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End-Diastolic Wall Thickness as a Predictor of Recovery of Function in Myocardial Hibernation

Relation to Rest-Redistribution Tl-201 Tomography and Dobutamine Stress Echocardiography

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OBJECTIVES The study assessed whether end-diastolic wall thickness (EDWT), measured with echocardiography, is an important marker of myocardial viability in patients with suspected myocardial hibernation, and it compared this index to currently established diagnostic modalities of dobutamine stress echocardiography (DSE) and rest-redistribution thallium-201 (Tl-201) scintigraphy.

BACKGROUND Because myocardial necrosis is associated with myocardial thinning, preserved EDWT may provide a simple index of myocardial viability that is readily available from the resting echocardiogram.

METHODS Accordingly, 45 patients with stable coronary artery disease and ventricular dysfunction underwent rest 2D echocardiograms, DSE and rest-redistribution Tl-201 tomography before revascularization and a repeat resting echocardiogram ≥2 months later.

RESULTS Global wall motion score index decreased from 2.38 ± 0.73 to 1.94 ± 0.82 after revascularization ($p < 0.001$). Thirty-eight percent of severely dysfunctional segments recovered resting function. Compared to segments without recovery of resting function, those with recovery had greater EDWT (0.94 ± 0.18 cm vs. 0.67 ± 0.22 cm, $p \leq 0.0001$) and a higher Tl-201 uptake (78 ± 13% vs. 59 ± 21%; $p < 0.0001$). An EDWT >0.6 cm had a sensitivity of 94% and specificity of 48% for recovery of function. Similarly, a Tl-201 maximal uptake of ≥60% had a sensitivity of 91% and specificity of 50%. Receiver operating characteristic curves for prediction of recovery of regional and global function were similar for EDWT and maximum Tl-201 uptake. Combination of EDWT and any contractile reserve during DSE for recovery of regional function improved the specificity to 77% without a significant loss in sensitivity (88%).

CONCLUSIONS End-diastolic wall thickness is an important marker of myocardial viability in patients with suspected hibernation, and it can predict recovery of function similar to Tl-201 scintigraphy. Importantly, a simple measurement of EDWT ≤0.6 cm virtually excludes the potential for recovery of function and is a valuable adjunct to DSE in the assessment of myocardial viability. (J Am Coll Cardiol 2000;35:1152–61) © 2000 by the American College of Cardiology

Residual myocardial viability in patients with stable coronary artery disease (CAD) and regional dysfunction is associated with improvement in contractile function after revascularization (1–3). Many noninvasive techniques have been used for distinguishing viable from irreversibly injured myocardium, and these have relied on detection of residual metabolic activity, radioisotope uptake or contractile reserve upon inotropic stimulation, most commonly with dobutamine stress echocardiography (DSE). Early pathologic studies have demonstrated that myocardial thinning occurs in areas of myocardial necrosis in chronic transmural infarction (4–7). Moreover, intraoperative biopsies from abnormally contracting myocardial segments have provided histologic evidence that areas of viable myocardium usually have less than 10% to 20% of muscle loss, whereas those with scar tissue have a greater extent of muscle loss (8,9). Furthermore, it has long been recognized that the presence

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Abbreviations and Acronyms

AUC	=	area under the curve
CAD	=	coronary artery disease
DSE	=	dobutamine stress echocardiography
EDWT	=	end-diastolic wall thickness
SPECT	=	single-photon emission computed tomography
T1-201	=	thallium-201
WMSI	=	wall motion score index

of myocardial thinning detected with echocardiography is a marker of chronic myocardial infarction (10,11). The present study was conducted, first, to evaluate the predictive accuracy of end-diastolic wall thickness (EDWT) measured with echocardiography in assessing recovery of function in patients with suspected hibernation; second, the study was done to compare the accuracy of EDWT with currently accepted modalities of rest-redistribution thallium-201 (Tl-201) uptake and DSE. If EDWT is an important parameter of myocardial viability, such a measurement could be performed from the resting portion of a DSE without additional procedures or cost.

METHODS

Consecutive patients with CAD (at least one major epicardial artery with ≥70% stenosis) and resting wall motion abnormality, who were already scheduled for revascularization, were enrolled in the study. Exclusion criteria included the presence of unstable angina or recent myocardial infarction (<6 weeks), significant valvular heart disease or sustained ventricular tachycardia. All patients signed an informed consent for participation in the study, approved by the Institutional Review Board of Baylor College of Medicine and The Methodist Hospital. The study protocol consisted of resting 2D echocardiography, low and high dose DSE, and a rest-redistribution Tl-201 tomographic study within one to seven days before revascularization. The results of the studies performed did not influence the decision to proceed with revascularization. A resting echocardiogram was performed >2 months after the procedure to evaluate recovery of function.

Rest and dobutamine echocardiographic studies. Images were obtained with a Hewlett-Packard ultrasound system (Sonos 1500 or 2500, 2.5 MHz transducer). Standard parasternal long, short axis, apical four- and two-chamber views were recorded on VHS tapes and digitized online at rest and during dobutamine. The protocol of DSE was performed as previously described, with similar safety end points (12). Briefly, dobutamine infusion was started at a dose of 2.5 μg/kg body weight/min and increased at 3-min intervals to 5, 7.5, 10, 20, 30, and 40 μg/kg/min. Images at baseline, 5, 7.5 and peak dobutamine dose were digitized on-line in a quad screen format for later interpretation. This format was previously shown to be optimal for evaluation of myocardial hibernation (12).

Echocardiographic analysis. The echocardiograms and thallium images were analyzed as previously described using a 13-segment model in which the inferior and posterior walls were combined to enhance the accuracy of matching segments in this region (13). The segments included the basal, mid- and apical portions of anterior wall, anterior septum, lateral and inferoposterior walls and the apex. The inferior septum (base and mid-ventricle) could not be differentiated well from the anterior septum in the nuclear studies and was therefore not measured separately in either echocardiographic or nuclear studies. Analysis of EDWT from the rest studies and DSE was performed in separate reading sessions and in random order.

WALL THICKNESS MEASUREMENT. Resting echocardiographic images were analyzed off-line by one observer without knowledge of any other data including DSE, postoperative 2D echocardiography, Tl-201 or coronary angiography. Videotaped and digital rest images were used to identify the best views and frames for measurements. End-diastolic wall thickness was measured at the center of each myocardial segment (Fig. 1) from the leading endocardial edge to leading epicardial edge, using the echocardiographic window that best identified the endocardial and epicardial borders. Parasternal views (long axis, short axis at the base and midventricle) were more often used for determination of thickness in the basal and midventricular segments, usually because of better endocardial and epicardial resolution (more axial resolution). Apical segments including the apical septum were measured from the apical window. Thickness in the conventionally separate inferior and posterior wall segments (14) (Fig. 1) at each level was averaged when possible to render this area as one inferoposterior segment, for matching purposes with nuclear segmentation. Measurements (in centimeters) for each segment were performed in triplicate and averaged, using an off-line station equipped with internal calipers (Digisonics EC 500). Intraobserver and interobserver variabilities in measurements of EDWT were assessed in 91 myocardial segments of seven randomly selected patients. Intraobserver and interobserver mean absolute differences were 0.05 ± 0.05 cm and 0.11 ± 0.11 cm, respectively.

ANALYSIS OF REGIONAL FUNCTION AND DSE RESPONSE. Analysis of regional function and response of the myocardium to DSE was performed as previously described (12) by another independent investigator without knowledge of any other data. Briefly, regional wall function was semiquantitated using a 5-grade scoring system, where normal = 1, mild hypokinesia = 2, severe hypokinesia = 3, akinesia = 4, and dyskinesia = 5. The contractile response to dobutamine of segments with abnormal contraction at rest was classified into four different patterns as previously described (12): biphasic, sustained improvement, worsening, and no change

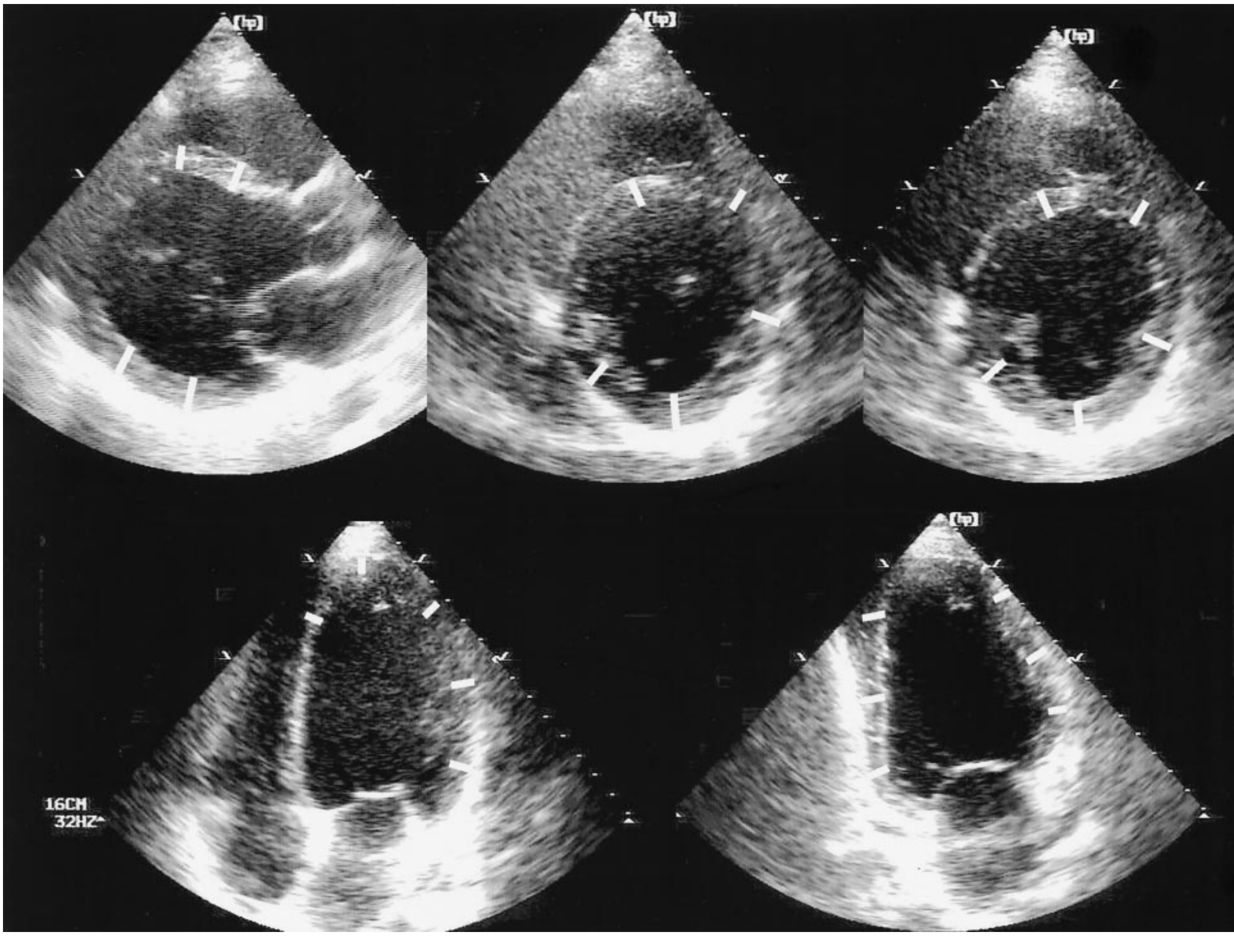

Figure 1. Parasternal long axis **(left upper panel)**, short axis at the base and midventricle (**middle** and **right upper panels**) and apical views **(lower panels)** showing location of measurements of end-diastolic wall thickness (EDWT) in the various myocardial segments (see text) in a patient with ischemic cardiomyopathy evaluated for myocardial viability. The inferior septum (at the base and midventricle) was not measured separately for the purposes of matching segments with Tl-201 scintigraphy. Parasternal windows usually provided a better resolution of basal and midventricular segments, whereas the apical windows allowed measurements of apical segments, in addition to others. As can be seen, EDWT of the apex was the most difficult to measure (see text) and was not recorded in this patient.

during DSE. Recovery of function within a segment was defined as a change of ≥2 grades in wall motion score from baseline to the follow-up study, based on a previous study of variability in our laboratory (12). A wall motion score index (WMSI) was derived as the sum of individual scores divided by the total number of segments analyzed. Ejection fraction was quantitated by the multiple-diameter method (15).

Rest redistribution Tl-201 scintigraphy. Both rest and 4-h redistribution Tl-201 single-photon emission computed tomography (SPECT) were performed after the intravenous (IV) administration of 3 mCi Tl-201 on the same day as DSE, before revascularization. The SPECT images were acquired as previously reported by our laboratory (16). A large-field-of-view rotating gamma camera with a high resolution, parallel-hole collimator was used. Data acquisition was obtained over a 180° arc (45° left posterior oblique to 45° right anterior oblique view) consisting of 32 frames. Reconstructed tomograms were oriented in the standard short, horizontal long and vertical long axes. Computerized two-dimensional polar maps of the three-dimensional myocardial radioactivity were generated and normalized to the highest pixel. Images were analyzed by experienced nuclear cardiologists blinded to all other information. The myocardial Tl-201 activity in each of the 13 segments was assessed in the center of the segment using a region of interest of 5 × 5 pixels, at rest and during redistribution. A maximal Tl-201 uptake (rest or redistribution) of ≥60% was used to denote myocardial viability, as this index was previously demonstrated to the most predictive of recovery of regional function after revascularization (13). Mean absolute differences in rest and redistribution Tl-201 uptake were determined from a previous evaluation of variability as 8.1 ± 8% and 11.6 ± 10.1%, respectively (13).

Coronary angiography. Selective coronary angiography was performed using standard techniques. The severity of coronary stenosis was determined with calipers and expressed as percent reduction of lumen diameter; this was done by an investigator who had no knowledge of all other data. Significant CAD was defined as ≥70% diameter stenosis of at least one major epicardial artery.

Statistical analysis. Results are expressed as mean value ± SD. Continuous data were compared using the Student *t* test. Categorical data were compared using the chi-square test. Differences in EDWT, Tl-201 uptake and DSE responses among groups were compared using analysis of variance (ANOVA). If the *F* value was significant, a Student-Newman-Keuls multiple comparison test was performed. To evaluate whether a myocardial region subtended by the revascularized artery responded in a statistically independent manner compared to adjacent regions, baseline WMSI and EDWT and changes in WMSI after revascularization in the revascularized and nonrevascularized regions were compared in the same patients using linear regression analysis and rank-sum test. Regression analysis was used to assess the correlation of EDWT with maximal Tl-201 uptake. To assess agreement between modalities, kappa statistics were used. Receiver operator characteristic curves were generated for the prediction of recovery of regional and global function by EDWT and maximum Tl-201 uptake. The area under the curve (AUC) was determined using the trapezoidal rule (17). Comparison of AUC was performed with the method developed by Hanley and McNeil (18). Statistical significance was set at $p \leq 0.05$.

Table 1. Baseline Characteristics of 45 Study Patients

Age (yr)	61 ± 10
Gender	38 men/7 women
Left ventricular ejection fraction	39 ± 13%
History of previous myocardial infarction	26 (58%)
Q-wave myocardial infarction	21 (47%)
Angina	34 (75%)
Congestive heart failure	21 (47%)
History of previous coronary bypass surgery	7 (15%)
History of previous coronary angioplasty	6 (13%)
Diabetes	13 (29%)
Hypertension	28 (62%)
Hyperlipidemia	29 (66%)
Smoking	26 (58%)
Cardiac medication	
Nitrates	31 (70%)
Beta-blockers	18 (40%)
Calcium channel blockers	15 (34%)
Angiotensin-converting enzyme inhibitors	19 (42%)
Diuretics	15 (33%)
Coronary angiography	
Single-vessel disease	14 (31%)
Multivessel disease	31 (69%)
Angiographic collaterals to revascularized area	17 (39%)

RESULTS

The study group consisted of 45 patients whose clinical and laboratory data are shown in Table 1. All patients underwent revascularization (coronary angioplasty in 31 patients, coronary artery bypass in 14). No clinical events occurred after the revascularization procedure except for one patient who died in heart failure 10 days after bypass surgery and was excluded from the analysis of recovery of function.

Relation of rest wall motion at baseline to EDWT and Tl-201 uptake. In the 45 patients, 555 of the 585 myocardial segments were visualized by echocardiography at rest. Two hundred twenty four were normal, 42 were mildly hypokinetic and 289 were severely dysfunctional (156 severely hypokinetic, 111 akinetic and 22 dyskinetic). Measurement of EDWT could be performed in 484 (83%) of all 585 segments and in 245 (85%) of the 289 severely dysfunctional segments. The majority of segments where thickness could not be reliably measured were in the apical area (96%): true apex in 38%, apical anterior wall in 23%, apical inferior wall in 15%, apical lateral wall in 14% and apical septum in 6%. Both EDWT and maximum Tl-201 uptake were significantly greater in myocardial segments with normal wall motion compared to those with hypokinesia, akinesia or dyskinesia (Fig. 2). End-diastolic wall thickness correlated significantly with maximum Tl-201 uptake ($r = 0.55$; $p < 0.0001$).

EDWT and recovery of function. For analysis of recovery of function after revascularization, only segments with severe baseline dysfunction (severe hypokinesia, akinesia or dyskinesia) were considered for analysis. A total of 234 severely dysfunctional segments were analyzed: 11 segments of the patient who died before follow-up were excluded. Of those, 181 segments were in revascularized territories and were the final objective of this study. Sixty-nine revascularized segments (38%) had functional recovery of ≥2 grades compared with 9 of 53 nonrevascularized segments ($p = 0.004$).

At baseline, there was no relation between WMSI of segments in the revascularized region and WMSI of segments in the nonrevascularized region in the same patients ($r = 0.02$; $p = 0.76$). Similarly, no relation was observed between EDWT of segments in the revascularized and nonrevascularized regions in the same patients ($r = 0.03$; $p = 0.66$). The change in WMSI of revascularized territory from baseline to after revascularization did not relate to change in WMSI of nonrevascularized segments ($r = 0.17$; $p = 0.07$). Segments that exhibited recovery of function had a thicker EDWT before revascularization compared to those without improvement in function (0.94 ± 0.18 cm vs. 0.67 ± 0.22 cm; $p < 0.0001$; Fig. 3). A receiver operator characteristic curve was generated to assess the prediction of recovery of function at different cutoffs of EDWT (Fig. 4). An EDWT of >0.8 cm provided the best balance between sensitivity (75%) and specificity (80%). However, the best cutoff from a clinical implication point of view for revascularization (high sensitivity with moderate specificity or higher) was 0.6 cm, which provided a sensitivity of 94%, a

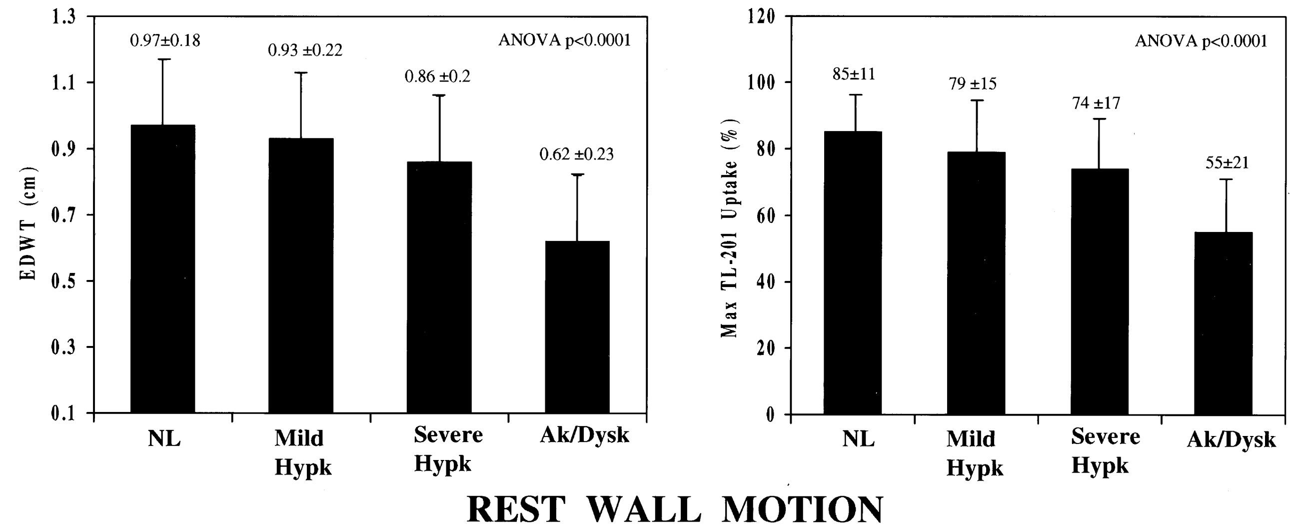

Figure 2. Relation of rest wall motion to end-diastolic wall thickness (EDWT) and rest-redistribution thallium-201 uptake. NL = normal; Hypk = hypokinesia; Ak = akinesia; Dysk = dyskinesia.

specificity of 48% and a high negative predictive value of 93% (Table 2, Fig. 4). The prediction of recovery of severely hypokinetic versus akinetic and dyskinetic segments is presented in Table 3. Overall sensitivity was higher and specificity was lower in hypokinetic segments.

Rest-redistribution Tl-201 scintigraphy and recovery of function. Maximum Tl-201 uptake was higher in revascularized segments that recovered function compared with those that did not (Fig. 3). The sensitivity and specificity of Tl-201 uptake ≥60% for predicting recovery of function was 91% and 50%, respectively (Table 2). Sensitivity was higher and specificity was lower in hypokinetic segments compared to akinetic and dyskinetic segments (Table 3). Overall results were similar to those obtained with EDWT (Tables 2 and 3). The EDWT was higher in segments with Tl-201 ≥60% compared to those with <60% uptake (Fig. 5). The receiver operating characteristic curve for maximal Tl-201 uptake is shown on Figure 4. The AUC for Tl-201 was 0.75 and was similar to that of EDWT (0.82; p = 0.09).

Dobutamine echocardiography and recovery of function. Of the 44 patients who underwent rest echocardiography, Tl-201 studies and revascularization, 43 had DSE before the procedure. All 43 patients finished the infusion protocol or reached ≥85% of their target heart rate, or achieved both end points. The different responses of the 169 severely dysfunctional segments to DSE were biphasic response in 48 (28%), sustained improvement in 39 (23%), worsening in 7 (4%) and no change in wall motion in 75 (44%). The prediction of recovery of function using biphasic response

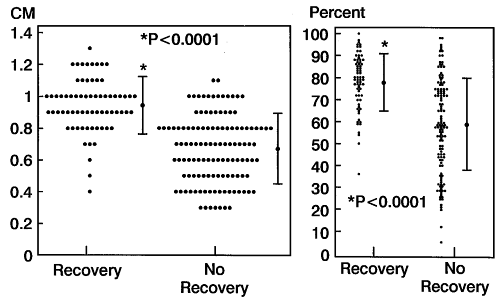

Figure 3. Scatter plot of individual measurements of end-diastolic wall thickness and maximum Tl-201 uptake in segments with and without recovery of systolic function after revascularization.

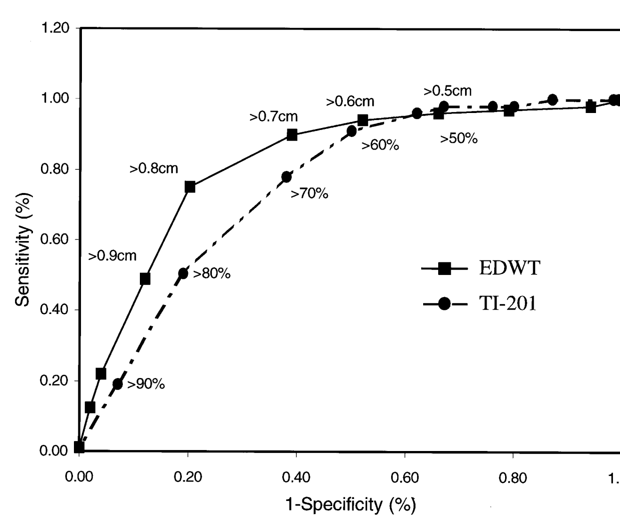

Figure 4. Receiver operating characteristic curves for prediction of recovery of function after revascularization with end-diastolic wall thickness (EDWT) and rest-redistribution Tl-201 uptake before revascularization.

Table 2. Accuracy of Different Modalities in Prediction of Recovery of Function in Severely Dysfunctional Segments

	Sensitivity	Specificity	PPV	NPV
EDWT >0.6 cm	65/69 (94%)	54/112 (48%)	65/123 (53%)	54/58 (93%)
Tl-201 (R-R) ≥60%	64/69 (91%)	56/112 (50%)	63/119 (53%)	56/62 (90%)
DSE (biphasic)	35/57 (61%)*	99/112 (88%)*	35/48 (73%)†‡	99/121 (82%)*
DSE (any improvement)	52/57 (91%)	77/112 (69%)†‡	52/87 (60%)	77/82 (94%)
EDWT >0.6 cm and DSE (any improvement)	50/57 (88%)	86/112 (77%)†‡	50/76 (66%)§	86/93 (92%)

Data are presented as number (%) of segments.
PPV = positive predictive value; NPV = negative predictive value; R-R = rest-redistribution.
*$p < 0.05$ vs. all other variables; †$p < 0.05$ vs. EDWT; ‡$p < 0.05$ vs. thallium-201; §$p = 0.07$ vs. EDWT.

and any contractile reserve during DSE (biphasic or sustained improvement) is shown in Table 2. Biphasic response alone had a sensitivity of 61% and a specificity of 88%. Any contractile reserve increased the sensitivity to 91% and decreased the specificity to 69%. Similar to Tl-201 and EDWT, higher sensitivity and lower specificity were found in hypokinetic segments (Table 3). The EDWT was thicker in segments with contractile reserve compared to those without (Fig. 5). Similar EDWT was observed in segments with biphasic response and in those with sustained improvement (0.88 ± 0.18 cm vs. 0.82 ± 0.23 cm; $p = 0.11$). In contrast, EDWT was thinner (0.64 ± 0.25 cm) in segments without change in function during DSE (ANOVA $p < 0.0001$).

Comparison of different modalities for prediction of recovery of function. Taking into consideration severely dysfunctional segments that were revascularized, a concordance of 72% was observed between what was judged to be viable by EDWT and Tl-201 maximum uptake (kappa = 0.38). A similar agreement was observed between DSE (any contractile reserve) and EDWT (73%, kappa = 0.45) and between DSE and Tl-201 (68%, kappa = 0.35). Comparison of sensitivity and specificity for recovery of function among different techniques (Tables 2 and 3) confirmed that biphasic response is more specific but less sensitive than EDWT and Tl-201. As expected, any contractile reserve during dobutamine increased sensitivity at the cost of decreasing specificity to levels closer to EDWT and Tl-201 scintigraphy. Because EDWT can be performed in the same setting as DSE, we investigated whether the incorporation of EDWT measurement with DSE would improve its diagnostic accuracy for prediction of recovery of function. The positive predictive value of preserved EDWT was improved with the addition of a biphasic response during DSE (from 53% to 74%, $p = 0.01$). The best combination was the addition of information from EDWT to any contractile reserve by DSE (Figs. 6 and 7). The combination of contractile reserve *and* EDWT >0.6 cm maintained a high sensitivity for recovery of function with a trend for improved specificity (Tables 2 and 3).

Analysis by patients. Global wall motion score index was 2.38 ± 0.73 at baseline and decreased to 1.94 ± 0.82 ($p < 0.001$) after revascularization. Similarly, ejection fraction increased from $39 \pm 13\%$ to $44 \pm 14\%$ ($p = 0.01$). Of the 44 patients who had follow-up, 41 had revascularization in the distribution of dysfunctional segments. The number of segments that recovered function by two or more grades correlated significantly with the difference in ejection fraction from baseline to after revascularization ($r = 0.89$; change in ejection fraction = $2.76 \times$ [number of segments with recovery of function] + 0.07). Nineteen patients had recovery of function of two or more segments, which corresponded to an improvement in ejection fraction of ≥5%, and 10 patients had an increase in ejection fraction of ≥9%. Table 4 shows the sensitivity and specificity of various parameters for predicting improvement in ejection fraction by ≥5%. Sensitivity and specificity for incremental extent in viability by the various methods (number of viable dysfunc-

Table 3. Prediction of Recovery of Function in Akinetic/Dyskinetic Segments and in Severely Hypokinetic Segments

	Severely Hypokinetic		Akinetic/Dyskinetic	
	Sensitivity	Specificity	Sensitivity	Specificity
EDWT >0.6 cm	52/53 (98%)	13/46 (28%)	13/16 (81%)	41/66 (62%)
Tl-201 (R-R) ≥60%	50/53 (94%)	18/46 (39%)	13/16 (81%)	38/66 (57%)
DSE (biphasic)	30/48 (62%)*	38/46 (83%)*	5/9 (56%)	61/66 (92%)§
DSE (any improvement)	46/48 (96%)	22/46 (48%)	6/9 (67%)	55/66 (83%)
EDWT >0.6 cm and DSE (any improvement)	45/48 (94%)	28/46 (61%)†‡	5/9 (56%)	58/66 (88%)§

Data represented as number (%) of segments.
R-R = rest-redistribution.
*$p < 0.05$ vs. all other variables; †$p < 0.05$ vs. EDWT; ‡$p < 0.05$ vs. thallium-201; §$p < 0.05$ vs. EDWT and thallium-201.

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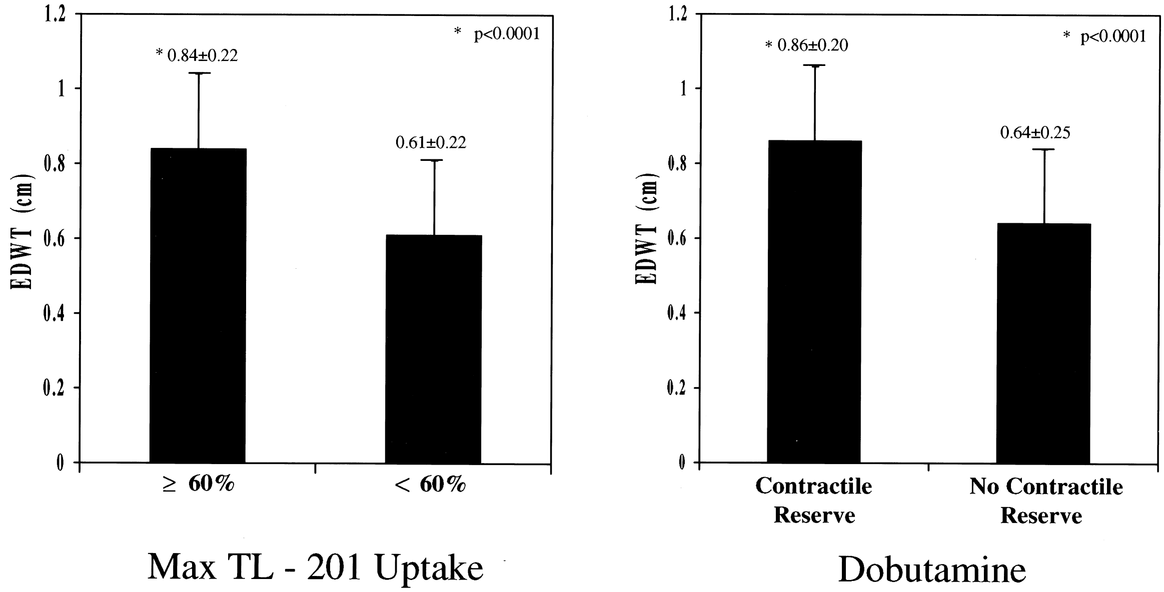

Figure 5. End-diastolic wall thickness at baseline grouped according to maximum Tl-201 uptake and contractile reserve during dobutamine echocardiography prior to revascularization.

tional segments that are revascularized) are shown. Overall, for identical segmental cutoffs, similar higher sensitivity and lower specificity were observed with EDWT, Tl-201 and any contractile reserve to DSE compared to biphasic response. This did not reach statistical significance. Balance between sensitivity and specificity was seen most commonly with three viable segments, except for biphasic response (two segments) (Table 4). A clinically desirable cutoff with high sensitivity and moderate specificity, however, was seen with a two-segment cutoff for most indices, except for biphasic response (≥1 viable segment). Using an increase in ejection fraction of ≥9% as a definition of an individual improvement in global function, based on previous variability studies (15,19), the best cutoff of number of viable segments increased by 1 for all modalities, with results similar to those reported in Table 4.

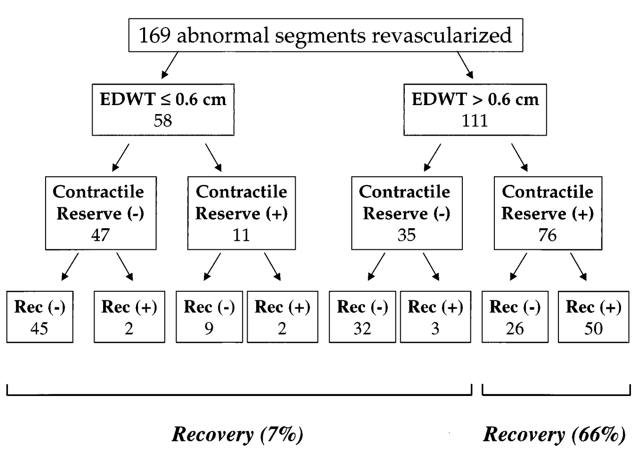

Figure 6. Diagram of the outcome of severely dysfunctional myocardial segments after revascularization grouped by end-diastolic wall thickness (EDWT) and contractile reserve to dobutamine. Rec = recovery of function.

DISCUSSION

The present study demonstrates that, in patients with suspected myocardial hibernation, a simple measurement of EDWT obtained with echocardiography is an important parameter of myocardial viability. A myocardial thickness of ≤0.6 cm virtually excludes recovery of function after revascularization. Of interest is that the diagnostic accuracy of EDWT in predicting recovery of function after revascularization is similar to that of quantitative rest-redistribution Tl-201 scintigraphy.

Prediction of viable myocardium by preserved EDWT. In the search for hibernating myocardium, several modalities are currently used to predict recovery of myocardial function, including preserved metabolic activity with positron emission tomography, myocardial radionuclide uptake, and contractile reserve with DSE. Early pathologic studies have demonstrated that myocardial thinning occurs in areas of myocardial necrosis in chronic transmural infarction (4–7). Data from autopsied hearts have previously shown that chronic transmural infarction is associated with myocardial thinning, frequently measuring less than 0.6 cm (7). Clinical observations of myocardial thinning in chronic myocardial infarction date back to the early days of echocardiography (10,11).

More recently, a reduction in EDWT relative to adjacent segments and increased acoustic reflectance of myocardial segments assessed visually were predictive of irreversibly

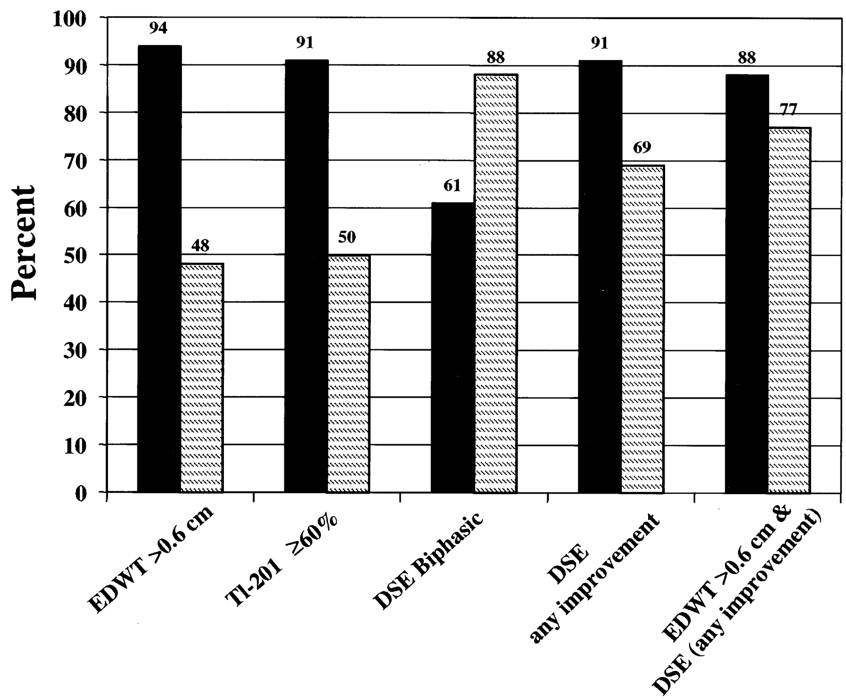

Figure 7. Sensitivity **(black bars)** and specificity **(shaded bars)** for recovery of function after revascularization using end-diastolic wall thickness (EDWT), rest-redistribution thallium uptake, and dobutamine stress echocardiography (DSE) responses.

damaged myocardium in 15 patients with healed Q-wave anterior myocardial infarction and single-vessel disease (20). The present study extends these earlier observations to patients with multivessel disease and demonstrates that quantitative, absolute measurement of EDWT is an important parameter of myocardial viability, with comparable accuracy to rest-redistribution T1-201 scintigraphy. An EDWT ≤0.6 cm is highly associated with irreversible injury (negative predictive value 93%) and virtually excludes myocardium with potential for functional recovery. A greater cutoff for wall thickness improved the specificity for recovery of function with a loss in sensitivity, as shown on the ROC curve. An EDWT >0.6 cm by itself overestimates the degree of recovery of function, similar to recent observations on myocardial thickness and viability with magnetic resonance imaging (21,22). This may be related in part to the "threshold phenomenon" of myocardial thickening (23). Because the endocardium is primarily responsible for systolic thickening, preserved thickness without thickening may be due to remnant viable tissue in epicardial layers in the presence of subendocardial infarction or an admixture of viable and nonviable myocardium (23–26). The positive predictive value of EDWT could be increased with the addition of biphasic response during DSE, which implies limited coronary flow reserve. Whether preserved myocardial thickness without recovery of function is associated with improvement in ventricular remodeling and clinical outcome after revascularization remains to be determined (27–30).

Relation of EDWT to Tl-201 scintigraphy. Thallium-201 uptake has been used extensively for the assessment of myocardial viability (31–33). Recent studies have also demonstrated a good inverse relation between Tl-201 uptake and percent fibrosis at myocardial biopsy (34). We hypothesized that the larger proportion of viable myocardium observed with higher Tl-201 uptake may relate to larger myocardial mass or thickness. Baseline wall motion, and thus in part viability, related similarly to both Tl-201 uptake and EDWT. A significant correlation (r = 0.55) was also found between maximum Tl-201 uptake and EDWT. These results are in agreement with previous observations in chronic infarctions on the relation of EDWT by magnetic resonance to fluorodeoxyglucose uptake in akinetic or dyskinetic segments (r = 0.59) (35) and to severity of Tl-201 defects (22,36). Importantly, in the present study, the predictive power of EDWT for recovery of function was similar to that of quantitative Tl-201 uptake using either segmental or global analysis, as demonstrated by the similar receiver operating characteristic curves. The cutoffs of 60% maximum Tl-201 uptake and EDWT of 0.6 cm provided similar high sensitivity and moderate specificity for the prediction of recovery of function.

EDWT and DSE: Clinical implications. Dobutamine stress echocardiography is currently the echocardiographic method of choice for evaluation of myocardial viability. A biphasic response of the dysfunctional myocardium to dobutamine implies viability and limited coronary flow reserve and hence has the highest specificity for recovery of function

Table 4. Sensitivity and Specificity for Improvement in Left Ventricular Ejection Fraction of ≥5% Using Increasing Cutoffs of Number of Viable, Dysfunctional Segments by EDWT, Tl-201 Scintigraphy and DSE

No. Viable Segments	EDWT		Tl-201		DSE (Biphasic)		DSE (Any Imp)		DSE and EDWT	
	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)	Sens (%)	Spec (%)
1	100	27	100	18	83	54	100	27	100	45
2	89	41	89	36	72	77	94	50	83	64
3	63	68	68	64	44	91	61	68	56	82
4	42	73	53	77	28	91	39	77	39	95

No. = Number of viable, dysfunctional segments that underwent revascularization; Imp = improvement in function; EDWT = end-diastolic wall thickness >0.6 cm; Tl-201 = rest-redistribution thallium-201 ≥60%; Sens = sensitivity; Spec = specificity.

after revascularization (12,13,19,37). The addition of sustained improvement to biphasic response (any improvement) increases the sensitivity of DSE at expense of specificity, because of lack of inducible ischemia and/or the possibility that the apparent increase in function may be due to myocardial tethering during DSE (12). In the present study, EDWT was more sensitive and less specific for recovery of function than was biphasic response, and it provided similar results to any contractile reserve during DSE. The combination of EDWT and DSE yielded results with the best accuracy and a good balance between sensitivity and specificity for recovery of function. The trend for improved specificity of any contractile reserve with the addition of EDWT may possibly be due to exclusion of thin, nonviable segments that exhibit tethering during DSE. End-diastolic wall thickness is a simple parameter that can be easily incorporated from the resting echocardiogram and is therefore a valuable adjunct to DSE in the assessment of myocardial viability. With the high negative predictive value of EDWT, one can conceivably forgo a DSE or other tests for viability if the dysfunctional area of the myocardium is ≤0.6 cm in thickness. However, in patients with an admixture of thin and preserved thickness of dysfunctional segments, DSE would be necessary to assess contractile reserve and ischemia in the latter segments.

Study limitations. Coronary angiography was not repeated in the follow-up period, and therefore restenosis or graft occlusion cannot be completely excluded. However, all patients were followed until the final study, and none complained of recurrent angina or had any other evidence of ischemia. Some discrepancy between echocardiographic and scintigraphic studies may be due to anatomic misregistration of segments, an inherent limitation of studies that attempt to compare different imaging modalities.

Both analysis and accuracy of EDWT depend on the quality of the echocardiogram. Measurement of EDWT in apical windows may be technically challenging owing to poor lateral resolution. Determination of EDWT in this study was performed from the window providing the best definition of the endocardial and epicardial borders, more often from the parasternal approach. Measurements were feasible in 85% of segments and had an acceptable reproducibility. In a previous study (20), measurement of thickness was feasible in only 7 of 15 patients. Since then, improvement in transducer technology has occurred.

More recently, the introduction of new modalities for quantitation of myocardial thickness (anatomic M-mode) and for improved endocardial delineation (harmonic imaging and contrast echocardiography) will undoubtedly improve the feasibility and accuracy of EDWT measurements with echocardiography. Increased ultrasound reflectivity has been associated with scarring and a lesser likelihood for recovery of function after myocardial infarction (20). It is subjective, however, and depends on several ultrasound settings. Whether quantitation of this phenomenon with addition of integrated backscatter can further enhance separation of viable from nonviable myocardium beyond that observed with EDWT measurements remains to be determined.

Conclusions. The EDWT measured at rest with 2D echocardiography can predict recovery of function in patients with suspected myocardial hibernation, similar to Tl-201 scintigraphy. Importantly, an EDWT ≤0.6 cm practically excludes relevant amount of viable myocardium and is an important simple adjunct to dobutamine echocardiography in the assessment of myocardial viability.

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