Left ventricular volume as a predictor of exercise capacity and functional independence in individuals with preserved ejection fraction

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Background: Cardiorespiratory fitness (CRF) is vital for independent living and is a powerful prognostic marker. Increased left ventricular (LV) volume has been linked with high CRF in athletes, but its utility as a diagnostic marker of low CRF across the entire health-disease continuum has yet to be tested.

Methods: This multi-center international cohort from Australia and Belgium examined the relationship between ventricular size on resting echocardiography and CRF (peakVO2 from cardiopulmonary exercise testing [CPET] or CPET with simultaneous echocardiography) in individuals with preserved LV ejection fraction (≥50%). LV end-diastolic volume (LVEDV) and LVEDV indexed to body surface area (LVEDVi) were tested as predictors of very low CRF (CRF associated with functional disability - peakVO2 < 1100ml or <18 ml/kg/min) and compared against other candidate measures of systolic and diastolic cardiac function that have been associated with heart disease. Thresholds for absolute and indexed LVEDV which best distinguished between lower and higher CRF status were identified.

Results: 2876 individuals (251 healthy non-athletes, 309 elite endurance athletes, 1969 individuals with unexplained dyspnea, 347 individuals with heart failure with preserved ejection fraction) were included. For the entire cohort, LVEDV had the strongest univariate association with peakVO2 ($R2 = 0.45$, standardized [std] β 0.67, $p< 0.001$) and, remained the strongest independent predictor of peakVO2 after adjusting for age, sex and body mass index (std β 0.44, $p < 0.001$). The relationship between LVEDV and VO2peak differed based on health/disease status (Figure 1). LVEDV demonstrated the greatest diagnostic capability in identifying functional disability (LVEDV AUC 0.72; LVEDVi AUC 0.71, Figure 2), outperforming ejection fraction, diastolic velocities, atrial volumes and pulmonary artery pressure estimates. The probability of achieving a peak VO2 below the threshold required for functional independence was highest for smaller ventricular volumes with LVEDV and LVEDVi of 88ml and 57 ml/m2 proving the optimal cut-points, respectively.

Conclusions: A small LVEDV is associated with a higher probability of poor exercise capacity, failure to achieve the peak VO2 required for functional independence and is the strongest independent echocardiographic predictor of CRF across the health-disease continuum.

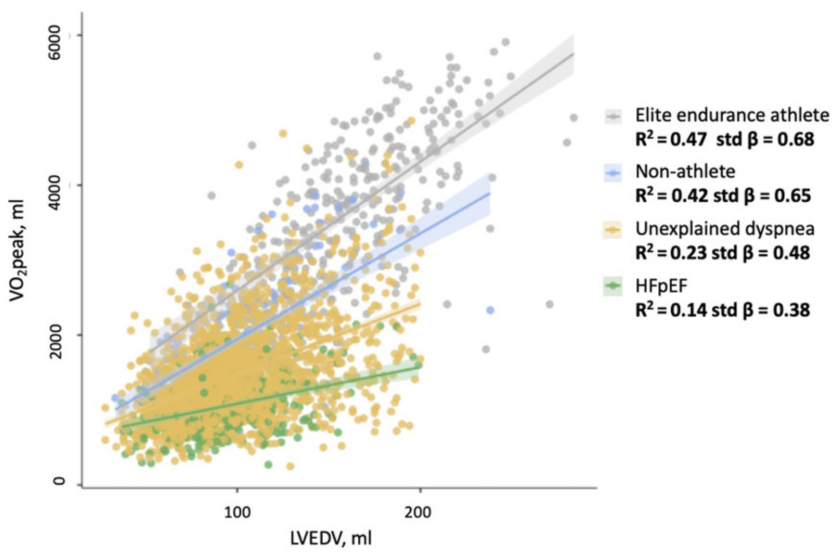

Figure 1. *Association between ventricular size and cardiorespiratory fitness by health/disease status*. Univariate linear regression with standard errors by health/disease status. Grey circles = elite endurance athletes; Blue circles = non-athletes; Yellow circles = participants with unexplained dyspnea; Green circles = participants with HFpEF. P < 0.0001 for all. LVEDV = left ventricular end-diastolic volume; HFpEF = heart failure with preserved ejection fraction. Std β = standardized β.

Figure 1. Ventricular Size and CRF

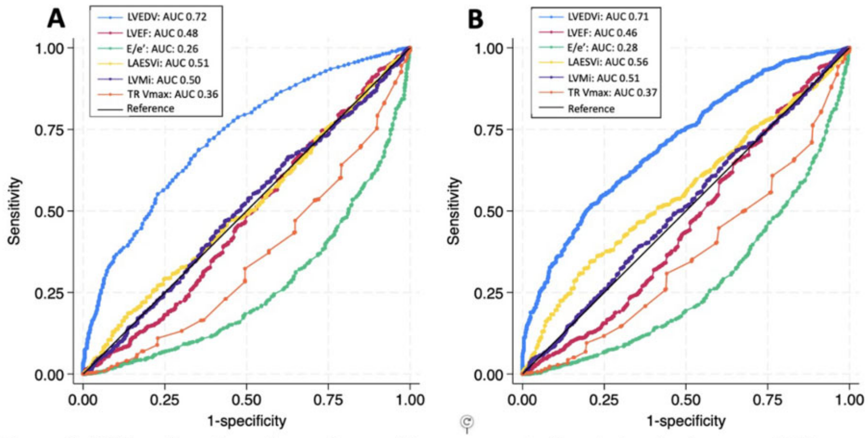

Figure 2. *Utility of resting echocardiographic measures in discriminating between CRF status.* ROC analysis for echocardiographic variables and ability to discriminate between (A) absolute peakVO_2 < 1100ml and ≥ 1100ml and (B) peakVO_2 < 18ml/kg/min and ≥ 18ml/kg/min. LVEDV = left ventricular end-diastolic volume; LVEDVi = LVEDV indexed to BSA; LAESVi = left atrial systolic volume indexed to body surface area; LVEF = left ventricular ejection fraction; GLS = average global longitudinal strain; LVMi = left ventricular mass indexed to BSA; TR Vmax = maximal tricuspid valve velocity at rest

Figure 2. Predictors of CRF status