Assessment of agreement between transthoracic and transesophageal echocardiography techniques for left ventricular longitudinal deformation imaging and conventional Doppler parameters estimation: a cross-sectional study

Sol ventrikül fonksiyonlarının değerlendirilmesinde kullanılan longitüdinal deformasyon görüntüleme ve geleneksel Doppler belirteçleri için transtorasik ve transözafajiyal ekokardiyografi teknikleri arasındaki uyumun değerlendirilmesi: Kesitsel bir çalışma

Enbiya Aksakal, Ahmet Kaya[1], Eftal Murat Bakırcı, Mustafa Kurt[1], İbrahim Halil Tanboğa, Serdar Sevimli, Mahmut Açıkel

Department of Cardiology, Faculty of Medicine, Atatürk University, Erzurum-*Turkey*
[1]Clinic of Cardiology, Erzurum Region Education and Research Hospital, Erzurum-*Turkey*

ABSTRACT

Objective: Studies investigating the comparison and interchangeability of transthoracic (TTE) and transesophageal echocardiography (TEE) regarding left ventricular (LV) systolic and diastolic function are limited. Therefore, in this study, we aimed to investigate agreement between TTE and TEE in the assessment of LV systolic functions by longitudinal myocardial deformation imaging (strain-S and strain rate-Sr) and LV diastolic functions by conventional Doppler parameters.

Methods: Thirty-five patients underwent a clinically indicated cross-sectional study on agreement between two methods. All the patients underwent TEE right after TTE. From both TTE and TEE Doppler parameters such as early and late diastolic velocities (E, A, E′ and A`) deceleration time (DT), averaged mitral annular systolic velocity (Sm), isovolumic relaxation time (IVRT), isovolumic contraction time (IVCT), ejection time (ET), myocardial performance index (MPI) and longitudinal deformation imaging parameters (S, Sr) and systolic velocities were recorded. Agreement between TTE and TEE were evaluated by Bland-Altman analysis.

Results: Bland-Altman analysis showed good agreement between TEE and TTE in terms of E, A, DT, E′, A′, IVRT, IVCT, ET and MPI measurements. However, there was poor agreement in segmental systolic velocities and segmental Sr parameters assessed by TTE and TEE. Besides, septal wall segmental S analysis showed a better agreement than lateral wall segmental analysis between TTE and TEE recordings.

Conclusion: TTE and TEE conventional Doppler parameters are compatible in the assessment of LV diastolic function; however, agreement was poor in longitudinal deformation parameters that have been used in the quantitative assessment of LV systolic function between two methods and cannot be used interchangeably. *(Anadolu Kardiyol Derg 2012; 12: 472-9)*

Key words: Deformation imaging, Doppler echocardiography, left ventricle

ÖZET

Amaç: Sol ventrikül (SV) sistolik ve diyastolik fonksiyonlarını değerlendirmede transtorasik (TTE) ve transözafajiyal (TEE) ekokardiyografinin karşılaştırıldığı ve birbirinin yerine kullanılabilirliğini araştıran çalışma sayısı oldukça azdır. Bundan dolayı biz bu çalışmada longitüdinal miyokart deformasyon görüntüleme (gerilim-S ve gerilim hızı-Sr) ile değerlendirilen SV sistolik fonksiyonları ve konvansiyonel Doppler parametreleri ile değerlendirilen SV diyastolik fonksiyonları için TTE ve TEE arasındaki uyumu incelemeyi amaçladık.

Yöntemler: İki yöntem arasındaki uyumun incelendiği bu kesitsel çalışmaya klinik endikasyonu olan 35 hasta alındı. Olgulara TTE sonrasında TEE uygulandı. Hem TTE, hem de TEE'de erken ve geç diyastolik velositeler (E, A, E′ ve A′) deselerasyon zamanı (DZ), ortalama mitral anüler sistolik velosite (Sm), izovolümetrik gevşeme zamanı (İVGZ), izovolümetrik kasılma zamanı (İVKZ), ejeksiyon zamanı (EZ) ve miyokardiyal performans

Address for Correspondence/Yazışma Adresi: Dr. Enbiya Aksakal, Atatürk Üniversitesi Tıp Fakültesi, Kalp Merkezi, Kardiyoloji Anabilim Dalı, 25100, Yakutiye, Erzurum-*Türkiye* Phone: +90 442 231 11 11 Fax: +90 442 236 10 14 E-mail: drenbiya@yahoo.com

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indeksi (MPI) gibi Doppler parametreleri ve longitüdinal deformasyon görüntüleme parametreleri (S, Sr) ve sistolik velositeler ölçüldü. TTE ve TEE arasındaki uyum Bland-altman analizi ile değerlendirildi.

Bulgular: Bland-Altman analiz sonuçları TTE ve TEE'den elde edilen E, A, DZ, E', A', İVGZ, İVKZ, EZ ve MPI parametreleri arasında iyi derecede uyum olduğunu gösterdi. Ancak TTE ve TEE ile ölçülen sistolik velositeler ve segmenter Sr değerleri arasındaki uyum zayıftı. TTE ve TEE'de segmenter S değerlendirmelerinde septal duvar segmentlerinde lateral duvar segmentlerine göre daha iyi uyum olduğu tespit edildi.

Sonuç: Sol ventrikül diyastolik fonksiyonlarının değerlendirilmesinde TTE ve TEE konvansiyonel Doppler verileri birbirleriyle uyumludur, ancak SV sistolik fonksiyonların nicel değerlendirilmesinde kullanılan longitüdinal deformasyon parametreleri için iki metot arasında uyum zayıftır ve birbiri yerine kullanılamaz. *(Anadolu Kardiyol Derg 2012; 12: 472-9)*

Anahtar kelimeler: Deformasyon görüntüleme, Doppler ekokardiyografi, sol ventrikül

Introduction

Although the left ventricular (LV) function is essentially evaluated by transthoracic echocardiography (TTE), they can also be evaluated by transesophageal echocardiography (TEE) (1). Two-dimensional, M-mode and tissue Doppler imaging (TDI) measurements used for evaluation of the LV function have comparable characteristics for TTE and TEE evaluation (2, 3). TDI derived longitudinal myocardial deformation imaging (strain-S and strain rate-Sr) allows also quantification of regional tissue velocities and deformation by consecutive phase shift of the reflected ultrasound from a contracting myocardium (4). TDI derived deformation imaging (S and Sr) has previously been studied in a number of trials for assessment of LV functions (5-7). Furthermore, TDI derived S by TTE has been proposed to provide prognostic and diagnostic information in many circumstances (5). Although there are studies demonstrating LV function with TTE S and Sr imaging, we found a limited number of studies reporting TEE applicability of S and Sr echocardiography compared with TTE in evaluating the LV function (8, 9).

TEE is used widely often to assess the systolic and diastolic LV functions especially in the intraoperative and perioperative period (10, 11). Moreover, TEE is an established imaging modality for the patients with inadequate transthoracic acoustic windows in terms of assessing the LV function. That is because, the agreement between TEE and TTE in both TDI derived longitudinal myocardial deformation imaging, a quantitative method for assessing the LV systolic function, and conventional Doppler parameters which are used for assessing the diastolic function of the LV is of great clinical importance. Maclaren et al. (12) reported that TDI derived LV S, Sr and velocity values was the most feasible technique in patients undergoing cardiac surgery, and there was a good concordance and agreement between TEE and TTE values of both TDI derived S imaging and two dimensional S imaging.

In this particular study, we aimed to investigate the agreement between TTE and TEE in the assessment of LV systolic and diastolic functions by conventional Doppler parameters and longitudinal myocardial deformation indices.

Methods

Study design

A cross-sectional, observational study on the agreement between TTE and TEE techniques for segmental longitudinal myocardial deformation imaging and conventional Doppler echocardiographic parameters assessment.

Study population

The present study was conducted in the cardiology departments of Atatürk University Faculty of Medicine and Erzurum Education and Research Hospital between January-April 2011. Thirty-five consecutive patients (11 female and 24 male; mean age 46±13 years and 46±17 years respectively) underwent a clinically indicated study. The TEE was indicated evaluation of suspected patent foramen ovale. The patients with atrial fibrillation and non-parallel alignment during TEE, a previous myocardial infarction, left bundle-branch block, pericardial disease, poor image quality, and inability to give consent were excluded from the study. All the subjects gave their written informed consent for the study.

Transthoracic echocardiography

For echocardiographic examination, a GE Vivid 7 Dimension (GE Vivid Ultrasound, Horten, Norway) Doppler echocardiographic unit was used. The LV end-diastolic and LV end-systolic diameters were measured in the parasternal long-axis view, and LV ejection fraction was assessed by apical four- and two-chamber views (biplane) with the modified Simpson's rule (1). Mitral inflow was assessed from the apical four- chamber view with pulse wave Doppler by placing a 1-2 mm sample volume between the tips of mitral leaflets during diastole. From the mitral inflow E and A wave velocity, E- deceleration time (DT) and E/A velocity ratio were measured. TDI was used to measure averaged lateral and septal mitral annular systolic, early and late diastolic (Sm, E' and A`) velocities and isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT), and ejection time (ET) by placing a 1-2 mm sample volume in the septal and lateral mitral annulus and these measurements were averaged (13). Myocardial performance index (MPI) was calculated as previously defined by Tei (14).

Transesophageal echocardiography

Transesophageal echocardiography was performed after 4-hour fasting period on all the patients. Ten percent lidocaine spray was used for posterior pharyngeal anesthesia. TEE probe was inserted with the subject lying in the left lateral position. The procedure was performed with continuous monitoring of heart rate, blood pressure, and a single lead electrocardiogram. Machine settings were optimized to obtain highest frame rate. A

Anadolu Kardiyol Derg
2012; 12: 472-9

TEE multiplane 5-MHz probe was introduced into the esophagus to obtain mid-esophageal 4-chamber views. All the recordings (Both TTE and TEE) were made during apnea at end-expiration simultaneously with electrocardiogram. TEE Doppler measurements were assessed similar to the TTE as mentioned above. TEE measurements were analyzed by a second observer who was blinded to the results of the TTE data. TEE was performed right after TTE. During the procedure, maximal effort was spent to prevent any significant differences between blood pressure and heart rate values. Atropin and sedation were not applied. All the images were recorded on workstation (EchoPC, GE Vingmed, Horten, Norway) for subsequent analysis.

Color Doppler myocardial imaging

Real time 2-dimensional color Doppler myocardial imaging (CDMI) data were recorded from the lateral wall and septum of LV. An appropriate velocity scale was chosen to avoid data aliasing. The narrowest image sector angle was used to achieve the maximum color Doppler frame rate possible. All data were acquired at a high frame rate of >120 frame/s. Utmost attention was paid to keep the region of interest at the center of the ultrasound sector to ensure an alignment as close to 0 as possible to long-axis motion (4-7, 15). In all the samples studied, we always selected three consecutive cardiac cycles, which were used for subsequent analysis.

Offline analysis

Color Doppler myocardial imaging data were stored in digital format and analyzed offline with dedicated software (EchoPC, GE Vingmed, Horten, Norway). This method allowed us to calculate local myocardial tissue systolic velocities (Vs), Sr, and S values. Analysis was performed for the basal, mid and apical segments of lateral wall and septum of LV. For longitudinal measurements, a computation area of 10 mm was chosen. To derive Vs and Sr profiles from a segment, the region of interest was maintained in a constant position within the segment being interrogated by using a semiautomatic tracking algorithm. S profiles were obtained by integrating the Sr values over time. Vs, Sr, and S curves were calculated in all patients over 3 cardiac cycles. Peak systolic values were calculated from the extracted curve.

Assessment of Doppler tissue velocity, strain rate and strain

Two-dimensional CDMI data for longitudinal function were recorded from the LV septum and lateral wall using standard apical four-chamber view. All data were acquired at a high frame rate of >120 frame/s. An appropriate velocity scale was chosen to avoid CDMI data aliasing. At least three consecutive cardiac cycles were recorded. Offline analysis of the CDMI data for regional Vs, Sr, and S curves were performed using a special software program (EchoPac 6.4 Vingmed, Horten, Norway). Vs was obtained by placing a sample volume (3×3 pixel) at the basal, mid and apical portion of LV lateral wall and septum. As calculable parameters of the TDI data, longitudinal S and Sr could be measured using the same software. They were assessed for the basal, mid and apical segments of the LV lateral wall and septum. In short, peak systolic Sr were estimated by measuring the spatial velocity gradient over a computation area of 10 mm longitudinally. To derive Vs and Sr profiles from a segment, the region of interest was maintained in a constant position within the segment being interrogated by using a semiautomatic tracking algorithm (15). The timing of end-systole (aortic valve closure) and end-diastole (onset of isovolumic contraction) of LV were derived using a myocardial tissue velocity profile. Natural S profiles were obtained by integrating the Sr values over time using end-diastole as the reference point S and Sr were analyzed by another physician blinded to the electrocardiographic findings (Fig. 1 and 2).

Statistical analysis

Statistical analyses were performed using statistical analysis software package (SPSS Inc., Chicago, IL., USA) version 15.0 for Windows. The data are expressed as mean±SD. The data obtained from TTE S and Sr imaging and TEE S and Sr imaging were compared. Bland-Altman analysis was used to compare the two measurement techniques (16). The differences between the groups were assessed by Mann-Whitney U test. A p value <0.05 was considered statistically significant.

Results

Table 1 shows the demographic and basal TTE parameters of the patients. The size of the left and right heart chambers and LV function of all the patients recruited in the study was normal (LV ejection fraction 71.5±7.1%). There were no significant differences between the TTE and TEE in terms of systolic and diastolic blood pressure and heart rate (p=0.51, p=0.31 and p=0.43, respectively). There were no significant differences between the TTE and TEE regarding LV diastolic parameters except for DT (p=0.05) (Table 2).

Table 1. The basal demographic and transthoracic echocardiographic parameters of the patients

Variables	n=35
Sex, male, %	68.5
Age, years	46.1±14
Body mass index, kg/m^2	26.1±3.2
Body surface area, m^2	1.87±0.2
Left ventricular end-diastolic diameter, mm	45.3±6.0
Left ventricular end-systolic diameter, mm	27.4±5.2
Left ventricular ejection fraction, %	71.5±7.1
Left atrial diameter, mm	34.2±6.8
Right atrial diameter, mm	36.3±4.0
Right ventricular diameter, mm	36.7±6.2

Results are shown as mean±standard deviation and numbers/percentages

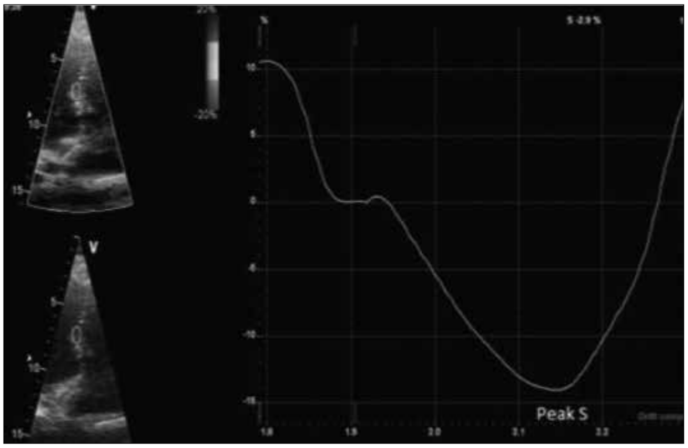

Figure 1. Mid septal segmental longitudinal strain analysis with transthoracic echocardiography

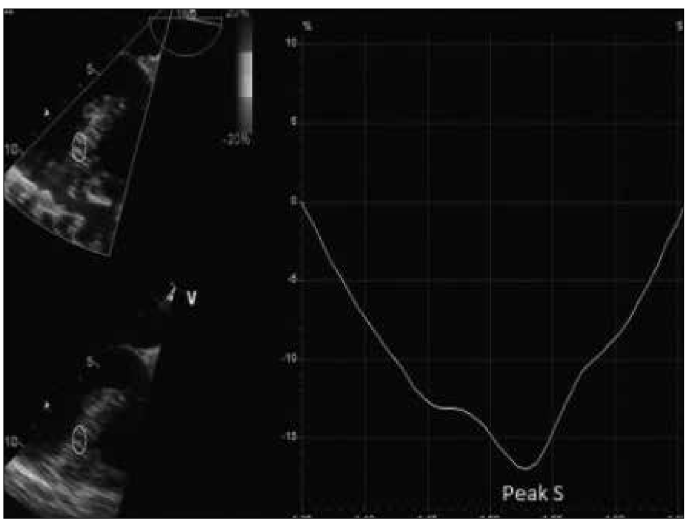

Figure 2. Mid septal segmental longitudinal strain analysis with transesophageal echocardiography

Bland-Altman analysis showed good agreement between TTE and TEE in terms of E, A, Sm, E′, A′, DT, IVRT, IVCT, ET and MPI measurements (Table 3). The analysis carried out with respect to longitudinal myocardial deformation parameters showed that while basal and mid septal Vs were found to be significantly different between TTE and TEE (p=0.002 and p=0.001, respectively), there were no significant differences in Vs, S and Sr apart from these two segments (p>0.05, for all) (Table 4). However, analysis for the longitudinal myocardial deformation parameters revealed poor agreement in segmental Vs and Sr parameters assessed by TTE and TEE. Besides septal wall segmental S analysis showed a better agreement than lateral wall segmental analysis between TTE and TEE recordings (Table 5) (Fig. 3a-f).

Discussion

Our study results indicate that, TTE and TEE parameters are compatible in LV diastolic indices assessed by conventional echocardiographic methods; however, agreement was poor in the quantitative assessment of segmental longitudinal myocardial systolic function between two methods. Therefore, we propose that TTE and TEE could be used interchangeably in the

Table 2. Comparison of transthoracic and transesophageal echocardiographic left ventricular diastolic function parameters

Variables	TTE	TEE	*p
E, m/s	1.2±0.14	1.1±0.10	0.33
A, m/s	0.62±0.10	0.61±0.10	0.29
E/A ratio	1.90±0.31	1.82±0.32	0.27
Sm, m/s	0.11±0.02	0.12±0.03	0.17
E′, m/s	0.12±0.02	0.10±0.03	0.06
A`, m/s	0.06±0.01	0.07±0.01	0.15
E/E′ ratio	10.1±1.5	10.5±1.7	0.31
DT, ms	231±19	217±20	0.05
IVRT, ms	86.1±13.6	89.8±11.1	0.24
IVCT, ms	42.2±8.1	44.1±9.3	0.39
ET, ms	322±24.1	319±28.1	0.72
MPI, %	0.40±0.09	0.42±0.07	0.51
SBP, mmHg	120.1±16.7	117.2±13.6	0.51
DBP, mmHg	70.0±8.5	72.6±7.1	0.31
Heart rate, beats/min	82.2±11.3	84.0±12.4	0.43

Results are shown as mean±standard deviation
*Mann-Whitney U test
A - conventional Doppler late diastolic velocity, A′ - tissue Doppler late diastolic velocity, DT - deceleration time, DBP - diastolic blood pressure, E - conventional Doppler early diastolic velocity, E′ - tissue Doppler early diastolic velocity, ET - ejection time, IVRT - isovolumic relaxation time, IVCT - isovolumic contraction time, MPI - myocardial performance index, Sm - averaged lateral and septal mitral annular tissue Doppler systolic velocity, SBP - systolic blood pressure, TEE - transesophageal echocardiography, TTE - transthoracic echocardiography

Table 3. The mean differences and limits of agreement of transthoracic and transesophageal echocardiography methods for left ventricular diastolic parameters

Variables	Mean difference	Limits of agreement 95%
E, m/s	0.09	-0.21 / 0.28
A, m/s	-0.1	-0.33 / 0.20
Sm, m/s	0.07	-0.17 / 0.28
E′, m/s	0.02	-0.04 / 0.06
A`, m/s	0.13	-0.22 / 0.37
DT, ms	15.9	-51 / 76
IVRT, ms	-3.1	-39 / 33
IVCT, ms	-4.2	-31 / 29
ET, ms	-9.9	-47 / 41
MPI	0.1	-0.44/0.56

Results are shown as numbers
Bland - Altman analysis
A - conventional Doppler late diastolic velocity, A′ - tissue Doppler late diastolic velocity, DT - deceleration time, E - conventional Doppler early diastolic velocity, E′ - tissue Doppler early diastolic velocity, ET - ejection time, IVCT - isovolumic contraction time, IVRT - isovolumic relaxation time, MPI - myocardial performance index, Sm - averaged lateral and septal mitral annular tissue Doppler systolic velocity

Table 4. Comparison of tissue Doppler parameters obtained from transthoracic and transesophageal echocardiographic studies

Segments	Vs, cm/s			S, %			SR, s^{-1}		
	TTE	TEE	*p	TTE	TEE	*p	TTE	TEE	*p
Basal lateral	5.4±0.5	4.9±1.7	0.14	20.2±7.0	18.1±5.8	0.34	2.1±0.76	2.1±0.93	0.75
Mid lateral	3.9±1.4	3.9±1.6	0.89	14.9±3.8	15.1±3.6	0.81	1.6±0.74	1.8±0.76	0.32
Apical lateral	2.4±1.3	2.6±1.8	0.64	10.7±3.2	9.8±4.1	0.28	1.2±0.84	1.0±0.41	0.31
Basal septal	5.3±1.5	3.8±1.4	0.002	18.7±4.3	18.3±5	0.71	1.4±0.78	1.4±0.62	0.71
Mid septal	4.8±1.6	3.7±1.3	0.001	14.2±3.3	14.3±3.9	0.88	1.2±0.38	1.3±0.45	0.46
Apical septal	1.8±0.9	1.8±0.6	0.69	10.9±4.6	9.8±5.3	0.21	1.1±0.71	1.2±0.76	0.33

Results are shown as mean±standard deviation
*Mann-Whitney U test
S - strain, Sr - strain rate, TEE - transesophageal echocardiography, TTE - transthoracic echocardiography, Vs - systolic velocity

Table 5. The mean differences and limits of agreement of transthoracic and transesophageal echocardiographic strain and strain rate imaging

Segments	Vs, cm/s		S, %		SR, s^{-1}	
	Mean difference	95% limits of agreement	Mean difference	95% limits of agreement	Mean difference	95% limits of agreement
Basal lateral	0.7	-2.7/3.5	2.3	-9.6/15.2	-0.15	-1.8/1.6
Mid lateral	0.3	-2.9/3.5	1.4	-9.2/12.3	0.17	-1.44/1.56
Apical lateral	-0.1	-2.2/2.0	1.6	-3.4/6.6	0.22	-0.56/0.65
Basal septal	0.6	-4.6/5.5	0.23	-1.33/1.51	1.1	-2.0/4.5
Mid septal	0.5	-7.9/8.2	1.4	-1.9/4.9	0.12	-1.29/1.38
Apical septal	2.5	-4.7/8.5	0.22	-1.44/1.56	0.38	-0.77/1.21

Results are shown as numbers
Bland-Altman analysis
S - strain, Sr - strain rate, TEE - transesophageal echocardiography, TTE - transthoracic echocardiography, Vs - systolic velocity

assessment of LV diastolic indices by conventional echocardiographic methods, however could not be used interchangeably for assessment of LV segmental longitudinal systolic function.

With the advances in echocardiography, TEE has facilitated the evaluation of more cardiac structures. Essentially, TEE is used in the evaluation of the left atrium, atrial appendages, aorta, and mitral and aortic valves (17-20). However, there are also studies evaluating the LV function (21, 22). TTE-TDI is a useful technique to assess LV systolic and diastolic function (23-26). It has been demonstrated that maximal longitudinal velocities during systole and diastole obtained from TDI are more sensitive to disturbances in LV function than ejection fraction. TDI is influenced less from heart rate and loading status and allows the evaluation of LV systolic and diastolic functions with a single recording (1). TDI may be applied as color coded as well as using the pulse-wave technique (27). In many studies, TDI was used in a TTE mode. Using TEE, it is often possible to visualize the septal, lateral, inferior and anterior myocardial wall, and corresponding parts of the mitral annulus. Although there are several studies demonstrating LV function with TTE-TDI there are few studies demonstrating LV function with TEE-TDI (22, 27-32).

Cheung et al. (30) investigated in animal study whether data obtained from TTE and TEE -CDMI during incremental atrial pacing were comparable. In this study, they evaluated peak isovolumic velocity, isovolumic acceleration during isovolumic contraction, ejection and diastolic E and A velocities from data obtained through TTE and TEE-TDI. Using isovolumic acceleration and isovolumic velocity from TTE-TDI, they found that systolic function evaluation had values comparable to those of TEE. However, they concluded that a velocity was incomparably different. Relying on these results, they have reported that TEE-TDI might be suitable for the monitorization of serial changes in LV function. This study was indeed different from ours, but it had positive results in terms of the evaluation of LV functions with TEE-TDI. In their study, Simmons et al. (31) showed that TEE-TDI could be used to evaluate LV function during cardiac surgery. In this study, they used CDMI. Nilsson et al. (32) determined in their study performed on 24 noncardiac patients under anesthesia that CDMI parameters they obtained from the LV septal, lateral and inferior walls were useful in the evaluation of global LV systolic and diastolic functions. CDMI requires offline analysis for mean velocity determination. This added step may limit its use-

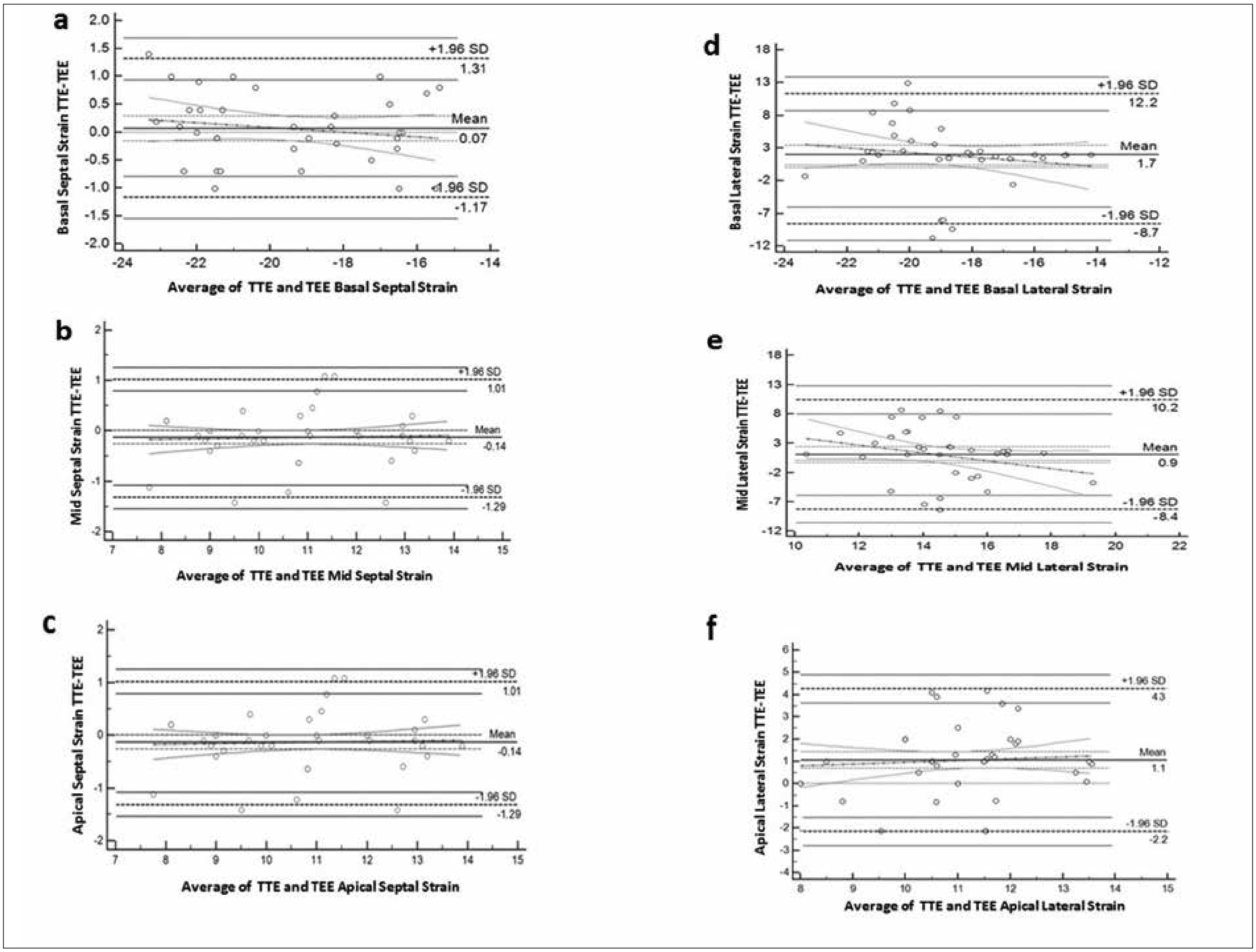

Figure 3. a-f) Bland-Altman analysis for segmental septal and lateral walls strain
TEE - transesophageal echocardiography, TTE - transthoracic echocardiography

fulness in the TEE. In other studies, in the evaluation of LV diastolic functions by TTE, TDI was applicable, and the best recordings of TDI could be obtained from mitral lateral annulus (3, 33). MacLaren et al. (12) carried out a study in which 19 patients undergoing cardiac surgery and only TEE performed and revealed that TDI of radial cardiac motion appears to be the most feasible technique of measuring myocardial velocity, strain, and strain rate during cardiac surgery. All of the earlier studies were performed intra-operatively on the patients under general anesthesia. Our data show that values for TDI data gained from TTE and TEE are comparable for E, A, E`, DT, IVRT, IVCT and MPI.

As a result, we found good agreement in the assessment of LV diastolic parameters between TTE and TEE. However, there was poor agreement in the TDI derived longitudinal deformation parameters (S, Sr and Vs) between TTE and TEE. The most probable reason for these results might be TDI derived S analysis. TDI derived S analysis has some limitations such as angle dependence, limited spatial resolution and deformation analysis in one dimension. In the studies between TTE and TEE by angle independent non Doppler S analysis revealed good agreement for deformation parameters like strain and strain rate (34, 35).

Study limitations

Our study was carried out on a limited number of subjects. S imaging is dependent on good 2D image quality. For this reason, poor 2D image quality results in a poor success rate. Especially foreshortening was seen in apical 4C and 2C views. In order to overcome this limitation we performed retroflexion maneuver.

Clinical implications

During the intra-operative period, assessment of the LV systolic and diastolic functions might be required in many patients. High-risk patients could easily undergo TEE in the operating room. Conventional echocardiographic parameters, which are widely used in the evaluation of LV diastolic functions in TTE practice, might also be used in TEE. However, physicians should pay special attention to segmental longitudinal LV systolic functions by TEE in the assessment of TDI derived S analysis.

Conclusion

TTE and TEE could be used interchangeably to assess LV diastolic function, however cannot be used interchangeably for assessment of LV segmental longitudinal systolic function.

Conflict of interest: None declared.

Authorship contributions. Concept - E.A., A.K., E.M.B.; Design - E.A., E.B.; Supervision - S.S., M.A.; Resource - E.M.B., A.K., E.A.; Materials - E.A.; Data collection&/or Processing - M.K., İ.H.T., E.M.B.; Analysis &/or interpretation - M.K., İ.H.T., A.K.; Literature search - S.S., M.A., E.A.; Writing - E.A., İ.H.T., M.K., A.K.; Critical review - E.A., S.S., M.A., M.K.

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