Assessment of the Left Atrial Appendage Mechanical Function by Three-Dimensional Echocardiography


Department of Cardiology and Institute for Cardiovascular Research, Medical Center VU, Amsterdam, The Netherlands

Aims: We evaluated the feasibility of three-dimensional echocardiography, in the assessment of left atrial appendage (LAA) function.

Methods and Results: Forty-five patients underwent multiplane transoesophageal echocardiography. In addition to Doppler and two-dimensional echocardiography reconstruction were obtained during transoesophageal echocardiography. Left atrial appendage ejection fraction based on three-dimensional echocardiography volume measurements (EFv) and two-dimensional echocardiography area measurements (EFa), coupled with other echocardiographic data, were related to left atrial appendage late peak emptying velocity, a frequently used indicator of left atrial appendage function. Multiple regression analysis has revealed a significant association of peak emptying velocity with EFv (P<0.0001), spontaneous echocardiographic contrast (P=0.01), tricuspid regurgitation (P=0.03) and left ventricular hypertrophy (P=0.05). No significant relation was observed between peak emptying velocity and EFa, presence or absence of atrial fibrillation, left ventricular dysfunction, mitral stenosis and insufficiency, left atrial dilatation, pulmonary venous peak systolic, diastolic and peak reverse flow velocity at atrial contraction as well as left atrial appendage volumes derived from two-dimensional echocardiography and three-dimensional echocardiography. In a simple linear correlation, the degree of association between peak emptying velocity and EFv was higher as between peak emptying velocity and EFa (r=0.7 vs 0.4, both P<0.001). Observer variabilities for calculating EFv were considerably lower than for two-dimensional echocardiography derived EFa. Ejection fractions determined by two-dimensional echocardiography area measurements at 45°, 90° and 135° cutplane angulations were related to EFv only at 135°.

Conclusions: Left atrial appendage ejection fraction calculation by three-dimensional echocardiography is feasible, more accurate than by two-dimensional echocardiography and has lower observer variability. Furthermore, an optimal cutplane angulation of the left atrial appendage view at 135° has been demonstrated.

Key Words: Left atrial appendage; transoesophageal echocardiography; atrial fibrillation.

Introduction

The left atrial appendage has an important role in cardiovascular performance[1]. Furthermore, its dysfunction is related to thromboembolic complications[2–5]. Thanks to transoesophageal echocardiography, it is possible to visualize the left atrial appendage and assess its function by means of Doppler flow velocity interrogation and even ejection fraction calculation[6,7].
The left atrial appendage is a structure that varies in volume and shape. This variability should be considered in particular when two-dimensional echocardiography is used for left atrial appendage ejection fraction calculation. Recently introduced three-dimensional echocardiography allows measurements without geometric assumption. It provides more accurate data than two-dimensional echocardiography, as far as the structures with complex three-dimensional anatomy are concerned. Therefore, it should be an ideal tool for studying the left atrial appendage function by means of volume and ejection fraction measurements. Besides Doppler evaluation of the left atrial appendage function, it can be important as left ventricular volume and ejection fraction calculations. To our knowledge, no data so far are available with respect to functional assessment of the left atrial appendage by three-dimensional echocardiography. Thus, the aims of this study were: (1) to evaluate feasibility of three-dimensional echocardiography for left atrial appendage volume and ejection fraction calculation. This was done by analysing the relation of left atrial appendage volumes and ejection fraction as well as other echocardiographic data to the left atrial appendage late diastolic peak emptying velocity. The variability of left atrial appendage ejection fraction from two-dimensional area measurements and three-dimensional volume measurements was compared using intra- and interobserver studies. Furthermore, (2) the effect of cutplane angulation on left atrial appendage area measurements was studied in order to define the optimal two-dimensional echocardiography tomographic imaging plane of the left atrial appendage.

**Methods**

**Patients**

The study population included 45 patients with an indication for transoesophageal echocardiography (20 men and 25 women) and ranged in age from 26 to 84 years (mean age 59.5 ± 14.4 years). Of these 45 patients, 17 had combined mitral valve stenosis and insufficiency, 22 pure mitral valve insufficiency, three patients had pure mitral stenosis and three were without mitral valve involvement. Twenty-nine (64%) patients were in sinus rhythm and 16 (36%) in atrial fibrillation during the transoesophageal echocardiography examination. Characteristics of the patients are shown in Table 1. The study patients were originally examined for mitral valve disease, i.e. mitral stenosis, mitral insufficiency or a combination of both. Because during acquisition of data for three-dimensional echocardiography reconstruction also the left atrial appendage was included, this study

---

**Table 1. Clinical and echocardiographic variables.**

| Age (yrs) | 59.5 ± 14.4 |
| Men/women | 20/25 |
| Sinus rhythm/atrial fibrillation | 29/16 |
| LAA peak emptying velocity (cm/s) | 35.6 ± 21.7 |
| LAA end-diastolic area (cm²) | 6.5 ± 2.9 |
| LAA end-systolic area (cm²) | 4.4 ± 2.7 |
| LAA end-diastolic volume (ml) | 13.8 ± 8.8 |
| LAA end-systolic volume (ml) | 9.9 ± 7.3 |
| EFa (%) | 35.3 ± 17.2 |
| EFv (%) | 34.4 ± 15.4 |
| Pulmonary peak systolic flow velocity (cm/s) | 36.8 ± 23.3 |
| Pulmonary pressure diastolic flow velocity (cm/s) | 38.8 ± 21.5 |
| Pulmonary reversal flow at atrial contraction (cm/s) | 13.7 ± 12.4 |

Left ventricular dysfunction (n=10)
- Mild: 0
- Moderate: 6
- Severe: 4

Mitral regurgitation (n=39)
- 1+: 23
- 2+: 7
- 3+: 9

Mitral stenosis (n=20)
| Area (cm²) | 1.53 ± 0.77 |

Tricuspid regurgitation (n=32)
| 1+ | 23 |
| 2+ | 7 |
| 3+ | 2 |

Left atrial spontaneous echocontrast
- 15

Left atrial dimension
- 44.9 ± 7.8

Left ventricular hypertrophy
- 3

LAA=left atrial appendage; EFa=percent area ejection fraction; EFv=percent volume ejection fraction.
population was suitable for three-dimensional echocardiography evaluation of the left atrial appendage.

**Echocardiography**

All enrolled patients underwent multiplane transoesophageal echocardiography examination, including a study of left atrial appendage function. Examinations were performed with a multiplane 5 MHz, 64-element transducer (Hewlett-Packard Co., Andover, Mass.) connected to a Hewlett-Packard Sonos 2500 or 5500 (Hewlett-Packard Co., Andover, Mass.). After the diagnostic multiplane transoesophageal study, the probe was located at midoesophageal level. A test sequence with 180° rotation of the transducer array was performed to ensure whether the left atrial appendage was encompassed within the conical dataset. The acquisition was performed at 3° increments with electrocardiographic (ECG) and respiratory gating. The data were stored on a magneto-optical disk and processed off-line using a three-dimensional echocardiography system (Echo-Scan 3.1, TomTec GmbH, Munich, Germany). two-dimensional echocardiography and Doppler studies were recorded on VHS videotape.

Left atrial appendage and pulmonary venous flow were evaluated by pulsed-wave Doppler interrogation. The peak emptying velocity, as an indicator of left atrial appendage mechanical function, was obtained in the left atrial appendage long-axis view with the sample volume placed 1 or 2 cm within the appendage outlet. The values of three and five measurements were averaged in patients with sinus rhythm and atrial fibrillation, respectively. In addition, the presence of spontaneous echocardiographic contrast was determined in the left atrial appendage. Mitral and tricuspid insufficiency was graded semiquantitatively according to the maximum regurgitant jet area as assessed by colour Doppler flow imaging. Left ventricular dysfunction was assessed by visual estimation and graded as mild, moderate and severe.

Left atrial appendage volumes and ejection fraction were calculated from the three-dimensional echocardiography volumetric dataset by using Simpson’s rule. After the long-axis view of the left atrial appendage had been selected, end-diastolic (EDV) and end-systolic volumes (ESV) were calculated by manual tracing of sequential short-axis views. In patients who were in sinus rhythm, left atrial appendage diastole was measured at the onset of the ECG P-wave and left atrial appendage systole at the ECG R-wave. Minimal and maximal areas were selected as end-diastole and end-systole in patients in atrial fibrillation. A line drawn from the limbus of the confluence of the left upper pulmonary vein and the left atrial appendage to the outermost portion of the mitral annulus was considered as a boundary between the cavity of the left atrium and the left atrial appendage. The paraplane technique was used to generate a series of equidistant cross-sections at fixed 3 mm slice thickness. When manual tracing was completed, the volume of the short-axis slice was calculated. Adding up the volumes of all slices provided the volume measurement (Fig. 1). The percent volume ejection fraction of the left atrial appendage (EFv) was calculated as (EDV – ESV)/EDV. The same three-dimensional echocardiography dataset was used to generate a two-dimensional long-axis view of the left atrial appendage. End-diastolic area (EDA) and end-systolic area (ESA) was planimetrised and percent area ejection fraction (EFa) was calculated (Fig. 2). Intra- and inter-observer reproducibility of all measurements was obtained in every patient by one observer at least two weeks apart and by two observers in a blinded fashion. In order to evaluate the errors caused by suboptimal cutplane selection, the left atrial appendage area and EFa was also measured in long-axis views angulated by 45°, 90° and 135° from the initially selected long-axis view. However, the cutplane angulations were not determined from the original two-dimensional echocardiography images but within a three-dimensional echocardiography data set; these views can be similar to real cutplanes during the multiplane transoesophageal echocardiography, because a 0° angulation is identical to a 0° imaging plane of multiplane transoesophageal echocardiography.

**Statistical analysis**

Data are reported as mean ± SD. The effect of several independent variables (those obtained during the diagnostic transoesophageal echocardiography study and three-dimensional echocardiography) upon peak emptying velocity was studied using multiple linear regression analysis. The subset of predictor variables which gives the best fitting model was calculated. Correlations were studied using the Pearson correlation test. A P-value <0.05 was considered significant. Observer variability was assessed by coefficient of variation (calculated as standard deviation of the differences between measurements divided by the average value). Furthermore, the correlation coefficient (r), the mean difference and standard deviation were used for the intra- and inter-observer study.

**Results**

Three-dimensional echocardiography reconstruction and volume calculation was feasible in all patients. The mean ± SD of the left atrial appendage EDV and ESV and ejection fraction obtained by three-dimensional echocardiography were: 13.8 ± 8.8 ml, 9.9 ± 7.3 ml and 34.4 ± 15.4%, respectively. The mean values ± SD of the left atrial appendage EDA and ESA and ejection fraction measurement using two-dimensional echocardiography were: 65 ± 2.9 cm², 4.4 ± 2.7 cm² and 35.3 ± 17.2%, respectively. In multiple linear regression analysis, peak emptying velocity was significantly related to three-dimensional echocardiography derived left
atrial appendage ejection fraction (EFv, \(P<0.0001\)), spontaneous echocardiographic contrast (\(P=0.001\)), tricuspid insufficiency (\(P=0.03\)) and left ventricular hypertrophy (\(P=0.05\)). There was no significant relation of peak emptying velocity to other observed variables: presence or absence of atrial fibrillation (\(P=0.4\)), left ventricular function (\(P=0.07\)), mitral stenosis (\(P=0.3\)), mitral insufficiency (\(P=0.09\)), ESV (\(P=0.2\)), EDV (\(P=0.3\)), ESA (\(P=0.2\)), EDA (\(P=0.3\)), EFa (\(P=0.1\)), left atrial dilatation (\(P=0.06\)), pulmonary venous peak systolic, diastolic and peak reverse flow velocity at atrial contraction (\(P=0.2, P=0.6, P=0.5\), respectively). Following a best subset selection a final regression model was: peak emptying velocity=30.87 – 5.64 tricuspid insufficiency + 63.97 EFv – 7.29 left atrial dilatation – 16.1 left atrial spontaneous echocardiographic contrast – 17.19 left ventricular hypertrophy. In a simple linear correlation, the degree of association between peak emptying velocity and EFv was higher than between peak emptying velocity and EFa (\(r=0.7\) vs \(r=0.4\), both \(P<0.001\), Fig. 3). Observer variabilities are presented in Table 2. There were considerably closer limits of agreement, lower variability and higher correlation in ejection fraction calculation by three-dimensional echocardiography as compared with two-dimensional echocardiography. Ejection fractions determined by

---

**Figure 1.** (a) Left atrial appendage volume measurement by three-dimensional echocardiography using Simpson’s rule. A slice of 3 mm thickness is measured in the long-axis plane of the left atrial appendage. (b) Contour tracing and labeling of the slice in the short axis. After tracing and labeling, the volume of the entire left atrial appendage is displayed in the reference image and the end-diastolic (c) and end-systolic (d) volume is calculated.
two-dimensional echocardiography area measurements at 45°, 90° and 135° cutplane angulation (mean ± SD: 34.1 ± 18.5%, 34.0 ± 19.2%, 34.3 ± 17.9%) were not significantly different (in multiple comparison each P-value not significant). However, by multiple regression analysis a significant relation was found between EFv and EFa measured at 135° cutplane angulation (P=0.008) but not at 45° and 90° angulation (P=0.3 and 0.8).

Discussion

Besides Doppler evaluation of the left atrial appendage, numerous studies have reported assessment of the left atrial appendage function by area and ejection fraction calculation. These studies led to recognition that the percent area ejection fraction of the left atrial appendage can be related to successful restoration of the sinus rhythm from atrial fibrillation[12]. Left atrial appendage dysfunction, using area ejection fraction calculations, was also demonstrated in patients with dilated and hypertrophic cardiomyopathy[13]. Similarly, these measurements based on two-dimensional echocardiography were used for presentation of more depressed left atrial appendage function in patients in atrial flutter with intermittent atrial fibrillation as compared to pure atrial flutter[14]. Improvement of the left atrial appendage ejection fraction after treatment of heart failure also revealed its relation to the overall cardiac performance[15]. In the study by Porte et al.[16], some discrepancy has been encountered in the assessment of left atrial appendage function after successful percutaneous mitral commissurotomy; peak emptying velocity was positively associated with successful commissurotomy as well as left atrial appendage ejection fraction derived from the transverse plane but not from the longitudinal plane. This was related to the difficulties inherent in the planimetry method carried out on two-dimensional images and rotational movements of the heart. In some reproducibility studies, percent area ejection fraction measurement is prone to observer variability, primarily because of complex three-dimensional anatomy of the left atrial appendage, which limits accurate definition of the standard tomographic imaging plane[4,15]. In our study, the correlation between EFa and peak emptying velocity was lower than the correlation between EFv and peak emptying velocity. In addition, there was higher reproducibility in EFv calculation than EFa in both the intra- and inter-observer studies. Besides the peak emptying velocity-EFv association, we found other echocardiographic correlations such as left atrial spontaneous echocardiographic contrast, tricuspid insufficiency and left ventricular hypertrophy. A negative correlation between peak emptying velocity and spontaneous echo contrast indicates a well known relation of left atrial appendage dysfunction to thrombus formation[17–20]. Influence of tricuspid insufficiency on left atrial appendage peak emptying velocity suggests that increased left atrial pressure transmitted to right heart chambers is inversely related to left atrial appendage function[21]. Association of peak emptying velocity and left ventricular hypertrophy in our study is consistent with the results of the Stroke Prevention in Atrial Fibrillation (SPAF-III) study, which confirmed that a history
of hypertension was more frequently associated with left atrial appendage thrombi and cardioembolic stroke.[22,23]

The above mentioned points to the probably higher accuracy of three-dimensional echocardiography in left atrial appendage ejection fraction calculation compared to two-dimensional echocardiography. As opposed to two-dimensional echocardiography, three-dimensional echocardiography provides a homogeneous dataset in which volume measurements are independent of the irregularities of the left atrial appendage and motion of the heart. The echocardiographic data in this study were related to the left atrial appendage late peak emptying velocity. This is an accepted functional index of the left atrial appendage and in vivo there is no other method to test the feasibility of three-dimensional echocardiography measurements.

The optimal tomographic imaging plane of the left atrial appendage has not been sufficiently defined. Therefore, we assessed the effect of cutplane angulation on the relation between EFa and EFv. Area ejection fraction at 135° angulation was only associated with EFv. This might be taken into account when multiplane transoesophageal echocardiography is used for left atrial appendage area measurements. Our observation is in agreement with the results found by Chan et al.,[24] who demonstrated greater left atrial appendage neck width and cross-sectional area at 135° than at 45° or 90°.

The present study has some important limitations: three-dimensional echocardiography is still time-consuming, although, future development of faster computers, application of automatic border detection and on-line acquisition by real-time three-dimensional echocardiography will shorten the time needed for three-dimensional reconstruction. Although one could argue that peak emptying velocity can be measured much easier than volume and ejection fraction, Doppler flow measurement does not reflect the degree of left atrial appendage enlargement. This can be important because severely hypokinetic and dilated left atrial appendage pre-disposes to thrombus formation in the same way as left ventricular aneurysm predisposes to thrombus formation. Therefore, we suppose that left atrial appendage volume and ejection fraction calculations can be just as important just as left ventricular volume and ejection fraction measurements.

Well established conditions (i.e. left ventricular function, mitral stenosis and atrial fibrillation) which would have affected peak emptying velocity, showed no significant relation in this study. The explanation could be that only four patients with severely impaired and six patients with moderately impaired left ventricular

Table 2. Intra- and inter-observer study.

<table>
<thead>
<tr>
<th></th>
<th>EFv</th>
<th>EFa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intra-observer</td>
<td>Inter-observer</td>
</tr>
<tr>
<td>Mean</td>
<td>Difference ± SD</td>
<td></td>
</tr>
<tr>
<td>Variability (%)</td>
<td>8.8</td>
<td>22.8</td>
</tr>
<tr>
<td>Correlation coefficient (r)</td>
<td>0.97</td>
<td>0.89</td>
</tr>
</tbody>
</table>

EFv=percent volume ejection fraction; EFa=percent area ejection fraction.

Figure 3. Scatterplot of linear regression analysis of the left atrial appendage volume ejection fraction (EFv) and area ejection fraction (EFa) vs left atrial appendage late diastolic peak emptying velocity.

Table 2. Intra- and inter-observer study.
function were present in this study. Regarding mitral stenosis, only three patients with pure mitral stenosis were included, the remaining 17 patients having combined mitral stenosis and insufficiency. It is likely that this heterogeneous group of patients with mitral valve disease failed to show a haemodynamic effect of mitral stenosis on left atrial appendage function. A lack of correlation between peak emptying velocity and atrial fibrillation may result from a wide continuum of left atrial appendage contractile dysfunction in patients with atrial fibrillation, from relatively preserved contraction to complete paralysis of the appendage. Despite the above mentioned, to our knowledge, this is the first study which has proved the feasibility of three-dimensional echocardiography in the assessment of left atrial appendage mechanical function.

In conclusion, three-dimensional echocardiography in the assessment of left atrial appendage ejection fraction is feasible and has lower observer variability compared with two-dimensional echocardiography. It may complement two-dimensional echocardiography and Doppler echocardiography in the assessment of left atrial appendage mechanical function. Future developments will simplify the procedure and expand its clinical applicability.

References