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EXPRESS PUBLICATIONS

Myocardial Wall Thickness Predicts Recovery of Contractile Function After Primary Coronary Intervention for Acute Myocardial Infarction

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OBJECTIVES We sought to determine whether end-diastolic wall thickness (EDWT) can predict recovery of regional left ventricular contractile function after percutaneous coronary intervention (PCI).

BACKGROUND Regional contractile function does not recover in all patients after PCI for acute myocardial infarction (AMI). Prediction of functional recovery after AMI may help in clinical decision making.

METHODS Forty consecutive patients with AMI were studied with left ventricular contrast echocardiography for accurate wall thickness and function measurement and myocardial perfusion immediately after and two months following PCI.

RESULTS Out of 640 segments, 175 (27%) dysfunctional segments in the infarct territory were analyzed for EDWT, wall function, and perfusion. One hundred and three (59%) dysfunctional segments presented with an EDWT <11 mm and 72 (41%) presented with an EDWT ≥11 mm. Perfusion (partial or complete) was present in 63 segments with an EDWT <11 mm (61%) and 71 segments with an EDWT ≥11 mm (99%) ($p < 0.001$). At two months' follow-up, 66 of 72 segments with an EDWT ≥11 mm (92%) improved, whereas only 35 of 103 of the dysfunctional segments with an EDWT <11 mm (34%) improved ($p < 0.0001$).

CONCLUSIONS Wall thickness is an easy parameter to predict recovery of function after revascularization. Moreover, combining EDWT and perfusion, segments with an EDWT ≥11 mm, and presence of perfusion have the highest chance of recovery; segments with an EDWT <11 mm and perfusion have an intermediate chance of recovery. In segments with an EDWT <11 mm and no perfusion, chances of recovery are very low. (J Am Coll Cardiol 2004;43:1489–93) © 2004 by the American College of Cardiology Foundation

Early revascularization by percutaneous coronary intervention (PCI) is associated with a good clinical outcome in patients with acute myocardial infarction (AMI) (1). However, in some patients successful PCI does not result in recovery of contractile function in the infarct territory (2). Two-dimensional contrast echocardiography allows assessment of wall function and myocardial perfusion simultaneously. It has been shown in several studies that myocardial contrast echocardiography (MCE) allows researchers to predict recovery of regional contractile function after reperfusion in AMI (3–6). Until now, the end-diastolic wall thickness (EDWT) was not used as a simple parameter to predict functional recovery after PCI. Therefore, myocardial wall thickness was assessed to determine its value as a predictor of recovery of regional contractile function late after PCI. In this study, contrast echocardiography was used for optimal endocardial border delineation (7).

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METHODS

Study patients. This prospective study comprised 40 consecutive patients without history of hypertension, left ventricular hypertrophy, and primary cardiomyopathy, but with ST-segment elevation AMI and who underwent PCI within 6 h of onset of symptoms. Baseline characteristics of the 40 patients (34 male, mean age 53 ± 13 years) are summarized in Table 1. The diagnosis of AMI was made on the basis of symptoms of myocardial ischemia for ≥30 min and ≥2 mm ST-segment elevation in ≥2 contiguous electrocardiographic leads. The infarct-related artery was identified by the site of the coronary occlusion, and stent implantation was performed. Left ventricular hypertrophy was defined according to recommendations of the American Society of Echocardiography and corrected following the suggestions of Devereux et al. (8). The left ventricular mass index was derived with normal limits defined as ≤ 125 g/m^2 for men and ≤ 110 g/m^2 for women (9). The local hospital ethics committee approved the study protocol, and all patients gave informed consent.

Echocardiography and contrast studies. Echocardiography was performed with a Sonos 5500 (Philips, Andover, Massachusetts) using second harmonic mode (1.8-MHz/

Abbreviations and Acronyms

AMI = acute myocardial infarction
EDWT = end-diastolic wall thickness
LVEF = left ventricular ejection fraction
MCE = myocardial contrast echocardiography
PCI = percutaneous coronary intervention

3.6-MHz), within 24 h following revascularization. After recording baseline, myocardial perfusion images were obtained in real time (power modulation) using a low mechanical index (0.1). A slow bolus of 0.75 ml of Sonovue (Bracco, Milan, Italy) was intravenously injected followed by a slow saline flush (5 ml) over 5 s. Imaging was started before contrast injection and "flash" imaging with high mechanical index (1.6) was used at peak contrast intensity for four frames to destroy the microbubbles in the myocardium, to exclude artifacts, and to visualize myocardial contrast replenishment. To obtain maximal image information, the segments related to the infarct territory were placed in the center of the echo sector reducing the problem of artifacts. After the real-time perfusion study, left ventricular opacification images were recorded in all standard parasternal and apical views to improve quantitative assessment of myocardial function (7). Left ventricular ejection fraction (LVEF) was measured using the standard biplane Simpson method. Improvement of LVEF ≥5% was considered significant (10). A follow-up study with MCE to reassess EDWT, function, and perfusion was performed at two months.

EDWT measurement. The EDWT was measured by two experienced observers unaware of the clinical data as previously described (11), using intravenous echo-contrast for better endocardial border detection (7). The EDWT was assessed at the center of each myocardial segment from the leading endocardial edge to the leading epicardial edge as the mean of three measurements. Dysfunctional segments were categorized as segments with an EDWT <11 mm and an EDWT ≥11 mm.

Table 1. Patient Characteristics

Age (yrs, ± SD)	53 ± 13
Men	34 (85%)
Smoking	25 (62%)
Diabetes mellitus	4 (10%)
Hypertension	0
Hypercholesterolemia	6 (15%)
Family history of CAD	13 (32%)
Previous myocardial infarction	5 (12%)
EF (%)	45 ± 6
CK peak (IU)	3,074 ± 2,245 (n < 200 IU)
Site of infarction	
Anterior	22 (55%)
Lateral	16 (40%)
Septal	2 (5%)
Inferior/posterior	19 (47%)
TIMI flow grade 3 after PCI	33 (82%)

CAD = coronary artery disease; CK = creatine kinase; EF = ejection fraction; SD = standard deviation; TIMI = Thrombolysis In Myocardial Infarction.

Analysis of echocardiograms. Regional wall motion and myocardial perfusion were scored using standard parasternal long- and short-axis views and apical two-, three-, and four-chamber views, employing a 16-segment model (12). Only segments related to acute infarct territory were considered for the analysis. Segments were graded as: 1 = normal, 2 = severe hypokinetic, 3 = akinetic, and 4 = dyskinetic. Myocardial contrast perfusion was scored semi-quantitatively using a 3-point grading scale: 2 = normal/homogenous opacification, 1 = reduced/patchy opacification, and 0 = no opacification. Segments with a severely hypokinetic, akinetic, or dyskinetic wall motion pattern were considered dysfunctional. Recovery of contractile function was defined as an improvement of segmental wall motion score by ≥1 grade at the follow-up.

Statistical analysis. All continuous data are expressed as mean ± SD; percentages are rounded. Differences between proportions were compared with the chi-square test. The agreement for the measurements of EDWT was assessed from 3 × 3 tables using weighted kappa statistics (13). A value of $p < 0.05$ was considered statistically significant. The EDWT that was related to a high likelihood of improvement of segmental contraction was determined by receiver operating characteristic curve analysis. The optimal cutoff value was the EDWT that yielded the highest sum of sensitivity and specificity.

RESULTS

Mean time from onset of chest pain to PCI was 3.8 ± 1.8 h. Of a total of 640 segments, 175 (27%) dysfunctional segments were located in the infarct-related territory, and EDWT, wall function, and myocardial perfusion were analyzed. A total of 103 (59%) segments had an EDWT <11 mm, and 72 (41%) had an EDWT ≥11 mm. Both intra- and inter-observer agreements for the assessment of EDWT were 0.96 and 0.93, respectively (kappa value). Mean EDWT was 9 ± 1 mm for the group with an EDWT <11 mm, and 12 ± 1 mm for the group with an EDWT ≥11 mm. Real-time perfusion MCE imaging demonstrated that 11 (11%) of the 103 dysfunctional segments with an EDWT <11 mm had normal perfusion, 52 (50%) had partial perfusion, and 40 (39%) had no perfusion. Of the 72 dysfunctional segments with an EDWT ≥11 mm, 33 (46%) had normal perfusion, 38 (53%) had partial perfusion, and 1 had absent perfusion.

Functional outcome. At two months' follow-up, 35 of the 103 (34%) segments with an EDWT <11 mm improved, whereas 66 of the 72 (92%) segments with an EDWT ≥11 mm improved ($p < 0.0001$) (Fig. 1). Sixty-nine of the 72 (96%) segments with an EDWT ≥11 mm became thinner at follow-up (12 ± 1 mm to 9 ± 1.5 mm; $p < 0.05$). Of these 69 segments, 64 (93%) had an EDWT <11 mm at follow-up. Seventy-two of the 103 dysfunctional segments with an EDWT <11 mm (70%) became thinner at follow-up (9 ± 1 mm to 7 ± 1.7 mm; $p < 0.05$). Of the 103

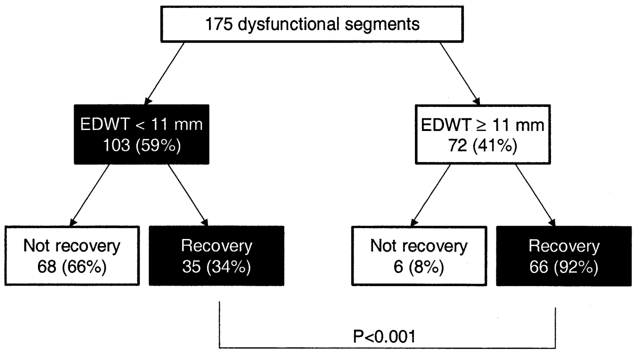

Figure 1. Relation between improvement of left ventricular contractile function and end-diastolic wall thickness (EDWT).

dysfunctional segments with an EDWT <11 mm, 33 (32%) had normal perfusion, 39 (38%) had partial perfusion, and 31 (30%) showed no perfusion at follow-up. In the 72 dysfunctional segments with an EDWT ≥11 mm, myocardial perfusion at follow-up was normal in 49 (68%), partial in 20 (28%), and absent in 3 (4%) segments.

A subanalysis was performed considering only the akinetic segments. Of the 100 akinetic segments, 31 of 33 (94%) with an EDWT ≥11 mm improved at follow-up, whereas only 20 of 67 (30%) segments with an EDWT <11 mm improved ($p < 0.001$).

Nearly all patients (15 of 16 patients, 94%) in which ≥50% of the dysfunctional segments had an EDWT ≥11 mm showed an improved LVEF at follow-up. Conversely, none of the 24 patients in which <50% of the dysfunctional segments had an EDWT ≥11 mm had an improved LVEF at follow-up.

Prediction of recovery by perfusion and wall thickness. To accurately predict functional recovery after revascularization in dysfunctional infarcted areas, information about perfusion and wall thickness should be combined (Table 2). Real-time perfusion MCE imaging demonstrated that perfusion was present in 134 of 175 (77%) dysfunctional segments. In particular, MCE showed that 44 (25%) of the 175 dysfunctional segments had normal perfusion, 90 (51%) had partial perfusion, and 41 (23%) showed no perfusion. However, only 98 (73%) of the adequately reperfused segments recovered at follow-up. Adding EDWT measurements of the adequately reperfused segments, 71 (53%) had an EDWT ≥11 mm and 63 (47%) had an EDWT <11 mm. At two months' follow-up, recovery of contractility was present in 66 (93%) of the adequately perfused segments with an EDWT ≥11 mm, whereas only 32 (51%) of the adequately perfused segments with an EDWT <11 mm recovered ($p < 0.001$) (Table 2, Figs. 2 and 3).

Table 2. Comparison Between EDWT and Myocardial Perfusion as Prognostic Indexes of Recovery of Contractile Function at Two Months' Follow-Up

Category	Number (%) of Segments With Functional Recovery
EDWT ≥11 mm	
P+	66/71 (93)
P−	0/1 (0)
EDWT <11 mm	
P+	32/63 (51)
P−	3/40 (7)

EDWT = end-diastolic wall thickness; P = perfusion (normal or patchy); + = present; − = absent.

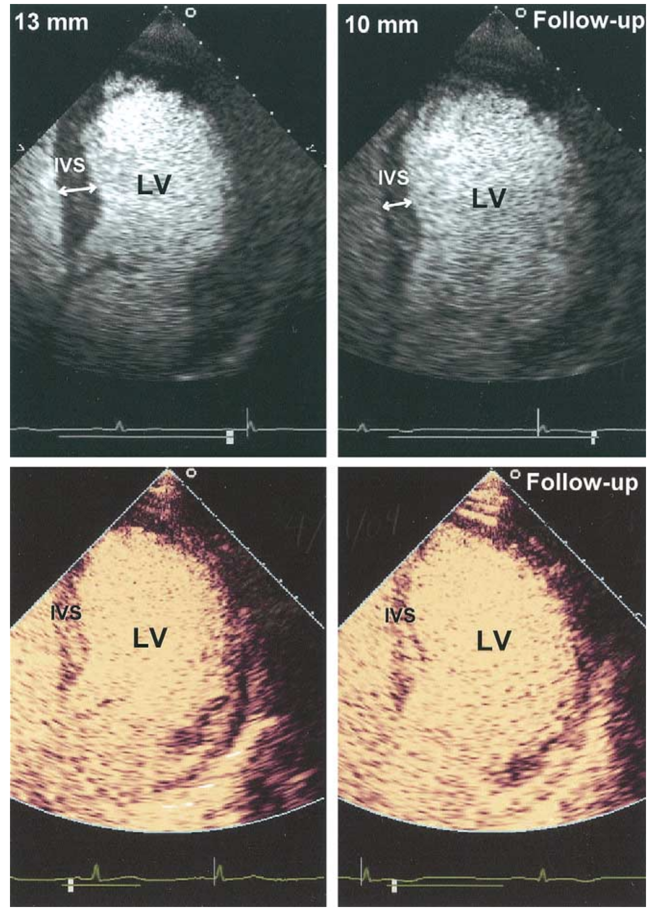

Figure 2. Two-dimensional echocardiograms showing end-diastolic wall thickness **(upper panels)** and perfusion **(lower panels)** in an infarcted region directly after percutaneous coronary intervention **(left panels)**, and after recovery at two months' follow-up **(right panels)**. IVS = interventricular septum; LV = left ventricle.

DISCUSSION

Restoration of coronary vessel patency does not automatically result in recovery of contractile function in patients undergoing PCI in the setting of AMI. The main finding of the present study is that a relatively simple measurement of EDWT, obtained with two-dimensional echocardiography combined with contrast agent, predicts recovery of regional contractile function after PCI for AMI. Using EDWT alone, dysfunctional segments with an EDWT ≥11 mm showed a high likelihood of recovery of regional contractile function two months after PCI. Moreover, it appears that when at least 50% of the dysfunctional segments show an EDWT ≥11 mm, global recovery may be anticipated. In the present study only 98 (73%) of the adequately reperfused dysfunctional segments had recovery of function at follow-

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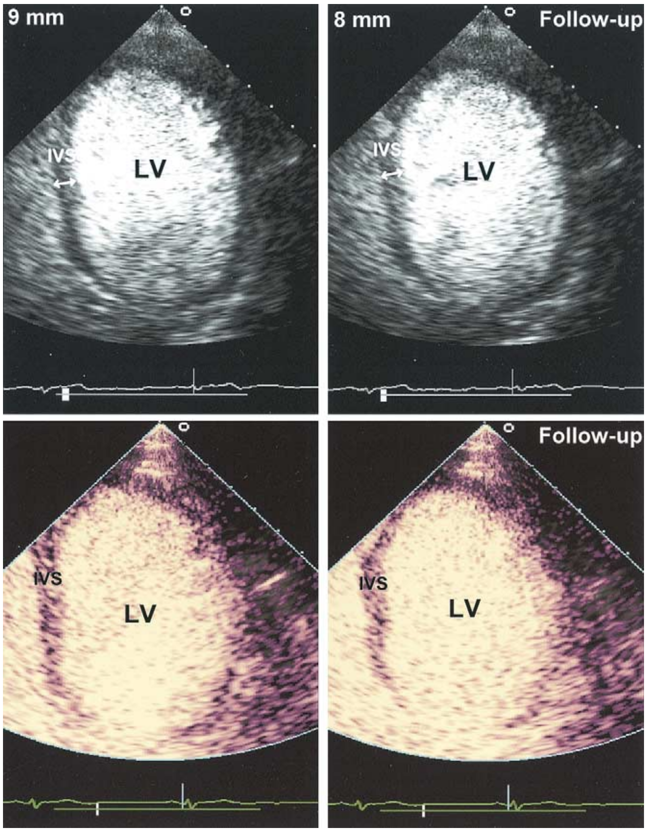

Figure 3. Two-dimensional echocardiograms showing end-diastolic wall thickness **(upper panels)** and perfusion **(lower panels)** in a patient directly after percutaneous coronary intervention **(left panels)** and at two months' follow-up **(right panels)**, in a case where regional function did not recover. IVS = interventricular septum; LV = left ventricle.

up. Combining wall thickness and perfusion, segments with an EDWT ≥11 mm and presence of perfusion have the highest chance of recovery (93%). An intermediate likelihood of recovery was observed in segments with an EDWT <11 mm and presence of perfusion (51%), whereas segments with an EDWT <11 mm and no perfusion nearly never improved. The present results indicate that perfusion data do not provide much additional information for the prediction of recovery of contractile function in segments with an EDWT ≥11 mm, because most of them recover at follow-up. Perfusion data are more relevant for the prediction of functional outcome in segments with an EDWT <11 mm.

Comparison to previous studies. In patients with AMI undergoing PCI, assessment of the amount of myocardial salvage is important for prediction of functional recovery and long-term prognosis. Main et al. (4) demonstrated that MCE compares favorably with low-dose dobutamine echocardiography for the assessment of myocardial viability after an acute anterior infarction. Balcells et al. (5) demonstrated that the extent of microvascular integrity assessed by MCE after PCI correlates with recovery of resting left ventricular function and contractile reserve. Lepper et al. (6) showed that assessment of restoration of myocardial perfusion by MCE after PCI corresponds closely to the evaluation of the microvascular integrity by coronary flow reserve. Moreover, an improvement of myocardial perfusion after revascularization was predictive for subsequent functional recovery. However, EDWT as a predictor of recovery of regional contractile function after PCI has not been specifically addressed.

Possible explanation for the findings. The pathophysiological mechanism underlying the relation between EDWT and long-term recovery of regional contractile function after PCI for AMI is currently not clear. It is conceivable (but speculative) that the high likelihood of recovery in segments with an EDWT ≥11 mm is related to hyperemia and tissue edema in adequately reperfused myocardium. During the early phase of reperfusion, reactive hyperemia may occur (14) followed by myocardial tissue edema within the reperfused myocardium (15). Further studies are needed to elucidate this issue.

Study limitations. A potential limitation of echocardiography to determine myocardial wall thickness is image quality. The use of contrast echocardiography in the present study overcame this limitation because endocardial border detection and EDWT measurements were more accurately assessed, as was shown by Thomson et al. (7). Another limitation is that wall thickness is heterogeneous throughout the left ventricle. The cut-off value of 11 mm, which was described previously (16), is therefore to some extent arbitrary.

Clinical implications and conclusions. The main finding of the present study is that a relatively simple measurement of EDWT, obtained with two-dimensional echocardiography combined with contrast agent, predicts recovery of regional contractile function after PCI for AMI. Dysfunctional segments with an EDWT ≥11 mm had a high likelihood of functional recovery two months after PCI. Moreover, combining wall thickness and perfusion, dysfunctional segments with an EDWT ≥11 mm and presence of perfusion have the highest chance of recovery, segments with an EDWT <11 mm and perfusion have an intermediate chance, whereas segments with an EDWT <11 mm and no perfusion have a very low likelihood of functional recovery at two months' follow-up. Prediction of recovery of contractile function early after AMI could be useful to identify patients who have irreversible left ventricular dysfunction. In these patients, tailored therapy can be started, also considering the possibility of automatic defibrillator implantation (17). Moreover, identification of stunning as the cause of ventricular dysfunction may provide a rationale for the aggressive support of the patients with mechanical methods and perhaps caution against the use of inotropic agents, which may adversely influence the recovery of potentially ischemic segments (18).

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