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Determinants of echocardiographic left atrial volume: implications for normalcy

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Aims The relative role of multiple determinants of left atrial volume index (LAVi) in athletes and non-athletes is not fully defined. Thus, we decided to prospectively assess the determinants of LAVi in healthy individuals and competitive athletes over a wide age range.

Methods and results Four hundred and eighteen healthy individuals (mean age 41.7 $\pm$ 15.6 years, range 16–84, 65% males, 38% competitive athletes) underwent Doppler echocardiography including assessment of LAVi by the biplane area-length method and of left ventricular (LV) diastolic function including the ratio of early diastolic peak LV inflow velocity to peak myocardial early diastolic velocity (*E*/*e*′). Mean LAVi was 32.2 $\pm$ 9.0 mL/m^2 in the pooled population. LAVi was larger in athletes than in non-athletes (38.9 $\pm$ 9.6 mL/m^2 vs. 28.4 $\pm$ 5.8 mL/m^2, $P < 0.0001$). In the pooled population a stepwise multiple linear regression analysis identified LV end-diastolic volume index (LVEDVi) ($\beta = 0.378$, $P < 0.0001$), LV mass index (LVMi) ($\beta = 0.260$, $P < 0.0001$), competitive sport activity ($\beta = 0.258$, $P < 0.0001$), and age ($\beta = 0.222$, $P < 0.0001$) as independent determinants of LAVi (model $R^2 = 0.54$, $P < 0.0001$). By separate analyses, although LVEDVi, age, and LVMi were predictors of LAVi in both groups, body mass index and the *E*/*e*′ ratio were additional predictors of LAVi only in non-athletes.

Conclusions In healthy individuals LV size, competitive sport, age, and LV mass are independent determinants of LAVi. Body mass index and the *E*/*e*′ ratio affect LAVi only in non-athletes. These findings may have practical implications when assessing normalcy of LA size in the clinical setting.

Keywords Left atrial volume • Ageing • Diastolic function • Athletes

Left atrial (LA) size is an independent predictor of adverse clinical outcome in several clinical conditions as well as in the general population.[1–4] Although the assessment of LA diameter is effectively used both for research and clinical purposes, because LA enlarges asymmetrically, LA volume indexed (LAVi) for body surface area (BSA) is now recognized as the most accurate measure of LA size obtainable by standard echocardiography.[5] Current recommendations encourage the clinical utilization of LAVi to quantify LA size[6] and support its use as a key element for the haemodynamic evaluation of diastolic function[7,8] and for the diagnosis of heart failure with normal ejection fraction.[9]

A number of demographic and anthropometric factors have been identified as determinants of LAVi[1] and the role of ageing is still debated.[10–12] Although the effects of competitive training activity on LA size have been previously investigated,[13–17] the relative role of multiple determinants of LAVi in athletes and non-athletes remains to be elucidated. The present study aimed to

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study a group of healthy individuals and competitive athletes over a wide range of ages in order to evaluate the relative effects of echocardiographic, demographic, and anthropometric variables on LAVi, aiming at investigating their potential implications when assessing normalcy of LAVi in the clinical setting.

Methods

Study population

Healthy individuals aged ≥16 years were consecutively identified and enrolled if they were normotensive, had a normal 12-lead ECG,[18] normal LV ejection fraction (>55%) and wall motion score index. Subjects were excluded if they had (i) arterial systemic hypertension (BP ≥135/85 mmHg as average of different three visits) and/or were on active anti-hypertensive treatment, (ii) overt coronary artery disease (defined as previous acute coronary syndrome and/or revascularization procedures, or positive stress tests of inducible ischaemia); (iii) primary cardiomyopathy and/or genetic cardiovascular disease (including Marfan syndrome); (iv) congenital heart disease; (v) mitral or aortic valvular insufficiency of higher degree than trivial, valvular stenosis of any degree, or any previous cardiac or vascular surgery or interventional procedure (including ablation of accessory pathways); (vi) previous chemotherapy and/or chest radiotherapy; (vii) documented episodes of atrial fibrillation or (AF) or atrial flutter (even if paroxysmal and remote), either complex or frequent (i.e. >10 ectopic beats per hour at Holter monitoring) supra-ventricular or ventricular arrhythmias; (viii) any kind of cardiac therapy; (ix) previous cardioembolic stroke, including transient ischaemic attacks; (x) diabetes mellitus or any kind of endocrinologic disorder.

Subjects were defined as *athletes* if engaged in competitive activities ≥5 consecutive years, and if declared eligible for that specific sport by board-certified practitioners according to well-defined protocols[18] within 6 months from the performance of the echocardiographic examination.

Height (in metre) and weight (in kilogram) were measured at the time of the echo examination; body mass index (BMI) was computed as weight/height squared and BSA calculated by the Du Bois and Du Bois formula. Comprehensive echocardiographic examinations were performed using a commercially available system (Vivid-7, GE Healthcare, Milwaukee, WI, USA) equipped with a multifrequency phased-array transducer. All examinations were performed and interpreted by the same investigator (S.N.) according to current guidelines[6] by averaging three consecutive cycles. Systolic and diastolic blood pressures were measured using a cuff sphygmomanometer at the end of the examination.

Echocardiography

LV end-diastolic and LV end-systolic volumes were calculated using the modified biplane Simpson's rule and indexed for BSA [LV end-diastolic volume index (LVEDVi) and LV end-systolic volume index (LVESVi), respectively]; LV mass was calculated using either M-mode tracings or linear measurements of 2D recordings of the left ventricle and also indexed to BSA (LVMi). The LV ejection fraction (EF) was calculated as [(LVEDVi − LVSVi)/LVEDVi] × 100 and LV stroke volume index measured as LVSVi = LVEDVi − LVESVi. Relative wall thickness was defined as 2 × LV end-diastolic posterior wall thickness/LV end-diastolic diameter.[6]

LA volume was assessed by the biplane area-length method and indexed for BSA. From the apical approach, care was taken to obtain multiple, dedicated views of the LA purposely oriented to maximize LA area with optimal definition of the LA wall; LA area was traced along the perimeter (avoiding the confluence of pulmonary veins and LA appendage) with a straight line connecting both sides of the mitral leaflet base attachment points to the valve ring taken as the superior border of the area outline. The long-axis selected for volume assessment was drawn perpendicularly to the midpoint of such atrioventricular plane.[6] Differences in infero-superior length ≤5 mm between the two planes were used as a quality control to avoid foreshortening.[1] Measurements were performed at the end of ECG-derived T-wave, just before the opening of the mitral valve. The heart rate was obtained from the loop used for each LAVi study.

Pulsed Doppler of LV mitral inflow was recorded in the apical four-chamber view at the tips of the mitral valve: early (E) and atrial (A) peak velocities (m/s), peak velocity E/A ratio and E velocity deceleration time (ms) were measured. Pulsed Tissue Doppler was performed as previously reported.[19] Systolic (s′) early diastolic (e′) and atrial (a′) velocities were measured at the septal and the lateral site of the mitral annulus and averaged. The ratio between transmitral E and average e′ (*E*/*e*′ ratio) was calculated as a non-invasive estimate of LV filling pressure degree.

Statistical analysis

Data are shown as mean ± SD. Comparisons of continuous variables between athletes and healthy subjects were performed using Student's *t*-test for independent samples. The χ^2 test was used to compare categorical variables. Univariate correlations were expressed using Pearson coefficients. To compare the slopes of the relationships of LAVi with other variables between athletes and non-athletes, GLM analysis was used to explore the significance of the interaction terms between those variables and the athletes status. Stepwise multiple regression analysis was used to explore independent predictors of LAVi as a continuous variable. A probability-of-*F*-to-enter ≤0.05 and a probability-of-*F*-to-remove ≥0.10 were used as selection criteria. Collinearity diagnostic was used to assess model stability. A *P*-value <0.05 was considered for statistical significance. All tests were two-tailed. The statistical package SPSS for Windows, Release 15.0, was used to perform all analyses.

Results

General features and atrial size

The study population included 418 individuals who satisfied the inclusion criteria (*Table 1*). Mean age was 41.7 ± 15.6 (range 16–84 years); 157 (38%) were competitive athletes, mostly ($n = 147$; 94%) involved in endurance sports (cycling, rowing, long-distance running and swimming, triathlon, soccer, basketball). BMI was ≤25 kg/m^2 in 288 patients (68%), between 25.1 and 30 kg/m^2 in 116 (28%), and >30 kg/m^2 in 14 (4%). Differences in anthropometric, demographic, and echocardiographic variables were observed between athletes and non-athletes as expected. Measurements of LV diastolic function were within normal range in the majority of the subjects. Twenty-one (5%) patients had a septal e′ < 8 cm/s, 24 (6%) had a lateral e′ < 10 cm/s, and none had an average *E*/*e*′ > 13.

Mean LAVi was 32.2 ± 9.0 mL/m^2 (range = 15.8–69.9 mL/m^2) in the pooled population and was larger in athletes than in non-athletes (38.9 ± 9.6 mL/m^2 vs. 28.4 ± 5.8 mL/m^2, respectively, $P < 0.0001$). LAVi values higher than the cut-off currently accepted for normality (28 mL/m^2)[6] were observed in the large majority of athletes ($n =$

Table 1 General characteristics of the study population

	Overall (n = 418)	Athletes (n = 157)	Non-athletes (n = 261)	P-value
Male gender (n, %)	310 (65.3)	158 (85.4)	152 (52.4)	<0.0001
Age (years)	41.7 ± 15.6	35.6 ± 14.9	45.3 ± 14.9	<0.0001
Height (m)	171.6 ± 9.0	176.4 ± 8.3	169.3 ± 8.4	<0.0001
Weight (kg)	71.5 ± 12.0	76.7 ± 11.2	68.3 ± 11.4	<0.0001
BSA (m^2)	1.84 ± 0.19	1.94 ± 0.18	1.78 ± 0.17	<0.0001
BMI (kg/h^2)	23.9 ± 3.1	24.3 ± 2.7	23.8 ± 3.2	0.36
Heart rate (bpm)	70.2 ± 13.1	63.2 ± 11.7	74.1 ± 12.1	<0.0001
SBP (mmHg)	125.2 ± 13.0	127.8 ± 14.1	123.8 ± 12.2	0.030
DBP (mmHg)	76.2 ± 7.9	76.4 ± 8.4	76.0 ± 6.2	0.86
LVMi (g/m^2)	83.0 ± 18.3	95.0 ± 17.8	76.0 ± 14.5	<0.0001
LVEDVi (mL/m^2)	63.3 ± 15.8	76.2 ± 16.2	55.6 ± 9.2	<0.0001
LVESVi (mL/m^2)	21.3 ± 7.0	26.2 ± 7.8	18.4 ± 4.5	<0.0001
LV ejection fraction (%)	66.6 ± 5.6	65.9 ± 5.5	67.0 ± 5.7	0.052
E velocity (m/s)	0.82 ± 0.15	0.83 ± 0.15	0.82 ± 0.15	0.19
A velocity (m/s)	0.58 ± 0.16	0.51 ± 0.16	0.62 ± 0.15	<0.0001
E/A ratio	1.54 ± 0.57	1.78 ± 0.65	1.40 ± 0.45	<0.0001
Deceleration time (m/s)	181.0 ± 42.3	181.1 ± 41.1	181.0 ± 43.0	0.99
Average s′ (cm/s)	11.0 ± 1.9	11.1 ± 2.1	10.9 ± 1.9	0.18
Average e′ (cm/s)	14.3 ± 3.3	15.1 ± 3.2	13.7 ± 3.2	<0.0001
Average a′ (cm/s)	9.9 ± 2.4	8.9 ± 2.5	10.4 ± 2.2	<0.0001
Average *E/e′*	6.0 ± 1.3	5.7 ± 1.2	6.2 ± 1.4	<0.0001

A, late diastolic peak velocity of the mitral flow; a′, peak late diastolic annular velocity; BMI, body mass index; BSA, body surface area; E, early diastolic peak velocity of the mitral flow; e′, peak early diastolic annular velocity; LV, left ventricular; LVEDVi, LV end-diastolic volume index; LVESVi, LV end-systolic volume index; LVMi, LV mass index; s′, peak systolic annular velocity.

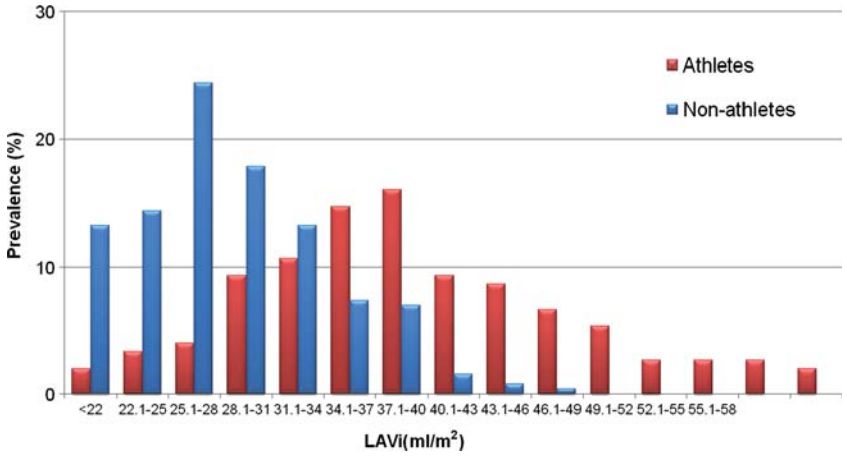

Figure 1 Distribution of left atrial volume index in athletes and non-athletes.

135; 86.0%) and in nearly half of non-athletes (n = 124; 47.5%) (*Figure 1*). Measures of LAVi above the reference value suggested by the current recommendations for the assessment of LV diastolic function (34 mL/m^2)[7] were found in 105 (66.9%) athletes and in 44 (16.9%) non-athletes. Specifically, a considerable percentage of athletes (37.6%) showed LAVi values over the cut-off point currently used to identify severe LA enlargement (40 mL/m^2)[6]. The 5th, 25th, 50th, 75th, and 95th percentiles of LA volume and LAVi distributions in the overall population and in the two study groups after stratification by gender are shown in *Table 2*.

Table 2 Main percentiles of left atrial volume and volume index in the study population, stratified by gender and competitive sport status

	Overall (n = 418)			Athletes (n = 157)			Non-athletes (n = 261)		
	All	Male	Female	All	Male	Female	All	Male	Female
LA volume (mL)									
5th	34.0	41.7	29.2	44.6	46.4	32.1	32.3	40.3	29.1
25th	45.7	52.1	37.2	61.0	65.5	50.2	41.5	47.9	36.8
50th	56.4	65.6	45.1	74.2	76.5	57.8	50.8	55.1	43.7
75th	70.5	77.4	55.0	90.1	91.8	62.5	57.7	63.2	53.3
95th	101.1	115.3	66.8	112.7	114.4	67.3	72.4	73.3	66.5
LA volume index (mL/m^2)									
5th	20.9	22.6	18.1	24.5	24.6	17.1	19.5	21.9	18.2
25th	25.9	27.5	23.1	32.6	32.7	31.7	24.3	26.0	22.8
50th	30.8	34.2	27.2	38.1	39.1	34.6	27.7	28.5	26.2
75th	37.3	39.5	32.1	44.3	45.9	36.9	31.9	32.6	30.7
95th	49.4	61.2	38.3	56.9	57.4	38.7	38.0	38.1	38.0

Table 3 Univariate correlations of left atrial volume index

Variable	Overall		Athletes		Non-athletes	
	R	P-value	R	P-value	R	P-value
LVEDVi	0.65	<0.0001	0.51	<0.0001	0.38	<0.0001
LV stroke volume index	0.61	<0.0001	0.49	<0.0001	0.29	<0.0001
LV mass index	0.63	<0.0001	0.53	<0.0001	0.43	<0.0001
LVESVi	0.57	<0.0001	0.40	<0.0001	0.34	<0.0001
Sport	0.57	<0.0001	—	—	—	—
Heart rate	−0.41	<0.0001	−0.28	<0.001	−0.23	0.0001
Sex	0.35	<0.0001	0.24	0.0013	0.19	0.0003
BMI	0.23	<0.0001	0.13	0.0007	0.32	<0.0001
SBP	0.17	0.0007	0.13	0.11	0.08	0.20
LV ejection fraction	−0.14	0.0031	−0.11	0.15	−0.12	0.053
DBP	0.08	0.11	0.09	0.28	0.08	0.19
Deceleration time	0.05	0.35	0.02	0.84	0.10	0.10
E/e'	0.05	0.28	0.20	0.015	0.22	0.0004
e'	0.02	0.63	−0.10	0.20	−0.27	<0.0001
Age	0.01	0.99	0.23	0.0039	0.22	0.0003

Abbreviations as in *Table 1*.

Predictors of left atrial volume index in the overall population

Univariate relationships of LAVi in the overall population and in the two study groups are shown in *Table 3*. Results of stepwise multiple regression analyses are shown in *Table 4*. In the pooled population, LVEDVi, competitive sport, age, and LVMi independently predicted LAVi. LVEDVi was the principal predictor, accounting for 72.6% of the total LAVi variability explained by the model. In an alternative analysis considering only clinical variables in the group of potential covariates, competitive sport activity ($\beta = 0.546$, $P < 0.0001$), age ($\beta = 0.157$, $P < 0.0001$), male gender ($\beta = 0.144$, $P = 0.0009$), and BMI ($\beta = 0.097$, $P = 0.023$) emerged as independent determinants of an LAVi (model $R^2 = 0.38$, $P < 0.0001$). Competitive sport activity was the principal determinant, accounting for 82.7% of the total variability explained by the model.

Predictors of left atrial volume index in athletes and non-athletes

LVEDVi, age, and LVMi independently predicted LAVi in both athletes and non-athletes (*Table 4*). Conversely, BMI and the E/e' ratio

Table 4 Predictors of left atrial volume index, as identified by stepwise multivariate regression analysis

Variable	β	P-value
Overall (model $R^2 = 0.54$, $P < 0.0001$)		
LVEDVi	0.378	<0.0001
LV mass index	0.260	<0.0001
Competitive sport	0.258	<0.0001
Age	0.222	<0.0001
Athletes (model $R^2 = 0.41$, $P < 0.0001$)		
LVEDVi	0.418	<0.0001
Age	0.343	<0.0001
LV mass index	0.261	0.0013
Non-athletes (model $R^2 = 0.35$, $P < 0.0001$)		
LVEDVi	0.341	< 0.0001
LV mass index	0.242	<0.0001
BMI	0.168	0.0043
E/*e*′	0.146	0.013
Age	0.124	0.047

Abbreviations as in *Table 1*.

were independently associated with LAVi only in non-athletes. Again, LVEDVi was the principal predictor in both models, accounting for 57.0%, and 41.5% of the total LAVi variability explained by the models in athletes and non-athletes, respectively. Among clinical variables, the heart rate ($\beta = -0.264$, $P = 0.0005$), age ($\beta = 0.248$, $P = 0.0010$), and male gender ($\beta = 0.206$, $P = 0.0060$) were associated with LAVi in athletes (model $R^2 = 0.17$, $P < 0.0001$), whereas BMI ($\beta = 0.238$, $P = 0.0002$), heart rate ($\beta = -0.181$, $P = 0.0021$), age ($\beta = 0.127$, $P = 0.040$), male gender ($\beta = 0.118$, $P = 0.0048$) predicted LAVi in non-athletes (model $R^2 = 0.16$, $P < 0.0001$). *Figure 2* depicts the different impact of predictors on LAVi in athletes and non-athletes, as identified by comparing the respective regression slopes. LVMi had a stronger impact in athletes than in non-athletes.

Regression equations

Table 5 shows the final regression equations for the full and clinical models in the overall population and separately in the two study groups. For practical purposes, we propose the following, simplified equation, which is applicable to whole study population irrespective of level of physical activity:

$$\text{LAVi(full model)} = \frac{\text{LVEDVi}}{5} + \frac{\text{Age}}{8} + \frac{\text{LVMi}}{8} + 5\,(\text{if competitive sport}) + 1$$

$$\text{LAVi(clinical model)} = \frac{\text{Age}}{10} + \frac{\text{BMI}}{3} + 3(\text{if male}) + 10\,(\text{if competitive sport}) + 16$$

Discussion

In the present study, we assessed the role of multiple anthropometric, demographic, and echocardiographic factors as determinants of LAVi, in a prospectively recruited study cohort of adult healthy subjects and competitive athletes over a wide range of age. The main findings of our study are the following: (i) LAVi appears to result from the complex interplay of LVEDVi, level of physical activity, age and LVMi, each contributing independently to LV size; (ii) different predictors of LAVi can be identified in healthy individuals according to their athletic status, BMI and *E*/*e*′ ratio playing a significant role only in non-athletes (iii); LAVi appears to be often greater than suggested by echocardiographic recommendations for normalcy,[6] particularly in athletes, challenging the applicability of current partition values to specific subsets of healthy individuals. These findings highlight the need of considering LAVi measurements in relation at least with patient's age, athletic status, LV volume and mass, and also a comprehensive Doppler-derived LV diastolic assessment,[7] rather than applying clear-cut LAVi values.[6]

Impact of demographic variables and body size on LA volume

Conflicting results have emerged from observational studies assessing the relationship between LA size and ageing.[1] They tended to explain age-related increase in LA volume with concomitant alterations of LV diastolic physiology occurring with age. In particular, Thomas *et al.*[10] demonstrated that an increase in LA size is an expression of pathology more than of a normal ageing in 92 healthy individuals (age range 17–86 years). On the contrary, our findings demonstrate that age is an independent determinant of LAVi in each of the proposed regression models, independent on the impact of age-dependent changes in LV diastolic properties.[19] Even in non-athletes, ageing retained an independent predictive value for LAVi. The present data, thus, confirm those observed in healthy elderly subjects of the Cardiovascular Health Study[11] and in participants of the MONIKA/KORA Study.[12]

The effect of gender on LA volume is currently considered to be negligible after indexation for BSA.[1] Our study substantially confirms these findings since the impact of male gender as an independent predictor of LA increase after adjusting for BMI and athletic status was lost in multivariate models including LVEDVi and LVMi.

Several studies identified BMI as an independent predictor of LA size in adults.[1,12,20] Our data provide additional information, showing that BMI is an independent predictor of LAVi only in the pooled population and in non-athletes, despite similar BMI values when compared with athletes. These observations may be clinically relevant given the recognized association between increased body size and AF.[21]

Left atrial size in athletes

Sport activities are well-known contributors of cardiac remodelling including LA size.[22–24] Extreme and uninterrupted endurance training over a 4- to 17-year period is not associated with changes in LV morphology or function but with a significant increase in LA antero-posterior diameter.[25] A frequent prevalence of mild-to-moderate LA enlargement (27.5%) has been recently observed in 615 elite athletes (age 28.4 ± 10.2 years, range 18–40) from a referral sports medicine centre.[14] Noteworthy, in that study, independent predictors of LAVi were training type

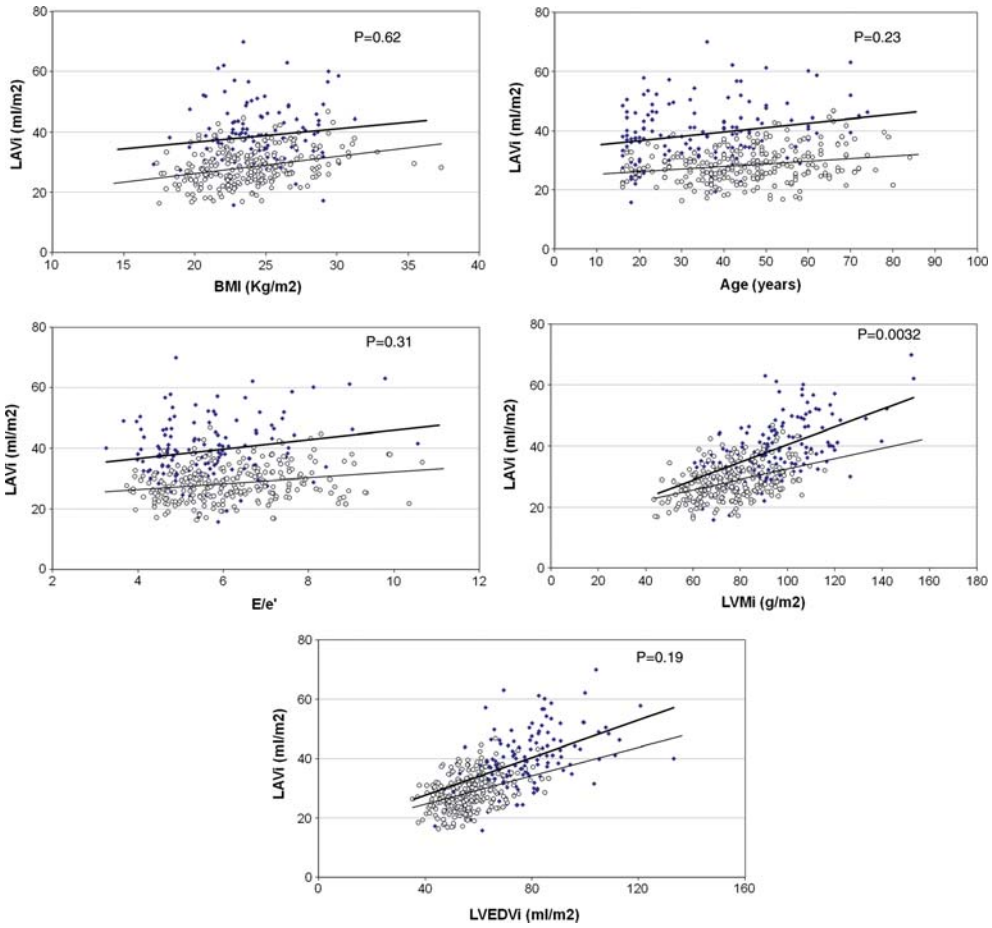

Figure 2 Impact of predictors on left atrial volume index in athletes (blue squares) and non-athletes (white squares). The *P*-value reported in each scatterplot refers to the comparison of the two slopes, as calculated by general linear model analysis.

Table 5 Regression equations for the prediction of left atrial volume index

Model	Equation
Overall	
Full model	0.21 · LVEDVi + 0.13 · LV mass index + 0.13 · Age + 4.8 (if competitive sport) + 1.2
Clinical model	0.09 · Age + 0.30 · BMI + 2.8 (if male) + 9.9 (if competitive sport) + 16.0
Athletes	
Full model	0.24 · LVEDVi + 0.14 · LV mass index + 0.22 · Age – 0.4
Clinical model	0.16 · Age – 0.22 · Heart rate + 5.9 (if male) + 42.1
Non-athletes	
Full model	0.21 · LVEDVi + 0.09 · LV mass index + 0.04 · Age + 0.33 · BMI + 0.60 · *E*/*e*′ – 3.4
Clinical model	0.05 · Age – 0.09 · Heart rate + 1.3 (if male) + 0.43 · BMI + 21.8

Abbreviations as in *Table 1*.

and duration, and LV end-diastolic volume.[14] In our study the prevalence of increased LAVi was higher, including 39% of athletes with severely dilated LAVi (i.e. >40 mL/m^2), but age was older and a substantial proportion of participants was engaged in sports (e.g. cycling) with strong impact on heart remodelling.[13,14,22] The older age of our athletes could have induced *per se* larger LA volumes but also as an equivalent of training duration.

Difference in determinants of LAVi between athletes and non-athletes of our study is worthy of note. Since LVEDVi and LVMi maintained their predictive value in each group, and *E*/*e*′ ratio was a predictor of LAVi only in non-athletes, it is conceivable that neuro-hormonal, metabolic, and cardiovascular factors other than LV size and mass (e.g. ventriculo-arterial coupling) might be responsible of these differences. Moreover, the fact that LV diastolic function has a significant impact on LAVi only in non-athletes over a wide range of *E*/*e*′ ratio values and age supports the concept that LAVi should not be considered a mere surrogate of comprehensive assessment of LV diastolic function.[3]

Recent data suggest endurance sport practice as a potential risk factor for AF and atrial flutter.[26–30] The association between AF and sport is complex, however, with a biphasic age-related influence of physical training in adults, prevalently in male athletes. The multifactorial pathophysiology of sport-related AF depends on the interaction of triggers, modulators, and substrates.[26,27] By demonstrating the independent role of age and sport activity on LAVi, our findings might provide a rationale for future studies addressing the impact of type and intensity of training on LAVi and possibly predisposition to AF in athletes.

Implications for normalcy

Since cardiovascular risk and LA size are continuously linked,[1–9] the identification of reference values for LAVi is of utmost importance for clinical purposes. To this regard, it should be reminded that values obtained by the three validated echocardiographic methods are not interchangeable.[31–33] In particular, the prolate-ellipse method systematically underestimates LAVi as compared both to the biplane Simpson and area-length methods, with more pronounced differences for larger LAVi.[33] Finally, accuracy of echocardiographic measurements heavily relies on multiple technical elements and is influenced by common pitfalls.[1] To lessen these potential limitations, we prospectively assessed LAVi using purposely oriented cine-loops (i.e. not using cine-loops stored for LV assessment) to maximize LA area.

The present study demonstrates that LAVi measurements should be considered in conjunction with patients' age, athletic status, LV size, and diastolic function consistent with the current recommendations.[7] Thus, our findings show that differences in terms of demographic, anthropometric, and training-related parameters would result into a potential misclassification of otherwise normal subjects when based on dichotomically suggested normal cut-off values.[6]

The utilization of specific normalcy criteria (e.g. >95th percentile), ideally partitioned according to gender and sport activity, could at least in part obviate this problem. Interestingly, in stable outpatients with coronary artery disease, a higher cut-off value for severe LAVi enlargement than that suggested by current recommendations (respectively 50 vs. 40 mL/m^2) provided more accurate prognostic information in terms of heart failure-related hospitalization and overall mortality.[34] The utilization of regression equations proposed in our study, resulting into an estimate of measured to predicted ratio for LAVi, could offer further potential advantages for better clinical identification of abnormally enlarged LAVi in individual patients.[11]

Study limitations

Participants of our study were selected because referring to echocardiography and not because part of a population-based study. Based on the low prevalence of overweight subjects, it is conceivable that a proportion of these individuals might have practiced light-to-moderate physical activity in leisure time or during their working hours, a minority having a truly sedentary lifestyle. Since different intensities in physical activity are related to increasing heart size[23] and LA remodelling,[35] this could have resulted into a relative overestimation of LAVi in non-athletes. However, it has to be taken into account that physical activity is part of the actual lifestyle in real world and a high proportion of individuals with these characteristics daily refer to outpatients cardiologic clinics.

Another limitation corresponds to the choice of *E*/*e*′ ratio as a comprehensive estimate of LV diastolic impairment. The accuracy of *E*/*e*′ ratio as a measure of LA pressures in a range <8 can be considered doubtful in a population as that of our study where abnormal LV filling pressure could not be expected. However, the use of *E*/*e*′ ratio as an hallmark of LV diastolic function is encouraged by recent recommendations on Doppler-derived LV diastolic function[7] it being also a prognostic indicator for cardiovascular disease.[36]

Clinical implications

By including athletes in a prospectively recruited healthy population, we demonstrated that multiple echocardiographic, anthropometric, and demographic variables independently contribute to the magnitude of LA volume. LVEDVi, age, and LVMi are predictors of LAVi both in athletes and non-athletes, whereas BMI and *E*/*e*′ ratio predict LAVi in non-athletes only. These finding should be taken into account when assessing normalcy of LA size in the clinical setting.

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