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Clinical Investigations

Early Prediction of 30-Day Mortality after Q-Wave Myocardial Infarction by Echocardiographic Assessment of Left Ventricular Function—A Pilot Investigation

ANDREW L. SMOCK, M.D., BRAD LARSON, M.D., CHRIS BROWN, M.D., C. RICHARD CONTI, M.D.

Cardiovascular Division, University of Florida, Gainesville, Florida, USA

Background: The GUSTO angiographic substudy demonstrated that left ventricular function measured 90 min after thrombolytic therapy was given had important prognostic implications at 30 days in patients with an acute myocardial infarction (MI).

Hypothesis: Thirty-day prognosis after Q-wave MI can be determined by early echocardiographic assessment of left ventricular function.

Methods: Using transthoracic echocardiography, semiquantitative ejection fraction and wall motion score index was assessed prospectively in 201 consecutive patients within 24 h following Q-wave MI. Independent experts blinded to the patient's status performed the echocardiographic assessment. All patients received standard medical care as dictated by the attending cardiologist.

Results: Of the 201 patients, 24 (11.9%) died within 30 days, with 70% of the deaths occurring within 10 days after the infarction. Three deaths occurred in the 120 patients with an ejection fraction ≥45% (2.5% mortality rate). In contrast, 21 deaths occurred among the 81 patients with an ejection fraction <45% (25.9% mortality rate) $p = 0.0003$. Two of the three patients who died in the high ejection fraction group died as a result of intracerebral hemorrhage from thrombolytic therapy. Ejection fraction was lower in nonsurvivors (32.3 ± 10.3 vs. 46.3 ± 13%) than in survivors, $p < 0.0002$. Wall motion score index (WMSI) of < 1.4 was associated with a 2.9% 30-day mortality (two deaths in 76 patients); WMSI of ≥ 1.4 was associated with a 17.6% 30-day mortality (22 deaths in 125 patients), $p = 0.0007$. Average WMSI was higher in the nonsurvivors (1.95 ± 0.5) than in survivors (1.52 ± 0.45), $p = 0.00001$.

Conclusions: Echocardiographic assessment of left ventricular function during the first 24 h after an acute Q-wave MI can be performed in all patients regardless of stability. High-risk patients are identified early in the hospital course, with relative ease, at no risk and at an acceptable cost. An ejection fraction <45% or WMSI ≥ 1.4 identifies patients who are at a high risk of dying within 30 days. These are the patients who may benefit most from aggressive medical therapy and early angiography to assess coronary pathology.

Key words: myocardial infarction, prognosis, echocardiography, left ventricular function

Introduction

In 1993, the Global Utilization of Streptokinase and t-PA for Occluded coronary arteries (GUSTO) investigators published the GUSTO angiographic substudy and compared left ventriculography (right anterior oblique [RAO] projection) at 90 min in 62 patients who died within 30 days with ventriculography in 915 patients who survived for 30 days or more.[1] They noted that left ventricular (LV) function was consistently worse in the nonsurvivors. The 90-min LV angiogram separated high-risk from low-risk patients. Mortality in those whose ejection fraction (EF) was ≥45% was 3.9% at 30 days compared with those whose EF was <45% and whose mortality was 14.7% ($p < 0.001$).

The Gruppo Italiano per lo Studio della Sopravvivenza nell' Infarto Miocardico (GISSI) investigators also noted a strong correlation between EF using echocardiography and 6-month mortality.[2] Echocardiography was performed at approximately 2 weeks after myocardial infarction (MI). Only patients who survived hospitalization and were discharged were included in the GISSI assessment of LV function. In these patients, there was a statistically significant increase in 6-month mortality when LVEF was <40%.

Address for reprints:

C. R. Conti, M.D.
P.O. Box 100277
1600 SW Archer Rd.
Gainesville, FL 32610, USA

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Transthoracic echocardiography (TEE), in contrast to RAO ventriculography, allows a complete assessment of LV function since the septum and lateral wall of the ventricle are visualized in addition to the anterior and inferior walls.

The use of transthoracic echocardiography (TTE) in the setting of acute MI has been studied by several other investigators since 1975.[3–6] None of these investigators reported using two-dimensional (2-D) echocardiograms performed in a systematic fashion in the first 24 h post Q-wave infarction; thus, any patient who died within 24 h was not included in these studies. We believe that we are the first to use 2-D TTE to assess LV function in the first 24 h following acute Q-wave MI. All patients who survived to reach the coronary care units are included in this assessment.

Although it would be ideal to perform TTE within 90 min after reperfusion therapy (similar to RAO LV angiography in the GUSTO angiographic substudy), it is not practical. However, it is practical to perform TTE within the first 24 h, as was done in this investigation.

The objective of this report is to investigate, in a prospective fashion, whether EF and wall motion score index (WMSI) determined by TTE within the first 24 h of Q-wave MI can discriminate high- from low-risk patients.

Patient Population

In all, 201 consecutive patients admitted to Shands Hospital at the University of Florida with Q-wave MI were evaluated during the first 24 h after admission. There were 136 men and 65 women. Of these, 92 had an anterior, 96 an inferior, 7 a lateral, and 6 a posterior MI (Table I). The majority were aged > 50 years, with an average of 59.7. Initial therapy was urgent percutaneous transluminal coronary angioplasty (PTCA) in 35, thrombolytic therapy in 130, and neither PTCA nor thrombolytic therapy in 36 patients.

Methods

Q-wave MI was defined as the presence of new Q-waves in two consecutive leads on 12-lead electrocardiogram (ECG) and positive cardiac enzymes (creatine kinase [CK] and CK-MB) at least two times normal. Neither CK-MB nor troponin were measured systematically after the first 24 h. Global assessment of LV function was determined using TTE within 24 h of the onset of the Q-wave MI. The septum, apex, anterior, lateral, and inferior walls were visualized. The EF and WMSI were estimated semi-quantitatively and were reported as a continuous variable by two expert echocardiographers who were blinded to the patient's condition. Ejection fraction was determined by direct visual estimation in multiple views. Wall motion score index was determined by assessing four standard views of the heart; parasternal long-axis, parasternal short-axis, apical four-chamber, and apical two-chamber views. The left ventricle was divided into 16 segments. Each segment was then scored in the following way: normal = 1, hypokinetic = 2, akinetic = 3, dyskinetic = 4, aneurysmal = 5. The numbers assigned to each segment were then added and divided by 16 to determine the LV WMSI.

Statistical analysis was performed using standard summary statistics including the Student's *t*-test and logistic regression. These techniques were used to determine the probability of death at 30 days, as well as the odds ratio (OR) of dying within 30 days, as a function of demographic characteristics and risk factors. The demographic characteristics analyzed were age, race, and gender. The echocardiographic factors were LVEF and WMSI.

We used LVEF and WMSI as dichotomous variables (LVEF < 45% or LVEF ≥ 45% and WMSI < 1.4 or WMSI ≥ 1.4). This optimized the clinical utility of these measurements.

Results

The overall 30-day mortality rate was 11.9%. Table II summarizes the relationship of 30-day mortality and EF in patients undergoing urgent angioplasty, thrombolytic therapy, or neither.

Most deaths occurred early (mean of 9.2 ± 7.9 days) after MI. The median time to death was 6 days, with over 70% of the deaths occurring within 10 days. Mechanism of death was arrhythmic in 10, asystole in 2, cardiogenic shock in 7, and central nervous system events in 5 (Fig. 1). Fourteen of 136 male patients (10.3%) and 10 of 65 female patients died (15.4%). Deaths occurred in 14 of 92 patients with an anterior

TABLE I Location of Q-wave myocardial infarctions of 201 male and female patients admitted consecutively to Shands Hospital at the University of Florida. All patients had an echocardiogram within 24 h of admission

	Anterior	Inferior	Lateral	Posterior	Total
Men	64	66	6	6	142
Women	28	30	1	0	59
Total	92	96	7	6	201

TABLE II 30-day mortality in patients with acute myocardial infarction whose ejection fraction was < 45% or ≥ 45%, and who were treated with urgent angioplasty, thrombolytic therapy, or neither

Therapy	No. of patients	30-Day mortality	
		EF < 45%	EF ≥ 45%
PTCA (%)	35	4 (11.4)	0 (0)
Thrombolysis (%)	130	12 (9.2)	2 (1.5)
Neither (%)	36	5 (13.9)	1 (2.8)
Totals (%)	201	21 (10.4)	3 (1.4)

Abbreviations: EF = ejection fraction, PTCA = percutaneous transluminal coronary angioplasty.

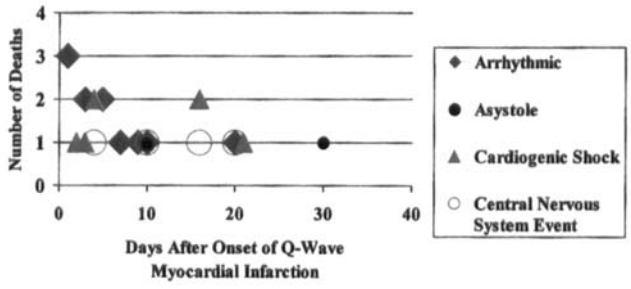

FIG. 1 Mechanism and timing of the 24 deaths up to 30 days post infarction.

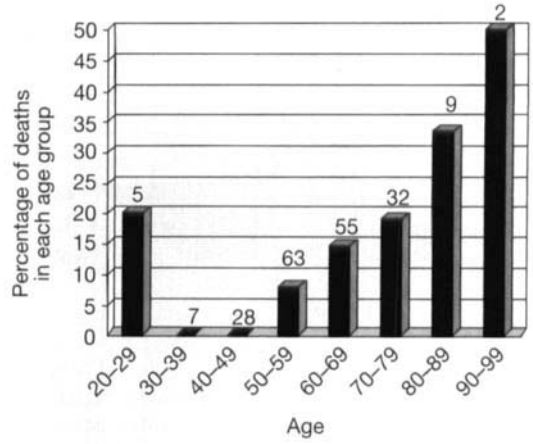

FIG. 2 Relationship of 30-day mortality to age in patients with Q-wave myocardial infarction. The percent of deaths in each age group increased in a linear fashion after age 49. The numbers above the vertical bars indicate the number of patients in each 10-year age group.

MI (15.2%), in 7 of 96 patients with an inferior infarction (7.3%), and in 3 of 13 patients (23%) with infarction in other locations.

Increasing age was a significant predictor of poor outcome, with an OR of 1.06 (95% confidence interval [CI] 1.02–1.10) risk of dying within 30 days with each increasing year of age (Fig. 2).

The average age of nonsurvivors (24 patients) was 67.6 ± 13.6 years. In contrast, the average age of the survivors (177 patients) was 58.6 ± 12.5 years ($p = 0.0006$).

Peak CK-MB was 262 ± 276 in survivors and 231 ± 276 in nonsurvivors ($p = 0.6$). All patients had several determinations of CK-MB to confirm the diagnosis of acute MI. No effort was made to quantify infarction size by CK-MB measurements.

Ejection Fraction and Survival

Ejection fraction was ≥ 45% in 120 patients; 3 died within 30 days (2.5% mortality rate), and 2 of the 3 had central nervous system hemorrhage as a result of thrombolytic therapy. In contrast, EF was < 45% in 81 patients; 21 died within 30 days (25.9% mortality) ($p = 0.0003$). Figure 3 compares 30-day mortality with LVEF and illustrates the steep increase in mortality as EF falls below 45%. Patients who had an LVEF < 45% had a 13.25 OR of dying within 30 days compared with those who had an LVEF ≥ 45% (CI 3.65–48.09) regardless of age, race, or gender. The average EF was 46.3 ± 13% in the survivors and 32.3 ± 10.6% in the nonsurvivors ($p < 0.0002$).

Wall Motion Score Index and Survival

A WMSI of one was normal. Wall motion score index was < 1.4 in 76 patients; 2 patients died (2.6% mortality). Of the patients studied, 125 had a WMSI ≥ 1.4; of these, 22 died (17.6% mortality) ($p = 0.0007$) (Fig. 4). The average WMSI in the survivors was 1.52 ± 0.45 and in the nonsurvivors 1.95 ± 0.5 ($p = 0.0001$). The WMSI was a powerful predictor of 30-day mortality with an OR of 7.76 (95% CI 1.71–35.12) for those with a WMSI of ≥ 1.4 compared with those with a WMSI of < 1.4.

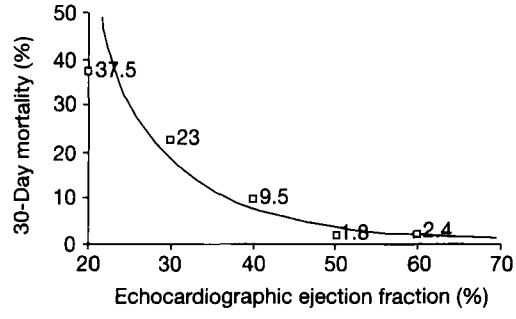

FIG. 3 Relationship of left ventricular ejection fraction in the first 24 h after Q-wave myocardial infarction to 30-day mortality in 201 consecutive patients. As left ventricular ejection fraction decreases, the percent of individuals in each group who died within 30 days increases in an exponential fashion.

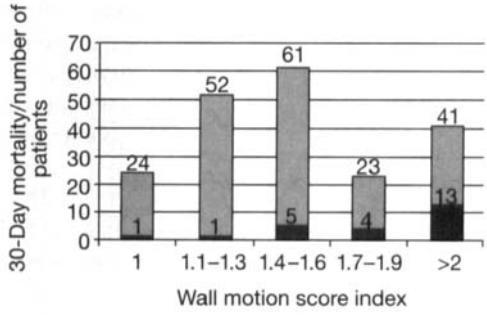

FIG. 4 Wall motion score index and 30-day mortality in 201 patients with Q-wave myocardial infarction. The numbers above the light bars are the total number of patients in each group. The numbers above the dark bars represent patients who died. ■ = Survivors, ■ = died.

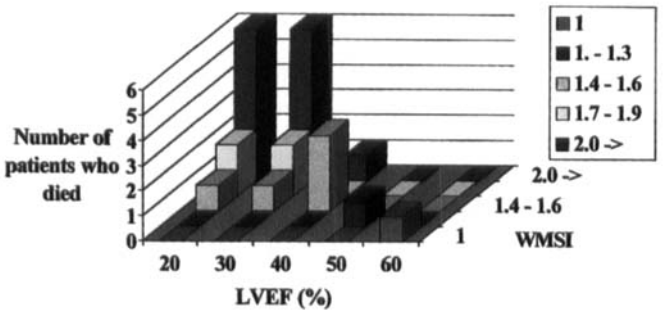

FIG. 5 Relationship of wall motion score index (WMSI) and left ventricular ejection fraction (LVEF) to 30-day mortality in 201 patients. Both WMSI and LVEF are powerful predictors of 30-day mortality. As both values are obtained from the same data set, there is no significant statistical advantage to using one method over the other.

The relationship between WMSI, LVEF, and 30-day mortality was analyzed and the results are shown in Figure 5. There was no statistical advantage of one method over the other, or of combining LVEF and WMSI to determine prognosis.

Discussion

Risk assessment early after MI begins with the history and physical examination. It has been shown that patients with a previous MI, increasing age, Killip class III or IV, the presence of a third heart sound, rales, elevated troponins, arrhythmias, or hypotension are at higher risk than those who do not have these features. Patients with ECG abnormalities in multiple leads as opposed to one or two leads also seem to be at higher risk.[7] Schroeder *et al.* reported that early resolution of the ST-segment elevation after thrombolysis at 180 min indicates a low-risk cohort of patients.[8] The chest x-ray, when clear, generally portends a better prognosis than when pulmonary edema or cardiomegaly is present. Creatine kinase/CK-MB can provide an index of the size of the MI if it is done in a systematic way, but in most instances CK and CK-MB are measured to confirm the diagnosis of MI. More quantitative information is required about troponin I and troponin T measurements in patients with Q-wave MI, but these measurements appear to correlate with development of cardiac events; for example, high troponin values are associated with a poorer prognosis than low troponin values.

The above data can be obtained within the first 24 h of admission and provide the clinician with a good sense of the patient's prognosis. Further refinements include exercise testing, ambulatory ECG, stress radionuclide, and stress echo studies. It is unlikely that any of these tests will be performed within the first 24 h because of the potential hazard to the patient in the early stages of an acute MI. However, Brown *et al.* reported 84 patients with acute MI who underwent dypyridamole myocardial perfusion imaging 2 to 4 days after the infarction.[9] They showed that early testing was safe and predictive of cardiac events.

Ideally, TTE could be performed within 90 min after admission to hospital or after reperfusion therapy (similar to RAO LV angiography in the GUSTO angiographic substudy), but it is not practical. However, it is practical to perform TTE within the first 24 h, as was done in this investigation.

Assessment of LV function during the first 24 h after an acute Q-wave MI can be easily and safely performed in patients regardless of their clinical condition. The only limitation is the inability to obtain satisfactory images. This limitation is diminished with the use of harmonic imaging and contrast agents.

In this cohort of 201 patients, TTE identified high-risk patients within the first 24 h of their hospital course. Seventy percent of deaths occurred within 10 days of the infarction. Two of the three patients with an LVEF $\geq 45\%$ died as a result of complications of thrombolytic therapy. No patients in the low EF group died as a result of central nervous system hemorrhage. In addition, LV function measurements early in acute MI may be lower than if measured several days after MI due to stunning of the myocardium. Cardiac ultrasound examination was not performed at a later time in any of these patients, so improvement or lack of improvement in LV function was not documented. Thus, despite the fact that early assessment of LV function may have included infarcted and stunned myocardium, our results demonstrate that LVEF determination within the first 24 h is highly predictive of subsequent clinical course.

When WMSI and LVEF are used in combination, there is little extra to gain as these two parameters are obtained by interpreting the same data (TTE) (Fig. 4). Based on our sample of 201 patients, it is most practical to use LVEF as the echocardiographic parameter to assess mortality risk. Although WMSI was a powerful predictor of 30-day mortality, clinically this is not used routinely. Focusing on LVEF currently seems to be the more practical of the two approaches to assess 30-day mortality within 24 h of admission.

Prognosis was worse in the older patients, but we did not try to correlate EF and age because the number of patients was too small to make multiple subset analyses.

A potential drawback to using visual versus computer-processed interpretations of LVEF determined by TTE is intraobserver variability.[10] Despite this potential for error, visual interpretation of TTE remains the usual clinical method for assessing LV function. In this investigation, two different expert echocardiographers assessed LV function blinded to the clinical condition of the patient.

Conclusions

In our cohort of 201 consecutive patients with Q-wave MI, echocardiographic assessment of LVEF within the first 24 h after onset of MI was a powerful predictor of 30-day mortality. Echocardiographic assessment of LV function is readily available and can be performed in all patients regardless of their clinical state. Patients are not excluded from assessment of LV

function because of instability. Results suggest that patients with the diagnosis of Q-wave MI should have an assessment of LV function within the first 24 h of the onset of MI. Echocardiography can identify high-risk patients early in their hospital course, with relative ease, at no risk to the patient and at an acceptable cost. In our patient cohort, high-risk patients were those who had an EF < 45%. This correlated well with what other investigators have found using ventriculography to determine LVEF at 90 min after thrombolysis. In patients with an LVEF < 45%, early coronary angiography may be warranted for better assessment of coronary artery pathology and for guidance in acute and chronic management strategies.

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