Use of a Regional Wall Motion Score to Enhance Risk Stratification of Patients Receiving an Implantable Cardioverter-Defibrillator

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Objectives. We postulated that preoperative assessment of both regional wall motion and left ventricular ejection fraction would serve as an accurate prognostic indicator of long-term cardiac mortality and functional outcome in patients treated with an implantable cardioverter-defibrillator.

Background. Long-term cardiac mortality has remained high in patients receiving an implantable cardioverter-defibrillator. The ability to risk stratify patients before defibrillator implantation is becoming increasingly important from a medical and economic standpoint.

Methods. The hypothesis was retrospectively tested in 74 patients who had received an implantable cardioverter-defibrillator. Left ventricular ejection fraction and regional wall motion score, derived from centerline chord motion analysis, were calculated for each patient from the preoperative right anterior oblique contrast ventriculogram. Wall motion score was the only significant independent predictor of long-term cardiac mortality and functional status by multivariate analysis because of its enhanced prognostic capability in patients with an ejection fraction in the critical range of 30% to 40%.

Results. Patients with an ejection fraction >40% had a 3-year cardiac mortality rate of 0% compared with 25% for those with an ejection fraction of 30% to 40% and 48% for those with an ejection fraction <30% ($p < 0.05$). Similarly, 75% of patients with an ejection fraction >40% were in New York Heart Association functional class I or II during long-term follow-up compared with 59% of those with an ejection fraction 30% to 40% and 29% of those with an ejection fraction <30%. Among patients with an ejection fraction of 30% to 40%, those with a wall motion score >16% had a 3-year cardiac mortality rate of 0% compared with 71% of those with a wall motion score ≤16% ($p = 0.002$). In addition, 86% of patients with a wall motion score >16% were in functional class I or II during long-term follow-up compared with 13% of those with a wall motion score ≤16% ($p = 0.001$).

Conclusions. Long-term cardiac mortality and functional outcome in patients receiving an implantable cardioverter-defibrillator can be predicted if the left ventricular ejection fraction and regional wall motion score are measured preoperatively.

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Since its introduction by Mirowski et al. (1) in 1980, the implantable cardioverter-defibrillator has become accepted as an effective therapy for preventing sudden death in patients with malignant ventricular arrhythmia. Despite a low incidence of sudden death (2,3), long-term cardiac mortality has remained relatively high after implantation of the device (2,4–9). The majority of nonsudden cardiac deaths have been attributed to progressive heart failure (2,4–9). Although major series have reported sudden death and total cardiac mortality rates, a significant limitation of these reports is that the late functional status of patients after defibrillator implantation has not been well characterized.

Both long-term cardiac mortality and functional outcome are important criteria by which to evaluate the overall benefit of implantable cardioverter-defibrillator therapy. For this reason, the ability to risk stratify patients before they receive the device into groups predicted to have a favorable or unfavorable outcome is becoming increasingly important from both a medical and economic standpoint (10). Several previous studies (8,11–17) have analyzed the effects of left ventricular ejection fraction on long-term cardiac mortality after defibrillator implantation. We (18) have reported that a preoperative wall motion score derived using centerline chord motion analysis is an independent predictor of long-term survival and functional outcome after aneurysmectomy and subendocardial resection for ventricular tachycardia. In that study, we demonstrated that a wall motion score ≤16% or >16% stratified patients into a high and a low risk group, respectively. We therefore postulated that a preoperative assessment of wall motion score in addition to measurement of ejection fraction would serve as an accurate prognostic

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Table 1. Clinical Characteristics of 74 Study Patients

Age (yr)	60 ± 12
Male	64 (86)
Female	10 (14)
Presenting arrhythmia	
Sustained monomorphic ventricular tachycardia	42 (57)
Cardiac arrest	20 (27)
Syncope (sustained monomorphic ventricular tachycardia at electrophysiologic study)	12 (16)
Structural heart disease	
Coronary artery disease	53 (72)
Dilated cardiomyopathy	13 (18)
Other (valvular, hypertrophic cardiomyopathy, no structural heart disease)	8 (10)
Inducible arrhythmia at baseline electrophysiologic study	
Sustained monomorphic ventricular tachycardia	56 (75)
Polymorphic ventricular tachycardia/ventricular fibrillation	9 (12.5)
Noninducible	9 (12.5)
Left ventricular ejection fraction (%)	35 ± 14
Wall motion score (%)	24 ± 22
Concomitant therapy	
Amiodarone	43 (58)
Type IA antiarrhythmic drugs	10 (14)
Coronary artery bypass grafting	26 (35)
Hospital deaths	2 (3)

Values presented are mean value ± SD or number (%) of patients.

indicator of both long-term cardiac mortality and functional outcome in patients who underwent defibrillator implantation. This hypothesis was retrospectively tested in a group of 74 patients who had undergone implantable cardioverter-defibrillator implantation at our institution.

Methods

Between June 1986 and July 1991, 85 patients received an implantable cardioverter-defibrillator at our institution. Eleven patients whose preoperative contrast left ventriculograms were technically inadequate for the analysis described in the study are excluded from this report. The clinical characteristics of the remaining 74 patients who comprised the study group are shown in Table 1.

Preoperative evaluation. All patients underwent preoperative contrast ventriculography and selective coronary angiography using standard techniques. A critically stenosed coronary artery was defined as ≥50% visual cross-sectional narrowing of the blood vessel in any angiographic view. Endocardial contours were traced from the preoperative right anterior oblique ventriculogram in end-systole and end-diastole. Global left ventricular ejection fraction was calculated as described by Sandler and Dodge (19) and Kennedy et al. (20) (Trinity Computing Systems). Centerline chord motion analysis, as described by Sheehan et al. (21), was used to assess quantitatively regional left ventricular function (Trinity Computing Systems) (Fig. 1). In this technique, endocardial motion is measured along 100 chords constructed perpendicular to a centerline drawn midway between the end-diastolic and end-systolic contours in the right anterior oblique projection. The last 20 chords are not analyzed because they primarily reflect motion of the mitral valve. The motion of each chord is then normalized for heart size by dividing by the length of the end-diastolic circumference. This value is then converted into units of standard deviation (SD) from the normal mean motion of each chord as derived from a normal reference population. Normal motion is considered to be between 1 and −1 SD from reference. Hypokinetic motion is defined as less than −1 SD and hyperkinetic motion as >1 SD from reference. In this study, wall motion score was defined as the number of chords displaying normal or hyperkinetic motion expressed as a percent of the 80 chords analyzed.

Surgical techniques. A left anterior thoracotomy approach was used in all patients who underwent defibrillator implantation alone. In the 26 patients who required concom-

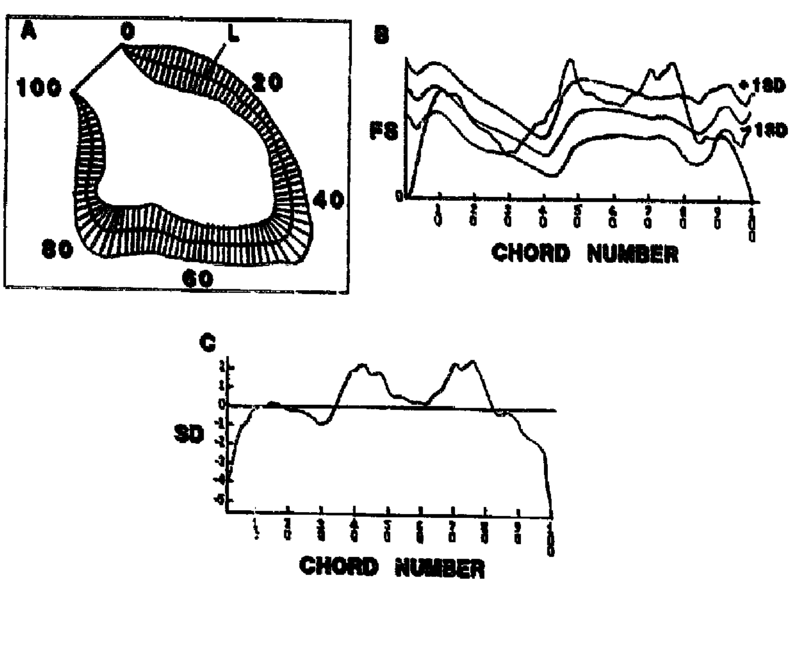


Figure 1. Centerline method of regional wall motion analysis. These data are from a normal patient studied in our catheterization laboratory. A, The centerline (L) is constructed midway between the end-diastolic and end-systolic left ventricular contours in the right anterior oblique projection. Motion is measured along 100 chords constructed perpendicular to the centerline. Chords 81 to 100 are not analyzed because they primarily reflect motion of the mitral valve. B, The motion of each chord is normalized by the end-diastolic circumference to yield a fractional shortening (FS). The fractional shortening of each chord is plotted along with the normal mean fractional shortening of each chord and 1 SD above and below this mean. C, The fractional shortening of each chord is plotted in units of SD from the normal mean motion.

Table 2. Univariate and Multivariate Analyses for Cardiac Mortality*

	All Patients (p value)		Patients With LVEF 30% to 40% (p value)	
	Univariate Analysis	Multivariate Analysis	Univariate Analysis	Multivariate Analysis
Gender	NS	NS	NS	NS
Age	NS	NS	NS	NS
Underlying heart disease	NS	NS	NS	NS
Presenting arrhythmia	NS	NS	NS	NS
Inducibility of ventricular tachycardia at electrophysiologic study	0.03	NS	NS	NS
LVEF	< 0.001	NS	NS	NS
Wall motion score	< 0.0001	< 0.0001	< 0.01	< 0.01
No. of diseased coronary arteries (≥50% diameter narrowing)	NS	NS	NS	NS
Coronary artery bypass grafting	NS	NS	NS	NS
Amiodarone use	NS	NS	NS	NS
Type 1A antiarrhythmic drug use	NS	NS	NS	NS

*Patients who underwent urgent heart transplantation were classified in the group with cardiac-related death in this analysis. LVEF = left ventricular ejection fraction; NS = p > 0.05.

itant coronary artery bypass grafting, a median sternotomy approach was used. An epicardial patch-patch configuration was used in all patients. The implantable cardioverter-defibrillator models used were models 1400, 1420, 1500, 1520, 1550 and 1600 (Cardiac Pacemakers, Inc.). All patients had an intraoperative defibrillation threshold ≤20 J. Defibrillation efficacy was retested before hospital discharge.

Long-term follow-up. Long-term follow-up was obtained in all 72 patients discharged from the hospital. Data concerning mortality and New York Heart Association functional class were obtained by direct or telephone contact with the patient, the patient's family members or the patient's local physician. Each patient was assigned a functional class at 6 and 24 months after hospital discharge. Cause of death was classified as either cardiac or noncardiac. Cardiac mortality was further divided into nonarrhythmic death (usually congestive heart failure) or sudden death (including arrhythmias associated with acute myocardial infarction) on the basis of criteria proposed by the Cardiac Arrhythmia Pilot Study investigators (22).

Statistical analysis. Data were compiled into a computerized data bank (RS1, BBN Software Products Corp.) and analyzed using BMDP (BMDP Statistical Software). Clinical variables (gender, age, type of structural heart disease, presenting arrhythmia, concomitant amiodarone use, concomitant type 1A antiarrhythmic drug use and concomitant coronary artery bypass grafting); electrophysiologic variables (inducibility of ventricular tachycardia at electrophysiologic study); and angiographic variables (left ventricular ejection fraction, wall motion score and the number of critically stenosed coronary arteries) were compared using a Cox regression analysis. In this model, variables are excluded in stepwise fashion whenever the p value for a significant association is >0.1. The Cox regression analyses and Kaplan-Meier survival curves were calculated using two methods. In the first method, the three patients who underwent urgent heart transplantation for heart failure or shock were counted as having had a cardiac nonarrhythmic death (Table 2). In the second method, these patients were censored from further mortality analysis at the time of transplantation. Data from both analyses are described in the following sections. Survival curves were compared using the Breslow test. Subgroup comparisons were made using the chi-square or Fisher exact test where appropriate. Statistical significance was defined as $p < 0.05$. All continuous variables were expressed as mean value ± SD.

Results

The mean ejection fraction for the entire study population was 35 ± 14%, and the mean wall motion score was 24 ± 22%. There was good linear correlation between wall motion score and ejection fraction for the entire study group ($r = 0.85$) (Fig. 2). Ejection fractions >40% were associated with a high wall motion score (>16%), and ejection fractions <30% were associated with a poor wall motion score (≤16%). However, in the 27 patients with an ejection fraction between 30% and 40%, there was often disparity between wall motion score and ejection fraction, with a poor linear correlation coefficient ($r = 0.17$).

Hospital mortality. Seventy-two patients (97%) were discharged from the hospital. The two in-hospital deaths were due to intractable heart failure (one patient) and to respiratory failure secondary to amiodarone-induced pulmonary toxicity (one patient).

Cardiac mortality. During a mean follow-up of 21 ± 13 months, there were 13 cardiac-related deaths (including in-hospital mortality) and 4 noncardiac-related deaths. An additional three patients underwent urgent heart transplantation because of intractable heart failure or incessant ven-

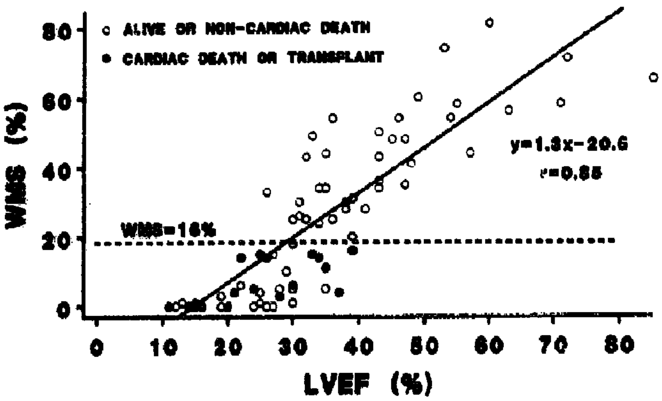


Figure 2. Relation between wall motion score (WMS) and left ventricular ejection fraction (LVEF). In patients with an ejection fraction in the range 30% to 40%, cardiac mortality or urgent heart transplantation was confined to those patients with a wall motion score ≤16%.

tricular arrhythmia, or both. Heart failure (nine patients) was the most common mode of death. There were only two sudden deaths during long-term follow-up. Inducibility of ventricular tachycardia at electrophysiologic study ($p < 0.05$), left ventricular ejection fraction ($p < 0.001$) and wall motion score ($p < 0.0001$) were all significant univariate predictors of cardiac mortality if patients who underwent heart transplantation were classified as having had a cardiac-related death. However, if these three patients were censored from further analysis at the time of transplantation, left ventricular ejection fraction ($p < 0.001$) and wall motion score ($p < 0.001$) were the only significant univariate predictors of cardiac mortality. By Cox regression analysis, wall motion score was the only significant independent predictor of cardiac mortality ($p < 0.001$), whether patients with heart transplantation were classified as having had a cardiac-related death or were censored from the mortality analysis at the time of transplantation.

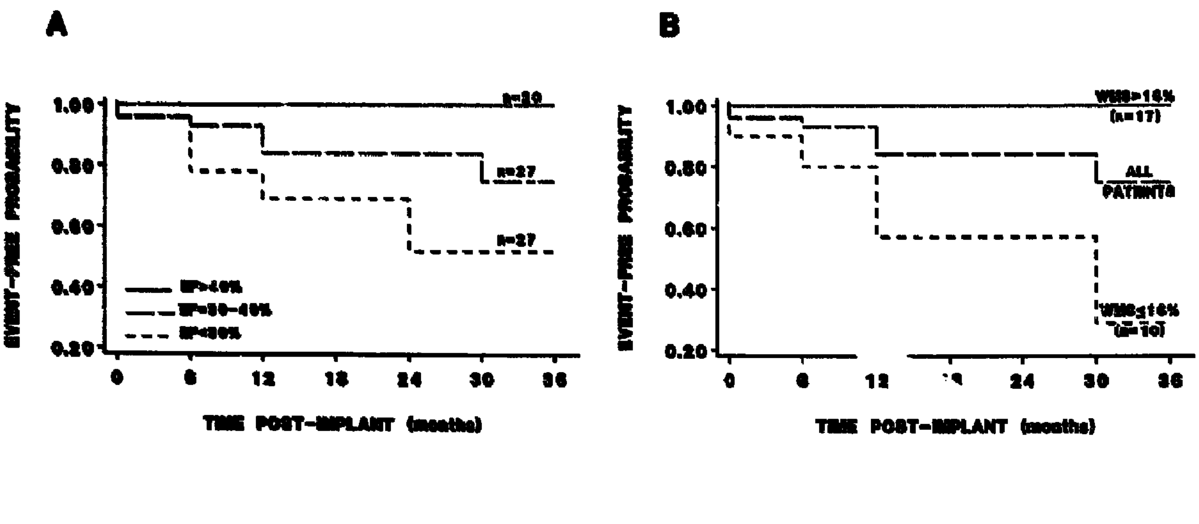
Life-table analysis for cardiac mortality is illustrated in Figure 3A. Patients with an ejection fraction >40% had a significantly better long-term survival than that of patients with an ejection fraction ≤40% ($p < 0.05$). There were no cardiac-related deaths among the 20 patients in the former group during a mean follow-up period of 29 ± 14 months. All patients with an ejection fraction >40% had a wall motion score >16%.

There were four cardiac-related deaths and two urgent cardiac transplantations among the 27 patients with an ejection fraction of 30% to 40% during a mean follow-up period of 22 ± 12 months. In this cohort, wall motion score was the only significant predictor of cardiac mortality (including or excluding the two transplant recipients as patients who died) (Table 2). A wall motion score ≤16% or >16% was effective in stratifying patients into a high or a low risk group, respectively (Fig. 3B). The 10 patients in this group who had a wall motion score ≤16% had a 3-year cardiac mortality rate of 71%, compared with a 0% cardiac mortality rate among the 17 patients with a wall motion score >16% ($p = 0.002$).

There were nine cardiac-related deaths and one urgent cardiac transplantation among the 27 patients with a left ventricular ejection fraction <30% during a mean follow-up period of 15 ± 11 months. Wall motion score was not helpful in risk stratifying patients in this group because all but one patient had a wall motion score ≤16%.

Functional status. Among the 72 patients discharged from the hospital, 74% were in functional class I or II at 6 months and 54% were in class I or II at 24 months after hospital discharge. Left ventricular ejection fraction and wall motion score were both univariate predictors of long-term functional class. However, after multivariate analysis, wall motion score was the only significant independent predictor of

Figure 3. Survival free of cardiac death or urgent transplantation. **A,** Patients are stratified by ejection fraction (EF). Patients with an ejection fraction >40% had a significantly better long-term survival than that of patients with an ejection fraction in the range 30% to 40% or <30% ($p < 0.05$). **B,** Patients with an ejection fraction between 30% and 40% are stratified by a wall motion score (WMS) >16% or ≤16%. Patients with a wall motion score >16% had a significantly better long-term survival than that of patients with a wall motion score ≤16% ($p = 0.002$). Post-implant = after implantation.



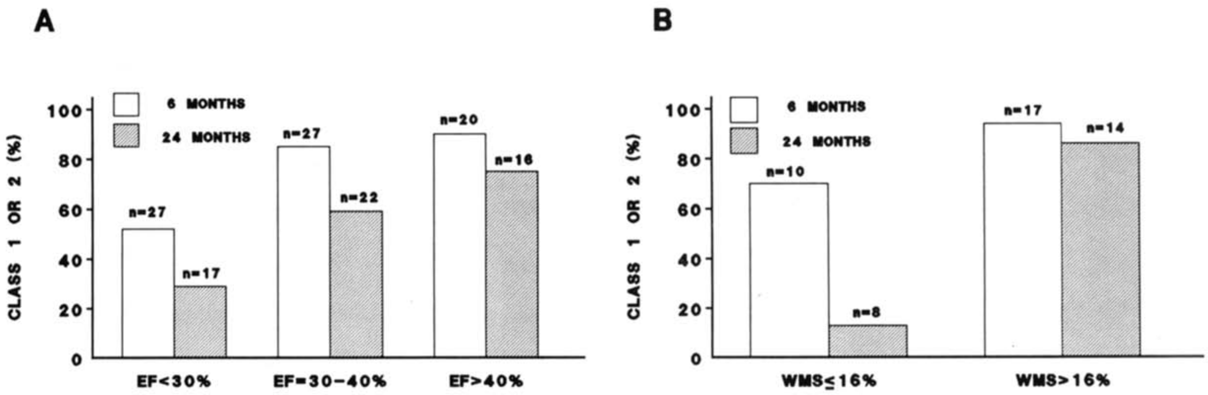


Figure 4. Functional class of patients at 6 and 24 months after receipt of an implantable cardioverter-defibrillator. A, Patients are stratified by ejection fraction (EF). Patients with an ejection fraction >40% were more likely to be in New York Heart Association functional class I or II (1 or 2) during long-term follow-up than were patients with an ejection fraction between 30% and 40% or <30%. B, Patients with an ejection fraction between 30% and 40% are stratified by a wall motion score (WMS) >16% or ≤16%. Patients with a wall motion score >16% were significantly more likely to be in functional class I or II during long-term follow-up than were patients with a wall motion score ≤16% ($p = 0.001$ at 24 months).

functional status at 6 months ($p < 0.01$) and 24 months ($p < 0.001$) after device implantation.

Patients with an ejection fraction >40% were more likely to be in functional class I or II during long-term follow-up than were patients with an ejection fraction ≤40% (Fig. 4A). At 6 months, 90% of the 20 patients in this group were in functional class I or II, and at 24 months 75% were in class I or II. Wall motion score was not helpful in predicting functional outcome in this patient group because all patients had a wall motion score >16%.

At 6 months, 85% of the 27 patients with an ejection fraction between 30% and 40% were in functional class I or II, and at 24 months 59% in were class I or II (p = NS vs. patients with an ejection fraction >40%). Patients in this group with a wall motion score >16% were more likely than patients with a score ≤16% to be in class I or II at 6 months (94% vs. 70%, respectively, p = NS) and at 24 months (86% vs. 13%, respectively, $p = 0.001$) after defibrillator implantation (Fig. 4B).

At 6 months, 52% of the 27 patients with an ejection fraction <30% were in functional class I or II, and at 24 months only 29% were in class I or II. All but one of the wall motion scores in this group were ≤16% and were therefore not helpful in predicting functional outcome.

Discussion

Our data indicate that by assessing preoperative regional wall motion using a reproducible quantitative technique in addition to measuring left ventricular ejection fraction, the long-term cardiac mortality and functional outcome of patients treated with an implantable cardioverter-defibrillator can be predicted with reasonable accuracy. Patients with an initial ejection fraction >40% had a good wall motion score and an excellent long-term survival and functional outcome. In contrast, patients with an ejection fraction <30% and a poor wall motion score had a significantly higher cardiac mortality rate and poorer long-term functional outcome. Wall motion score was most helpful in patients in an intermediate group with an ejection fraction between 30% and 40%. This cohort, which included 27 (36%) of 74 of our study patients, could be further stratified into high and low risk groups by a quantitative measurement of regional wall motion. In this group, patients with a wall motion score ≤16% had a 3-year cardiac mortality rate of 71%, and an additional 25% had symptomatic heart failure within 2 years of implantation. In contrast, no patient in this group with a wall motion score >16% had a cardiac-related death, and only 7% had symptomatic heart failure within the same time interval.

Previous studies. Previous studies (8,11–17) have reported the prognostic importance of preoperative left ventricular ejection fraction on subsequent survival after defibrillator implantation. Patients with an ejection fraction ≥30% have been shown to have a significantly better long-term survival rate than that of patients with an ejection fraction <30% (8,13,15–17). Akhtar et al. (16) reported a 3-year total mortality rate of 22% in 96 patients with an ejection fraction of 30% to 40% receiving an implantable cardioverter-defibrillator. However, most other studies (8,13–15,17) have not included a separate analysis of patients with an ejection fraction in this range.

The reported 3-year survival rates for patients with an ejection fraction <30% have ranged from 57% to 81% (8,12–17). Axtell et al. (12) observed a 3-year survival rate of 81% in 68 patients with an ejection fraction <30%. However, 79% of their patients were in functional class I or II before surgery, 21% were in class III, and no patient was in class IV. Other series (8,13) that have included a higher percent of patients who were in functional class III or IV have reported lower long-term cardiac survival rates in patients with an ejection fractions <30%.

Although functional class in a patient in stable condition can effectively predict prognosis, it may be difficult to assess functional class in patients in the early recovery period after a recent myocardial infarction or cardiac arrest with its associated complications, a scenario common in implantable cardioverter-defibrillator recipients. This study demonstrates that by quantitatively measuring preoperative regional wall motion in addition to ejection fraction, an objective assessment of long-term mortality risk and functional outcome can be obtained before defibrillator implantation.

Clinical implications. The long-term cardiac mortality and functional outcome of patients treated with an implantable cardioverter-defibrillator can be predicted with reasonable accuracy by measuring both ejection fraction and regional wall motion. Patients with an ejection fraction >40% or in the range 30% to 40% associated with a wall motion score >16% have an excellent long-term survival and functional outcome after implantable cardioverter-defibrillator implantation. In contrast, patients with an ejection fraction <30% or of 30% to 40% and a wall motion score ≤16% remain at high risk for cardiac mortality and the development of symptomatic heart failure during long-term follow-up. In this high risk group of patients, the same degree of long-term benefit from implantable cardioverter-defibrillator implantation should not be anticipated. Although sudden death may be prevented, death of nonarrhythmic origin or a reduced quality of life due to heart failure frequently occurs.

Assessment of both ejection fraction and regional wall motion may allow better medical and economic utilization of the implantable cardioverter-defibrillator. High risk patients may be referred earlier for heart transplantation or treated initially with the best available pharmacologic therapy because there is limited long-term benefit from the implantable cardioverter-defibrillator in this group of patients. However, a randomized study of implantable cardioverter-defibrillator therapy versus pharmacologic therapy has not been reported to date. Patients who improve clinically and whose condition remains stable with medical therapy may later be considered candidates for implantable cardioverter-defibrillator as an adjunct or alternative to antiarrhythmic drug treatment. The implantable cardioverter-defibrillator may conceivably be used as a "bridge to transplantation" in this high risk group; however, even this use may be of limited benefit owing to the different mechanisms responsible for sudden death in these patients (23).

Limitations of study. There was some inevitable selection bias during the period of the study. Patients with an ejection fraction <20% and ventricular arrhythmias were usually not considered candidates for receipt of an implantable cardioverter-defibrillator unless they had a reasonable functional status. Patients with both a low ejection fraction and a poor baseline functional status were usually referred for heart transplantation, or a decision was made to treat them conservatively with only the best available pharmacologic therapy. This clinical practice may have resulted in a better long-term outcome in the patients with the lowest ejection fractions (i.e., <30%) than if all such patients had received an implantable cardioverter-defibrillator.

Three of the 16 patients classified as having a cardiac-related death in the study were heart transplant recipients. We believe that we are justified in classifying these patients in the group with cardiac death because each was hospitalized in an intensive care unit with either intractable heart failure or incessant ventricular arrhythmias and was anticipated to have had a very limited survival without transplantation. However, when they are censored at the time of transplantation, the same general conclusions about the value of wall motion score still apply.

Our data can be strictly applied only to second-generation implantable cardioverter-defibrillators. Newer, more capable implantable cardioverter-defibrillators are now undergoing clinical trials (24). These devices may require less invasive implantation procedures, may require less concomitant antiarrhythmic drug therapy and may convert many arrhythmias by antitachycardia pacing, rather than by shocks. Although not yet clinically proved, these advantages might lead to reductions in total mortality and improvement in functional outcome after implantation.

There are radionuclide and echocardiographic techniques that may be used for regional wall motion analysis. It may be possible to adapt the methods used for contrast ventriculogram analysis to these techniques and thus achieve the same prognostic information using a noninvasive approach.

Finally, this was a retrospective study in a relatively small number of patients. However, measurement of a wall motion score is relatively simple, and our observations could be confirmed both retrospectively and prospectively by other centers.

Conclusions. Long-term cardiac mortality and functional outcome in patients receiving an implantable cardioverter-defibrillator for sustained ventricular tachycardia or ventricular fibrillation can be effectively predicted if the left ventricular ejection fraction and regional wall motion score are measured preoperatively. Assessment of both of these factors may allow better medical and economic utilization of these expensive but potentially lifesaving devices.

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