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Research Article

Transesophageal Versus Transthoracic Echocardiography for Assessment of Left Ventricular Diastolic Function

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ABSTRACT

Background: Transesophageal echocardiography (TEE) has not been compared to transthoracic echocardiography (TTE) for assessment of left ventricular diastolic function (LVDF). Left ventricular diastolic dysfunction is common in systemic lupus erythematosus (SLE), a disease model of premature myocardial disease.

Methods: 66 patients with SLE (mean age 36±12 years, 91% women) and 26 age-and-sex matched healthy volunteers (mean age 34±11 years, 85% women) underwent TEE immediately followed by TTE. From basal four-chamber views, mitral inflow E and A velocities, E/A ratio, E deceleration time, isovolumic relaxation time, septal and lateral mitral E' and A' velocities, septal E'/A' ratio, mitral E to septal and lateral E' ratios, and pulmonary veins systolic to diastolic peak velocities ratio were measured. Measurements were averaged over 3 cardiac cycles and performed by 2 independent observers.

Results: LVDF parameters were worse in patients than in controls by TEE and TTE (all $p \le 0.03$). Most LVDF parameters were similar within each group by TEE and TTE (all $p \ge 0.17$). By both techniques, mitral E and A, mitral and septal E/A ratios, septal and lateral E', septal and lateral E/E' ratios, and average E/E' ratio were highly correlated (r = 0.64 - 0.96, all $p \le 0.003$); E deceleration time, isovolumic relaxation time, and septal A' velocities were moderately correlated (r = 0.43 - 0.54, all $p \le 0.03$); and pulmonary veins systolic to diastolic ratio showed the lowest correlation (r = 0.27, p = 0.04).

Conclusion: By TEE and TTE, LVDF parameters were worse in SLE patients than in controls; and in both groups, LVDF parameters assessed by TEE and TTE were similar and significantly correlated.

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Introduction

Left ventricular diastolic dysfunction with preserved ejection fraction is increasing in prevalence and is associated with increased morbidity and mortality [1-6]. Left ventricular diastolic function (LVDF) is accurately assessed by transthoracic echocardiography (TTE), the current standard method for evaluation of LVDF [7]. The American Society of Echocardiography guidelines for performing a comprehensive transesophageal echocardiogram (TEE) recommend TEE for evaluation of LVDF in technically difficult situations or when TEE is being performed for other purposes [8]. However, to our knowledge, there is no comparative data of TEE versus TTE for assessment of LVDF. Evaluation of LVDF using intraoperative TEE in highly selected

populations has shown to be of diagnostic and prognostic value [9-15]. However, these TEE studies were not compared to pre-operative TTE, were performed in selected patients with severe heart disease, and interpretation of TEE findings was generally not blinded and consequently was prone to interpretation bias. Therefore, data on LVDF derived from intra-operative TEE studies may not be applicable to general populations undergoing TEE under conscious sedation.

Left ventricular diastolic dysfunction is more common in patients with systemic lupus erythematosus (SLE) than in age and sex matched controls without SLE [16-20]. Therefore, SLE is a disease model of premature myocardial disease. Therefore, this prospective and controlled study is aimed to compare TEE versus TTE in the assessment of LVDF in patients with SLE and age and sex matched controls without SLE.

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Methods

I Study Population

This study population was part of a prospective and controlled protocol funded by the National Institutes of Health and approved by the Institutional Review Board of the University of New Mexico for the study of the association of cardiovascular and cerebrovascular disease in patients with SLE [21].

The study was conducted according to the declaration of Helsinki and all participants provided signed informed consent. Sixty-six consecutive SLE patients [age 36 ± 12 years (range, 18-60 years), 91% women] participated in the study. Patients were recruited from 266 well-characterized patients actively followed at the Rheumatology Clinics of the University of New Mexico Health Sciences Center.

As approved and limited by the institutional review board, 26 age-and-sex matched volunteers [age 34 ± 11 years (range, 18-57), 85% women] with a negative medical history and normal physical examination were studied. The control group was mainly intended to validate blinded interpretation of studies and to provide reference values. Exclusion criteria: age <18 or >60 years, pregnancy, atrial fibrillation or flutter, cardiomyopathy with LV ejection fraction <50%, renal dysfunction with a creatinine level >1.2 mg/dL, or drug abuse. On the same day, each participant underwent clinical and laboratory evaluations and TEE immediately followed by TTE.

II Clinical and Laboratory Evaluations

Patients and controls underwent assessment of demographics, traditional atherogenic risk factors, and basic laboratory data. Patients were also characterized regarding SLE duration, activity, damage, standard serologies, autoantibodies, and therapy.

III Assessment of Left Ventricular Diastolic Function by TEE and TTE

All subjects underwent TEE immediately followed by TTE (within 5 minutes) using the I-E33 imaging systems (Philips; Andover, MA, USA). Multiplane TEE studies were performed using a 7-MHz transducer and were immediately followed by complete TTE studies using a 5 MHz transducer. Intravenous Fentanyl and Midazolam with half-life elimination of 2-4 hours and 1.8 to 6.8 hours, respectively, were used for conscious sedation during the TEE studies. During TEE and TTE assessment of LVDF, 3 to 6 heart rates and 3 to 6 automatic brachial blood pressures were obtained and matched in time with measurement of LVDF parameters.

The basal 4-chamber TEE and apical 4-chamber TTE views were used for assessment of LVDF. Using pulsed-wave Doppler with a sample volume of 1-3 mm and tissue Doppler imaging with a sample volume of 5-10 mm, standard parameters of LVDF were assessed according to the 2016 American Society of Echocardiography guidelines and included: (1) mitral inflow early filling (E wave) and late atrial contraction (A wave) peak velocities (cm/sec) obtained at the leaflets' tips; (2) mitral E/A ratio; (3) E-wave deceleration time (msec); (4) isovolumic relaxation time (IVRT) in msec using the lateral mitral annulus tissue Doppler recordings, (5) early (E') and late (A') peak tissue Doppler

velocities (cm/sec) obtained at the septal and lateral mitral annulus; (6) mitral E/septal E' ratio, (7) mitral E/lateral E' ratio, and (8) average mitral E/E' ratio; and (9) left upper (by TEE) and right upper (by TTE) pulmonary veins inflow peak systolic to diastolic velocities ratio [7]. TEE and TTE measurements of LVDF were performed off-line using electronic calipers and averaged over 3 cardiac cycles.

To avoid bias and assure blinded interpretation of echocardiograms, all TEE and TTE studies were de-identified and codified. Also, studies of patients and controls were randomly intermixed and TEE and TTE studies were interpreted by 2 independent and experienced observers unaware of each other results.

IV Statistical Analysis

Student t tests and Fisher's exact tests were used for comparison of continuous and binary variables among groups, respectively. Paired t-tests were used for the comparison of parameters of LVDF between TEE and TTE. Pearson's correlation coefficients were calculated to assess the correlation between TEE and TTE for each parameter of LVDF. A 2-tailed p value <0.05 was considered significant.

Table 1: Clinical and Laboratory Data in SLE Patients and Controls.

| Parameter | Patients | Controls | P value | |
|-----------------------|---------------------|-------------------|---------|--|
| | $(\mathbf{N} = 66)$ | (N= 26) | | |
| Age (years) | 36.0 ± 11.9 | 34.1 ± 11.2 | 0.51 | |
| Female gender | 91% | 85% | 0.46 | |
| Ethnicity | 63%/23% | 50%/31% | 0.52 | |
| (Hispanic/non- | | | | |
| Hispanic white) | | | | |
| Body mass index | 27.3 ± 5.7 | 26.5 ± 5.2 | 0.54 | |
| Hypertension | 9% | 0 | 0.18 | |
| (>140/90 mmHg) | | | | |
| Dyslipidemia | 45% | 36% | 0.48 | |
| Cholesterol (mg/dl) | 179.0 ± 43.7 | 192.0 ± 45.2 | 0.24 | |
| LDL cholesterol | 110.0 ± 40.2 | 111.3 ± 31.6 | 0.85 | |
| (mg/dl) | | | | |
| HDL cholesterol | 50.1 ± 16.4 | 50.4 ± 18.1 | 0.95 | |
| (mg/dl) | | | | |
| Triglycerides (mg/dl) | 148.4 ± 68.7 | 159.3 ± 102.1 | 0.65 | |
| Diabetes mellitus | 4.8% | 0 | 0.55 | |
| Glucose (mg/dl) | 89.7 ± 26.7 | 83.5 ± 8.6 | 0.10 | |
| Smoking currently | 31% | 23% | 0.61 | |
| Postmenopausal | 6.2% | 0 | 0.58 | |
| Hemoglobin (g/dl) | 13.1 ± 1.5 | 14.1 ± 1.5 | 0.008 | |
| White blood cell | 6.2 ± 2.7 | 6.4 ± 1.4 | 0.66 | |
| count (x10^3/mm3) | | | | |
| Platelets | 245.1 ± 76.3 | 272.0 ± 41.6 | 0.04 | |
| (x10^3/mm3) | | | | |
| Creatinine (mg/dl) | 1.03 ± 1.14 | 0.74 ± 0.12 | 0.07 | |
| Albumin (g/dL) | 3.8 ± 0.6 | 4.2 ± 0.4 | 0.002 | |
| Quantitative D-dimer | 1.0 ± 2.7 | 0.34 ± 0.38 | 0.07 | |
| (mg/dL) | | | | |

Cell formats are mean \pm SD (n) or frequency (%).

SLE: systemic lupus erythematosus; LDL: low density lipoprotein; HDL: high density lipoprotein.

Results

I Clinical and Laboratory Data in Patients and Controls

As shown in (Table 1), patients as compared to controls had similar age, sex, ethnicity, body mass index, and prevalence of traditional atherogenic risk factors (all $p \ge 0.18$). Expectedly, patients had lower

haemoglobin, platelets, and albumin (all p≤0.04). As shown in (Supplemental Table 1), patients had SLE duration of 8 years, a mean age of 29 years at diagnosis of SLE, and 60% had antiphospholipid antibodies. Regarding therapy, 41% were on corticosteroids, 50% on antimetabolite immunosuppressive, 68% on antimalarial, and 43% were on antithrombotic therapy.

Table 2: Parameters of Left Ventricular Diastolic Function in Patients and Controls by TEE and TTE.

| Parameter | TEE | | | TTE | | |
|----------------------|------------------|-----------------|---------|------------------|-----------------|---------|
| | Patients | Controls | P value | Patients | Controls | P value |
| | N = 66 | N = 26 | | N = 66 | N = 26 | |
| E velocity (cms/sec) | 80.1 ± 22.0 | 77.7 ± 15.7 | 0.69 | 87.8 ± 23.9 | 83.0 ± 21.9 | 0.31 |
| A velocity (cms/sec) | 63.0 ± 25.0 | 44.5 ± 9.4 | < 0.001 | 68.6 ± 28.4 | 47.2 ± 10.4 | < 0.001 |
| E/A ratio | 1.4 ± 0.6 | 1.8 ± 0.4 | 0.009 | 1.4 ± 0.5 | 1.8 ± 0.4 | 0.002 |
| EDT (msec) | 184.5 ± 57.2 | 157.7 ± 32 | 0.04 | 174.7 ± 54.6 | 173.6 ± 26 | 0.99 |
| IVRT (msec) | 75.7 ± 18.6 | 70.0 ± 18.7 | 0.04 | 73.5 ± 14.8 | 69.2 ± 12.9 | 0.18 |
| Septal E' (cm/sec) | 9.1 ± 3.0 | 11.8 ± 2.7 | 0.001 | 9.6 ± 2.7 | 11.5 ± 2.1 | 0.002 |
| Septal A' (cm/sec) | 8.2 ± 1.7 | 8.3 ± 1.8 | 0.77 | 8.5 ± 2.0 | 8.1 ± 1.8 | 0.36 |
| Septal E'/A' ratio | 1.1 ± 0.4 | 1.49 ± 0.45 | 0.003 | 1.2 ± 0.5 | 1.5 ± 0.48 | 0.009 |
| Lateral E' (cm/sec) | 12.0 ± 3.4 | 14.9 ± 2.4 | 0.002 | 13.1 ± 4.4 | 15.6 ± 3.2 | 0.02 |
| Septal E/E' ratio | 10.0 ± 4.6 | 6.9 ± 1.8 | 0.005 | 10.0 ± 5.2 | 7.3 ± 2.1 | 0.02 |
| Lateral E/E' ratio | 7.6 ± 4.9 | 5.4 ± 1.2 | 0.05 | 7.8 ± 5.3 | 5.6 ± 1.7 | 0.06 |
| Average E/E' ratio | 8.5 ± 4.4 | 6.0 ± 1.3 | 0.02 | 8.6 ± 5.0 | 6.2 ± 1.8 | 0.03 |
| PV S/D ratio | 1.8 ± 0.6 | 1.6 ± 0.4 | 0.06 | 1.4 ± 0.6 | 1.2 ± 0.4 | 0.05 |

Abbreviations: TEE: transesophageal echocardiogram; TTE: transthoracic echocardiogram; E/A ratio: mitral inflow E and A peak velocities ratio; EDT: mitral E-wave deceleration time; IVRT: isovolumic relaxation time; septal E' and A': early (E') and late (A') peak tissue Doppler velocities of the septal mitral annulus; PV S/D: pulmonary veins systolic and diastolic peak velocities ratio.

Table 3: Correlation of parameters of Left Ventricular Diastolic Function by TEE and TTE in Patients.

| Parameter | TEE | TTE | P value | Pearson Correlation | P value |
|----------------------|------------------|------------------|---------|---------------------|---------|
| | N = 66 | N = 66 | | | |
| Heart rate (bpm) | 76.1 ±13.4 | 73.3 ± 12.1 | 0.08 | 0.80 | < 0.001 |
| Systolic BP (mmHg) | 120.3 ± 17.0 | 118.4 ± 13.3 | 0.28 | 0.62 | < 0.001 |
| Diastolic BP (mmHg) | 68.5 ± 15.6 | 67.2 ± 13.1 | 0.90 | 0.67 | < 0.001 |
| Mean BP (mmHg) | 85.8 ± 15.04 | 84.2 ± 12.6 | 0.63 | 0.67 | < 0.001 |
| E velocity (cms/sec) | 80.1 ± 22.0 | 87.8 ± 23.9 | 0.002 | 0.69 | < 0.001 |
| A velocity (cms/sec) | 62.9 ± 24.9 | 68.6 ± 28.4 | 0.02 | 0.85 | < 0.001 |
| E/A ratio | 1.4 ± 0.6 | 1.4 ± 0.5 | 0.56 | 0.76 | < 0.001 |
| EDT (msec) | 184.5 ± 57.2 | 174.7 ± 54.6 | 0.50 | 0.45 | < 0.001 |
| IVRT (msec) | 75.7 ± 18.6 | 73.5 ± 14.8 | 0.42 | 0.54 | < 0.001 |
| Septal E' (cm/sec) | 9.1 ± 3.0 | 9.6 ± 2.7 | 0.28 | 0.64 | < 0.001 |
| Septal A' (cm/sec) | 8.2 ± 1.7 | 8.5 ± 2.0 | 0.17 | 0.43 | 0.008 |
| Septal E'/A' ratio | 1.1 ± 0.40 | 1.2 ± 0.5 | 0.64 | 0.71 | < 0.001 |
| Lateral E' (cm/sec) | 12.1 ± 3.4 | 13.1 ± 4.4 | 0.62 | 0.79 | < 0.001 |
| Septal E/E' ratio | 10.0 ± 4.6 | 10.0 ± 5.2 | 0.83 | 0.77 | < 0.001 |
| Lateral E/E' ratio | 7.6 ± 4.9 | 7.8 ± 5.3 | 0.05 | 0.96 | < 0.001 |
| Average E/E' ratio | 8.5 ± 4.4 | 8.6 ± 5.0 | 0.36 | 0.91 | < 0.001 |
| PV S/D ratio | 1.8 ± 0.6 | 1.4 ± 0.6 | < 0.001 | 0.27 | 0.04 |

Bpm: beats per minute; BP: blood pressure. Other abbreviations as in (Table 2).

II Parameters of LVDF in Patients versus Controls by TEE and $\ensuremath{\mathsf{TTE}}$

As shown in (Table 2), most parameters of LVDF were worse in patients than in controls by both TEE and TTE (all $p \le 0.05$).

III Comparison and Correlation of Parameters of LVDF within Patients and within Controls by TEE and TTE

As shown in (Tables 3 & 4), heart rate and blood pressures were similar during TEE and TTE in patients and controls (all $p \ge 0.08$) suggestive of a persistent effect of conscious sedation during the performance of TTE studies. Of most importance, most values of LVDF by TEE as compared

to TTE were similar within patients and within controls (all p \geq 0.17). In patients, the mitral inflow E and A velocities were lower by TEE as compared to TTE (both p \leq 0.02) (Table 3). This is probably explained by a stronger effect in patients on heart rate and reduction of preload of conscious sedation during TEE. However, these statistical but not clinically relevant differences did not affect the similarity of the E/A ratio (p=0.56) between the 2 techniques. In controls, the E deceleration

time was lower by TEE than by TTE (p = 0.04) (Table 4). However, the value of E deceleration time is within normal ranges by both techniques. In both patients and controls, the pulmonary vein systolic to diastolic peak velocities ratio was higher by TEE than by TTE, which may be explained by a better alignment of the sampling Doppler with the upper pulmonary vein and better defined spectral waveforms by TEE than by TTE. However, in both groups, these ratios were within normal limits.

Table 4: Correlation of parameters of Left Ventricular Diastolic Function by TEE and TTE in Controls.

| Parameters | TEE | TTE | P value | Pearson | P value |
|---------------------|-----------------|-----------------|---------|-------------|---------|
| | N = 26 | N = 26 | | Correlation | |
| Heart rate (bpm) | 66.6 ± 11.8 | 65.3 ± 10.3 | 0.52 | 0.55 | 0.003 |
| Systolic BP (mmHg) | 110.9 ± 0.0 | 108.9 ± 0.6 | 0.28 | 0.74 | < 0.001 |
| Diastolic BP (mmHg) | 62.3 ± 11.4 | 61.2 ± 11.6 | 0.83 | 0.73 | < 0.001 |
| Mean BP (mmHg) | 78.5 ± 10.1 | 77.1 ± 10.7 | 0.60 | 0.74 | < 0.001 |
| E velocity (cm/sec) | 77.7 ± 15.7 | 83.0 ± 21.9 | 0.24 | 0.72 | < 0.001 |
| A velocity (cm/sec) | 44.5 ± 9.4 | 47.2 ± 10.4 | 0.18 | 0.68 | < 0.001 |
| E/A ratio | 1.8 ± 0.4 | 1.79 ± 0.42 | 0.70 | 0.68 | < 0.001 |
| EDT (msec) | 157.7 ± 32 | 173.6 ± 26 | 0.04 | 0.47 | 0.03 |
| IVRT (msec) | 70.0 ± 18.7 | 69.2 ± 12.9 | 0.62 | 0.52 | 0.01 |
| Septal E' (cm/sec) | 11.8 ± 2.7 | 11.5 ± 2.1 | 0.85 | 0.74 | < 0.001 |
| Septal A' (cm/sec) | 8.3 ± 1.8 | 8.1 ± 1.7 | 0.36 | 0.52 | 0.01 |
| Septal E'/A' ratio | 1.49 ± 0.45 | 1.5 ± 0.48 | 0.38 | 0.69 | < 0.001 |
| Lateral E' (cm/sec) | 14.9 ± 2.4 | 15.6 ± 3.2 | 0.07 | 0.70 | < 0.001 |
| Septal E/E' ratio | 6.9 ± 1.8 | 7.3 ± 2.1 | 0.90 | 0.69 | < 0.001 |
| Lateral E/E' ratio | 5.4 ± 1.2 | 5.6 ± 1.6 | 0.61 | 0.64 | 0.003 |
| Average E/E' ratio | 6.0 ± 1.3 | 6.2 ± 1.8 | 0.85 | 0.69 | < 0.001 |
| PV S/D ratio | 1.6 ± 0.4 | 1.2 ± 0.4 | 0.002 | 0.47 | 0.02 |

^{*}Abbreviations as in previous Tables.

Of most importance, in patients and controls, all parameters of LVDF by TEE and TTE were significantly correlated (all p \leq 0.04) (Tables 3 & 4). In each group, mitral E and A velocities, mitral E/A ratio, septal E' and lateral E' velocities, septal E'/A' ratio, septal E/E' ratio, lateral E/E' ratio, and average E/E' ratio were all highly correlated (r=0.64 to 0.96, all p \leq 0.008). In patients, the lateral and average E/E' ratios showed the strongest correlation (both r \geq 0.95 and p<0.001). In both groups, the E deceleration time, isovolumic relaxation time, and septal A' velocities demonstrated moderate correlations (r=0.43 to 0.54, all p \leq 0.03). In patients, the pulmonary veins systolic to diastolic peak velocities ratio showed the lowest correlation (r=0.27, p=0.04).

Discussion

I Major Findings

To our knowledge, this is the first controlled study to demonstrate that standard parameters of LVDF obtained by TEE during conscious sedation are overall similar and moderately to highly correlate with those obtained by TTE during a semi-awake or awake state. Therefore, assessment of LVDF by TEE in appropriate clinical settings may be of similar diagnostic and prognostic value as those of TTE.

Lateral E/E' and average E/E' ratios obtained by both modalities showed the strongest correlation. According to the current American Society of Echocardiography guidelines for the evaluation of LVDF by TTE and the largest intraoperative TEE study including 905 patients, lateral and average E/E' ratios are two of five most important parameters for

assessment of LVDF, are probably the best two discriminators of the presence of LV diastolic dysfunction and are also the best predictors of major cardiovascular events [7, 10, 18]. In addition, previous TTE studies have shown that in patients with normal ejection fraction, lateral E' velocity, lateral E'/A' ratio, and mitral E/lateral E' ratio have the strongest correlation with invasive measurement of pulmonary capillary wedge pressure and indices of LV filling pressures and LV stiffness [21-24]. Furthermore, in this study, values of lateral and septal E' velocities and mitral E/lateral, septal, and average E' ratios by both techniques are similar to values reported in previous TTE studies [16-20, 25, 26]. Finally, parameters of LVDF by both TEE and TTE in this study's control group of young females (predominantly 20 to 40 years old) are similar to currently reported normal values [27].

This study also confirms previous reports that parameters of LV diastolic dysfunction are worse in young SLE patients than in age-and-sex matched controls without SLE [16-20, 28]. Controlled Doppler echocardiography series in asymptomatic SLE patients without arterial hypertension and normal LV systolic function have demonstrated prevalence rates of LV diastolic dysfunction ranging from 8% to 35% [16-20, 28]. In these series, longitudinal, circumferential, and radial myocardial strain and strain rate are reported to be the most sensitive parameters for detecting LV diastolic dysfunction followed by tissue-Doppler and then by mitral inflow Doppler parameters [28].

However, LV diastolic dysfunction in most series including young women, as in this study, has been defined with different criteria to those proposed by the American Society of Echocardiography. Subclinical LV diastolic dysfunction occurs more frequently in patients with longer

disease duration and higher disease activity and severity [26]. LV diastolic dysfunction in SLE patients is believed to be predominantly due to endothelial dysfunction–mediated microvascular coronary artery disease, as supported by a decrease in coronary flow reserve in young patients with active SLE and normal coronary arteries [29-33]. The second most common cause of LV diastolic dysfunction in SLE patients is probably arterial hypertension, which is a highly prevalent condition (25% to 35%) in these patients [34, 35]. Premature peripheral arterial stiffness independent of arterial hypertension causing increased LV afterload and LV mass may be another pathogenetic factor [36]. Finally, primary myocarditis is a rare cause of LV diastolic dysfunction in these patients.

II Comparison with Previous TEE Studies

To our knowledge, there is no previous similar study comparing TEE versus TTE for assessment of LVDF. However, 7 clinically relevant studies have been reported using intra-operative TEE for assessment of LVDF in highly selected patients undergoing cardiac, thoracic, vascular, orthopedic, and general surgery [9-15]. These TEE studies determined prevalence rates, type distribution, time of occurrence and resolution, and prognostic value of intraoperative LV diastolic dysfunction. These studies included highly variable populations ranging from 8 to 905 subjects, predominantly men (67% to 100%) with a mean age ≥61 years, used variable parameters of LVDF (E/A ratio, E deceleration time, septal and lateral E' velocities, mitral E/lateral E' ratio, and pulmonary veins inflow systolic to diastolic peak velocities ratio) and variable definitions of LV diastolic dysfunction. Five of these 7 TEE studies were conducted in patients undergoing coronary artery bypass surgery, combined coronary artery bypass surgery and valve repair or replacement, valve repair or replacement alone, re-do coronary artery bypass surgery or valve surgery, congenital heart disease surgery, or heart transplant [9-13]. The 2 other studies included patients undergoing lung, vascular, orthopedic, or general surgery [14, 15]. An expectedly high prevalence of significant LV diastolic dysfunction was found (30% - 100%), worsening in LV diastolic dysfunction occurred immediately after and into 4 hours after cardiopulmonary bypass with return to baseline 20 hours after. Of most importance, LV diastolic dysfunction was associated with more prolonged cardiopulmonary bypass time, more frequent and higher requirement of positive inotropic or vasopressor support, and with a longer intensive care unit stay.

In the largest of these intraoperative TEE series including 905 subjects, a simplified two-variables algorithm of lateral E' velocities <10 cm/sec and mitral E/lateral E' ratio <8 or >8 as compared to a four-variables algorithm was able to grade better the presence of LV diastolic dysfunction (99% versus 62%, respectively) and was a better predictor of major cardiovascular events during follow-up [10]. These studies were performed in patients with predominantly severe heart disease, interpretation of TEE findings was generally not blinded and therefore prone to interpretation bias, and standard parameters of LVDF were not always included. However, their findings are clinically relevant and support the important diagnostic and prognostic value of intra-operative TEE assessment of LVDF.

Understandably, TTE should continue to be the preferred method for assessment of LVDF due to its accuracy, easily availability and portability, safety, and cost as compared to TEE. However, in patients undergoing TEE for appropriate clinical indications including intra-

operative TEE, assessment of LVDF by TEE is feasible and of diagnostic and prognostic value.

III Study Limitations

The study population included predominantly young women. Therefore, the current American Society of Echocardiography guidelines for the definition of LV diastolic dysfunction are not applicable to this type of population. Thus, a future study comparing TEE versus TTE for assessment of LVDF including a larger control group, wider age ranges, equal gender distribution, and LV diastolic dysfunction in different populations including those with hypertensive heart disease is necessary. In addition, left atrial volume index and pulmonary artery systolic pressure, 2 of 5 proposed criteria for LV diastolic dysfunction by TTE cannot be applied to TEE due to limited visualization of the entire left atria and limited assessment of peak tricuspid regurgitation velocity by this technique.

These limitations 1) precluded an accurate assessment of the prevalence of LV diastolic dysfunction by either technique according to recommended criteria, and 2) precluded assessment of the sensitivity, specificity, and predictive values of TEE as compared to TTE for detecting LV diastolic dysfunction. However, the primary purpose of the study was to assess the equivalence of values for most parameters of LVDF obtained by both TEE and TTE independently of the population' age, sex, and underlying disease. This study did not include assessment of LV strain. However, at this point, strain parameters are not yet well standardized, are not part of routine clinical practice, and are not currently recommended parameters for routine assessment of LVDF by the American Society of Echocardiography [7].

Conclusion

Parameters of LVDF assessed by TEE appear to be similar and significantly correlated with those obtained by TTE. These study findings support the 2013 American Society of Echocardiography guidelines for performing a TEE to evaluate LVDF in technically difficult situations or when TEE is being performed for appropriate clinical indications as a primary diagnostic test or as a complementary test to TTE.

Author Contributions

Theingi Tiffany Win, M.D. Participated in the conduction of the study, completed TTE and TEE measurements of left ventricular diastolic function, participated in the analysis and interpretation of the data, and wrote the manuscript. Ihab B. Alomari, M.D. Participated in the conduction of the study, performed TTE measurements of left ventricular diastolic function, participated in the analysis and interpretation of the data, and reviewed and edited the manuscript. Khaled Awad, M.D. Participated in the conduction of the study, performed TEE measurements of left ventricular diastolic function, participated in the analysis and interpretation of the data, and reviewed and edited the manuscript. Michelle D. Ratliff, M.D. Critically reviewed and edited the manuscript. Clifford R. Qualls, Ph.D. performed all statistical analyses and reviewed and edited the manuscript. Carlos A. Roldan, M.D. Designed and conducted the study, performed all transesophageal echocardiograms, analyzed and interpreted the data, and critically reviewed and edited the manuscript.

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Conflicts of Interest

None.

Human Rights Statements and Informed Consent

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions. Informed consent was obtained from all patients for being included in the study.

Supplemental Table 1: Clinical, Laboratory, and Therapy Data in Patients with SLE

| Characteristic | Patients $(N = 66)$ |
|---|---------------------|
| Duration of SLE (years) | 7.5 ± 6.2 |
| Age at diagnosis of SLE (years) | 28.6 ± 12.2 |
| Total SLE disease activity (units) | 11.9 ± 9.9 |
| Total SLE damage (units) | 3.1 ± 2.3 |
| dsDNA titer | 129.8 ± 352.7 |
| ANA titer | 646.9 ± 704.1 |
| C3 (mg/dl) | 95.8 ± 33.1 |
| C4 (mg/dl) | 19.2 ± 22.3 |
| CH50 (mg/dl) | 78.43 ± 40.30 |
| Fibrinogen (mg/dl) | 350.0 ± 96.0 |
| C-reactive protein (mg/dl) | 1.1 ± 1.4 |
| Erythrosedimentation rate (mm/hr) | 29.9 ± 24.1 |
| Ribonucleoprotein titer (dilutions) | 0.4 ± 0.5 |
| SSA antibody positive | 40% |
| SSB antibody positive | 22% |
| Any antiphospholipid antibody positive | 60% |
| Beta-2 glycoprotein I antibody positive | 26% |
| Lupus-like inhibitor positive | 34% |
| IgG, IgM, or IgA anticardiolipin positive | 45% |
| IgM anticardiolipin antibody (units) | 17.5 ± 32.4 |
| IgG anticardiolipin antibody (units) | 17.0 ± 24.3 |
| IgA anticardiolipin antibody (units) | 8.5 ± 14.6 |
| Prednisone therapy | 41% |
| Prednisone current dose (mg/d) | 8.8 ± 15.8 |
| Prednisone (years) | 6.0 ± 5.4 |
| Cyclophosphamide therapy | 32% |
| Cyclophosphamide therapy (years) | 0.5 ± 0.8 |
| Any immunosuppressive therapy (beyond prednisone) | 50% |
| Hydroxycloroquine or cloroquine therapy | 68% |
| Aspirin, warfarin, or either | 29%, 14%, 43% |

Cell formats are mean \pm SD (n) or frequency/n (%).

DNA: double stranded nuclear antibody; ANA: antinuclear antibody; SSA: Ro antibody; SSB: La antibody.

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