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Limited utility of the subcostal view for the echocardiographic evaluation of left ventricular mass in epidemiological studies of older persons

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Abstract

Background: Epidemiological estimates of left ventricular mass are based on echocardiographic imaging from the parasternal view, which is often unavailable in subjects with obesity or lung disease. This study was undertaken to assess whether the subcostal view is a valid alternative to estimate left ventricular mass in an unselected older population. *Methods:* In a cross-sectional study of all the residents in Dicomano, Italy, aged ≥ 65 years, echocardiography was performed with a systematic attempt to obtain both the parastermal and the subcostal views. *Results:* The parasternal view was missing in 73/614 participants, 48 of whom were imaged from the subcostal view. In participants imaged from both views, the subcostal view underestimated left ventricular cavity dimension and, consequently, left ventricular mass [79.7 (1.3) vs. 93.3 (1.5) g/m^2; $p < 0.001$]. Furthermore, the subcostal view was only 25% sensitive for the diagnosis of hypertrophy. Several multivariate regression models, developed in an equation development subgroup and tested in a validation subgroup, failed to correct the prediction of left ventricular mass based on measures taken from the subcostal view, also after inclusion of demographic, anthropometric, and spirometric covariates. *Conclusions:* In unselected older persons, the subcostal view does not improve the accuracy of echocardiographic estimation of left ventricular mass, which remains biased in epidemiological studies.

Keywords: Epidemiology; Validity; Population studies; Echocardiography; LV hypertrophy; Aging

1. Introduction

Left ventricular hypertrophy is a powerful, independent predictor of cardiovascular morbidity and mortality in patients with high blood pressure and other conditions [1–4]. Two-dimensional guided M-mode echocardiography from the parasternal approach is the standardized technique of choice to quantitate left ventricular mass and diagnose left ventricular hypertrophy [5]. Echocardiographic measures of left ventricular mass are reliable, reproducible [6,7], and predictive of subsequent outcomes [3,8,9].

However, the quality of echocardiographic images from the parasternal view is often poor in persons who are older, obese or have pulmonary disease [10,11]. This limitation may be particularly problematic in epidemiological studies of older populations. For instance, due to this, in the Cardiovascular Health Study (CHS), the echocardiographic estimation of left ventricular mass was unavailable in 34% of 5201 participants aged 65 years and older. Measurements of left ventricular mass were selectively missing in male participants who were older, heavier and taller, or had a history of coronary artery disease, hypertension, and diabetes [10,12], all conditions that are associated with an increased left ventricular mass.

Thus, such selective data loss could significantly bias the echocardiographic estimate of the prevalence of left ventricular hypertrophy and the risk associated with it [11]. Magnetic resonance imaging provides highly accurate estimates of left ventricular mass [13], but because of its costs and poor transportability, it is unlikely that it

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could substitute echocardiography in large epidemiological studies.

For clinical purposes, the subcostal view is commonly used as an alternative to the standard parasternal view [14]. However, comparisons between measures of left ventricular mass obtained from the parasternal and the subcostal views have been conducted only in small clinical series, with conflicting results [15,16]. We conducted this study to determine whether the subcostal view is a reliable alternative for the echocardiographic measurement of left ventricular mass in epidemiological studies when the parasternal approach is unavailable.

2. Materials and methods

2.1. Study population and protocol

This study is part of an epidemiological survey on heart failure in the elderly ("Insufficienza Cardiaca negli Anziani Residenti a Dicomano", ICARe Dicomano Study), which enrolled the entire home-dwelling, elderly (≥ 65 years) population recorded in the City Registry Office of Dicomano, Italy. The design of the study, which followed the principles outlined in the Declaration of Helsinki on biomedical research involving human subjects, have been published elsewhere [17].

2.2. Data collection

After informed consent, participants received a complete clinical exam, 12-lead EKG, M-mode, two-dimensional and color Doppler echocardiography, and spirometry. Body height (cm) and weight (kg), and waist circumference (cm) were measured. Hypertension was defined as a blood pressure of >140/90 mm Hg, or drug treatment [18]. History and EKG criteria were used to define the presence of coronary artery disease, which included previous myocardial infarction (medical records or typical symptoms associated with EKG changes), angina (typical chest pain, as assessed with Rose questionnaire, or positive stress test), and myocardial revascularization procedures (medical records).[17] The Minnesota coding system was used to define left ventricular hypertrophy on EKG (codes 3–1, 3–3, and 3–4).[19] Smoking status was classified as previous or current smoker versus never smoker.

2.3. Echocardiographic examination

Echocardiography was performed with a mechanical sector scanner (Challenger, 3.5–2.5 MHz dynamically focused transducer, ESAOTE Biomedica). In all cases, attempts were made at visualizing the left ventricular chamber from both the parasternal and subcostal approaches. Images from the parasternal view were obtained at expiratory apnea in the left decubitus position, whereas subcostal images were obtained at deep inspiratory apnea in the supine position.

In both the parasternal and the subcostal views, orientation of the ultrasound beam was optimized in two-dimensional long-and short-axis images. Two-dimensionally guided M-mode images were videotaped and stop frame images were digitized (TomTec^{P90} System, TomTec Imaging Systems) for quantitative analysis. The criteria proposed by Schieken [20] were used to judge technical acceptability of M-mode images from either parasternal or subcostal view. As commonly accepted [5,21], linear measures were taken from parasternal two-dimensional images when M-mode orientation was suboptimal (less than 10% of cases).

Left ventricular wall thickness and internal dimensions were measured according to the American Society of Echocardiography (ASE) convention [22]; at least three to five measures were averaged in participants in sinus and non-sinus rhythm, respectively. Left ventricular mass was calculated by the adjusted ASE method and left ventricular hypertrophy was defined as left ventricular mass/body surface area >116 g/m^2 in men and >104 g/m^2 in women [23].

Regional wall motion abnormalities were scored semi-quantitatively as hypokinesia, akinesia, or dyskynesia on the basis of reduced, absent, or paradoxical endocardial motion and myocardial thickening of 16 left ventricular segments.

2.4. Spirometry

Pulmonary functional assessment was performed with standard spirometric methods [24]. Forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1), expressed as percent of predicted values [25], and their ratio (FEV1/FVC) was used to diagnose obstructive lung disease.

2.5. Analytic procedures

Statistical analysis was performed with the SPSS for Windows 10.1 package. Mean values are expressed as mean

Table 1
Characteristics of the 614 study participants

	Mean (S.E.M.)	*N* (%)
Age (years)	73.4 (0.25) (range: 65–94)	
Male gender		256 (41.7)
Body height (cm)	157.4 (0.37)	
Body weight (kg)	67.4 (0.51)	
Body mass index (kg/m^2)	27.2 (0.18)	
Waist circumference (cm)	94.3 (0.47)	
Coronary artery disease		96 (15.7)
Hypertension		441 (71.8)
Smoking (current or past)		264 (43.0)
Non-sinus rhythm		38 (6.2)
EKG left ventricular hypertrophy		49 (8.0)
Left ventricular wall motion abnormalities		63 (10.3)

		Subcostal		
		Yes	No	Total
Parasternal	Yes	323	218	541
	No	48	25	73
Total		371	243	614

Fig. 1. Availability of parasternal and subcostal views in the study participants.

(S.E.M.). Relative frequencies were compared with the χ^2 test, where continuous anthropometric variables were categorized into tertiles. Logistic regression was used to identify the independent predictors of a missing left ventricular mass value. To this purpose, candidate predictors were considered all the variables that in bivariate comparisons tended to be associated with the outcome ($p < 0.1$). Redundant variables were backward deleted from a complete initial model, to obtain a final parsimonious model of prediction.

Left ventricular mass estimates and the corresponding measures from the parasternal and subcostal approaches were compared using the paired *t* test in the 323 participants who had both views available. The comparison was then restricted to the 282 participants in this group who were in sinus rhythm and had no left ventricular wall motion abnormalities. Because left ventricular mass differed significantly between the two views, multivariate regression analyses were used to adjust the original subcostal estimate. To this purpose, the 282 participants were randomly assigned to an equation development subgroup ($n = 146$) and a cross-validation subgroup ($n = 136$), where spirometric data were missing in 13 and 6 participants, respectively. Equations were developed and validated either predicting directly the parasternal view left ventricular mass from the subcostal mass estimate, or predicting the parasternal left ventricular diastolic dimension from the subcostal measure and then using this adjusted value to recalculate left ventricular mass. In both sets of equations, age, gender, height, weight (or, alternatively, waist circumference), and spirometric data were entered stepwise as covariates, with *p* values of < 0.05 for entry and of < 0.1 for exiting variables.

Competitive models were compared in terms of their explained variance (unadjusted R^2 value). Predictive equations were validated in the cross-validation subgroup by regressing the predicted values on the corresponding values measured from the parasternal view, and assessing whether the slope and the intercept of the regression equation differed significantly from one and zero, respectively. Finally, the difference between observed and predicted values was regressed on the observed parasternal values. A two-tailed *p* value < 0.05 was considered statistically significant.

3. Results

As of April 25, 1995, there were 899 residents in Dicomano aged 65 years and over, of whom 864 were initially eligible. Of them, 614 were included in the present study, whereas 21 died or were institutionalized before data collection and 229 refused to participate. Mean age of eligible persons who did and did not participate in the cardiopulmonary assessment was 73.4 (0.3) and 75.8 (0.5) years ($p < 0.001$), with almost an even distribution of non-

Table 2
Factors associated with a missing mass value

		Parasternal view			Subcostal view		
		N (%) LV mass not available	Odds ratio	95% Confidence interval	*N* (%) LV mass not available	Odds ratio	95% Confidence interval
Age (years)	65–74	39 (9.7)	1.0	–	153 (37.9)	1.0	–
	75–84	21 (12.5)	1.3	0.8, 2.4	70 (41.7)	1.2	0.8, 1.7
	≥85	13 (31.0)	4.2	2.0, 8.7*	20 (47.6)	1.5	0.8, 2.8
				p for trend < 0.001			
Male gender	No	30 (8.4)	1.0	–	143 (39.9)	1.0	–
	Yes	43 (16.8)	2.2	1.3, 3.6***	100 (39.1)	1.0	0.7, 1.3
Body mass index (kg/m^2)	< 25.1	19 (9.3)	1.0	–	69 (33.8)	1.0	–
	25.1–28.5	22 (10.8)	1.2	0.6, 2.2	82 (40.2)	1.3	0.9–2.0
	≥ 28.5	30 (14.7)	1.7	0.9, 3.1	90 (44.1)	1.5	1.0, 2.3**
Waist circumference (cm)	< 90	14 (7.0)	1.0	–	69 (34.7)	1.0	–
	90–99	26 (12.2)	1.8	0.9, 3.6	83 (39.0)	1.2	0.8–1.8
	≥99	32 (16.0)	2.5	1.3, 4.9*	89 (44.5)	1.5	1.0, 2.3**
				p for trend = 0.024			
Current/past smoking	No	27 (7.7)	1.0	–	145 (41.4)	1.0	–
	Yes	46 (17.4)	2.5	1.5, 4.2***	98 (37.1)	0.8	0.6, 1.2
Obstructive lung disease	No	38 (9.3)	1.0	–	152 (37.2)	1.0	–
	Yes	21 (16.7)	2.0	1.1, 3.5***	46 (36.5)	1.0	0.6, 1.5

*$p < 0.01$ vs. first tertile.
**$p < 0.05$ vs. first tertile.
***$p < 0.001$ vs. No.

participants between men and women (46.4% vs. 53.6%; $p = 0.205$).

The principal characteristics of the study population are summarized in Table 1. As reported in Fig. 1, the parasternal view was inadequate to obtain a measurable left ventricular imaging in 73 participants (11.9%). Age, male gender, smoking, larger waist circumference, and obstructive lung physiology (but not body weight and height, history of hypertension and of coronary artery disease, and presence of wall motion abnormalities; data not shown) were bivariate predictors of missing left ventricular mass values from the parasternal view (Table 2). All the candidate predictors, identified from bivariate associations ($p < 0.1$) where entered in a multivariate logistic regression model; after backward deletion of redundant variables, smoking, age, and waist circumference remained the only independent predictors of a missing parasternal view (Table 3).

The subcostal view was available in 371 participants (60.4%), 48 of whom had not been adequately imaged from the parasternal approach. Therefore, measures of left ventricular cavity and wall thicknesses were available from the subcostal view in 65.8% (48/73) of participants who could not be imaged from the parasternal view (Fig. 1). Body mass index or waist circumference were the only bivariate predictors of missing subcostal left ventricular mass values (Table 2).

3.1. Parasternal and subcostal estimates of left ventricular mass

Interobserver reproducibility of echocardiographic readings was assessed in the first 109 participants. No significant difference was observed between two readers (MDB, RP) for septum and free wall thickness. Mean values of left ventricular diastolic dimension were slightly different (mean error 0.8 mm, $p = 0.029$) between the two readings. However, this did not affect the estimates of left ventricular mass, which were comparable between the two readers.

Table 3
Multivariate predictors of a missing left ventricular mass value from the parasternal view

		Odds ratio	95% Confidence interval
Age (years)	65–74	1.0	–
	75–84	1.4	0.8, 2.6
	≥85	6.4	2.9, 14.1*
			p for trend = 0.001
Male gender	No	1.0	–
	Yes	1.0	0.5, 2.1
Waist circumference (cm)	< 90	1.0	–
	90–99	1.9	0.9, 3.8
	≥99	3.1	1.5, 6.2**
			p for trend = 0.003
Current/past smoking	No	1.0	–
	Yes	2.7	1.3, 5.6***

The presence of obstructive lung physiology was backward deleted from the initial model.

* $p < 0.001$ vs. first tertile.

** $p = 0.002$ vs. first tertile.

*** $p = 0.007$ vs. No.

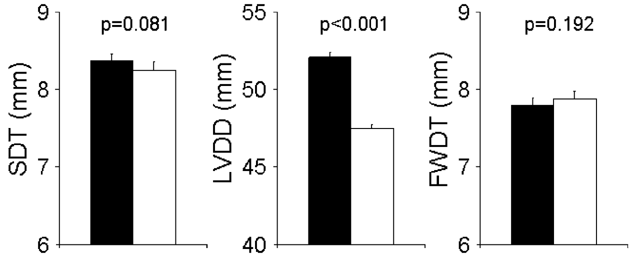

Fig. 2. Paired comparisons of M-mode echocardiographic parameters from the parasternal view (solid bars) and the subcostal view (open bars) in 282 participants. SDT: ventricular septum diastolic thickness, LVDD: left ventricular diastolic dimension, FWDT: free wall diastolic thickness.

Left ventricular imaging was adequate from both the parasternal and subcostal views in 323 participants. Overall, left ventricular mass was underestimated from the subcostal view [subcostal: 79.7 (1.3) vs. parasternal: 93.3 (1.5) g/m^2; $p < 0.001$], which was only 33% sensitive (24/73 cases) and 99% specific (247/250), as compared to the parasternal view, in the diagnosis of left ventricular hypertrophy. Such underestimation persisted even after restricting the comparison to the 282 participants who were in sinus rhythm and had no left ventricular wall motion abnormalities [subcostal: 76.7 (1.3) vs. parasternal: 90.2 (1.5) g/m^2; $p < 0.001$], with a sensitivity as low as 25% (14/55 cases) and unchanged specificity (225/227, 99%) for the diagnosis of left ventricular hypertrophy. This difference originated mainly from an underestimation of left ventricular diastolic dimension, whereas septum and free wall thicknesses from the two views were comparable (Fig. 2).

Multivariate regression models were built from measurements obtained in the randomly selected 146 participants assigned to the equation development subgroup, in order to improve the prediction of left ventricular mass using data obtained from the subcostal view. A first set of equations was developed on the direct prediction of left ventricular mass, following a hierarchical approach for entering potential

Table 4
Prediction of parasternal left ventricular mass from echocardiographic data obtained from the subcostal view in 146 participants of the equation development subgroup

Model no. (n)	Variables*	R^2	p Value
1 (146)	Subcostal LV mass	0.52	< 0.001
2 (146)	Model 1 + weight	0.54	< 0.001
3 (146)	Model 2 + subcostal LV mass squared	0.56	< 0.001
4 (133)**	Model 3 + FVC	0.59	< 0.001

LV: left ventricular; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s. Spirometric variables expressed as percent of their predicted values [25].

* Variables entered and stepwise deleted were: in Step 2, age and gender; in Step 4, FEV1 and FEV1/FVC.

** Case number in Model 4 is less than in other models due to unavailability of spirometric data in 13 participants.

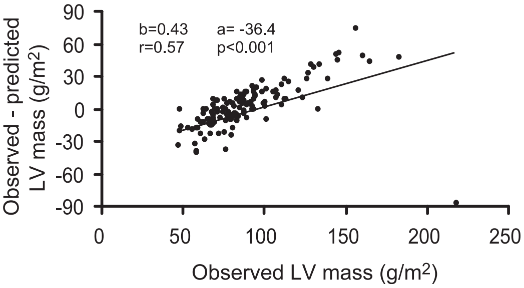

Fig. 3. Regression of the difference between observed (from parasternal view) and predicted (from subcostal view) left ventricular mass on observed left ventricular mass, in the cross-validation subgroup ($n = 130$).

covariates (Table 4). In a first model, the subcostal left ventricular mass alone explained 52% of the variance of parasternal left ventricular mass. The progressive inclusion of body weight (Model 2), a squared term for subcostal left ventricular mass (Model 3), and FVC (Model 4) increased the explained variance only marginally. Age, gender, height, FEV1, and FEV1/FVC were not retained in any model. The substitution of waist circumference for weight, or of body mass index for height and weight, did not substantially improve the amount of explained variance. When the model providing the highest R^2 (Model 4) was applied to the participants in the cross-validation subgroup, the predicted value correlated moderately well with that obtained from the parasternal view ($r = 0.67$). However, the 95% confidence interval for the slope ($b = 0.80$, 95% confidence interval: 0.65, 0.95) and the intercept ($a = 19.6$, 95% confidence interval: 5.9, 33.3) of the regression equation did not include one and zero, respectively, indicating that the regression was diverging significantly from the line of identity. Furthermore, the predicted left ventricular mass value substantially and systematically underestimated the observed value, as shown by a significant correlation between the difference of the two estimates and the observed parasternal value (Fig. 3).

The alternative approach of modeling left ventricular diastolic dimension using the subcostal measure, again with sequential inclusion of several potential covariates, did not improve the accuracy of the prediction of left ventricular mass, recalculated with the adjusted left ventricular dimension value. The variance of parasternal left ventricular dimension explained by regression models respectively not adjusted and fully adjusted as previously described, ranged from 42% to 51%. Left ventricular mass calculated from predicted left ventricular dimension values still substantially underestimated parasternal left ventricular mass, and did not improve the results illustrated in Fig. 3.

4. Discussion

Echocardiographic estimates of left ventricular mass were achieved from the parasternal view in 88% of our community-dwelling older persons. This figure is higher than usually reported in previous studies [10,11], including CHS, where only 66% of participants had a valid left ventricular mass estimate. Since body size is a major determinant of successful echocardiographic imaging, our results may derive from a lower proportion of overweight participants in the present study sample. Yet, even in such a thinner population, several factors, such as older age, larger body size, and smoking habit systematically reduced the availability of left ventricular mass from the parasternal approach. This confirms the presence of a selection bias in the echocardiographic assessment of left ventricular mass and hypertrophy in older persons. Differently from CHS, other factors, such history of coronary artery disease, were not associated with the unavailability of parasternal view. However, this difference with previous findings should be interpreted cautiously, as our sample size may be underpowered to detect these associations.

Devereux et al. [21] recently reported that left ventricular mass was immeasurable in 9% of 3501 participants in the Strong Heart Study, aged 45–74 years. Even with such a low proportion of cases with unavailable left ventricular mass, missing data was confirmed to be non-randomly associated with several clinical characteristics, such as more advanced age, larger body mass index, and poorer spirometric performance. In that study, it was reassuring that the proportion of incident cardiovascular events in the follow-up was independent of the availability of left ventricular mass measurements. However, this finding might not be generalizable to older individuals, such as those included in the sample enrolled in the present study.

The subcostal view is frequently available also in older persons with poor acoustic accessibility from the parasternal view [14]. However, standard formulas to calculate left ventricular mass have been validated anatomically only for linear M-mode measures taken from the parasternal view [26]. In the ICARe Dicomano study, an attempt at imaging the left ventricular from the subcostal view was systematically performed independent of the availability of the parasternal view. This allowed for an unbiased evaluation of the usefulness of the subcostal approach in the assessment of left ventricular mass.

An adequate subcostal view was obtained in a substantially lower percentage of subjects (60%) than the parasternal view, including more than 65% (48/73) of the participants who could not be imaged from the parasternal approach. The availability of an adequate subcostal view was unrelated to factors such as age and smoking, therefore possibly reducing the selection bias in estimating left ventricular mass. This prompted us to validate left ventricular mass estimates from subcostal view.

Previous validation studies were limited to small, selected series of younger individuals and reported conflicting findings [15,16]. The results of the present study, which enrolled a large sample of unselected older persons, indicated that left ventricular mass from the subcostal approach was substantially underestimated, even when the analysis was restricted to participants without arrhythmias and left ventricular wall motion abnormalities. As a consequence, the sensitivity of the subcostal view in the diagnosis of left ventricular hypertrophy was very poor. These negative findings were marginally mitigated by the fact that septum and free wall thickness was not statistically different between the parasternal and the subcostal approaches, therefore suggesting that the latter might be occasionally used to replace a missing thickness measure from the parasternal view.

Body size and shape affect the orientation of the ultrasound beam, thereby contributing to the poor agreement between measures of the same cardiac structure from the parasternal and subcostal approaches. Indeed, measures of body size and shape, as well as of lung physiology, were significant covariates in predicting parasternal left ventricular mass from the subcostal view. However, the explained variance was less than 60% and, most importantly, a systematic error was detected in the prediction (Fig. 3). This error was not reduced when the correction was alternatively based on adjustment of left ventricular dimension from the subcostal view, followed by recalculation of left ventricular mass.

Strengths of the present study are its population-based design, the systematic attempts at visualizing the left ventricular chamber from both parasternal and subcostal views, and the availability of numerous, prospectively acquired demographic and clinical measures, permitting an adjustment for a broad spectrum of potential covariates. Despite this, we were unable to obtain a satisfactory prediction of left ventricular mass based on subcostal measures, even after a complex adjustment procedure. As a study limitation, we must acknowledge that better echocardiographic equipments and newer technologies, or adjustment for other variables not available in our database, might improve such prediction.

Our findings have clear implications for epidemiological studies of older populations, but they should be considered also in the clinical setting. Echocardiography, indeed, is frequently used to assess the presence of left ventricular hypertrophy as an end-organ damage, or to evaluate the effect of treatment, in patients with high blood pressure. According to our results, estimates of left ventricular mass obtained from the subcostal view are often inaccurate and cannot validly substitute for a missing parasternal view. When assessment of left ventricular mass has a high clinical relevance and cannot be obtained from the parasternal view, other techniques, such as magnetic resonance imaging, should be probably considered [13].

In conclusion, our findings indicate that inclusion of the subcostal view as currently performed would not increase the yield, or improve the accuracy, of echocardiographic estimation of left ventricular mass in epidemiological studies of older populations. These findings give a strong evidence-based support to the ASE recommendations, which were issued only on a consensus basis, to the use of the parasternal view as the only approach to quantitate left ventricular mass [5]. These limitations of echocardiography should be considered in studies on the epidemiology of left ventricular hypertrophy and of its associated risk.

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References

[1] Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Intern Med 1991;114: 345–52.

[2] Haider AW, Larson MG, Benjamin EJ, Levy D. Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. J Am Coll Cardiol 1998;32:1454–9.

[3] Bikkina M, Levy D, Evans JC, Larson MG, Benjamin EJ, Wolf PA, et al. Left ventricular mass and risk of stroke in an elderly cohort. The Framingham Heart Study. JAMA 1994;272:33–6.

[4] Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med 1990;322: 1561–6.

[5] Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography committee on standards, subcommittee on quantitation of two-dimensional echocardiograms. J Am Soc Echocardiogr 1989;2:358–67.

[6] de Simone G, Muiesan ML, Ganau A, Longhini C, Verdecchia P, Palmieri V, et al. Reliability and limitations of echocardiographic measurement of left ventricular mass for risk stratification and follow-up in single patients: the RES trial. Working Group on Heart and Hypertension of the Italian Society of Hypertension. Reliability of M-mode Echocardiographic Studies. J Hypertens 1999;17:1955–63.

[7] Dai S, Ayres NA, Harrist RB, Bricker JT, Labarthe DR. Validity of echocardiographic measurement in an epidemiological study. Project heartbeat! Hypertension 1999;34:236–41.

[8] Levy D. Left ventricular hypertrophy. Epidemiological insights from the Framingham Heart Study. Drugs 1988;35(Suppl. 5):1–5.

[9] Gardin JM, McClelland R, Kitzman D, Lima JA, Bommer W, Klopfenstein HS, et al. M-mode echocardiographic predictors of six- to seven-year incidence of coronary heart disease, stroke, congestive heart failure, and mortality in an elderly cohort (the Cardiovascular Health Study). Am J Cardiol 2001;87:1051–7.

[10] Gardin JM, Siscovick D, Anton-Culver H, Lynch JC, Smith VE, Klopfenstein HS, et al. Sex, age, and disease affect echocardiographic left ventricular mass and systolic function in the free-living elderly. The Cardiovascular Health Study. Circulation 1995;91: 1739–48.

[11] Whalley GA, Gamble GD, Doughty RN, MacMahon S, Sharpe N.

Selection bias in clinical research when subjects are excluded because of failure to estimate left ventricular mass by echocardiography. J Am Soc Echocardiogr 1998;11:1050–5.

[12] Gardin JM, Arnold A, Gottdiener JS, Wong ND, Fried LP, Klopfenstein HS, et al. Left ventricular mass in the elderly. The Cardiovascular Health Study. Hypertension 1997;29:1095–103.

[13] Myerson SG, Bellenger NG, Pennell DJ. Assessment of left ventricular mass by cardiovascular magnetic resonance. Hypertension 2002;39: 750–5.

[14] Feigenbaum H. Echocardiographic evaluation of cardiac chambers. In: Feigenbaum H, editor. Echocardiography. Philadelphia: Lea and Febiger; 1986. p. 127–87.

[15] Rein AJ, Azancot I, N'Guyen AV, Adda JL, Georgiopoulos G, Piekarski A, et al. Subcostal M-mode computerised echocardiography. An alternative or complementary approach to parasternal echocardiography? Br Heart J 1983;50:21–6.

[16] Abergel E, Cohen A, Vaur L, Khellaf F, Menard J, Chatellier G. Accuracy and reproducibility of left ventricular mass measurement by subcostal M-mode echocardiography in hypertensive patients and professional bicyclists. Am J Cardiol 1993;72:620–4.

[17] Di Bari M, Marchionni N, Ferrucci L, Pini R, Antonini E, Chiarlone M, et al. Heart failure in community-dwelling older persons: aims, design and adherence rate of the ICARe Dicomano Project, an epidemiologic study. J Am Geriatr Soc 1999;47:664–71.

[18] Di Bari M, Salti F, Nardi M, Pahor M, De Fusco C, Tonon E, et al. Undertreatment of hypertension in community dwelling older adults: a drug-utilization study in Dicomano, Italy. J Hypertens 1999;17: 1633–40.

[19] Prineas RJ, Crow RS, Blackburn H. The Minnesota code manual of electrocardiographic findings. Standards and procedures for measurement and classification. London: John Wright-PSG; 1982.

[20] Schieken RM, Clarke WR, Mahoney LT, Lauer RM. Measurement criteria for group echocardiographic studies. Am J Epidemiol 1979; 110:504–14.

[21] Devereux RB, Roman MJ, Liu JE, Lee ET, Wang W, Fabsitz RR, et al. An appraisal of echocardiography as an epidemiological tool. The Strong Heart Study. Ann Epidemiol 2003;13:238–44.

[22] Sahn DJ, De Maria AN, Kisslo J, Weiman A. The committee on M-mode standardization of the American Society of Echocardiography. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.

[23] Devereux RB, Dahlof B, Levy D, Pfeffer MA. Comparison of enalapril versus nifedipine to decrease left ventricular hypertrophy in systemic hypertension (the PRESERVE trial). Am J Cardiol 1996; 78:61–5.

[24] American Thoracic Society. Standardization of spirometry, 1994 update. Am J Respir Crit Care Med 1995;152:1107–36.

[25] Enright PL, Kronmal RA, Higgins M, Schenker M, Haponik EF. Spirometry reference values for women and men 65 to 85 years of age. Cardiovascular Health Study. Am Rev Respir Dis 1993;147: 125–33.

[26] Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450–8.