Grand Rounds

The Electrocardiogram as a Predictor of Left Ventricular Systolic Function:

Correlation with Gated SPECT Imaging

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Abstract

Background: Left ventricular systolic function, expressed as ejection fraction (LVEF), is an important determinant of prognosis for cardiac disease, and is the basis for therapeutic decisions. Several imaging modalities are used for measuring LVEF. All require time, appropriate technology and professional attention, and most expose patients to small doses of radiation. We studied the correlation between surface electrocardiogram (ECG) and nuclear angiography in 673 patients. The purpose of our study was to determine whether normal ECG reliably predicts normal LVEF. Gated single-photon emission computed tomography (GSPECT) imaging was used as the reference.

Methods and Results: A total of 673 patients (273 men, 400 women) with known or suspected coronary artery disease and normal ECGs underwent GSPECT Tc99m sestamibi stress tests (exercise stress for 405 patients, pharmacological stress for 268). Post-stress images were gated 30–60 minutes after stress. LVEF was determined using QGS Cedar-Sinai commercial software.

Results were grouped according to type of stress (exercise or pharmacological) and the interpretation of perfusion imaging (normal or abnormal). LVEF was similar after exercise and pharmacological stress in patients with normal (69±7 vs 69±7) and abnormal (61±9 vs 62±10) stress perfusion. LVEF was < 45% (lower limit of normal) in only 7/673 patients (1%).

Conclusions: Normal ECG reliably predicts normal LVEF measured by post-stress GSPECT. Absolute LVEF value is lower in patients with stress perfusion defects.

Key Words: Ejection fraction, ECG, gated SPECT, GSPECT.

LEFT VENTRICULAR SYSTOLIC FUNCTION, commonly expressed as the ejection fraction (LVEF), is an important determinant of prognosis for patients with cardiac disease, and often forms the basis for therapeutic decisions (1, 2). Measurement of LVEF by contrast angiography, echocardiography, radionuclide angiography, magnetic resonance, or gated single-photon emission computed tomography (GSPECT) imaging requires time, technology and professional attention, and may expose patients to radiation.

Correlations between left ventricular function and findings on 12-lead surface electrocardiography (ECG), a readily available and inexpensive test, have been studied for a limited number of patients using contrast angiography or nuclear angiography as a reference standard (3–7). Normal ECG is both consistent with normal left ventricular function and independently predictive of a favorable prognosis (8).

LVEF measurements acquired by GSPECT at the time of myocardial perfusion imaging correlate closely with ejection faction (EF) values derived by other modalities (9, 10). Automated calculation of LVEF by GSPECT is reproducible with relatively little interobserver variation (11).

The purpose of this study was to examine whether a normal ECG at rest predicts normal left ventricular systolic function, as assessed by GSPECT imaging in patients referred for stress test myocardial perfusion imaging.

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Methods

A database of patients referred for GSPECT Tc99m sestamibi stress testing because of known or suspected coronary artery disease with a normal resting ECG was searched over an 18- month period (from 1/00 to 6/01). Of a total of 5,311 patients, 673 consecutive patients with normal rest ECGs were identified (273 men and 400 women). Of them, 405 patients (mean age 59±11 years) underwent symptom-limited treadmill exercise testing, and 268 (mean age 64±13 years) underwent pharmacological stress testing. Medications were given routinely unless the referring physician requested interruption.

A standard 12-lead ECG was acquired at rest for all patients, and was interpreted according to the Minnesota code (12) by cardiologists blinded to the results of perfusion imaging. The only abnormal pattern considered normal for the purpose of this analysis was sinus bradycardia at rates (heart rate ≤ 59 bpm).

Exercise testing was performed according to the Bruce protocol (13), with the heart rate, blood pressure and 12-lead electrocardiogram recorded before, during and after exercise. Exercise was terminated when limiting cardiac symptoms (chest pain or shortness of breath) or fatigue occurred, or when there was greater than a 2 mm horizontal and/or downsloping ST-segment depression measured 80 milliseconds after the J-point over at least three consecutive beats. In patients unable to exercise adequately, dipyridamole (0.56 mg/kg) or adenosine (140 μg/kg for 6 minutes) was infused intravenously.

GSPECT imaging was performed using a dual-head camera (Vertex Plus; ADAC Laboratories, Milpitas, CA) using stop-and-shoot acquisition with 64 stops, 180° arc from right anterior oblique to left anterior oblique, and a 64×64×16 matrix, VXGP collimator. Tc99m sestamibi was injected at rest and at peak stress (same day, single isotope protocol). Image acquisition began 30–60 minutes after tracer injection, and only the post-stress images were gated.

Stress and rest perfusion images were evaluated subjectively and semi-quantitatively by experienced nuclear cardiologists, who were not blinded to the clinical history or resting ECG findings. Imaging results were classified as normal or abnormal. LVEF was determined using commercial software (QGS, Cedar-Sinai, Los Angeles, CA) (13), with 45% considered the lower limit of normal.

Statistical analysis involved the Student t-test for unpaired variables, with significance accepted at the 99% confidence limit ($p<0.01$).

Results

Patients were grouped according to the type of stress (exercise or pharmacological) and the perfusion imaging results (normal or abnormal). Patients who underwent exercise testing (n=405) were younger (59±1 years) than those who underwent pharmacological testing (n=268 patients, age 64±13 years, $p<0.01$). Perfusion during stress was normal in 431 patients and abnormal in 242; the LVEF was higher in those with normal perfusion (69±7 vs 62±10%, $p<0.001$). In patients with normal perfusion, LVEF was no different after exercise than after vasodilator administration (69±7% vs 69±7%, p=ns) (Table 1). LVEF was <45% in 7 of the 673 patients in this cohort (1%), and stress perfusion was abnormal in each of these; 25 patients (3.7%) had an EF <50%. No patient had LVEF <40% (Table 2).

Discussion

Our data indicate that for this group of patients with known or suspected coronary artery disease (CAD), a normal 12-lead ECG pattern correlated well with a normal, or minimally abnormal, LVEF as measured on post-stress

TABLE 1
LVEF (%) According to Type of Stress and Stress Perfusion Findings

Perfusion	Exercise Stress Test (n=405)	Pharmacological Stress Test (n=268)
Normal (n=431)	69±7	69±7
Abnormal (n=242)	61±9*	62±10**

*p = 0.01, **p <0. 01 when compared to normal perfusion.
LVEF = left ventricular ejection fraction.

TABLE 2
Distribution of LVEF Values (n=673 patients)

LVEF (%)	Number of patients (%)
≥50	648 (96.3%)
45–49	18 (2.7%)
40–44	7 (1%)
<40	0

LVEF = left ventricular ejection fraction.

GSPECT imaging. The LVEF is lower in patients with stress-induced perfusion defects than in patients without such defects.

Previous investigators have found that LVEF (measured by contrast ventriculography) was normal in patients with normal ECG at rest, including occasional patients with mild hypokinesis limited to a single wall segment (3). In another study the sum of the R-wave amplitudes in six precordial and two augmented limb leads was used and compared to angiographic LVEF during a sinus beat and during a post-extrasystolic beat. The sum of R waves correlated with the LVEF in both types of beats (4). Among patients with known or suspected CAD and normal resting ECG in the Cardiac Arrhythmia Suppression Trial (CAST) registry (n=4,034), LVEF measured by contrast ventriculography was >50% in 92%, mildly abnormal in 8% and ≤35% in 0.6% of patients (5). More recently, Khan et al. (6) used a 29- point scoring system based on the QRS complex in 391 patients undergoing coronary angiography and contrast ventriculography. LVEF was >50% in 93% of patients with normal QRS complex scores. When the ECG was classified subjectively as normal by cardiologists, the LVEF was normal in 98% of patients.

In 874 patients with suspected CAD but no clinical history of myocardial infarction and a normal ECG, the LVEF measured by resting radionuclide ventriculography (gated blood pool imaging) was >50% in 95% (7). For 1,154 patients with angina pectoris, the five-year and 10-year survival rates (87% and 71%, respectively) were greater for patients with normal baseline ECG than for those with abnormal tracings (71% and 46%, respectively).

Taken together with our observations, these data confirm that a normal resting ECG is associated with good left ventricular function and with a favorable prognosis. To apply these correlations in clinical practice requires a strict definition of ECG normalcy: even minor repolarization abnormalities may have different diagnostic implications. It should also be emphasized that the finding of a normal LVEF does not exclude significant (even multivessel) CAD. Stress perfusion imaging was abnormal in 36% of our patients, many of whom may have harbored epicardial CAD. The absolute value of LVEF was lower in patients with abnormal stress perfusion (Table 1). This finding can be explained by either presence of chronic segmental wall motion abnormalities or by ischemic stunning (or a combination of both mechanisms). GSPECT imaging data were collected beginning 30–60 minutes after stress, and stress-induced ischemic ventricular dysfunction may persist beyond this interval, particularly after exercise (14).

Study Limitations

Using GSPECT imaging, we could not diagnose significant mitral regurgitation, which has both therapeutic and prognostic significance and thus limits the generalizability of our data. Nuclear cardiologists, who reported the LVEF value, were not blinded to the ECG tracings and myocardial perfusion results. However, since the calculation of the LVEF is fully automated, reporting bias is unlikely.

Conclusions

Our findings confirm that a normal surface ECG is associated with a high likelihood of normal post-stress left ventricular ejection fraction determined by GSPECT in patients undergoing stress testing for evaluation of suspected or known coronary artery disease. Additional or repeat use of more sophisticated methods to measure left ventricular systolic function in this group of patients may be unnecessary and associated with the undesirable waste of health care dollars.

References

1. SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fraction and congestive heart failure. N Engl J Med 1991; 325:293–302.
2. MERIT-HF Study Group. Effect of metoprolol CR/XL in chronic heart failure: metoprolol CR/XL randomized intervention trial in congestive heart failure. Lancet 1999; 353:2001–2007.
3. Swartz MH, Pichard AD, Meller J, et al. The normal electrocardiogram as a predictor of left ventricular function in patients with coronary artery disease. Br Heart J 1977; 39:208–211.
4. Askenazi J, Parisi AF, Freedman WB, Braunwald E. Value of the QRS complex in assessing left ventricular ejection fraction. Am J Cardiol 1978; 41:494–499.
5. Rihal CS, Davis KB, Kennedy JW, Gersh BJ. The utility of clinical, electrocardiographic, and roentgenographic variables in the prediction of left ventricular function. Am J Cardiol 1995; 75:220–223.
6. Khan MA, Sinha S, Hayton S, et al. A normal electrocardiogram precludes the need for left ventriculography in the assessment of coronary artery disease. Heart 1998; 79:262–267.
7. O'Keefe JH, Zinsmeister AR, Gibbons RJ. Value of normal electrocardiographic findings in predicting resting left ventricular function in patients with chest pain and suspected coronary artery disease. Am J Med 1989; 86:658–662.
8. Connolly DC, Elveback LR, Oxman HA. Coronary artery disease in residents of Rochester, Minnesota. IV. Prognostic value of the resting electrocardiogram at the time of initial diagnosis of angina pectoris. Mayo Clin Proc 1984; 59:247–250.

9. Nichols K, Tamis J, DePuey EG, et al. Relationship of gated SPECT ventricular function parameters to angiographic measurement. J Nucl Cardiol 1998; 5:295–303.
10. Cwajg E, Cwajg J, He ZX, et al. Gated myocardial perfusion tomography for assessment of left ventricular function and volumes: comparison with echocardiography. J Nucl Med 1999; 40:1857–1865.
11. Germano G, Kiat H, Kavanaugh PB, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. J Nucl Med 1995; 36:2138–2147.
12. Blackburn H, Keys A, Simonson E, et al. The electrocardiogram in population studies: a classification system. Circulation 1960; 21:1160–1175.
13. Froelicher VF. Manual of exercise testing. St. Louis (MO): Mosby; 1994.
14. Johnson LL, Verdesca SA, Aude WY, et al. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. J Am Coll Cardiol 1997; 30:1641–1648.