

# RELATIONSHIP OF LEFT VENTRICULAR SIZE TO LEFT ATRIAL AND LEFT ATRIAL APPENDAGE SIZE IN SINUS RHYTHM PATIENTS WITH DILATED CARDIOMYOPATHY

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## Original paper

### SUMMARY

**Introduction:** Thromboembolic events are a frequent cause of mortality in patients with congestive heart failure. The aim of our study was to evaluate the relationship of left ventricular end diastolic diameter (LVEDD) to left atrial (LA) size and left atrial appendage (LAA) size in patients with dilated cardiomyopathy in sinus rhythm, as well as to determine the prevalence of thrombi in LV and LA/LAA. **Methods:** This was a prospective cross-sectional study, conducted from December 2009 until

December 2011. The study included 95 patients with dilated cardiomyopathy in sinus rhythm. Patients with swallowing problems, acute myocardial infarction, atrial fibrillation/flutter, severe systolic dysfunction, and/or patients who were taking oral anticoagulation therapy were excluded. **Results:** Mean patient age was  $58.6 \pm 12.2$  years and 68.4% were men. Mean LVEDD of our population was  $66.5 \pm 6.5$  mm, while mean LA atrium, LA volume and LAA maximal area were  $46 \pm 5.1$  mm,  $87.2 \pm 38.7$  cm<sup>3</sup> and  $4.7 \pm 1.2$  cm<sup>2</sup>, respectively. LA diameter ( $p < 0.001$ ) and

LAA maximal area ( $p = 0.01$ ) showed to be independent predictors of LV size. LV thrombus was detected in 13 (13.7%) patients, while LAA thrombus in 46 (48.4%) patients of our study population. **Conclusions:** In conclusion, dilated LV size is associated with enlarged LA and LAA size. On the other hand, dilation of LV, LA and LAA is related to high prevalence of left chamber cardiac thrombi. **Key words:** thrombus, dilated cardiomyopathy, left atrial appendage area.

## 1. INTRODUCTION

Dilated cardiomyopathy is characterized by enlargement of one or both ventricles associated by systolic and diastolic contractile impairment (1). Thromboembolic events are a frequent cause of mortality in patients with congestive heart failure, accounting for about 30% of such patients (2).

The aim of our study was to evaluate the relationship of left ventricular end diastolic diameter (LVEDD) to left atrial (LA) size and left atrial appendage (LAA) size in patients with dilated cardiomyopathy in sinus rhythm, as well as to determine the prevalence of thrombi in LV and LA/LAA.

Our hypothesis was built upon the following logics. Dilated cardiomyopathy is known to be correlated to intraventricular thrombosis. Dilated LV induces dilation of the LA, which in turn brings on the en-

largement of the LAA (Figure 1). We hypothesized that dilated LV will be associated to dilated LA and dilated LAA; this will contribute to favorable circumstances for LAA thrombus formation, as well.

## 2. PATIENTS AND METHODS

This was a prospective cross-sectional study, conducted from December 2009 until December 2011 in the settings of University Clinical Center of Kosova. The study included 95 patients with dilated cardiomyopathy in sinus rhythm. Exclusion criteria included patients with: swallowing problems, acute myocardial infarction, atrial fibrillation/flutter, severe systolic dysfunction, and/or patients who were taking oral anticoagulation therapy.

The study was approved by our Ethical Board and written informed consent was taken from every patient that entered the study.

Thorough demographic information, history data, physical examination, laboratory tests, ECG, chest X-ray, transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were acquired for every patient that entered our study.

Several previous ECGs along with the ECG of the day the patient was enrolled in the study were analyzed with the main aim of determining the sinus rhythm. To our best awareness patients that were included in the study did not have episodes of atrial fibrillation.

### 2.1. Echocardiography

TTE and TEE (Phillips iE 33) were performed in every patient.

TTE examinations and measurements were performed with the subject in the left lateral decubitus position, according to the recommendations of the American Society of Echocardiography (3). LVEDD, left

	n=95
Age, yr	58.64 ± 12.26
Female (%)	30/95 (31.58)
Current smokers (%)	28/95 (29.47)
Alcohol users (%)	8/95 (8.42)
Hypertension (%)	48/95 (50.53)
Diabetes Mellitus (%)	28/95 (29.47)
Dyslipidemia (%)	23/95 (24.21)
BMI, kg/m <sup>2</sup>	28.52 ± 4.05
Coronary artery disease (%)	55/95 (57.89)
Peripheral vascular disease (%)	5/95 (5.26)

**Table 1.** Baseline patient characteristics\* \*Data are presented as mean ± SD or No. (%).

	n=95
IVSd, mm	9.85 ± 2.01
PWd, mm	9.71 ± 1.46
LVEDD, mm	66.52 ± 6.15
LVESD, mm	53.59 ± 7.49
LVEF, %	38.87 ± 6.39
LA, mm	46.02 ± 5.07
LA area 4CH, cm <sup>2</sup>	25.15 ± 6.93
LA area 2CH, cm <sup>2</sup>	25.59 ± 6.31
Left atrial volume, cm <sup>3</sup>	87.22 ± 38.7
MR area, cm <sup>2</sup>	4.13 ± 3.15
LAA maximal area, cm <sup>2</sup>	4.71 ± 1.16
LAA minimal area, cm <sup>2</sup>	2.52 ± 1.43
LAA EF, %	47.84 ± 21.41

**Table 2.** Basic echocardiographic data of the study population\* \*Data are presented as mean ± SD. IVSd: diastolic interventricular septum; PWd: diastolic posterior wall; LVEDD: left ventricular end diastolic diameter; LVESD: left ventricular end systolic diameter; LV: left ventricular; EF: ejection fraction; LA: left atrium; CH: chamber; MR: mitral regurgitation; LAA: left atrial appendage.

ventricular end systolic diameter, septal and posterior wall thickness were measured from parasternal M-mode recordings according to standard criteria. LA diameter was measured at end-ventricular systole in parasternal short axis at the level of aortic valve. Measurement of LA volume was done with the area-length method using apical 4-chamber and apical 2-chamber views at ventricular end-systole (maximum LA size), while L was measured from back wall to line across hinge points of mitral valve. Subsequently, calculation of LA volume was obtained according to American Society of Echocardiography, with the following formula:  $8/3\pi[(A1)(A2)/(L)]$  (3). LV ejection fraction (EF%) was determined from apical views with a modified Simpson's rule.

Thrombus was defined as presence of distinct echogenic intracavity mass, identifiable in at least two

different views.

TEE was performed with multi-plane transesophageal transducer. Patients were in a fasted state before the procedure. Intraoral lidocaine spray and intravenous midazolam were administered to every patient. The procedure was performed by one cardiologist trained for the procedure and another experienced cardiologist observing it. Any discrepancy was resolved by the third cardiologist and consensus.

TEE projections and measurements were completed according to the recommendations (4).

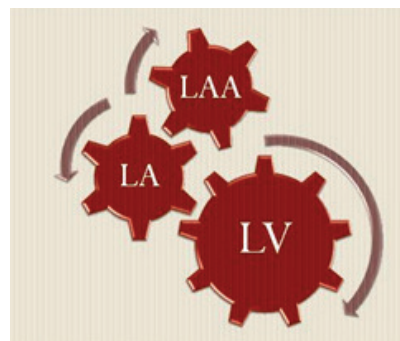
Maximum and minimum LAA area was measured by planimetry method, from the best obtained view. LAA area was measured from the top of the limbus of the upper pulmonary vein along the entire appendage endocardial border. The maximal area of the LAA was measured during LAA diastole, which corresponds to the onset of the ECG P wave, while the LAA minimal area was measured at R wave. The LAA EF was calculated from the following equation:  $LAAEF (\%) = 100 \times (LAA \max - LAA \min) / LAA \max$ .

	p
LA diameter	<0.001
LAA maximal area	0.01
Coefficient of determination ( $r^2$ )=0.27	
Adjusted for degrees of freedom: 0.25	
95% CI: $0.12 \leq r^2 \leq 0.42$	

**Table 3.** Multiple regression analysis for LVEDD. LVEDD: left ventricular end diastolic diameter; LA: left atrium; LAA: left atrial appendage.

### Statistical analysis

All data were expressed as mean ± standard deviation (SD) and percentages. Correlation of selected variables was estimated using Pear-



**Figure 1.** Hypothesis: Dilated LV induces dilation of LA, which in turn induces dilation of LAA.

son correlation test. Simple and multiple regression analyses were performed to determine if LA and LAA size were associated with LVEDD dimensions. Variables with a value of  $p < 0.05$  in simple regression were considered significant and included in the multivariate model. Non-significant variables were removed. All statistical analysis were performed using statistical software SPS, version 2.80, 2005.

### 3. RESULTS

Mean patient age was  $58.6 \pm 12.2$  years and 68.4% were men, whereas the rest of patients' baseline data are presented in Table 1.

Haemostatis tests were within normal range in all patients included in the study.

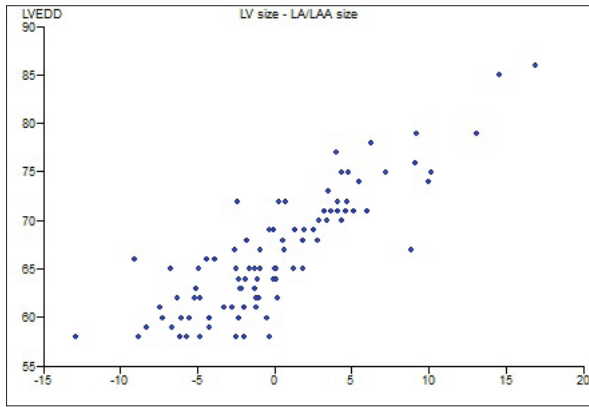
Mean LVEDD of our population with dilated cardiomyopathy was  $66.5 \pm 6.5$  mm, while mean LV EF was  $38.9 \pm 6.4$  %. Basic TTE and TEE parameters are shown in Table 2. LVEDD correlated significantly with LA diameter ( $r=0.47$ ,  $p < 0.001$ ), LA area at four-chamber view ( $r=0.53$ ,  $p < 0.001$ ), LA area at two-chamber view ( $r=0.49$ ,  $p < 0.001$ ), LA volume ( $r=0.45$ ,  $p < 0.001$ ), LAA maximal area ( $r=0.33$ ,  $p < 0.001$ ). Furthermore, LAA maximal area correlated significantly with all LA measurements, as follows: LA diameter ( $r=0.28$ ,  $p=0.003$ ), LA area at four-chamber view ( $r=0.31$ ,  $p=0.001$ ), LA area at two-chamber view ( $r=0.22$ ,  $p=0.02$ ), LA volume ( $r=0.22$ ,  $p=0.02$ ).

In a multiple regression analysis for LVEDD predictors we included only LA diameter (as most widely measured LA parameter in every day clinical practice) and LAA maximal area, thus avoiding the collinearity effect. Both, LA diameter ( $p < 0.001$ ) and LAA maximal area ( $p=0.01$ ), showed to be independent predictors of LV size (Table 3 and Figure 2).

LV thrombus was detected in 13 (13.7%) patients, while LAA thrombus in 46 (48.4%) patients of our study population.

### 4. DISCUSSION

Our hypothesis proved to be right, as LVEDD correlated significantly to LA and LAA size. In ad-



**Figure 2.** Diagram presenting LVEDD as a dependent variable and LA diameter and LAA area as predictors of LV size in a multiple regression model.

dition, LA diameter, LA area and LA volume demonstrated a significant correlation to LAA maximal area. Mean LVEDD of our patients with dilated cardiomyopathy was  $66.5 \pm 6.1$  mm, and mean LA diameter ( $46 \pm 5$  mm), which also resulted to be above the normal range. Dilated LV, LA and LAA are known to be associated with thromboembolic events. LV thrombus was found in around 14% of our patients, whereas LAA thrombus was found 3.5 fold more frequently.

In this context, Dittrich et al. also found that LVEDD dimension correlates well with LA diameter in adult patients with atrial fibrillation (5). There are also data that illustrate that an enlarged LA on TEE is associated significantly with enlarged LAA (6). Earlier we reported that LAA maximal area was significantly larger in patients with dilated cardiomyopathy compared to the controls, however patients with atrial fibrillation were also included in the study, which might have influenced enlargement of LAA area (7). At present, we are not aware of any study that correlated directly LVEDD to LAA size. Furthermore, our current study demonstrated that LAA maximal area measured by TEE was an independent predictor of LV size.

Gottdiener et al. had found thrombus in around 36% of patients with chronic dilated cardiomyopathy (8). The annual risk of systemic embolization in patients with dilated cardiomyopathy is 1.4-12% (8, 9).

Dilated LA is also shown to be an independent risk factor for stroke

in several studies. Framingham Heart Study investigators found that LA size remained a significant predictor of stroke in men and death in both genders after adjusting for age, hypertension, diabetes, smoking, left ventricular hypertrophy, prevalent atrial fibrillation, and prevalent congestive heart failure or myocardial infarction (10). The Northern Manhattan Stroke Study (NOMAS) also showed that LA size was associated with an increased risk of ischemic stroke (11). However, some studies have shown that the relation of LA size to stroke was attenuated after addition of LV hypertrophy and low LV EF (12).

LAA dilation is a widely recognized factor that contributes in LAA thrombus formation in patients at sinus rhythm and atrial fibrillation (6, 13). In a study where intravenous contrast agent was used, the LAA is shown to be significantly larger in patients with thrombus than in those without (14). LAA area of  $>6$  cm<sup>2</sup> is considered a risk factor for arterial embolic events (15).

## 5. CONCLUSIONS

In conclusion, dilated LV size is associated with enlarged LA and LAA size. On the other hand, dilation of LV, LA and LAA is related to high prevalence of left chamber cardiac thrombi.

### Abbreviations


- ECG - Electrocardiography.
- EF - Ejection fraction.
- LA - Left atrium/atrial.
- LAA - Left atrial appendage.
- LV- Left ventricle/ventricular
- LVEDD - Left ventricular end - diastolic diameter.
- TEE - Transesophageal echocardiography.
- TTE - Transthoracic echocardiography.

**Conflict of interest: none declared.**


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