

Long-term Prognostic Importance of Transient Left Ventricular Dilation During Pharmacologic Stress Echocardiography

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Objectives: We sought to evaluate the prognostic significance of left ventricular (LV) transient ischemic dilation (TID) for patients with a positive stress echocardiogram (SE).

Background: TID during SE has been related to the presence of extensive coronary artery disease, but its long-term prognostic implications have not been reported.

Methods: In all, 99 consecutive patients with a positive SE comprised the study group. LV volumes were evaluated according to the modified Simpson's rule. TID during SE was defined as the presence of an increase in LV end-diastolic volume during the stress test. A clinical history was fulfilled for each patient and all of them were followed up.

Results: Of 99 patients, 32 (32.3%) showed TID. Mean age was 65.8 ± 9.8 years for non-TID group

and 70.2 ± 8.4 for TID group ($P = .048$). Baseline characteristics and subsequent treatment were similar in both groups. Mean follow-up was 21.4 ± 15.8 months. In non-TID group the mean survival free of acute myocardial infarction was 47.28 months and 39.7 months in TID group (log rank = 0.012). In the univariate and multivariate analysis only TID and the wall motion score index were found as independent predictors related to long-term prognosis (risk ratio = 6.9; 95% confidence interval = 0.8-59.6; $P = .042$; and risk ratio = 0.4; 95% confidence interval = 0.18-0.89; $P = .047$, respectively).

Conclusions: LV TID during SE is an easy and independent prognostic marker. It helps to select patients with increased risk. (J Am Soc Echocardiogr 2005;18:57-62.)

Stress echocardiography (SE) is an useful diagnostic tool to assess coronary artery disease.¹⁻³ The evaluation of myocardial ischemia with SE has become an accurate and standard method; as such it has demonstrated its growing use during the last years. A wide number of studies have defined its exact role in assessing myocardial ischemia and other specific cardiac conditions such as myocardial viability or coronary flow reserve.⁴⁻⁸ Different kinds of stress protocols have been used and all of them play, with variable diagnostic accuracy, an important role in the evaluation of patients with proven or suggested ischemia.

Left ventricular (LV) transient ischemic dilation (TID) has been studied by several research groups with different diagnostic methods. TID has been related to the presence of large myocardial perfusion defects and extensive coronary artery disease.^{9,10} Nevertheless,

long-term prognostic implications of TID during SE have not been reported.

Our aim was to assess the long-term prognosis of patients with TID during a positive SE and compare it with the long-term prognosis of patients with a positive SE without TID. In this way, we would be able to evaluate whether TID has further prognostic implications.

METHODS

Patient Population

This study was conducted at our hospital, which is both a primary care hospital for a local population of 500,000 people and a university-based referral center for cardiac diagnostic tests and operations. All patients with an echocardiographic positive result among those referred to undergo a SE during the inclusion period comprised the study group. Patients were recruited between March 1998 and September 2002. They underwent a SE to detect myocardial ischemia for diagnostic and prognostic purposes. Patients with a negative SE, those without a good or acceptable acoustic window in all the protocol phases, and those with significant valvular disease were not enrolled.

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SE

All patients underwent a pharmacologic SE (dobutamine or dipyridamole) according to our standard laboratory protocols. Before starting the test informed consent was obtained from each patient. Exercise echocardiography was not performed because this technique is not typically used in our daily practice. Dipyridamole SE was contraindicated in those patients with severe chronic obstructive pulmonary disease, severe bradycardia, high-degree auriculoventricular (AV) block, significant sinus node disease, or cerebrovascular disease. Dipyridamole SE was performed by administering dipyridamole intravenously at an infusion rate of 0.84 $\mu\text{g/kg/min}$ for 6 minutes. Four minutes later, 1 mg of atropine was delivered. Dobutamine SE was contraindicated in cases of uncontrolled atrial fibrillation, high blood pressure, severe aortic stenosis, hypertrophic obstructive cardiomyopathy, and severe ventricular arrhythmias. Dobutamine SE was performed by infusing dobutamine intravenously at an infusion rate of 10 $\mu\text{g/kg/min}$, increased every 3 minutes by 10 $\mu\text{g/kg/min}$ up to a dose of 40 $\mu\text{g/kg/min}$ during 6 minutes. If negative results were obtained after full dobutamine infusion or maximal heart rate was not yet achieved, atropine (1 mg) was then administered. Baseline vital signs and electrocardiogram were performed before the pharmacologic infusion and at the end of each stage. Reasons for procedure interruption included positive echocardiographic test, reaching 85% of maximal heart rate, symptomatic angina, significant ventricular arrhythmias, and hypotension or marked systemic hypertension.

Imaging

Images were acquired using a device (Sonos 5500, Phillips Medical Systems, Andover, Mass) device with harmonic images (transmission and reception frequency 1.8-3.6 MHz). Echocardiographic images were obtained from parasternal long- and short-axis views and apical 4- and 2-chamber views. In every case, a digitally acquired SE study was used. Images were stored at baseline, low dose, peak stress, and recovery phase. The study was recorded on videotape and in a digital/optical disk cineloop system. Segmental wall-motion images were interpreted by quantitative comparison according to the 16-segment scheme recommended by the American Society of Echocardiography. Segments were scored on a 4-point scale (1 = normal, 2 = hypokinetic, 3 = akinetic, 4 = dyskinetic). Ischemia was defined as new regional wall-motion abnormalities or the worsening of pre-existing ones in at least two segments belonging to the same coronary artery distribution. Neither baseline wall-motion abnormalities nor the development of dyskinesia during stress in an akinetic segment were considered as ischemic responses. When the patient failed to achieve 85% of maximum age predicted heart rate in dobutamine protocol, the test was considered inconclusive.

LV Dilation

LV volumes were evaluated according to the modified Simpson's rule. For this purpose, 4- and 2-chamber apical views were obtained in all patients and LV end-systolic volume (LVESV) and LV end-diastolic volume (LVEDV) were analyzed offline by two skilled and independent operators who were unaware of other study data. Measurements were averaged from 3 cardiac cycles. LV dilation during SE was defined as the presence of an increase in LVEDV when compared with the baseline study. The variable TID was defined as a binomial variable, as we intend to define an easy prognostic marker. As the physiologic response to pharmacologic stress is the reduction on LV volumes, any degree of TID was considered significant. The interobserver reproducibility of all the aforementioned echocardiographic volumes was calculated.

Follow-up

On each patient a clinical history was fulfilled. Clinical charts were periodically reviewed and patients were followed up as outpatients in our outpatient clinic. If any of them were admitted to hospital for any reason, clinical chart was reviewed and telephone contact, if necessary, was made. Cardiac death and myocardial infarction were considered major cardiac events. Cardiac death was defined as any death in the setting of a cardiac decompensation or any sudden death in the absence of any symptom or sign attributable to any extracardiac origin. The diagnosis of acute myocardial infarction (AMI) was established by using the criteria of an increase in cardiac troponin I above 0.1 with a typical curve of AMI. The development of new Q waves, preferably accompanied by symptoms compatible with typical ischemic chest pain, supported this diagnosis. When myocardial infarction and death occurred during the same admission the event was recorded as death only. The first cardiac event was used in the statistical analysis. Secondary end points were hospital admission because of unstable angina or heart failure.

Statistical Analysis

We used a statistical software package (SPSS, Version 11.0; SPSS Inc, Chicago, Ill). Quantitative data were expressed as media $\pm$ SD. Qualitative data were expressed as number (percentage). Comparison of qualitative data was assessed by χ^2 test or Fisher exact test when appropriated and comparison of quantitative data was assessed by *t* test. Interobserver and intraobserver reproducibility was evaluated by means of the absolute agreement intraclass correlation coefficient (ICC) with reproducibility being considered almost perfect if the ICC was between 0.81 and 1.0. Survival curves were estimated by the Kaplan-Meier method and curves were compared using the log rank test. The effects of all the parameters were studied with univariate and multivariate regression analysis (proportional hazards model). Variables with a *P* value $< .1$ in the univariate analysis were included in the multivariate

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