Assessing Left Ventricular Dimensions in Patients During Coronary Artery Bypass Surgery by Transoesophageal Echocardiography

Koroner Arter Bypass Ameliyatı Boyunca Sol Ventrikül Boyutlarının Transözofajyal Ekokardiyografi İle Değerlendirilmesi

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Objective: Normative values for left ventricular (LV) end-diastolic area (EDA) and diameter (EDD) for intra-operative transoesophageal echocardiography (TOE) have not been established. We aimed to define the ranges of LV EDA and EDD for intra-operave TOE examinations in patients undergoing coronary artery bypass graft (CABG) surgery.

Methods: A MEDLINE search for studies reporting LV EDA and EDD in patients undergoing CABG surgery was performed. Individual-level data set from 333 anaesthetised and ventilated patients with preserved LV function (study population) was obtained from eight studies. EDA and calculated EDD in the study population were compared with summary EDD values obtained using transthoracic echocardiography (TTE) in two studies of 500 awake patients with coronary artery disease (CAD). Further, the influence of pre-specified factors on EDD was evaluated in a multivariate regression model.

Results: The EDA and EDD values measured using TOE in the anaesthetised CABG patients were 16.7±4.7 cm² and 4.6±0.6 cm, respectively. TOE values of EDD in anaesthetised patients were 10%-13% less than those measured using TTE in two studies of awake patients (p<0.001). Body surface area, age and fractional area change, but not sex were factors that affected LV EDD.

Conclusion: The values for LV EDD measured through intra-operative TOE in anaesthetised ventilated CABG patients were 10%-13% less than the corresponding values measured using TTE in awake CAD patients. This finding indicates that independent normative values specific for intra-operative TOE should be established for guiding intra-operative clinical decisions.

Keywords: Echocardiography, transthoracic echocardiography, transoesophageal echocardiography, cross-sectional, coronary artery bypass surgery

Amaç: İntraoperatif transözofajyal ekokardiyografi (TOE) için sol ventrikül (SV) diyalostal alan (EDA) ve çapının (EDD) normal değerleri belirlenmemiştir. Bu çalışmamızın amacı, koroner arter bypass greft (KABG) ameliyatı geçiren hastalarda yapılan intraoperatif TOE incelemeleri için SV EDA ve EDD aralıklarını tanımlamaktır.

Yöntemler: KABG ameliyatı geçiren hastalarda SV EDA ve EDD değerlerini rapor eden çalışmalar için bir MEDLINE araştırması yapıldı. Korunmuş SV fonksiyonu olan 333 anestezi ve ventilasyon uygulanan hastanın (çalışma popülasyonu) bireysel verileri 8 çalışma ele edildi. Çalışma popülasyonundaki EDA ve hesaplanmış EDD değerleri, koroner arter hastalığı (KAH) olan 500 bilinçli hastaya içeren iki çalışmada transorakal ekokardiyografi (TTE) kullanılarak elde edilen özet EDD değerleri ile karşılaştırıldı. Ayrıca, önceden belirlenmiş faktörlerin EDD üzerindeki etkisi multivaryant regresyon modeli kullanılarak değerlendirildi.

Bulgular: Anestezi altındaki KABG hastalarında TOE kullanılarak ölçülen EDA ve EDD değerleri sırasıyla 16.7±4.7 cm² ve 4.6±0.6 cm olarak bulundu. Anestezi uygulanmasında TOE ve EDD değerleri, bilinçli hastalar üzerinde yapılan iki çalışmada TTE kullanılarak ölçülen değerlerde göre %10-13 daha düşük (p<0.001), Vücut yüzey alanı, yaş ve fraksiyonel alan değişimi SV EDD’yi etkileyen faktörler olarak saptanırken, cinsiyetin etkilediği görüldü.


Anahtar sözcükler: Ekokardiyografi, transorakal ekokardiyografi, transözofajyal ekokardiyografi, kesitsel, koroner arter bypass ameliyatı
Introduction

Transoesophageal echocardiography (TOE) has been recommended for all patients undergoing cardiac surgery and is accepted worldwide for the evaluation of unexplained haemodynamic instability in intra-operative management and decision-making (1, 2).

The left ventricular (LV) end-diastolic chamber dimensions, i.e. LV end-diastolic area and diameter (EDA and EDD), are regularly used to identify patients with low or normal LV volaemia and to guide intravenous administration of fluids (2-5). However, the clinical utility of EDA and EDD for intra-operative decisions and prognosis depends on the accuracy and reliability of normal values. In fact, the availability of normative reference values for cardiac chamber quantification is a prerequisite for accurate clinical application of echocardiography (6). Two large studies recently published normal values as assessed using transthoracic echocardiography (TTE) in young and healthy patients (6, 7). However, such values might not necessarily apply for patients with coronary heart disease. Further, even if normative values obtained using transoesophageal echocardiography (TOE) in awake subjects are applied (6, 7), anaesthetic drugs, positive pressure ventilation and patient positioning may have systematic effects on cardiac function and loading conditions causing small, but important differences in LV EDA and EDD measurements in the anaesthetised and ventilated patients (8-10).

Finally, TTE values might be different from those for TOE as a consequence of small differences in the position of the echo probe and the slightly different standard echocardiographic cross-sectional views used in the two techniques (11). Nonetheless, reference values for LV EDA and EDD obtained from TTE studies performed in awake healthy patients are commonly applied as diagnostic criteria for the intra-operative TOE examination (12, 13).

The aim of this study was (1) to define the physiologic ranges of LV EDA and EDD in anaesthetised and mechanically ventilated patients undergoing coronary artery bypass graft (CABG) surgery as obtained using TOE immediately before surgery; (2) to compare the values obtained by intra-operative TOE with reference values obtained using TTE in awake, spontaneously breathing patients with coronary artery disease (CAD) and (3) to determine which patient factors affect LV EDA and EDD in patients undergoing CABG surgery. We hypothesised that the ranges for LV EDA and EDD measured using intra-operative TOE are different from those measured using TTE studies in awake patients.

Methods

This is individual-level data analysis including data from several published studies (3, 14-19). All patient data from studies included in this analysis were approved by the local institutional review boards, and written informed consent was obtained from all included patients.

Study population

We searched the MEDLINE database to identify studies reporting on EDA or indexed EDA (EDAI) values measured using transgastric TOE in the short-axis view at the transgastric mid-papillary level (TG mid SAX) in patients undergoing CABG surgery (20). The search included the period between January 1990 and May 2014. The following search terms were applied: ‘transoesophageal echocardiography cardiac surgery’, ‘transoesophageal echocardiography CABG left ventricle’, ‘transoesophageal echocardiography aorto-coronary bypass’, ‘transoesophageal echocardiography CABG short-axis’, ‘transoesophageal echocardiography CABG LVEDA’, ‘echocardiography cardiac surgery anaesthesia’, ‘CAD end-diastolic’, ‘CAD EDA’, ‘CAD LVEDA’, ‘CAD EDAI’ and ‘CAD LVEDAI’. We identified a total of 1131 citations. Eligibility criteria consisted of EDA values measured using TOE in the TG mid SAX view (20), including the papillary muscle (21). Further eligibility criteria were clinically stable haemodynamic conditions without the use of vasopressors or vasodilators during measurements and EDA measurements without the use of automatic border detection for the determination of EDA. Fifteen studies satisfied the eligibility criteria. The corresponding authors were contacted and requested to provide individual patient-level data. We obtained the original data from seven publications (3, 14-19). The authors of the eight other studies did not respond and were not able or willing to provide individual patient data. In addition, a co-author (JP) shared individual patient data from an unpublished TOE study that also satisfied the eligibility criteria. We thereby selected the study population including 333 patients who fulfilled the following additional pre-specified individual patient criteria: (1) preserved LV function defined as LV ejection fraction (EF) ≥45% or fractional area change (FAC) ≥40% (22); (2) isolated CABG surgery; (3) no previous cardiac surgery requiring sternotomy and (4) no relevant valvular heart diseases. The collected data of the study population included patient demographics, LV EDA and LV end-systolic area (ESA). In two studies (13, 16), the TOE data immediately before surgery but after anaesthesia induction and at the end of surgery were available for 78 patients. In both studies, ‘before surgery’ was defined as the time after induction of anaesthesia but before sternotomy, and ‘after surgery’ was defined as the time after sternal closure but before transfer to the intensive care unit.

Awake population

To compare EDD and EDA values in anaesthetised and awake patients, we searched MEDLINE for studies providing EDA values in awake CAD patients. Because the search retrieved no studies using the above-described MEDLINE search strategy, we expanded the search to include EDD using the following terms: ‘CAD echocardiography’, ‘CAD end-diastolic diameter’ and ‘CAD LVEDD’. We identified a total of 876 citations. Eligibility criteria consisted of haemodynamically stable CAD patients with preserved LV function (EF ≥45% or FAC ≥40%) and the availability of TTE estimates of LV
EDD in the parasternal long-axis (LAX) view. Two studies including 139 and 361 patients fulfilled these criteria (23, 24). Because we were unable to obtain individual patient data from these two studies, we compared the TOE values from the study population with the summary estimates reported in the two TOE studies in the awake population.

Endpoints
The endpoints were LV EDA and EDD measured in the TG mid SAX view. EDD values were reported in only one TOE study. In contrast, the summary values in the awake population consisted exclusively of EDD measurements (23, 24). To compare EDD values, the TOE EDA values were mathematically converted into EDD values. Considering the circular symmetry of the LV cavity at the TG mid SAX view (20), we used the equation: EDD=√ (4×EDA/π).

Factors influencing EDA/EDD values
Patient factors potentially influencing LV EDA and EDD values were tested using a linear regression model as described below. In addition, we tested if EDA values and calculated EDD values were different among male and female patients. Further, we analysed whether EDA values obtained immediately before surgery were different from those obtained immediately after surgery using data from two studies.

Statistical analysis
No formal sample size calculation was performed for this study. Data were presented as mean±standard deviation (SD) or number (percentage) as appropriate. Mean±SD (95% confidence interval [CI]) of the pooled data were compared using a two-sided t test for unpaired and paired measurements as appropriate. To evaluate factors influencing EDA and EDD, we inserted four pre-specified independent variables into the linear regression model. Sex was inserted as a dichotomous variable, whereas age (per year increase), LV FAC (per % increase) and body surface area (BSA; per m² increase) were entered as continuous variables into the model. A p value <0.05 was considered significant. Statistical analyses were performed using the IBM Statistical Package for Social Sciences software (version 21; IBM Corp., Armonk, NY, USA).

Results
Characteristics of the study population and the awake population
Individual data sets were obtained from 304 patients in seven published studies (3, 14-19) and from 85 patients in one unpublished study (Table 1). In all studies, LV EDA and ESA were measured using manual planimetry of the endocardial boarders at end-diastole and end-systole according to the guidelines provided by Lang et al. (21). The average LV EDA (mean±SD) obtained from each study is shown in Figure 1. Data from 56 patients were excluded due to impaired LV function (EF <45% or FAC <40%) providing a final sample size of 333 patients in the study population. Patient characteristics and the average LV dimensions from the study population are listed in Tables 2 and 3. The mean age in the study population was 64±9 years, and the proportion of male patients was 82%.

The two studies reporting EDD values measured in awake CAD patients enrolled 139 and 361 patients with preserved LV function, with 101 (73%) and 301 (83%) male patients (23, 24), respectively. The mean ages were 54±9 years and 58±10 years. Both TTE studies used M-mode imaging and LV EDD and end-systolic diameter were measured in the parasternal LAX view using the leading-edge-to-leading-edge technique at end-diastole and end-systole according to the guidelines provided by Lang et al. (21).

EDA and EDD values
The average LV EDA and calculated LV EDD values in the study population were 16.7±4.6 cm² and 4.6±0.6 cm, respectively. Excluding the patients from the unpublished study did not change these values. The average LV EDD values reported by Ghali et al. (23) and by Gruchala et al. (24) were 5.1±0.5

Table 1. Characteristics of studies providing individual data of 389 patients

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Patients</th>
<th>Male</th>
<th>Age (years)</th>
<th>Normal LV function*</th>
<th>Main anaesthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheung et al., 1994 (3)</td>
<td>31</td>
<td>N/A</td>
<td>N/A</td>
<td>25 (81)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Seeberger et al., 1998 (18)</td>
<td>76</td>
<td>63 (83)</td>
<td>61±8</td>
<td>73 (97)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Skarvan et al., 2003 (19)</td>
<td>42</td>
<td>35 (83)</td>
<td>64±10</td>
<td>33 (78)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Poelaert et al., 2004 (16)</td>
<td>42</td>
<td>33 (79)</td>
<td>64±10</td>
<td>42 (100)</td>
<td>Propofol</td>
</tr>
<tr>
<td>Preismann et al., 2005 (17)</td>
<td>16</td>
<td>14 (88)</td>
<td>63±8</td>
<td>11 (69)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Michaux et al., 2006 (15)</td>
<td>47</td>
<td>42 (84)</td>
<td>63±8</td>
<td>40 (85)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Couture et al., 2007 (14)</td>
<td>50</td>
<td>38 (76)</td>
<td>68±8</td>
<td>44 (88)</td>
<td>Volatile</td>
</tr>
<tr>
<td>Poelaert, N/P</td>
<td>85</td>
<td>N/A</td>
<td>63±11</td>
<td>65 (76)</td>
<td>Propofol</td>
</tr>
</tbody>
</table>

Data are numbers (percent) or mean±standard deviation. All patients subsequently underwent coronary artery bypass graft (CABG) surgery. *Normal left ventricle (LV) function was defined as ejection fraction (EF) ≥45% or fractional area change (FAC) ≥40%.
N/A: not available; N/P: not published.
cm and 5.3±0.7 cm, respectively (Figure 2). These TTE LV EDD values were 10%-13% greater than the calculated LV EDD values of 4.6±0.6 cm in the TOE study population (p<0.001 for both comparisons).

Factors influencing EDA and EDD values

The average TOE LV EDA values in females (15.3±4.6 cm²; n=44) were less than those in males (17.2±4.7 cm²; n=199; p=0.012). The average LV EDD values were also less in females compared to males (4.4±0.7 cm vs. 4.6±0.6 cm, p=0.008). When using indexed values corrected to BSA, LV EDAI and EDDI values were comparable among female and male patients.

In the multivariable linear regression model, BSA (0.83, 95% CI 0.40-1.26, p<0.001) and age (0.010, 95% CI: 0.002-0.018, p=0.020) were positively correlated with LV EDD, whereas FAC (−0.024, 95% CI: −0.030-0.019, p<0.001) was negatively correlated with LV EDD. Sex did not correlate with LV EDD (p=0.224). Similar correlations were obtained using LV EDA as the independent variable.

Among the 78 patients who had TOE measurements before and after surgery, postoperative TOE LV EDA values (16.2±6.3 cm²) were significantly less than preoperative values (17.4±6.0 cm²; p=0.006), whereas LV ESA did not change significantly. FAC also did not change significantly before and after surgery (50±15% vs. 49±16%; p=0.410).

Discussion

Based on individual-level data from 333 patients from eight clinical studies, LV EDA and EDD measured using intra-operative TOE in anaesthetised and mechanically ventilated CABG patients with preserved LV function during haemodynamically stable conditions prior to thoracotomy were 16.7±4.6 cm² and 4.6±0.6 cm, respectively. Intra-operative LV EDD values measured using TOE were 10%-13% less than published LV EDD values measured using TTE in awake CAD patients. This finding suggests that the common clinical practice of applying reference values obtained using TTE in awake patients as normative values for anaesthetised and ventilated patients assessed using TOE might be misleading and result in inappropriate intra-operative decisions regard-
ing choice of therapy and prognosis. Further, this discrepancy between TTE and intra-operative TOE measurements highlights the need for studies designed to establish normative reference values specifically for intra-operative TOE studies in anaesthetised and ventilated patients. This conclusion is in agreement with two recently published studies (6, 7) which also claimed for reliable and accurate TTE reference values for chamber quantitation.

However, the normative values described by TTE in young and healthy individuals may not be representative for other populations to which they are applied (6, 7, 12, 13). Although some studies have reported nearly identical LV EDA and EDD values by both TTE and TOE in awake patients (25-27), the discrepancy between TOE and TTE measurements of LV EDA found in this study can be explained by several real, but subtle differences in the standard clinical imaging protocols used in TOE and TTE. Where-as the different echocardiographic approach, i.e. TTE vs. TOE, is unlikely to be causative factor (25-27), the standard cross-sectional imaging planes for measuring LV cavity dimensions in TTE and TOE are slightly but significantly different. Diameter measurements using the TTE para-sternal LAX view are performed at the level of tips of the mitral valve leaflets (28). In contrast, LV cavity diameter in the study population was measured by using the TOE TG LV SAX view at mid-papillary level as recommended in the TOE guidelines published in 1999 (20) and valid until 2013. The normal anatomic shape of the LV has a smaller diameter at the mid-papillary level (closer to the LV apex) where the TOE measurements are performed compared to the diameter at the mitral valve leaflet tips (closer to the LV base) where the TTE measurements are performed. The recently updated TOE guidelines acknowledged this difference between TOE and TTE cross-sectional imaging planes for measuring LV cavity diameter and recommended to measure LV diameter using the TG LAX or the TG two-chamber views (2). Although this methodological difference between TTE and TOE is a convincing explanation for the differences found in the current study and may be minimised in the future with the updated TOE guidelines (2), reference ranges for LV EDA and EDD using this newly recommended approach have not been established. Clinici ans are therefore likely to continue using the TG mid SAX view to measure LV EDA and EDD according to the first set of published guidelines (3, 20).

Interestingly, the normative value of LV EDD was determined as 4.43±0.48 cm using TTE in the NORRE study including young and healthy individuals (6). This value is comparable to the LV EDD value of 4.6±0.6 cm as determined in our TOE population but substantially lower in the studies by Ghali et al. (23) and Gruchala et al. (24), which report LV EDD values between 5.1 and 5.3 cm as assessed using TTE. It seems likely that the older age and cardiac comorbidities including CAD increase end-diastolic dimensions (29). However, the use of anaesthetic drugs and positive pressure ventilation as well as a relative intra-operative hypovolaemia might compensate for the ‘dilative effect’ of older age and cardiac disease on chamber dimensions.

Anaesthetic drugs and positive pressure ventilation may have relevantly influenced LV cavity dimensions in the TOE study population by affecting systemic vascular resistance, venous tone and venous return (30). The physiologic effects of general anaesthesia and positive pressure ventilation on LV cavity size were recently demonstrated in a magnetic resonance imaging study in healthy adults (10) and several echocardiographic studies in healthy subjects and in patients with cardiac disease (9, 31-33). All these studies reported that LV cavity dimensions were reduced during anaesthesia and positive pressure ventilation, most likely as a consequence of decreased venous return and LV preload.

The analysis of factors potentially affecting LV dimensions revealed that LV EDA and LV EDD were larger in males compared to females, but EDA and EDD values indexed for BSA became comparable. In agreement, there was no association of sex with EDDI and EDAI in the linear regression model after adjustment for BSA. Some weak positive associations between age and LV EDD were found, which is in agreement with normal changes that occur in the aging heart (29). Also, in agreement with earlier studies (3, 34), we found that LV EDA varied in response to differences in systolic function measured by FAC. Finally, LV EDA was significantly less immediately after surgery compared to its value immediately before sternotomy. Changes in heart rate, autonomic nervous system tone, decreased intravascular volume, or diastolic dysfunction as a consequence of reperfusion may all have contributed to the reduced LV EDA after surgery.

Study limitations
This retrospective study has several strengths and limitations: First, the study was based on pooled values from published studies that were identified by using detailed search strategies and predefined eligibility criteria; however, the literature search was limited to a single electronic database and did not comply formally with current standards for systematic reviews. However, the original objective of the study was to collect individual patient-level data from the previously published studies rather than comparing the summary data from different studies. Further, EDD was not included as a search term in the primary MEDLINE search, but a post-hoc search that included ‘EDD’ and ‘end-diastolic diameter’ as search terms did not reveal any additional TOE studies in anaesthetised patients, which could have been included in the analysis. Second, not all individual patient-level data sets were complete regarding patient characteristics and comorbidities. Third, the study relied on the investigators to adhere to the methodology described in their studies for performing the echocardio- graphic measurements. The studies were not standardised.
measurements performed using the standard cross-sectional specific normative reference values for intra-operative TOE
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question the common practice of applying normative values
similar population of awake CAD patients. These findings
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The study found that values for LV EDD obtained using in-
through intra-operative TOE using the TG mid SAX view.
ventilated patients with preserved LV function measured

Conclusion

Data from prior studies were used to determine the physi-
ological ranges for LV EDA and EDD in anaesthetised and venti-
ated patients with preserved LV function measured through
intra-operative TOE using the TG mid SAX view. The study
found that values for LV EDD obtained using in-
tra-operative TOE in the study population was 10%-13%
less than corresponding TTE reference values obtained in a
similar population of awake CAD patients. These find-
ings question the common practice of applying normative values
defined using TTE in awake patients for guiding intra-oper-
ative decisions and prognosis and indicate a need to establish
specific normative reference values for intra-operative TOE
measurements performed using the standard cross-sectional imaging planes.

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Informed Consent: Written informed consent was obtained from
all patients who participated in this study.

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M.D.S.; Data Collection and/or Processing - C.P., D.B., G.L.B.,
A.T.C., P.C., I.M., J.P., S.P., K.S., M.D.S.; Analysis and/or Inter-
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