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EDITORIAL COMMENT

Risk Stratification by Stress Echocardiography Beyond Wall Motion Analysis*

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Left bundle branch block (LBBB) is a frequent, etiologically heterogeneous, clinically and diagnostically challenging entity. Approximately 2% of patients referred for cardiac stress testing show stable or intermittent LBBB (1). Although LBBB is a recognized predictor of unfavorable cardiac outcome (2–4), the prognosis primarily is determined by underlying cardiac pathology, including coronary artery disease, hypertension, idiopathic dilated cardiomyopathy, and aortic valve stenosis (5,6).

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The presence of LBBB makes the electrocardiogram (ECG) uninterpretable for ischemia and, therefore, a stress imaging technique is necessary for the identification of coronary artery disease (7). Despite the difficulty posed by abnormal wall motion, stress echocardiography is the best option for the diagnosis of coronary artery disease (8–10): it is more specific than perfusion imaging (8,10) and its sensitivity is good, albeit reduced, in the left anterior descending territory only in the presence of a dyskinesis in the baseline echocardiogram (9). The prognostic value of pharmacologic stress echocardiography is excellent, additive when compared with clinical and resting echocardiographic variables, and especially pronounced in patients without myocardial infarction (11). The negative predictive value of stress echocardiography in these patients is similar to that obtained with this technique and with nuclear techniques in patients without conduction abnormalities (12).

In this issue of *iJACC*, Bouzas-Mosquera et al. (13) demonstrate—in a patient population of a little more than 600—that exercise echocardiography provides significant prognostic information for prediction outcome in those with LBBB. Patients with a normal exercise echocardiogram have a very good prognosis, whereas those with abnormal results are at increased risk of death and major cardiac events. Bouzas-Mosquera et al. (13) demonstrate the additive prognostic value of wall motion abnormalities at peak exercise stress echocardiography in a prospective study analyzing hard end points. This evidence is another piece in the larger framework of the prognostic power of stress echocardiography.

The present results are consistent with previous studies evaluating the outcome of patients with LBBB. The recommendations of the American Society of Echocardiography and the European Association of Echocardiography consider physical and pharmacological stressors comparable in their diagnostic and prognostic accuracy and the choice of one over the other is strictly due to relative contraindications and ability of patients to exercise (7,14). Both physical and pharmacological stress echocardiography has been previously demonstrated to be accurate in identifying the subset of patients at greater risk of experiencing hard events in the follow-up in patients with LBBB (8–11,15). A recent meta-analysis confirmed the prognostic accuracy of noninvasive imaging techniques showing a relative risk 7-fold greater in the presence of test positivity (16) in this subset of patients.

Perhaps, however, we might expect more from stress echocardiography in the evaluation of patients with LBBB. The yearly death rate in the group of patients with a negative test is approximately 1% (13), almost double that compared with other reports (12) and supporting the role of LBBB as the manifestation of a subtle underlying cardiomyopa-

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thy. If so, which are the stress echocardiographic parameters that can be used in risk stratification beyond wall motion analysis? Would it have also been possible to risk stratify the negative subset beyond the conventional wall motion analysis?

In the last few years several parameters, such as coronary flow reserve and myocardial contractility, have been added to stress echocardiography to identify patients who, despite a negative test, have some risk of becoming troublemakers in the long run. Coronary flow reserve (CFR) evaluated by pulsed Doppler echocardiography associated with vasodilator stress recently has entered the stress echocardiography laboratory (17). A reduced CFR is an additional parameter of severity of ischemia in the risk stratification of the stress echocardiographic response, whereas patients with a negative test for wall motion criteria and normal CFR have a favorable outcome during dipyridamole stress echocardiography (18). The measurement of CFR also provides independent prognostic information in diabetic and nondiabetic patients with known or suspected coronary artery disease and negative dipyridamole stress echocardiography for wall motion criteria (19) and in patients with chest pain syndrome and normal coronary arteries (20). The prognostic impact of CFR also has been recently proven in patients with nonischemic dilated cardiomyopathy (21): an abnormal CFR detectable by Doppler echocardiography identifies a subset of patients at greater risk of spontaneous events (death and worsening of clinical status). The lack of increment of end-systolic pressure-volume relationship evaluation has been demonstrated to identify patients at greater risk of mortality in the face of a negative test for wall motion criteria (22).

Last, but not least, almost 30% of patients in the present study were on antianginal medical therapy, 4% on beta-blockers, 29% on nitrates, and 16% on calcium channel blockers. Antianginal medical therapy exerts a powerful effect on the diagnostic accuracy of stress echocardiography (23,24), offsetting the recognition of ischemic burden through a series of conventional stress echocardiographic parameters: number of ischemic segments and severity of induced dysfunction (both expressed by peak wall motion score index), exercise workload, and time of onset of ischemia. Drug therapy also has an important influence on the evaluation of prognosis in patients with known or suspected coronary artery disease. In the presence of concomitant anti-ischemic therapy, a positive test is more prognostically malignant and a negative test is less prognostically benign (25). A spectrum of stratification is possible among both positive and negative test results. A large extent of inducible myocardial ischemia expressed by the variation of wall motion score index between rest and peak stress at a low workload will identify patients with an underlying severe coronary artery disease. It also is possible to stratify the negative response into a spectrum of different risks, including therapy at time of testing, CFR on left anterior descending artery, and myocardial contractility (Table 1). The addition of these parameters to conventional stress echocardiography will enrich the test, making it an extraordinary tool to identify the risk of several classes of patients: those with diabetes, pre-clinical cardiomyopathies, and microvascular disease as well as those with overt coronary artery disease.

Table 1. The Risk of Patients With a Negative Test Result

Risk	Not So Low	Very Low
Dose/load	Submaximal	Maximal
Diabetes	+	−
Therapy	+	−
Coronary flow reserve	<2	>2
Force-frequency relationship	Flat-biphasic	Steep
Death/year	>3%	<1%

In patients at low risk, such as those with a negative test for wall motion criteria, a small subset will be at risk in the long term according to other parameters beyond wall motion analysis.

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Key Words: LBBB ■ prognosis ■ stress echocardiography ■ coronary flow reserve ■ contractility.