, r=−0.375, P=0.001; E/e’, r=0.275, P=0.012).

Based on multivariate logistic regression analysis using the continuous variables age, hypertension, LVEDD index, LV mass index, RWT, E velocity, A velocity, E/A, DT, e’ velocity, and E/e’ as univariate factors, DT was the only independent predictor for DLVOTO during DSE (P=0.002, β=1.019, 95% CI: 1.007–1.031).

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**Table 4.** Exercise Treadmill Test Parameters vs. Presence of DLVOTO

|                      | No DLVOTO (n=50) | DLVOTO (n=52) | P-value |
|----------------------|------------------|---------------|---------|
| Pre-exercise SBP (mmHg) | 121±14          | 125±13        | 0.14    |
| Pre-exercise DBP (mmHg) | 78±10           | 81±7          | 0.16    |
| Pre-exercise HR (beats/min) | 78±16          | 78±12         | 0.96    |
| Peak exercise SBP (mmHg) | 163±25          | 172±18        | 0.06    |
| Peak exercise DBP (mmHg) | 80±15           | 82±11         | 0.38    |
| Peak exercise HR (beats/min) | 150±19         | 147±15        | 0.31    |
| Exercise time (min)    | 7.9±2.1         | 6.8±2.1       | 0.02    |
| Work (MET)             | 10.3±2.2        | 9.2±2.2       | 0.04    |
| Patients with ST-segment deviation (n) | 22            | 17            | 0.39    |
| No. leads with ST-segment deviation (n) | 2.7±1.0        | 2.9±0.7       | 0.49    |
| DTS                   | 6.1±4.1         | 3.9±4.1       | 0.02    |

Data given as n or mean±SD. DTS, Duke treadmill score; MET, metabolic equivalent of task. Other abbreviations as in Tables 1,2.

**Table 5.** Indicators of Stress Peak LVOT Pressure Gradient

| Indicator                        | Coefficient | P-value | Age-adjusted coefficient | P-value |
|----------------------------------|-------------|---------|--------------------------|---------|
| LVEDD index                      | −0.229      | 0.022   | −0.232                   | 0.022   |
| LVESD index                      | −0.131      | 0.197   | −0.070                   | 0.502   |
| LVEF                             | 0.181       | 0.071   | 0.169                    | 0.126   |
| LV mass index                    | 0.220       | 0.040   | 0.217                    | 0.045   |
| RWT                              | 0.428       | <0.001  | 0.353                    | 0.001   |
| LVOT diameter index              | −0.065      | 0.525   | −0.087                   | 0.406   |
| LAD index                        | 0.158       | 0.117   | 0.020                    | 0.850   |
| E velocity                       | −0.119      | 0.238   | −0.011                   | 0.915   |
| A velocity                       | 0.321       | 0.001   | 0.217                    | 0.045   |
| E/A                              | −0.288      | 0.004   | −0.148                   | 0.173   |
| DT                               | 0.328       | 0.001   | 0.259                    | 0.016   |
| e’ velocity                      | −0.301      | 0.002   | −0.157                   | 0.149   |
| E/e’                             | 0.219       | 0.029   | 0.095                    | 0.384   |

Abbreviations as in Table 2.
In the present study, patients with DLVOTO had a higher LV mass index and higher RWT than those without DLVOTO. The prevalence of hypertension was also higher in patients with DLVOTO. It is well known that LV hypertrophy leads to increased oxygen demand, and that hypertension and LV hypertrophy may reduce effort tolerance and induce chest discomfort. Another possible explanation for this ischemic-like response could be a high myocardial oxygen demand imposed by the mid-to-apical LV walls as a result of obstruction. During systole, the effective intraventricular pressure might be higher than the aortic pressure, which would eventually reduce subendocardial perfusion.

Interestingly, but not surprisingly, the present study indicated that patients with DLVOTO had worse LV diastolic function, even when adjusted for age. The presence of DLVOTO was significantly correlated with LV concentric remodeling and LV diastolic parameters. The present patients did not have severe LV hypertrophy or high LV mass index. With aging, the mitral annular e’ velocity and transmitral E velocity decrease and transmitral A velocity increases. As shown in Table 5, when adjusted for age, only A velocity and DT were associated with stress peak LVOT pressure gradient. On multivariate analysis including age, only DT remained as a significant parameter for DLVOTO. These patients had preserved LVEF and rarely had LV diastolic dysfunction >grade 2. Therefore, prolonged DT meant worse LV diastolic function in these patients.

In the elderly, limited exercise tolerance in the presence of normal LV systolic but disturbed diastolic function is common. Henein et al suggested that stress-induced DLVOTO during DSE could be a potential cause of dyspnea in the elderly, although they did not confirm this in the coronary arteries.15

Given that we excluded patients with regional wall motion abnormalities at baseline and inducible myocardial ischemia by dobutamine infusion, the present patients represent a rela-
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Recently low to moderate risk group according to DTS. Exercise time is the main determinant of DTS. Indeed, in the present study, there was no difference in the DTS according to presence of CAD. In other words, DLVOTO and exercise intolerance were correlated regardless of the presence of CAD. Therefore, patients with LV diastolic impairment and significant DLVOTO during DSE may be prone to the development of diastolic heart failure.

The prevalence of DLVOTO during DSE is reported in 13–23% of all study patients. In one study, DLVOTO during DSE developed in 20 of 52 patients (38%) with normal coronary arteries and unexplained chest pain. In the present study, 51% of the patients had DLVOTO, which is significantly higher than in other published studies. One possible explanation for this is that we studied women only. It has previously been shown that dynamic LV cavity obliteration is associated with female sex and smaller LV, and Korean women are known to generally have smaller LV than Western women. Sohn et al recently reported that 17 of 26 Korean women (63%) had dynamic intraventricular obstruction during DSE, although the number of patients in that study was very small. The prevalence of DLVOTO and the degree of LVOT pressure gradient needs to be investigated in various conditions.

Other structural parameters such as sigmoid ventricular septum (SVS) and systolic anterior movement of mitral leaflet (SAM) can be considered as possible mechanisms. Recently, Tano et al reported that 40 of 64 patients (73±8 years) with SVS had DLVOTO during DSE, and these 40 patients had SAM. SVS is considered part of the normal aging process and is common in elderly patients. A few of the present patients (n=4; mean age, 57±10 years) had SVS according to the criteria, but this was not sufficient to show a relationship between DLVOTO and SVS. SAM has been considered to play an ancillary role in blood acceleration in the genesis of intraventricular obstruction in patients with LV hypertrophy and hypertrophic cardiomyopathy. In the present study, SAM was observed in 8 (15.4%) of 52 patients with DLVOTO on DSE, but was not related to the degree of LVOT pressure gradient.

We observed hypotension during DSE in 9 patients, but there was no relationship between hypotension and DLVOTO or the degree of LVOT pressure gradient. The relationship between hypotension and DLVOTO during DSE is not clear. Pellikka et al suggested that the development of dynamic intraventricular obstruction leads to hypotension during DSE. Other studies, including the present one, have found no relationship between hypotension and DLVOTO. We therefore assume that the hypotension is not a result of intraventricular obstruction.

In patients with hypertrophic cardiomyopathy, β-blockers or calcium channel blockers might be effective to reduce LVOT pressure gradient. Data on medical intervention with these drugs in patients with DLVOTO, however, are scarce, therefore, further studies are required.

There are several limitations to the present study. First, this registry study was conducted in tertiary hospitals, and all of the patients who underwent ETT, DSE, and CAG were enrolled. This could have resulted in referral and selection biases. Second, we excluded 23 patients who had poor quality echo imaging and no LVOT Doppler parameters, particularly at peak stress. Although some patients had significant color turbulence in the LVOT area, it was not possible to obtain clear Doppler images.

There is one study in which DSE-provoked LVOTO was shown to be an independent positive predictor of future episodes of chest pain and syncope and/or near syncope, although the subjects included both men and women, and the presence of CAD was not investigated. In the present study, we were not able to demonstrate any long-term clinical significance.

Finally, the presence of microvascular angina could not be excluded in this study. At least some of the present patients fulfilled the diagnostic criteria for syndrome X, namely, effort chest discomfort, positive ETT, and normal coronaries. A number of studies, including the National Heart, Lung, and Blood Institute-sponsored Women’s Ischemia Syndrome Evaluation (WISE) study, have reported that up to half of all patients undergoing CAG are found to have normal or non-obstructive epicardial coronary arteries. Furthermore, in several studies, DSE was documented to induce an ischemic chest pain response or ST changes despite normal coronary arteries, and to induce hyperkinetic contractile response in syndrome X patients. Some of the present patients who had DSE-provoked DLVOTO-associated chest pain, therefore, may represent a subgroup of patients with syndrome X or microvascular angina.

Conclusions

In Korean women with suspected CAD, DSE-provoked DLVOTO is correlated with LV concentric remodeling and LV diastolic dysfunction, and may be associated with limited exercise tolerance and symptoms of chest pain. Follow-up in the KoROSE study is ongoing, and this may provide further insights into the clinical significance of DLVOTO during DSE in women.

Disclosures

None.

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