Bratisl Lek Listy 2009; 110 (3)
146 – 151

CLINICAL STUDY

Left atrial volume as a predictor of heart function

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Abstract: *Objectives:* This study was designed to identify an association between left atrial volume and systolic and diastolic functions of the left ventricle.
Background: Several studies have shown a relationship between the left atrial volume and different cardiovascular risk factors.
Methods: Transthoracic echocardiographic results of 268 patients (136 women and 132 men, mean age 60.2±17.3 years) were studied retrospectively. Key echocardiographic variables of systolic and diastolic function were related to the left atrial volume and its indexed value.
Results: The mean indexed left atrial volume in a subgroup of patients with normal echocardiography, was 25.3±6.7 ml/m^2. Left atrial volume significantly (p<0.0001) increased in deteriorating diastolic function (impaired relaxation, pseudonormalized pattern, and restrictive physiology): 33.6±11.6, 48.7±21.8 and 84.5±60.5 ml/m^2, respectively. There were also significant (p=0.0001) differences in cases with normal systolic function (EF>50 %) and systolic dysfunction (EF<50 %): 37.9±24.1 vs 54.9±34.7 ml/m^2. There were no significant differences in the left atrial volumes (33.1±10.9 ml/m^2 and 38.3±15.4 ml/m^2, p=0.13) in patients with normal systolic function and impaired relaxation compared to patients with systolic dysfunction. However, in both cases these values were different from those with normal echocardiography (p<0.0001). In multiple regression analysis the best predictor of enlarged left atrial volume was the left ventricular mass.
Conclusion: We found a strong association between left atrial volume and left ventricular systolic and diastolic dysfunction. The strongest association appeared between increasing left atrial volume and left ventricular mass *(Tab. 2, Fig. 4, Ref. 26)*. Full Text (Free, PDF) *www.bmj.sk.*
Key words: left atrial volume, left ventricular systolic dysfunction, left ventricular diastolic dysfunction.

Left atrial size as assessed by M-mode echocardiography has been proved as a strong prognostic marker of cardiovascular events (1). However, it has only recently been shown that left atrial volume (LAV) and its indexed value (LAVI) more precisely determine its size as a single linear measurement from M-mode or two-dimensional echocardiography (2).

We undertook this study to determine whether LAV/LAVI is altered by left ventricular systolic and diastolic dysfunction.

Patients and methods

We retrospectively analysed 448 transthoracic echocardiographic findings recorded from January to September 2006. Standard transthoracic two-dimensional echocardiography and Doppler examination were performed by one echocardiographer (VG) according to established clinical laboratory practice using two commercially available instruments: Siemens Sequoia (Siemens Medical Solutions), and Vivid Five (GE Medical Systems).

Of these, 268 individuals (mean age 60.2±17.3 years, 136 women and 132 men) were selected after obtaining the key echocardiographic variables of systolic and diastolic function. Patients with mitral stenosis and left atrial myxoma were excluded.

Left ventricular ejection fraction (EF) was measured using the modified biplane Simpson's rule. Left ventricular mass (LVM) and its indexed value (LVMI) was assessed by the method proposed by Devereux et al (3). LAV was measured by biplane Simpson's method in apical four and two-chamber views and indexed to body surface area. Timing of the measurement was defined at maximal expansion of left atrium (Fig. 1). Left ventricular diastolic filling pattern was obtained by pulse-wave Doppler. Peak velocity of early filling (E wave), peak velocity at atrial contraction (A wave), their ratio (E/A), deceleration time of early filling, and isovolumic relaxation time (IVRT) were measured. In addition, flow propagation velocity (Vp) of the left ventricle was assessed using color Doppler M-mode echocardiography (4, 5). Impaired relaxation was defined as follows: E/A <1, E wave deceleration time >240 ms, IVRT >100 ms. Pseudonormalized pattern: E/A >1, E wave deceleration time normal (160–240 ms), IVRT normal (60–100 ms), Vp <45 cm/s. Restric-

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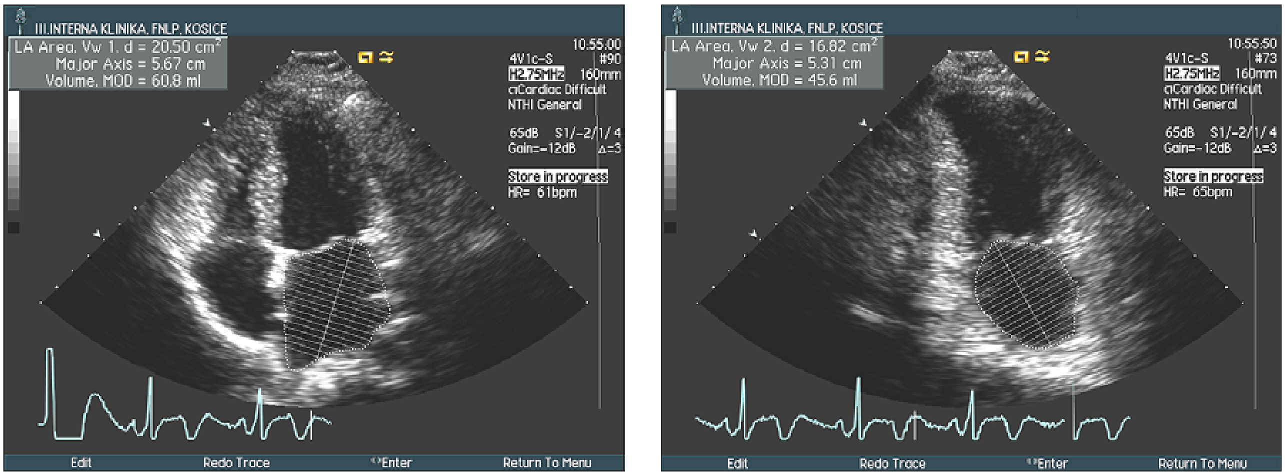

Fig. 1. Measurement of the left atrial volume by biplane Simpson's method in apical four (A) and two-chamber view (B).

tive physiology was: E/A >2, E wave deceleration time <160 ms, IVRT <60 ms, Vp <45 cm/s. Mitral and aortic regurgitation were assessed semiquantitatively by color Doppler flow mapping and graded as mild, moderate or severe.

Tei index, an indicator of combined ventricular systolic and diastolic function was also evaluated. It was assessed by Doppler as the time interval from end to onset of left ventricular inflow waveforms (a), left ventricular ejection time (b), and calculated according to the formula (a – b)/b (6).

We defined several subgroups of patients: 1) With "structurally normal heart": ejection fraction >50 %, absence of left and right ventricular hypertrophy, absence of wall motion abnormalities, absence of aortic and mitral valve stenotic or regurgitant lesions, absence of tricuspid and pulmonary stenotic or regurgitant lesions, absence of ventricular septal defect or atrial septal defect, and absence of a prosthetic valve. 2) Patients with different forms of diastolic dysfunction as mentioned above (impaired relaxation, pseudonormalized pattern, and restrictive physiology). 3) Patients with preserved systolic function (EF >50 %) and systolic dysfunction (EF <50 %). 4) Patients with impaired relaxation combined with systolic dysfunction (EF <50 %) and preserved systolic function (EF >50 %).

Statistical analysis

Continuous variables are expressed as mean±SD. Differences among the groups were examined by a paired or unpaired *t* test. Several groups were compared by ANOVA test. Significance was set for p value <0.05. Multivariate logistic regression analysis was used to explore associations of LAV/LAVI to parameters of left ventricular systolic and diastolic functions.

Results

The analysed echocardiographic variables are presented in Table 1. The distributions of LAVI across different forms of systolic and diastolic dysfunctions are shown in Figures 2–4. In the whole group of patients, multiple linear regression analysis revealed a significant relation of LAVI to age (p=0.04), EF (p=0.008), Tei index (p=0.03), ratio of E/A (p=0.03), and grade of mitral regurgitation (p=0.02). There were no relations of LAVI to other parameters: LVM (p=0.3), LVMI (p=0.9), E wave (p=0.5), E wave deceleration time (p=0.8), A wave (p=0.05), IVRT (p=0.8), Vp (p=0.4), E/Vp ratio (p=0.3), and aortic regurgitation (p=0.6).

Table 1 Mean ± SD of the analysed echocardiographic variables.

	Age	LVM (g)	LVMI (g/m²)	LAV (ml)	LAVI (ml/m²)	EF (%)	TEI	E (cm/s)	DT E (ms)	A (cm/s)	E/A	IVRT (ms)	Vp (cm/s)	E/Vp
Normal (n=53)	43.2±15.8	144.7±43.7	78.2±21.8	46.2±12,6	25.3±6.7	60.4±7.6	0.2±0.1	79.6±16.7	186.7±36.8	64.3±14.9	1.2±0.4	88±15	54±14.4	1.5±0.4
Impaired relaxation (n=116)	66.8±11.2	208.9±62.6	112±32.7	62.7±20,7	33.6±11.6	55.4±8.2	0.4±0.2	59.5±15.1	260.2±59.7	84.1±16.8	0.7±0.1	114.1±25.1	39.1±0.6	1 .7±0.6
Pseudonormalized pattern (n=51)	64.4±15.9	273.4±98.9	150.3±54.6	90.2±43.8	48.7±21.8	35.9±11.7	0.4±0.3	76±11.7	152.3±53.8	67.2±19.5	1.1±0.4	85.4±33.3	33.7±14.3	2.6±1.22
Restrictive physiology (n=48)	66.1±13.3	330.4±113.4	165±46.1	172.1±139.9	84.5±60.5	35.5±14.6	0.7±0.4	123.7±17.7	105±23.5	48.7±14.8	2.6±0.6	55.5±15.1	35.4±10. 1	3.7±1.1
EF > 50% (n=226)	59.9±17	190.2±69.7	101.3±34.9	70±42.7	37.9±24.1	58.4±5	0.3±0.1	74.8±22.8	210.7±66.2	75±22.2	1±0.5	99.2±25.5	45.8±15.9	1.8±0.9
EF < 50% (n=42)	68.6±12	276.2±94.7	149.7±47.1	105±75.4	54.9±34.7	34.9±7.5	0.6±0.2	79.3±29.6	189.7±83.4	70.6±23.5	1.2±0.9	97.7±36.4	31.9±11.6	2. 6±1.2
Impaired relaxation and EF > 50% (n=95)	66.7±11.5	199.9±55.8	106.3±26.6	61.8±19.4	33.1±10.9	58±5	0.3±0.1	60.9±14.7	259.6±58.7	84.6±16.8	0.7±0.1	113±25.1	40.4±17	1.7±0. 6
Impaired relaxation and EF < 50% (n=21)	67.6±9.6	271.4±74.6	148.6±45.7	70.2±27.3	38.3±15.4	39±6	0.6±0.2	51.1±15.6	264.3±70.7	82.5±16.4	0.6±0.1	120.1±25.3	31.3±13.6	1.8 ±0.6

LVM = left ventricular mass, LVMI = left ventricular mass index, LAV = left atrial volume, LAVI = left atrial volume index, EF = ejection fraction, TEI = Tei index, E = E wave, DT E = E wave deceleration time, A = A wave, IVRT = isovolumic relaxation time, Vp = flow propagation velocity.

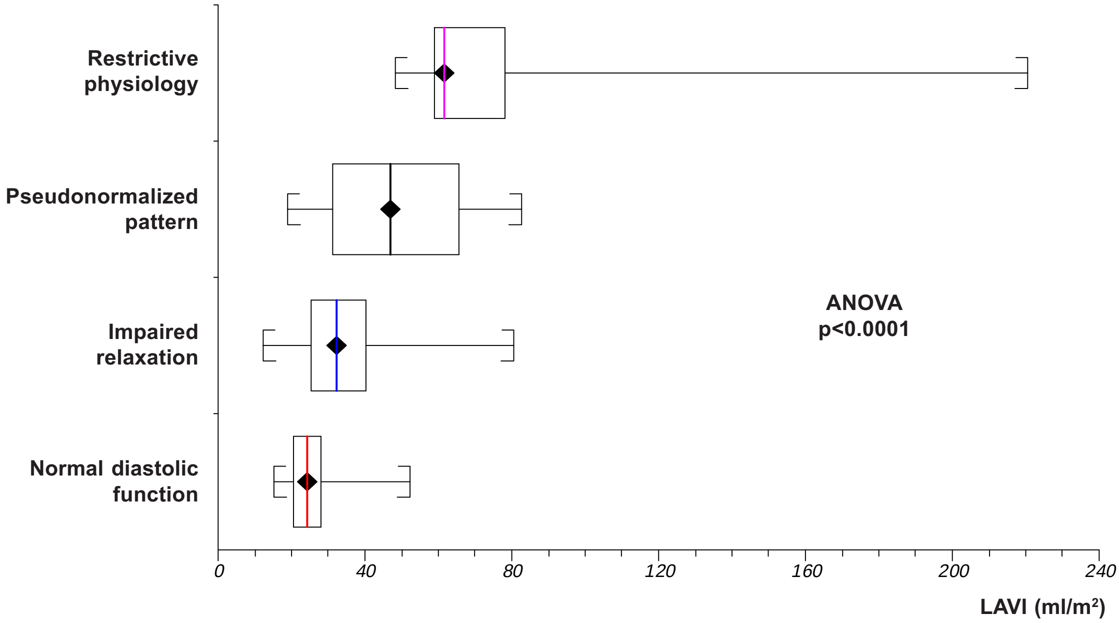

Fig. 2. Box and whisker plots of the relation between various forms of diastolic dysfunction and left atrial volume index (LAVI).

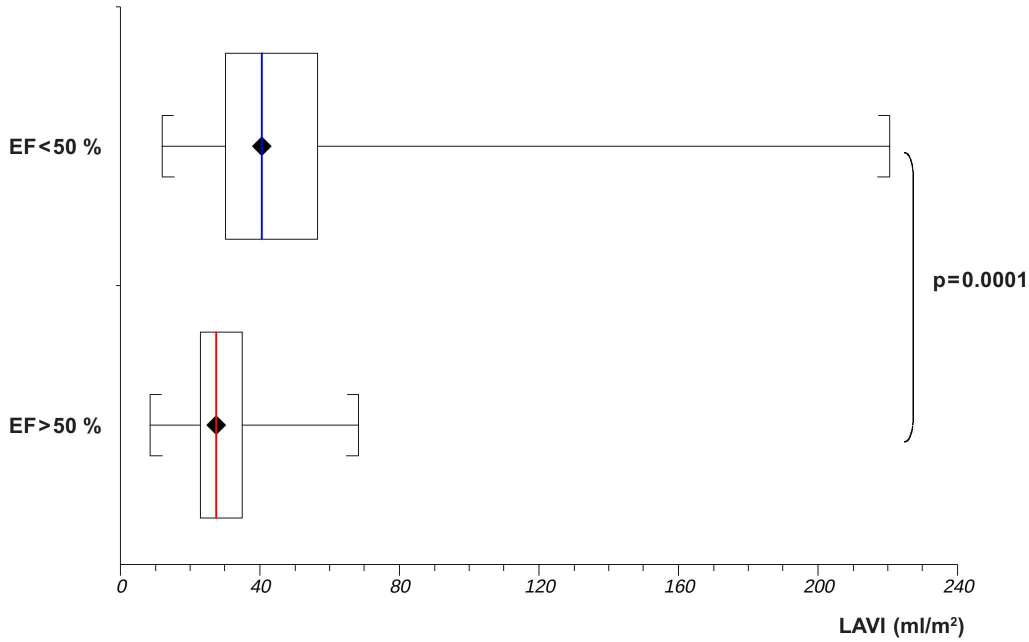

Fig. 3. Box and whisker plots of the relation between left atrial volume index (LAVI) and systolic dysfunction and normal systolic function.

In a subgroup of patients with impaired relaxation, LAVI was significantly related to: age (p=0.03), LVM (p=0.02), LVMI (p=0.002), Tei index (p=0.005), and mitral regurgitation (p=0.04). There were no relations of LAVI to other parameters in this subgroup of patients: EF (p=0.08), E wave (p=0.6), E wave deceleration time (p=0.5), A wave (p=0.3), E/A ratio (p=0.2), IVRT (p=0.7), Vp (p=0.6), E/Vp ratio (p=0.8), and aortic regurgitation (p=0,9).

In a subgroup of patients with pseudonormalized pattern of diastolic dysfunction, LAVI was significantly related only to LVM (p<0.0001) and LVMI (p<0.0001). In multiple comparison (Sheffé test), LAVI was not related to age (p>0,9), EF (p=0.9), Tei index (p=0.2), E wave (p=0.8), E wave deceleration time (p=0.07), A wave (p>0,9), E/A ratio (p=0.3), IVRT (p=0.9), Vp (p=0.9), E/Vp ratio (p=0.3), mitral regurgitation (p=0.3), and aortic regurgitation (p=0.2).

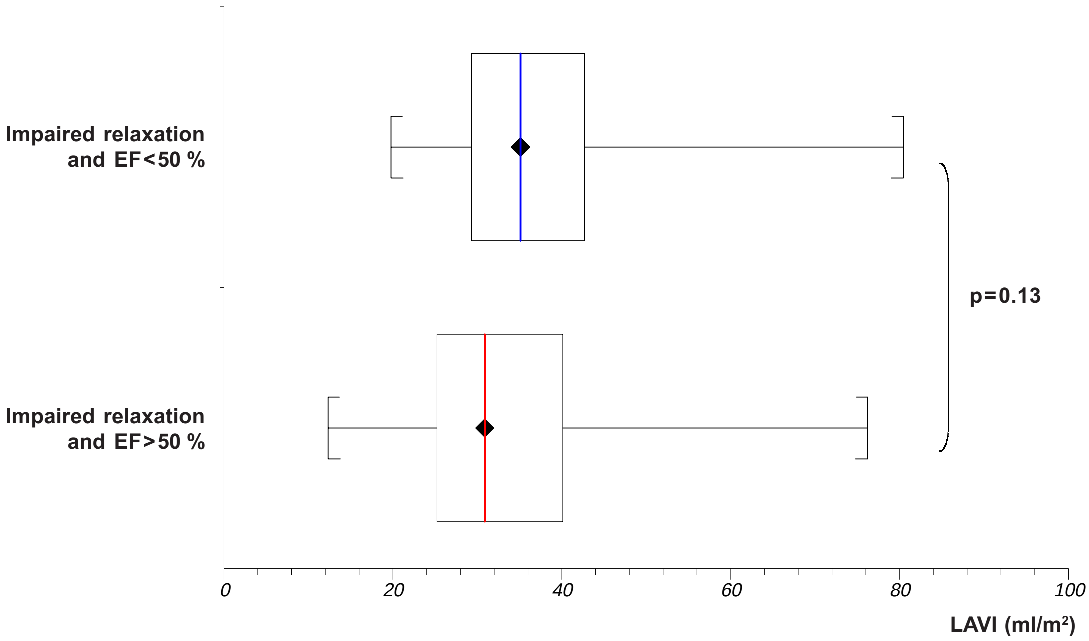

Fig. 4. Box and whisker plots of the relation between left atrial volume index (LAVI) and impaired relaxation with systolic dysfunction and preserved systolic function.

In a subgroup of patients with restrictive physiology, LAVI was significantly related only to LVM (p<0.0001) and LVMI (p=0.02). There was no relation of LAVI to: age (p>0.9), EF (p=0.8), Tei index (p=0.08), E wave (p=0.9), E wave deceleration time (p=0.9), A wave (p=0.9), E/A ratio (p=0.1), IVRT (p=0.9), Vp (p=0.7), E/Vp ratio (p=0.1), mitral regurgitation (p=0.1), aortic regurgitation (p=0.08).

Relations between LAVI and the analysed echocardiographic parameters are presented in Table 2.

Discussion

The volume of left atrium is an important biomarker of the heart function. Although left atrial size assessed as a single linear measurement of the anteroposterior diameter obtained from M-mode or two-dimensional echocardiography was shown as an independent prognostic indicator of cardiovascular events, LAV/LAVI has been shown as a stronger predictor (7–10). Left atrium is considered as a "barometer" of the heart function. Doppler assessment of the transmitral inflow provides information related to instantaneous pressures in the left ventricle and atrium. LAV/LAVI is a measure of chronicity and severity of systolic and diastolic dysfunction and is less load-dependent. It has been linked to "glycosylated hemoglobin" in the assessment of left ventricular filling pressures.

There are different methods in the assessment of LAV using two-dimensional echocardiography (left atrial planimetry, area-length method, monoplane or biplane Simpson's method). Several studies have proved that LAV assessed by three-dimensional echocardiography, which can be considered as a gold standard

Table 2 P values of the relations between left atrial volume index (LAVI) and echocardiographic variables in different forms of diastolic dysfunction

	All	Impaired relaxation	Pseudonormalized pattern	Restrictive physiology
Age	**0.04**	**0.03**	>0.9	>0.9
LVM (g)	0.3	**0.02**	**<0.0001**	**<0.0001**
LVMI (g/m²)	0.9	**0.002**	**<0.0001**	**0.02**
EF (%)	**0.008**	0.08	0.9	0.8
Tei index	**0.03**	**0.005**	0.2	0.08
E (cm/s)	0.5	0.6	0.8	0.9
DT E (ms)	0.8	0.5	0.07	0.9
A (cm/s)	0.05	0.3	>0.9	0.9
E/A	**0.03**	0.2	0.3	0.1
IVRT (ms)	0.8	0.7	0.9	0.9
Vp (cm/s)	0.4	0.6	0.9	0.7
E/Vp	0.3	0.8	0.3	0.1
Mitral regurgitation	**0.02**	**0.04**	0.3	0.1
Aortic regurgitation	0.6	0.9	0.2	0.08

in the assessment of LAV, is significantly related to the methods of two-dimensional echocardiography. Therefore, two-dimensional echocardiographic methods of LAV measurements can be used for the follow-up evaluation in daily clinical practice (11–14).

In a population-based study by Pritchett et al (n=767, age ≥45 years) with no cardiovascular disease and normal systolic and diastolic function, the normal value for LAV indexed to body surface area was 21.46±5.14 ml/m^2. In obese participants (BMI >28 kg/m^2), LAVI was larger (22.85±5.40 ml/m^2) (15). In our study in case of „structurally normal“ echocardiographic findings, LAVI was slightly larger as in the above mentioned study (25.3±6.7 ml/m^2). The effect of normal aging on LAV in different studies is controversial (16, 17). In our study we found a significant relation of LAV to age when analysing the whole group and patients with impaired relaxation, however, in other subgroups we did not find any relation of LAV to age. Left atrial function is not influenced by sex (18).

LAV in relation to systolic and diastolic function is determined by its active and passive emptying (19). Left atrial emptying is decreased in patients with systolic and diastolic dysfunction, which leads to enlarged LAV (20, 21). It has been shown that abnormal left atrial histology may represent a precursor state for left atrial dilatation (22). Left atrium plays an important role in failing heart, including patients with systolic dysfunction but also patients with diastolic dysfunction and preserved systolic function (23).

LAV above 60 ml or its indexed value above 30–40 ml/m^2 is an important predictor of many cardiovascular events (24). Similarly, LAV >32 ml/m^2 is an independent predictor of postoperative and recurrent atrial fibrillation (25). The echocardiographic substudy of the GISSI trial proved in low-risk acute myocardial infarction patients the existence of not only left ventricular remodeling but also left atrial remodeling which was demonstrated by increased LAV (26).

In our study we analysed the relation between LAV and each of both, systolic and diastolic functions. In a subgroup of patients with normal echocardiography, the mean indexed LAV was 25.3±6.7 ml/m^2. LAV significantly increased in case of deteriorating diastolic function (impaired relaxation, pseudonormalized pattern, and restrictive physiology): 33.6±11.6 ml/m^2, 48.7±21.8 ml/m^2, and 84.5±60.5 ml/m^2, respectively, all p<0.0001. There was also a significant difference in LAV in case of normal systolic function (EF >50 %) and systolic dysfunction (EF <50 %): 37.9±24.1 ml/m^2 versus 54.9±34.7 ml/m^2 (p=0.0001). When comparing the patients with preserved systolic function and impaired relaxation with those suffering from systolic dysfunction there were no significant differences in LAV (33.1±10.9 ml/m^2 and 38.3±15.4 ml/m^2, p=0.13), however, in both cases the values were significantly higher than in case of „structurally normal“ echocardiographic findings (p<0.0001). In multiple regression analysis the best predictor of enlarged LAV was the LVM.

The limitation of our study is that we did not use pulmonary venous flow and tissue Doppler imaging for comprehensive assessment of diastolic dysfunction. However, flow propagation velocity (Vp) of the left ventricle in our experience can be helpful in the differentiation of different forms of diastolic dysfunction, mainly to distinguish the pseudonormalized pattern from normal diastolic flow.

Conclusion

We found a strong association between increased LAV/LAVI and deteriorated systolic and diastolic function of the left ventricle. The strongest association was found between enlarged LAV/LAVI and mass of the left ventricle.

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Received January 18, 2008.
Accepted December 18, 2008.