HEART FAILURE AND CARDIOMYOPATHY

Left atrial volume provides independent and incremental information compared with exercise tolerance parameters in patients with heart failure and left ventricular systolic dysfunction

Andrea Rossi, Mariantonietta Ciccoira, Stefano Bonapace, Giorgio Golia, Luisa Zanolla, Lorenzo Franceschini, Corrado Vassanelli

Heart 2007;93:1420–1425. doi: 10.1136/hrt.2006.101261

See end of article for authors' affiliations

Correspondence to:
Dr A Rossi, Divisione di
Cardiologia Ospedale
Maggiore, P.le Stefani, 1,
37126 Verona, Italy;
andrea.rossi@univr.it

Accepted 3 October 2006
Published Online First
12 December 2006

Objective: Left atrial volume (LAV) is a powerful predictor of outcome in patients with chronic heart failure (CHF) independently of symptomatic status, age and left ventricular (LV) function. It is unknown whether LAV provides independent and incremental information compared with exercise tolerance parameters.

Methods: 273 patients with CHF (mean (SD) 62 (9) years; 13% female) prospectively underwent echocardiography and exercise testing with maximal oxygen consumption (VO_2). The primary end point was composite and included cardiac death, hospitalisation for worsening heart failure or cardiac transplantation.

Results: At Cox proportional hazard analysis, LAV normalised for body surface area (LAV/BSA) was strongly associated with mortality (hazard ratio (HR) = 1.027 (95% CI 1.018 to 1.04), $p < 0.001$). The predictive value of LAV/BSA was independent of VO_2 and LV ejection fraction (EF) (HR = 1.014 (1.002 to 1.025), $p = 0.02$; HR = 0.95 (0.91 to 0.99), $p = 0.02$; HR = 0.89 (0.82 to 0.98), $p = 0.02$ for LAV/BSA, EF and VO_2 , respectively). Receiver operator characteristic (ROC) curve analysis identified the best cut-off values for prediction of the end point. LAV/BSA > 63 ml, EF $< 30\%$ and $\text{VO}_2 < 16$ ml/kg/min were considered to be risk factors. Patients with three risk factors had an HR of 38 (95% CI 11 to 129) compared with patients with no risk factors.

Conclusion: LAV provides powerful prognostic information incrementally and independently of VO_2 . LAV, EF and VO_2 can be used to build a risk prediction model, which can be used clinically.

In patients with chronic heart failure, echocardiography is of fundamental importance in studying the mechanism and defining the severity of the disease. In the presence of dilated and hypocontractile left ventricle, Doppler-derived measures of left ventricular (LV) diastolic function have been shown to predict cardiovascular mortality and morbidity.^{1–2} However, because of the strong load dependency of these measures, attention has also focused on other markers of diastolic dysfunction, such as left atrial volume (LAV). It has recently been shown that LAV is closely associated with LV diastolic function.^{3–4} LAV provides a sensitive morphophysiological expression of the severity of LV dysfunction and seems to be a useful index of cardiovascular risk.⁵ We and others have recently demonstrated that left atrial enlargement is a powerful marker of poor prognosis in patients with chronic heart failure.^{6–11} It should be acknowledged that the left atrium may dilate for reasons other than diastolic dysfunction, such as left ventricular remodelling, mitral regurgitation or atrial fibrillation.^{6–12–14} This is noteworthy because these pathophysiological variables are all associated with poor prognosis.^{15–17} Consequently, the left atrium might be a unifying factor among multiple causes of impaired survival, and this might explain its considerable prognostic power.

Before LAV can be widely accepted as a simple marker of outcome, however, there is a need to verify whether it provides prognostic information independently of parameters obtained by cardiopulmonary exercise testing. Peak oxygen consumption (VO_2) and minute ventilation-carbon dioxide production ($\text{VE}-\text{VCO}_2$) have become the most widely used markers for assessing the clinical severity of the disease and for selecting patients for

heart transplantation.^{18–19} It is also important to ascertain whether LAV provides prognostic information about the mode of death. Therefore the hypotheses underlying this prospective study were (a) LAV predicts prognosis, independently of and incrementally to that obtained using routine cardiopulmonary exercise testing such as peak oxygen consumption (VO_2) and $\text{VE}-\text{VCO}_2$; (b) LAV provides prognostic information about different modes of death in patients with chronic heart failure.

METHODS

The patients were recruited prospectively and consecutively from those routinely referred to the outpatient clinic of Verona City Hospital with a diagnosis of chronic heart failure (ie, heart failure which had lasted for more than 1 year) and LV systolic dysfunction (LV end-diastolic volume > 70 ml/m² and ejection fraction (EF) $< 50\%$). All patients had a complete Doppler echocardiographic examination in our echocardiography laboratory. On the same morning, patients underwent exercise testing with gas exchange monitoring. Follow-up information was obtained from clinical records, death certificates and correspondence.

The primary end point was composite and included cardiac death, hospitalisation for worsening of heart failure or cardiac

Abbreviations: AUC, area under the curve; BNP, brain natriuretic peptide; BSA, body surface area; DTE, deceleration time; EF, ejection fraction; HR, hazard ratio; LAV, left atrial volume; LV, left ventricular; ROC, receiver operator characteristic; VE, minute ventilation; VCO_2 , carbon dioxide production; VO_2 , maximal oxygen consumption

Table 1 Clinical and echocardiographic characteristics of the overall population and the subgroups of patients, divided according to survival status

Characteristics	Overall	Without events	With events	p Value
Age (years)	62 (9)	59 (13)	63 (14)	0.08
QRS duration (ms)	124 (32)	122 (34)	126 (27)	0.5
Ischaemic aetiology	61	70	58	0.08
NYHA III–IV (%)	33	23	56	<0.001
AFib (%)	12	8	18	0.03
ACE inhibitor (%)	90	91	90	0.9
β Blockers (%)	72	74	68	0.6
ARBs (%)	8	5	9	0.4
Spironolactone (%)	27	24	37	0.1
AICD	18	16	25	0.2
BPS (mm Hg)	126 (14)	126 (13)	125 (16)	0.6
BPD (mm Hg)	79 (8)	79 (8)	77 (8)	0.06
Na	140 (2.8)	140 (2.7)	139 (3.1)	0.055
K	4.5 (2.4)	4.5 (2.7)	4.4 (0.5)	0.7
Creatinine	106 (32)	104 (30)	114 (37)	0.03
VO ₂	16.2 (4.5)	17 (4.5)	13.4 (3.2)	<0.001
VE–VCO ₂ slope	37 (6)	36 (6)	40 (7)	<0.001
RQ	1.14 (0.1)	1.15 (0.12)	1.14 (0.1)	0.5
Duration of exercise (min)	9.4 (2.4)	9.8 (2.2)	8.0 (2.3)	<0.001
LAD/BSA (mm/m ²)	23 (3.7)	23 (3.6)	25 (3.3)	0.005
LAV/BSA (ml/m ²)	57 (25)	52 (20)	71 (34)	<0.001
LVMAS/BSA (g/m ²)	184 (57)	178 (55)	201 (60)	0.04
LVD/BSA (ml/m ²)	143 (50)	139 (51)	156 (47)	<0.05
LVS/BSA (ml/m ²)	98 (45)	94 (45)	111 (40)	0.02
CI (l/min/m ²)	2.6 (0.5)	2.7 (0.5)	2.6 (0.6)	0.4
EF (%)	33 (8)	34 (8)	30 (7)	<0.001
E (m/s)	0.64 (0.3)	0.6 (0.2)	0.78 (0.3)	<0.001
E/A (ratio)	1.19 (1.2)	1.08 (0.9)	1.6 (1.7)	0.01
DTE (ms)	212 (81)	223 (78)	172 (78)	<0.001
RMFP (%)	18	12	57	<0.001
MR (scale 0–6)	1.2 (1.1)	1.0 (0.9)	1.8 (1.3)	<0.001

Results are shown as mean (SD) unless stated otherwise.

NYHA, New York Heart Association; AFib, atrial fibrillation; ARBS, angiotensin receptor blockers; AICD, automatic intracardiac defibrillator; BPS, systolic blood pressure; BPD, diastolic blood pressure; VO₂, maximal oxygen consumption; VE–VCO₂ ventilatory response to exercise; RQ, respiratory ratio; LAD/BSA, left atrial diameter normalised for body surface area; LAV/BSA, left atrial volume normalised for body surface area; LVMAS/BSA, left ventricular mass normalised for body surface area; LVD/BSA, left ventricular diastolic volume normalised for body surface area; LVS/BSA, left ventricular systolic volume normalised for body surface area; CI, cardiac index; EF, ejection fraction; E, E-wave velocity; DTE, deceleration time; RMFP, restrictive mitral filling pattern; MR: mitral regurgitation.

transplantation. Secondary end points were considered to be cardiac death and sudden death.

Patients who died from non-cardiac causes were censored as alive on the date of death.

In the event of death, the underlying cause was obtained from the hospital chart or from interviews with the referral doctor or relatives. Deaths were classified as cardiac death, sudden death, or death resulting from other causes. Sudden

Table 2 Cox proportional hazard model for predictors of primary and secondary end points (univariate analysis)

Characteristics	Cardiac death and CHF		Cardiac death		Sudden death	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Age	1.017 (0.99 to 1.024)	0.2	1.008 (0.98 to 1.036)	0.5	1.008 (0.97 to 1.044)	0.6
QRS	1.002 (0.99 to 1.01)	0.5	1.005 (0.99 to 1.02)	0.3	1.003 (0.99 to 1.02)	0.6
NYHA	2.7 (1.77 to 4.11)	<0.001	2.0 (1.21 to 3.31)	0.007	1.45 (0.79 to 2.65)	0.2
AFib	1.7 (0.95 to 3.16)	0.07	2.2 (1.005 to 4.83)	0.05	2.67 (1.06 to 6.75)	0.04
Na	0.93 (0.86 to 1.01)	0.09	0.95 (0.86 to 1.05)	0.3	1.013 (0.88 to 1.16)	0.6
K	1.01 (0.86 to 1.19)	0.8	0.99 (0.77 to 1.30)	0.99	0.99 (0.75 to 1.31)	0.8
Creatinine	1.006 (1.00 to 1.01)	0.03	1.003 (0.99 to 1.01)	0.4	0.99 (0.98 to 1.01)	0.8
VO ₂	0.83 (0.78 to 0.88)	<0.001	0.84 (0.78 to 0.91)	<0.001	0.88 (0.81 to 0.92)	0.001
VE–VCO ₂	1.09 (1.05 to 1.13)	<0.001	1.09 (1.04 to 1.14)	<0.001	1.042 (0.98 to 1.11)	0.2
LVMAS/BSA	1.007 (1.002 to 1.01)	0.007	1.008 (1.002 to 1.01)	0.01	1.007 (1.00 to 1.02)	0.07
LAD/BSA	1.14 (1.05 to 1.25)	0.02	1.14 (1.02 to 1.27)	0.02	1.103 (0.96 to 1.27)	0.2
LVD/BSA	1.006 (1.001 to 1.01)	0.02	1.007 (1.00 to 1.013)	0.03	1.005 (0.99 to 1.015)	0.1
LVS/BSA	1.007 (1.002 to 1.01)	0.007	1.008 (1.002 to 1.02)	0.01	1.006 (0.99 to 1.012)	0.2
EF	0.96 (0.91 to 0.97)	<0.001	0.93 (0.89 to 0.97)	0.001	0.93 (0.88 to 0.98)	0.007
LAV/BSA	1.027 (1.018 to 1.04)	<0.001	1.026 (1.015 to 1.04)	<0.001	1.027 (1.014 to 1.04)	<0.001
E	6.65 (3.13 to 14.1)	<0.001	7.86 (3.28 to 18.8)	<0.001	6.7 (2.27 to 19.8)	<0.001
E/A	1.36 (1.14 to 1.61)	0.001	1.43 (1.19 to 1.72)	0.001	1.32 (1.01 to 1.72)	0.04
DTE	0.989 (0.98 to 0.99)	<0.001	0.99 (0.98 to 0.993)	0.001	0.99 (0.98 to 0.999)	0.02
RMFP	3.5 (1.99 to 6.2)	<0.001	3.99 (1.92 to 8.3)	0.001	3.09 (1.24 to 7.74)	0.02
MR	1.6 (1.34 to 1.97)	<0.001	1.59 (1.26 to 2.01)	<0.001	1.55 (1.16 to 2.07)	0.003

CHF, chronic heart failure; HR, hazard ratio. Other abbreviations as in table 1.

Table 3 Cox proportional hazard model for predictors of survival free of hospitalisation (multivariate analysis)

Characteristics	HR (95% CI)	p Value
<i>Model A</i>		
NYHA	1.7 (1.04 to 2.95)	0.04
LAV/BSA	1.014 (1.002 to 1.025)	0.02
EF	0.95 (0.91 to 0.99)	0.02
VO ₂ max	0.89 (0.82 to 0.98)	0.02
RMFP	1.2 (0.69 to 2.53)	0.5
MR	1.11 (0.84 to 1.47)	0.4
<i>Model B</i>		
NYHA	2.1 (1.3 to 3.4)	0.004
LAV/BSA	1.013 (1.001 to 1.025)	0.03
EF	0.95 (0.91 to 0.99)	0.03
VE-VCO ₂	1.038 (0.99 to 1.08)	0.1
RMFP	1.3 (0.66 to 2.61)	0.4
MR	1.19 (0.9 to 1.55)	0.4

Abbreviations as in table 1.

In model B, VO₂ was replaced by VE-VCO₂.

death was defined as witnessed cardiac arrest, death within 1 hour of the onset of acute symptoms, or unexpected, unwitnessed death in a patient known to be without symptoms within the previous 24 hours.

Echocardiography

LAV was measured at end LV systole from the apical four-chamber view (monoplane, area-length method). LV end-diastolic and end-systolic volumes (area-length method) and EF were measured on line from the apical four-chamber view.²⁰ Mitral E (E) and A (A) wave velocities, E/A ratio and E-wave deceleration time (DTE) were also measured offline. DTE was measured as the interval (in milliseconds) from peak early mitral filling to an extrapolation of the deceleration to 0 m/s. All measurements were obtained from the mean of three beats for patients with sinus rhythm and five beats for those with atrial fibrillation. Restrictive mitral filling pattern was defined as E/A >2 or E/A between 1 and 2 and DTE <140 ms or DTE <140 ms in cases of atrial fibrillation. Five regurgitant grades were routinely determined and reported directly to the study database (0, no regurgitation; 1, mild; 2, mild to moderate; 3, moderate; 4, moderate to severe; 5, severe).

Figure 1 Hazard ratios and 95% confidence intervals for LAV/BSA in various subgroups of patients.

Cardiopulmonary exercise testing

All patients underwent a symptom-limited bicycle ergometer exercise test at a constant cadence of 60 rpm. A continuous ramp protocol was used in which work rate was increased by 10 W/min. Gas exchange was monitored during the exercise test with a computerised metabolic cart (SensorMedics, Yorba Linda, CA, USA; Vmax 229). VO₂, VE-VCO₂ and the respiratory exchange ratio were measured online every 10 seconds using a standard inert gas dilution technique. VO₂ was defined as the highest VO₂ achieved during exercise and was expressed in ml/kg/min. The slope of the relation between ventilation and carbon dioxide production (VE/VCO₂) was calculated from the exercise data and taken as an index of the ventilatory response to exercise.

Statistical analysis

Continuous data are presented as mean (SD). Comparisons of all measurements were made using the unpaired *t* test or χ^2 test, as appropriate. Receiver operator characteristic (ROC) curves were constructed to compare predictive values of different clinical and echocardiographic variables. Differences between curves were assessed with the z-statistic. The best prognostic cut-off point for survival status of different variables was defined as that which gave the highest product of sensitivity and specificity. The relation of specific variables to mortality was investigated univariately using the Cox proportional hazard model. To assess the independence of the predictive value of LAV normalised for body surface area (LAV/BSA) from that of other predictors, multivariate analysis was performed. The variables selected to be entered in the multivariate models were chosen from those which had shown a highly significant ($p < 0.001$) association with outcome at univariate analysis. E and DTE were not entered in the model because of the similar pathophysiological meaning of the restrictive mitral filling pattern. Survival rate was analysed by the Kaplan-Meier method, and survival curves were compared by the log-rank test. To perform these analyses two different statistical programs were employed: Statview 5.0 (Abacus Concepts, SAS Institute, Cary, USA) and MedCalc 5.0 (Mariakerke, Belgium). A *p* value <0.05 was considered significant.

RESULTS

The study group comprised 273 patients (mean age 62 (9) years; 13% female) with chronic heart failure and LV systolic dysfunction. Table 1 shows the clinical and echocardiographic

Figure 2 Hazard ratios of the four groups of patients defined according to the number of risk factors.

Figure 3 (A) Survival rate in patients divided according to VO_2 level of 16 ml/kg/min; (B) survival rate according to the number of risk factors.

characteristics. Patients who reached the clinical end point were slightly older, had more severe clinical impairment as measured by NYHA grade and exercise tolerance, and worse left ventricular systolic and diastolic function. They also had an 8.6% ($p = 0.005$) higher left atrial diameter, and more importantly a 37% ($p < 0.001$) larger LAV than patients who had no cardiac events.

Survival analysis

During a mean follow-up of 45 (20) months, 44 patients died. Four patients had non-cardiac deaths and accordingly their follow-up was censored at the time of death. Forty patients died from cardiac causes, and of these, 24 patients (60%) died suddenly. Twenty-two patients were admitted to hospital for worsening heart failure and 13 patients underwent cardiac transplantation. Consequently, the primary end point was reached by 75 patients. Survival analysis was performed using the Cox proportional hazard model. Table 2 shows the results of univariate analysis. LAV/BSA was strongly associated with outcome, with a 2.7% increase in risk for every 1 ml/m² of LAV. Different multivariate models (table 3) showed that LAV/BSA was associated with outcome independently of the most powerful measures of ventricular function and exercise tolerance. Interestingly, left atrial diameter was associated with prognosis at univariate analysis but not independently of the New York Heart Association (NYHA) grade and EF, which underlines the superiority of volume compared with diameter in defining atrial size. Figure 1 shows hazard ratios (HRs) and 95% confidence intervals for LAV/BSA in predicting the primary end point in different subgroups of patients.

As regards the mode of death, LAV/BSA had a strong prognostic power for both cardiac death and sudden death, with HRs similar to that of the primary end point (1.026 and 1.027, respectively). At multivariate analysis, LAV/BSA predicted sudden death (HR = 1.02 (95% CI 1.005 to 1.04); $p = 0.009$) independently of VO_2 (HR = 0.9 (95% CI 0.8 to 1.02); $p = 0.1$), EF (HR = 0.96 (95% CI 0.91 to 1.006); $p = 0.08$) and E (HR = 3.3 (95% CI 0.76 to 14.7); $p = 0.1$).

Prediction model

To better define cardiac risk for individual patients in clinical practice, a non-invasive predictive model was developed on the basis of the independent risk factors identified by multivariate analysis—namely, VO_2 , LAV/BSA and EF. The best cut-off value for these variables was defined as that which gave the highest sensitivity and specificity as assessed by ROC curves. The best cut-off value for LAV/BSA was 63 ml/m² (sensitivity 83% (95% CI 77% to 88%) and specificity 55% (95% CI 43% to 67%), while for EF it was 30% (sensitivity 73% (95% CI 66% to 79%) and specificity 60% (48% to 71%) and for VO_2 16 ml/kg/min

(sensitivity 63% (95% CI 56% to 70%) and specificity 76% (65% to 85%). The prediction model made it possible to identify four risk groups of patients (according to the number of risk factors). The areas under the curve (AUCs) were 0.68 (0.04) (95% CI 0.62 to 0.74) for LAV/BSA < 63 ml/m², 0.69 (0.04) (0.63 to 0.74) for $\text{VO}_2 < 16 \text{ ml/kg/min}$, 0.66 (0.04) (0.60 to 0.72) for EF < 30% and 0.80 (0.03) (0.74 to 0.84) for the prediction model. The AUC of the prediction model was significantly higher than the AUC of VO_2 ($p < 0.001$).

The Cox proportional hazard model showed that patients with three risk factors had an HR of 38 (95% CI 11 to 129) compared with patients with no risk factors (fig 2). At 58 months of follow-up, the survival rate free of hospitalisation was 95% in patients with no risk factors as against 28% in those with three risk factors, with intermediate groups showing results between these figures (fig 3).

DISCUSSION

To the best of our knowledge, this is the first study to show that LAV provides powerful prognostic information that is independent of and incremental to cardiopulmonary exercise testing in patients with chronic heart failure due to LV systolic dysfunction. Furthermore, we provide evidence that LAV is a powerful predictor of different modes of death. In particular, LAV was the only independent predictor of sudden death in patients with chronic heart failure.

The correct classification of patients at high risk of death is a great clinical challenge. One of the most important aims is the identification of individual patients who will benefit most from heart transplantation. In the past decade, the most important parameters for selecting patients have been exercise parameters, especially peak oxygen consumption,^{18 19 21} but there is still a need for improved selection criteria based on objective markers of cardiac dysfunction. Left ventricular EF has frequently been used as a marker of the severity of the disease. However, a large majority of patients with reduced EF are asymptomatic, and among symptomatic patients reduced EF can be associated with a quite different clinical course, which contributes to the uncertainty in judging the prognosis of individual patients. Furthermore, nowadays it is clear that up to 50% of patients with heart failure have preserved EF of the left ventricle.²² Diastolic dysfunction is more clearly related to the severity of the disease, as shown by exercise tolerance and prognosis.^{1 2 23 24} The presence of a restrictive filling pattern has been shown to be a powerful marker of prognosis independently of EF and VO_2 .²⁵ Nevertheless, restrictive filling is highly load dependent and can change dramatically after treatment.²⁶ This can be very useful in following up a patient and checking

the efficacy of medical treatment, but limits its use as a marker of the severity of disease.

LAV is often enlarged in patients with chronic heart failure, whether with reduced or preserved EF.^{6, 27} LAV has been proposed as a morphophysiological marker of diastolic dysfunction,^{3, 4} but in patients with LV systolic dysfunction, it also reflects the degree of ventricular remodelling, the severity of mitral regurgitation, the presence of atrial fibrillation and the duration of the disease. Recently, the strong prognostic power of LAV has been shown to be independent of any of its determinants.⁶ Therefore LAV is a potential candidate for a simple marker of the severity of disease. The present study's demonstration that LAV has incremental and independent value compared with peak Vo_2 highlights the usefulness of this easy measurement in the clinical evaluation of patients with chronic heart failure.

Although LAV was a powerful predictor both in the overall population and in many subgroups of patients, it must be emphasised that there was quite a large overlap of this variable between survivors and non-survivors. Furthermore, multivariate analysis showed that other variables such as Vo_2 and EF have a major role in the selection of high-risk patients. Several studies have shown that a combination of factors most accurately predicts survival, but they frequently neglected Vo_2 and never included LAV. In our study a prediction model was constructed on the basis of independent risk variables identified at multivariate analysis. A combination of three variables, LAV, Vo_2 and EF, greatly enhanced risk stratification compared with Vo_2 alone. The major advantage of this prediction model is that the variables evaluated in the present study are readily available in clinical practice and are cost effective. However, it must be conceded that the prediction model presented here needs to be tested in a prospective study of a separate cohort of patients with chronic heart failure.

A new result of our study is that LAV provides valuable information about the risk of sudden death in patients with heart failure and LV systolic dysfunction. Since sudden death is generated by lethal ventricular arrhythmias directly related to the severity of LV dysfunction, the fact that LAV displaced both E-wave velocity and EF from the multivariate model further supports the idea that it should be considered an integrated index with the ability to summarise global systolic and diastolic modifications of the left ventricle throughout the entire duration of the disease. This is important because the worldwide risk stratification for sudden death, and then for implantation of an automatic cardioverter-defibrillator, is based on the level of EF alone.²⁸ So better risk stratification might improve the cost effectiveness of electrical treatment.²⁹ Interestingly, Vo_2 did not predict sudden death when LAV was inserted into the multivariate model. This is particularly intriguing, and a possible explanation should be sought in the multiple determinants of Vo_2 . In fact cardiac,³⁰ vascular³¹ and muscular factors³² influence peak oxygen consumption, probably making this measure a better predictor of cardiac death and worsening heart failure than of sudden death. Of course, to confirm these findings, additional studies in large populations with heart failure are needed.

A main limitation of this study is the lack of neurohormonal measurements, in particular of brain natriuretic peptide (BNP), which has been shown to have strong prognostic power in patients with chronic heart failure. LAV is linked to the BNP level,³³ and it has been shown that atrial size is a predictor of mortality in patients with heart failure independently of BNP.⁸ This is important because in that study, left atrial size was assessed on the basis of diameter, which has been shown to be a suboptimal way of measuring the left atrium³⁴; in the present study it was shown to have a lower predictive value than volume.

In conclusion an increased LAV is associated with increased risk for adverse events in patients with heart failure and LV systolic dysfunction. Our study has shown that this information is independent of other variables such as maximal oxygen consumption, LV ejection fraction, NYHA class and restrictive mitral filling, which are widely used in everyday clinical practice for risk stratification. The central clinical implication should be to implement LAV in the clinical management of patients with heart failure.

Authors' affiliations

A Rossi, M Cicoira, S Bonapace, G Golia, L Zanolla, L Franceschini, C Vassanelli, Department of Biomedical and Surgical Sciences, Section of Cardiology, University of Verona, Italy

Competing interests: None declared.

REFERENCES

- 1 Pinamonti B, Di Lenarda A, Sinagra G, et al. Restrictive ventricular filling pattern in dilated cardiomyopathy assessed by Doppler echocardiography: clinical, echocardiographic and hemodynamic correlation and prognostic implication. *J Am Coll Cardiol* 1993;**22**:808-15.
- 2 Giannuzzi P, Temporelli PL, Bosimini E, et al. Independent and incremental prognostic value of Doppler-derived mitral deceleration time of early filling in both symptomatic and asymptomatic patients with left ventricular dysfunction. *J Am Coll Cardiol* 1996;**28**:383-90.
- 3 Appleton CP, Galloway JM, Gonzales MS, et al. Estimation of left ventricular filling pressure using two-dimensional and Doppler echocardiography in adult patients with cardiac disease. Additional value of analyzing left atrial size, left atrial ejection fraction and the difference in duration of pulmonary venous and mitral flow velocity at atrial contraction. *J Am Coll Cardiol* 1993;**22**:1972-82.
- 4 Tsang TS, Barnes ME, Gersh BJ, et al. Left atrial volume as a morphophysiological expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. *Am J Cardiol* 2002;**90**:1284-9.
- 5 Tsang TS, Barnes ME, Gersh BJ, et al. Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography. *J Am Coll Cardiol* 2003;**42**:1206-7.
- 6 Rossi A, Cicoira M, Zanolla L, et al. Determinants and prognostic value of left atrial volume in patients with dilated cardiomyopathy. *J Am Coll Cardiol* 2002;**40**:14-25.
- 7 Modena MG, Muia N, Sgura FA, et al. Left atrial size is the major predictor of cardiac death and overall clinical outcome in patients with dilated cardiomyopathy: a long-term follow-up study. *Clin Cardiol* 1997;**20**:553-60.
- 8 de Groote P, Dagorn J, Soudan B, et al. B-type natriuretic peptide and peak exercise oxygen consumption provide independent information for risk stratification in patient with stable congestive heart failure. *J Am Coll Cardiol* 2004;**43**:1584-9.
- 9 Lanfranchi PA, Braghiroli A, Bosimini E, et al. Prognostic value of nocturnal Cheyne-Stokes respiration in chronic heart failure. *Circulation* 1999;**99**:1435-40.
- 10 Moller JE, Hillis GS, Oh JK, et al. Left atrial volume: a powerful predictor of survival after acute myocardial infarction. *Circulation* 2003;**107**:2207-12.
- 11 Dini FL, Cortigiani L, Baldini U, et al. Prognostic value of left atrial enlargement in patients with idiopathic dilated cardiomyopathy and ischemic cardiomyopathy. *Am J Cardiol* 2002;**89**:518-23.
- 12 Popescu BA, Macor F, Antonini-Canterin F, et al. GISSI-3 Echo Substudy Investigators. Left atrium remodeling after acute myocardial infarction (results of the GISSI-3 Echo Substudy). *Am J Cardiol* 2004;**93**:1156-9.
- 13 Rossi A, Golia G, Gasparini G, et al. Left atrial filling volume can be used to reliably estimate the regurgitant volume in mitral regurgitation. *J Am Coll Cardiol* 1999;**33**:212-7.
- 14 Sanfilippo AJ, Abascal VM, Sheehan M, et al. Atrial enlargement as a consequence of atrial fibrillation. A prospective echocardiographic study. *Circulation* 1990;**82**:792-7.
- 15 Wong M, Staszewsky L, Latini R, et al. Severity of left ventricular remodeling defines outcomes and response to therapy in heart failure: valsartan heart failure trial (Val-HeFT) echocardiographic data. *J Am Coll Cardiol* 2004;**43**:2022-7.
- 16 Blondheim DS, Jacobs LE, Kotler MN, et al. Dilated cardiomyopathy with mitral regurgitation: decreased survival despite a low frequency of ventricular thrombus. *Am Heart J* 1991;**122**:763-71.
- 17 Carson PE, Johnson GR, Dunkman WB, for the V-HeFT VA Cooperative Studies Group, et al. The influence of atrial fibrillation on prognosis in mild to moderate heart failure. The V-HeFT Studies. *Circulation*, 1993;**87**(suppl VII), 102-10.
- 18 Mancini DM, Eisen H, Kussmaul W, et al. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. *Circulation* 1991;**83**:778-86.
- 19 Cicoira M, Davos CH, Francis DP, et al. Prediction of mortality in chronic heart failure from peak oxygen consumption adjusted for either body weight or lean tissue. *J Card Fail* 2004;**10**:421-6.
- 20 Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006;**79**:108.

- 21 Cohn JN, Johnson GR, Shabetai R, *et al*. Ejection fraction, peak oxygen consumption, cardiothoracic ratio, ventricular arrhythmias, and plasma norepinephrine as determinants of prognosis in heart failure. *Circulation*, 1993;**87**(Suppl VI), VI-5-16.
- 22 Senni M, Tribouilloy CM, Rodeheffer RJ, *et al*. Congestive heart failure in the community: a study of all incident cases in Olmstead County, Minnesota in 1991. *Circulation* 1998;**98**:2282-9.
- 23 Rihal CS, Nishimura RA, Hatle LK, *et al*. Systolic and diastolic dysfunction in patients with clinical diagnosis of dilated cardiomyopathy. Relation to symptoms and prognosis. *Circulation* 1994;**90**:2772-9.
- 24 Packer M. Abnormalities of diastolic function as a potential cause of exercise intolerance in chronic heart failure. *Circulation*, 1990;**81**(Suppl III), III-78-86.
- 25 Hansen A, Haass M, Zugck C, *et al*. Prognostic value of Doppler echocardiographic mitral inflow patterns: implications for risk stratification in patients with chronic congestive heart failure. *J Am Coll Cardiol* 2001;**37**:1049-55.
- 26 Hurrell DG, Nishimura RA, Ilstrup DM, *et al*. Utility of preload alteration in assessment of left ventricular filling pressure by Doppler echocardiography: a simultaneous catheterization and Doppler echocardiographic study. *J Am Coll Cardiol* 1997;**30**:459-67.
- 27 Rossi A, Ciccoira M, Florea V, *et al*. Chronic heart failure with preserved left ventricular ejection fraction: diagnostic and prognostic value of left atrial size. *Int J Cardiol* 2006;**110**:386-92.
- 28 Kadish A, Dyer A, Daubert JP, *et al*. Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) Investigators. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med* 2004;**350**:2151-8.
- 29 Gehi A, Haas D, Fuster V. Primary prophylaxis with the implantable cardioverter-defibrillator: the need for improved risk stratification. *JAMA* 2005;**294**:958-60.
- 30 Lapu-Bula R, Robert A, De Kock M, *et al*. Relation of exercise capacity to left ventricular systolic function and diastolic filling in idiopathic or ischemic dilated cardiomyopathy. *Am J Cardiol* 1999;**3**:728-34.
- 31 Bonapace S, Rossi A, Ciccoira M, *et al*. Aortic distensibility independently affects exercise tolerance in patients with dilated cardiomyopathy. *Circulation* 2003;**107**:1603-8.
- 32 Ciccoira M, Zanolla L, Franceschini L, *et al*. Skeletal muscle mass independently predicts peak oxygen consumption and ventilatory response during exercise in noncachectic patients with chronic heart failure. *J Am Coll Cardiol* 2001;**37**:2080-5.
- 33 Rossi A, Enriquez-Sarano M, Burnett JC, *et al*. Natriuretic peptide levels in atrial fibrillation. A prospective hormonal and Doppler-echocardiography study. *J Am Coll Cardiol* 2000;**35**:1256-62.
- 34 Lester SJ, Ryan EW, Schiller NB, *et al*. Best method in clinical practice and in research studies to determine left atrial size. *Am J Cardiol* 1999;**84**:829-32.

IMAGES IN CARDIOLOGY

doi: 10.1136/hrt.2006.104786

An unusual origin of the left coronary system

A 72-year-old man presented with a history of exertional angina with a positive exercise test at a low workload. Risk factors included hypertension and hyperlipidaemia. An initial coronary angiogram showed a vestigial remnant of the left main stem arising from the left coronary cusp. An anomalous origin of the left main stem (ALMO) was suspected. The right coronary artery ostium was normally positioned.

CT scanning of the aortic root confirmed a left main stem arising adjacent to the right coronary ostium in an anterior position. Coronary angiography was then repeated. Engagement of the anomalous left coronary ostium was obtained using a Q4 guide catheter and was seen supplying the mid-portion of the left anterior descending artery. Proximally the left anterior descending artery (PLAD) continued as the circumflex vessel. There was severe disease in the proximal and mid left anterior descending artery, the circumflex artery (LCx) was mildly diseased, but the right coronary artery was heavily diseased with a significant bifurcation lesion at the crux (panel A).

Anomalies of coronary artery anatomy affect about 1% of the general population. Usually the left coronary system originates from the right coronary cusp. In this case, however, the left main stem (LMS) had a separate origin from the anterior aspect of the aortic root and adjacent to the right coronary ostium (panel B). The circumflex artery then arose as a continuation from the left anterior descending artery and this is thought to be a very rare occurrence.

In view of the findings the patient was accepted for surgical revascularisation.

A Msairi, R Hornung, N D Palmer
adelmsairi@doctors.org.uk