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Cardiac Imaging

Role of Left Atrial Size in Risk Stratification and Prognosis of Patients Undergoing Stress Echocardiography

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Objectives The purpose of this study was to evaluate the role of diastolic dysfunction as measured by left atrial (LA) size in patients undergoing stress echocardiography (SE).

Background Left atrial size is a surrogate marker of diastolic function. However, its prognostic value in patients referred for SE is not well defined.

Methods We evaluated 2,705 patients (60 ± 13 years, 47% men) undergoing SE (56% dobutamine). Patients with significant mitral valve disease (mitral stenosis or ≥ moderate mitral regurgitation) were excluded. Enlarged LA was defined as a LA size indexed to body surface area ≥2.4 cm/m^2. Follow-up (mean 2.7 ± 1.0 years) for nonfatal myocardial infarction or cardiac death (n = 122) was obtained.

Results A dilated LA was able to further risk-stratify both the normal and abnormal SE groups. In the presence of a dilated LA, an abnormal SE portends a worse prognosis compared with patients with normal LA size. Cox proportional modeling showed that a dilated LA added incremental value over traditional risk factors, stress electrocardiographic, rest echocardiographic, and SE variables for the prediction of hard events (global chi-square increased from 90.4 to 113.1 to 176.1 to 184.4 to 190.5; $p < 0.05$ all groups). Left atrial size was a significant predictor of events independent of left ventricular systolic dysfunction and ischemia (relative risk = 1.84, 95% confidence interval 1.19 to 2.85; $p = 0.006$).

Conclusions In patients referred for stress echocardiography, LA size provides independent and incremental value over standard risk factors including left ventricular systolic dysfunction and ischemia. Left atrial size is a powerful prognosticator and should be routinely used in the prognostic interpretation of stress echocardiography. (J Am Coll Cardiol 2007;50:1254–62) © 2007 by the American College of Cardiology Foundation

As measured by M-mode echocardiography, an increase in left atrial (LA) dimension is a risk factor for atrial fibrillation, stroke, and death and is closely related to general cardiovascular risk burden (1,2). Left atrial size is also a marker of left ventricular (LV) diastolic function in patients without significant mitral valve disease or systolic heart failure. Left atrial size reflects the chronicity and magnitude of the increased LV filling pressure (3) and is thus a marker of the severity and duration of diastolic dysfunction (4). It has been suggested (5) that Doppler indexes of diastolic function reflect filling pressures at one point in time, whereas increased LA reflects the cumulative effect of filling pressures over time and hence has been compared to hemoglobin A1c for diabetes.

It has recently been demonstrated (6) that the size of the LA is better described by volume rather than diameter. However, unidimensional measurement is still the most common method worldwide to quantify LA size.

Stress echocardiography is increasingly used for diagnosis, risk stratification, and prognosis of patients with known or suspected coronary artery disease (CAD) (7–11). However, the role of LA size in risk stratification of patients referred for stress echocardiography is not defined. We thus sought to evaluate the role of a routinely measured unidimensional measurement of LA size at further risk stratification of patients with known or suspected CAD referred for stress echocardiography. Our objective was 2-fold: 1) to evaluate the role of LA size as a risk factor for cardiovascular events, and 2) to evaluate the prognostic impact of LA size in risk stratification and prognosis during stress echocardiography.

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Methods

Study population. We identified 3,260 consecutive patients referred for stress echocardiography. Successful prospective follow-up for future cardiac events after testing was obtained in all patients. Patients with acute myocardial infarction (<3 days), hemodynamically significant valvular abnormalities, hemodynamic instability, poor acoustic windows (<13 of 16 segments visualized by echocardiography), pregnancy, and inability to give informed consent were excluded from the study. Patients with significant mitral valve disease (mitral stenosis or moderate to severe mitral regurgitation by color Doppler) were excluded from this analysis (n = 555), leaving a cohort of 2,705 patients. Informed written consent was obtained from all patients, and the study was approved by the institution's review board.

Exercise echocardiography protocol. Maximal exercise treadmill testing was performed using standard Bruce protocol. Patients exercised to general fatigue, with premature termination for severe angina, ventricular tachycardia, hemodynamically significant arrhythmias, or hemodynamic instability. The maximal degree of ST-segment change at 80 ms after the J point on the electrocardiogram (ECG) was measured. Patients with ≥1 mm ST-segment change after stress were considered to have a positive stress ECG response. After-exercise echocardiographic images were acquired within 30 to 60 s after termination of treadmill exercise.

Dobutamine echocardiography protocol. Dobutamine was administered intravenously beginning at a dose of 5 to 10 μg/kg/min and increased by 5 to 10 μg/kg/min every 3 min to a maximum of 50 μg/kg/min or until a study end point was achieved. The end points for termination of the dobutamine infusion included development of new segmental wall-motion abnormalities, attainment of 85% maximum age-predicted heart rate (MPHR), or the development of significant adverse effects related to the dobutamine infusion. Atropine was administered intravenously in 0.25-mg increments every 3 min to a maximum of 2 mg if a study end point was not achieved at the maximum dobutamine dose.

Beta-blockers were held on the morning of the test, as is the protocol in our laboratory for both types of stress. During both types of stress echocardiography, transthoracic echocardiographic images were obtained with the patient in the left lateral decubitus position using commercially available ultrasound equipment (Acuson Sequoia, Mountain View, California; Hewlett Packard Sonos 5500, Andover, Massachusetts). Four standard echocardiographic views were obtained with each acquisition: parasternal long-axis, parasternal short-axis, apical 4-chamber, and apical 2-chamber views. Echocardiographic images were acquired at baseline, with each increment of dobutamine infusion, and during the recovery phase. Cardiac rhythm was monitored throughout the stress echocardiography protocol, and 12-lead ECGs and blood pressure measurements were obtained at baseline, at each level of stress, and during the recovery phase.

Abbreviations and Acronyms

CAD = coronary artery disease
ECG = electrocardiogram
ICC = interclass correlation
LA = left atrial/atrium
LV = left ventricular
MI = myocardial infarction
RR = risk ratio
WMSI = wall motion score index

Echocardiographic image analysis. The LV was divided into 16 segments as recommended by the American Society of Echocardiography, and a score was assigned to each segment at baseline, with each stage of stress, and during the recovery phase (12). Each segment was scored as follows: 1 = normal, 2 = mild to moderate hypokinesis (reduced wall thickening and excursion), 3 = severe hypokinesis (marked reduced wall thickening and excursion), 4 = akinesis (no wall thickening and excursion), and 5 = dyskinesis (paradoxical wall motion away from the center of the LV during systole) (9). All echocardiograms were interpreted by consensus agreement of experienced echocardiographers who were blinded to patients' treatment and outcome.

A normal response to stress was defined as normal wall motion at rest, with an increase in wall thickening and excursion during stress. An abnormal response to stress was defined as: 1) an LV wall segment that did not increase in thickness and excursion during stress (fixed wall motion abnormality); 2) deterioration of LV segment wall thickening and excursion during stress (increase in wall motion score of ≥1 grade); and/or 3) a biphasic response with dobutamine stress. The peak wall motion score index (WMSI) following stress was derived from the cumulative sum score of 16 LV wall segments divided by the number of visualized segments. The stress echocardiogram, with a peak WMSI of 1.0, was considered normal, and those with a WMSI >1.0 were considered abnormal. Maximal severity of ischemia was the score of the LV wall segment(s) with the greatest value (worst wall motion grade) at peak stress (range 0 to 5) (13). Ischemic extent was the number of new (ischemic) wall motion abnormality during stress that increases in wall motion score of ≥1 (range 0 to 16) (13). Resting ejection fraction used in the study analysis was a visual estimation by experienced echocardiographers.

LA size. For each patient, LA size was measured as per the recommendation of the American Society of Echocardiography with the use of a leading-edge-to-leading-edge measurement of the maximal distance between the anterior and the posterior LA wall at end-systole (14), and this measurement was done at the time of stress echocardiography. Wade et al. (15) have demonstrated low interobserver (r = 0.97) and intraobserver (r = 0.97) variability in the M-mode measurements of LA dimension using these guidelines. A dilated LA was defined as a LA size ≥3.9 cm in women or ≥4.1 cm in men or LA size indexed to body surface area ≥2.4 cm/m^2, as recommended by the American Society of Echocardiography and the European Association of Echocardiography (16). Indexing the size of body surface area