Resting echocardiographic assessment of regional wall motion, thickness and reflectivity in chronic ischemic cardiomyopathy: an alternative to the viability test?

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Background. **A resting echo showing a regional end-diastolic wall thickness ≤ 6 mm with a hyperechoic texture is pathognomonic of scar tissue and of non-viable myocardium. The aim of this study was to assess the prognostic value of the resting echo scar texture in patients with chronic ischemic cardiomyopathy evaluated prior to coronary artery bypass surgery.**

Methods. **The preoperative clinical and echocardiographic data of 70 patients with a mean ejection fraction of 29.8 ± 4% scheduled for coronary revascularization were correlated to the cardiac events observed during a mean follow-up of 24 ± 12 months after surgery. Akinetic segments of the left ventricular wall with a reduced diastolic thickness and increased echoreflectivity were judged scarred.**

Results. **Sixty-eight patients were discharged alive from hospital. On the basis of ROC analysis, we identified: group A (27 patients) with > 5 and group B (41 patients) with ≤ 5 scarred segments. There were 10 events (3 deaths, 4 heart transplants and 3 refractory heart failures), 8 in group A (29%) and 2 in group B (5%). At multivariate analysis the only independent predictor of the clinical outcome after revascularization was whether the patient was included in group A or B (Wald 6.3, p < 0.012). One year after surgery, the ejection fraction improved only in group B patients (p < 0.03).**

Conclusions. **The extent of scarred myocardial tissue as assessed at resting echocardiography predicted the benefit of revascularization in patients with chronic ischemic left ventricular dysfunction. This simple and straightforward echo parameter should be taken into consideration when assessing the instrumental value of more technologically demanding and costly viability testing.**

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In patients with severe left ventricular dysfunction due to coronary artery disease, the presence of an adequate amount of contractile reserve is considered a prerequisite for obtaining the greatest benefit from myocardial revascularization[1-4]. In the selection of patients for revascularization, positron emission tomography, 201-thallium scintigraphy and low-dose dobutamine echocardiography can be used by clinicians as a quantitative relationship between the preoperative amount of myocardial viability and clinical benefits of coronary surgery which have been proved[2-10].

Resting echocardiography is an easy-to-use and reliable method for the evaluation of left ventricular performance, but the analysis of wall motion is not accurate for the assessment of myocardial viability mainly because even severely dysfunctional segments of the left ventricular wall can improve after revascularization[11,12]. On the contrary, histological and clinical studies have shown that resting echocardiography is reliable in identifying irreversible myocardial damage consisting of scar tissue (i.e., thinning and increased echoreflectivity of akinetic segments of the left ventricular wall)[11,13,14].

The aim of this study was to evaluate whether in patients with chronic ischemic cardiomyopathy, the echocardiographic assessment of the extent of scarred ventricular tissue may be a useful method for predicting the clinical outcome after revascularization.

Methods

Patient selection. From January 1995 through September 1998, 156 candidates for coronary artery bypass grafting with multivessel coronary artery disease and a left ventricular ejection fraction ≤ 35% at baseline echocardiography were considered for the study. The decision to revascularize was based on clinical, angiographic and instrumental criteria according to current practice in that period. Eighty-six patients were excluded from the study because of: previous coronary surgery, need of adjunctive heart surgery, unstable angina or recent (< 1 month) myocardial infarction or inadequate echocardiographic images. The clinical and instrumental data of the remaining 70 patients were collected prospectively.

Echocardiography. The echocardiographic examinations were carried out with the patients in the left lateral decubitus position during the fortnight prior to surgery and repeated 1 year later using a Vingmed CFM 750 (Vingmed Sound, Utah) machine with a 3.25 MHz transducer. All the two-dimensional studies included standard parasternal, subcostal and apical views. M-mode images were also obtained from the parasternal and/or subcostal view in order to optimize the evaluation of the left ventricular wall motion and thickness. The echocardiograms were recorded on SVHS videotape for subsequent analysis.

Echocardiographic analysis. The echocardiograms were reviewed by two independent observers who had no knowledge of the clinical and angiographic characteristics of the patients. The regional wall motion of the left ventricle was assessed using the 16-segment model recommended by the American Society of Echocardiography[15], with each segment being judged as normal, hyperkinetic, hypokinetic, akinetic or dyskinetic on the basis of the visual evaluation of the systolic wall motion. On the basis of the results of previous studies[11,13], the akinetic or dyskinetic segments with an end-diastolic thickness of < 7 mm or < 30% of that of an adjacent normal segment, associated with an abnormal increase in acoustic reflectance, were defined as scarred (i.e. not viable). An increase in acoustic reflectance was defined as the presence of highly echoreflective linear echoes replacing the fine granular texture of myocardial tissue. For those myocardial regions in which it was impossible to obtain a reliable measure of the wall thickness, a qualitative evaluation was made of the distortion of the diastolic endocardial profile of the left ventricular cavity at the level of the akinetic/dyskinetic segments, according to the method of Faletra et al.[11].

The left ventricular end-diastolic and end-systolic volumes were determined from the apical 2- and 4-chamber views using the Simpson biplane formula recommended by the American Society of Echocardiography[15]: left ventricular ejection fraction was calculated as (end-diastolic – end-systolic volume)/end-diastolic volume. The antero-posterior diameter of the left atrium was measured in the long-axis parasternal view. The severity of mitral regurgitation was estimated by means of color Doppler echocardiography and assessed in terms of the distance within the left atrium reached by the flow from the mitral valve orifice and in terms of the maximum regurgitant jet area and of the percentage that the latter occupied of the left atrial area. Mitral regurgitation was classified using a 4-point scale (trivial = 1+, mild = 2+, moderate = 3+, severe = 4+).

Operative, early postoperative and late follow-up data. A record was kept of the type of conduit (saphenous vein or internal mammary artery), the number of grafts and the in-hospital course of the patients. The survival after hospital discharge was determined. After discharge, the clinical status of patients was yearly assessed by direct contact or by telephone interview. The following cardiac events were considered: cardiac death (sudden and unexplained death or else death due to myocardial infarction or pump failure), heart transplantation, myocardial infarction, and the persistence of severe congestive heart failure despite optimized medical therapy.

Statistical analysis. The results are expressed as mean values ± SD. A p value < 0.05 was considered statistically significant. Univariate analysis was performed using the Student's unpaired t-test for numerical or the χ^2 test for categorical data, with Yates' correction if necessary. Pre- and post-therapy data were compared by means of the Student's paired t-test. Linear regression was used to assess the correlation between variables and the regression coefficient was calculated to assess the goodness of fit. ROC analysis was used to find the level of a given prognostic factor that optimizes specificity and sensitivity. Multivariate analysis was performed using a logistic regression model in order to evaluate the independent prognostic factors of events, with the variables being added by means of the forward stepwise method. Results are expressed as the significance level for the Wald statistic of the regression coefficients. The survival curves were estimated using the Kaplan-Meier method and compared by means of the log-rank test.

Results

Baseline characteristics. Seventy patients were included: 65 men and 5 women with a mean age of 61.5 ± 8 years (range 41-73 years). The clinical and echocardiographic data are shown in table I: 80% of patients had a history of a previous Q-wave myocardial infarction, 29% had chronic angina, and 40% were in NYHA functional class III or IV but none required inotropic medication. The mean ejection fraction was 29.8 ± 4% (range 21-35%). Out of 509 akinetic segments (mean 7.3 ± 3/patient, 383 involving the apical, septal, anterior or lateral wall and 126 involving the inferior wall), 301 (59%, mean 4.3 ± 3/patient) were scarred (224 involving the apical, septal, anterior or lateral wall and 77 involving the inferior wall). Fifty-eight patients (84%)

Table I. Baseline characteristics of the study population.

Age (years)	61.5 ± 8
Male sex	64 (93%)
Diabetes mellitus	16 (23%)
Hypertension	34 (49%)
Prior Q-wave MI	55 (80%)
Angina	20 (29%)
NYHA class III-IV	28 (40%)
LVEDV (ml)	193 ± 44
LA (mm)	43 ± 3
LVEF (%)	29.8 ± 4
MR 3+4+	9 (13%)
Akinetic LV segments	7.3 ± 3
Scarred LV segments	4.3 ± 3
No. grafts	2.5 ± 0.7
IMA (% patients)	47 (66%)

IMA = internal mammary artery; LA = left atrial diameter; LV = left ventricular; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MR = mitral regurgitation.

had at least one scarred segment (range 1-10). Mitral regurgitation 3+/4+ or 4+/4+ (moderate-severe) was present in 9 patients (13%): in this subgroup of patients, the number of scarred segments was significantly higher than in the remaining patients (6 ± 1/patient vs 4 ± 2/patient, $p < 0.0001$), whereas the left ventricular ejection fraction and left ventricular end-diastolic volume were similar (29 vs 30%, p = NS, and 210 vs 191 ml, p = NS, respectively).

Operative and postoperative care. The mean number of grafts/patient was 2.5 ± 0.7. The territory of the left anterior descending coronary artery was revascularized in all patients (using the internal mammary artery in 68%) and the territories of the left circumflex and right coronary arteries were revascularized in 45 and 43 patients respectively.

In no case did a myocardial infarction occur perioperatively.

Two patients (3%) died before hospital discharge respectively 1 and 15 days after surgery: one of fatal ventricular arrhythmias and one of cardiac failure.

Delayed postoperative outcome. The 68 survivors were followed for a mean period of 24 ± 12 months (range 3-50 months). During this period, 10 patients (14%) experienced cardiac events: one patient died suddenly and two died of refractory heart failure, 5, 8 and 24 months respectively after hospital discharge; 4 underwent heart transplantation after 3-24 months and 3 patients had progressive refractory heart failure (all required several hospitalizations and one is listed for heart transplantation). Three patients, all of whom without cardiac events, died of non-cardiac causes 24-50 months after discharge. The overall mortality was 9%. No myocardial infarction nor recurrence of angina was observed during the follow-up period.

Prediction of events. At univariate analysis (Table II) patients who experienced cardiac events significantly differed from those without events for the larger number of severely dysfunctional segments, the larger number of scarred segments, and for the higher incidence of moderate-severe mitral regurgitation at preoperative echocardiography. The correlation among the number of akinetic segments and the number of scarred segments was not strong (r = 0.59; Fig. 1): in fact, patients with many severely dysfunctional segments may exhibit a variable extent of scarred tissue. ROC analysis

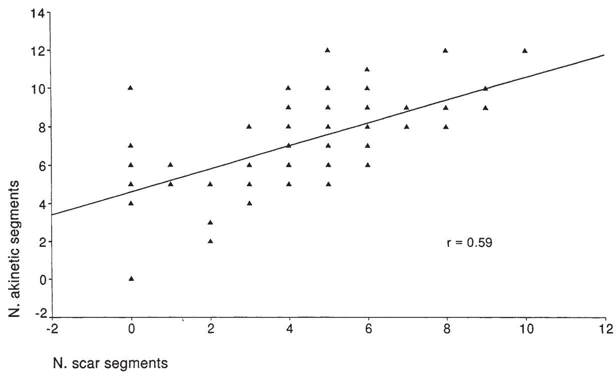

Figure 1. *Scatterplot showing the relationship between akinetic and scarred segments at baseline echocardiography.*

Table II. Univariate predictors of the outcome after myocardial revascularization.

	Patients with events (n = 10)	Patients without events (n = 58)	p
Age (years)	60 ± 6	62 ± 8	< 0.4
Prior Q-wave MI	8 (80%)	45 (76%)	< 1
LVEDV (ml)	217 ± 44	190 ± 4	< 0.1
LA (mm)	46 ± 6	43 ± 6	< 0.3
LVEF (%)	28 ± 5	30 ± 4	< 0.24
MR 3+4+	4 (40%)	5 (9%)	< 0.028
Akinetic LV segments	9 ± 2	6.9 ± 2.6	< 0.02
Scarred LV segments	6.2 ± 3	3.9 ± 2.5	< 0.034
No. grafts	2.5 ± 0.5	2.5 ± 0.7	< 0.9

Abbreviations as in table I.

showed that the number of scarred left ventricular segments that best predicted post-revascularization cardiac events was 5 [sensitivity 80% (8/10) and specificity 64% (38/58)] whereas for akinetic segments the number that best predicted the post-revascularization outcome was 8 [sensitivity 70% (7/10) and specificity 60% (35/58)] (Fig. 2).

On the basis of these results, the study population was divided into two groups for the subsequent analysis: group A consisted of 27 patients with > 5 scarred segments at preoperative echocardiography and group B consisted of 41 patients with ≤ 5 scarred segments. Group A patients significantly differed from those of group B in that they more frequently had moderate or severe mitral regurgitation ($p < 0.032$) (Table III).

Eight cardiac events occurred in group A patients (29%) (3 deaths, 2 heart transplants, 3 severe congestive heart failures) and 2 in group B (5%) (2 heart transplants). The event-free survival 24 months after coronary surgery was significantly poorer in group A than in group B ($p < 0.005$; Fig. 3). When the 9 patients with moderate or severe mitral regurgitation were excluded

Table III. Differences in baseline characteristics.

	Group A (n = 27)	Group B (n = 41)	p
Age (years)	62 ± 8	61 ± 9	< 0.4
Diabetes mellitus	6 (22%)	10 (25%)	< 1
Hypertension	11 (40%)	23 (56%)	< 0.3
Angina	4 (15%)	16 (40%)	< 0.06
NYHA class III-IV	12 (44%)	16 (39%)	< 0.85
LVEDV (ml)	196 ± 44	191 ± 45	< 0.67
LA (mm)	44 ± 5	43 ± 7	< 0.8
LVEF (%)	30 ± 5	30 ± 4	< 0.95
MR 3+4+	7 (26%)	2 (5%)	< 0.032
No. grafts	2.5 ± 0.6	2.5 ± 0.8	< 0.7

Abbreviations as in table I.

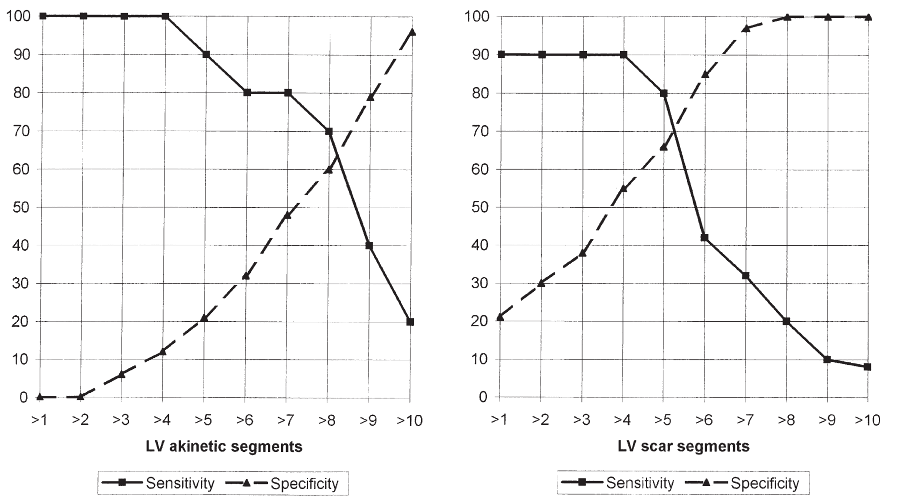

Figure 2. *ROC analysis showing the different levels of sensitivity and specificity in predicting the clinical outcome after coronary artery bypass grafting for different numbers of akinetic left ventricular (LV) segments* (left panel) *and the subgroup of akinetic and scarred segments* (right panel) *at preoperative echocardiography.*

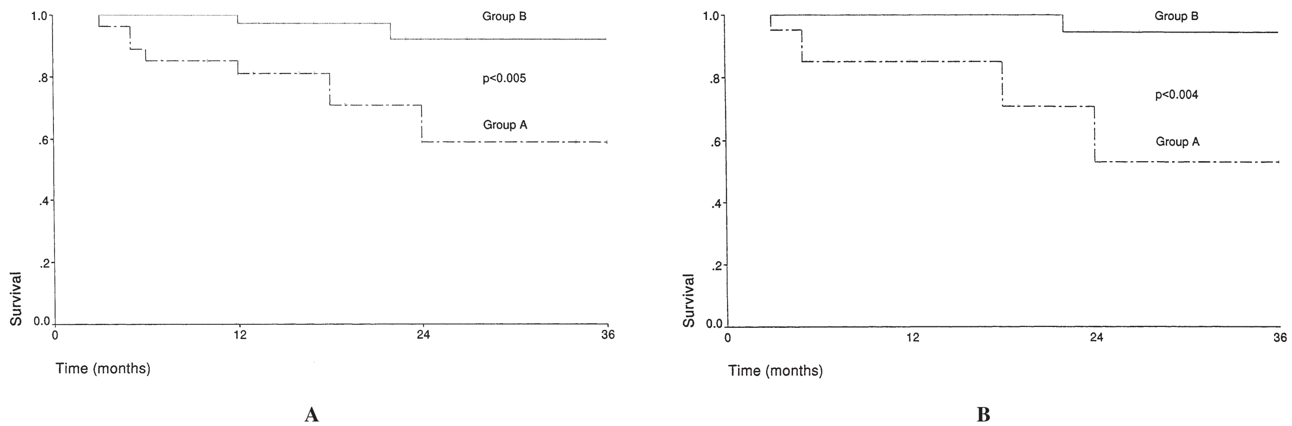

Figure 3. *Kaplan-Meier analysis: comparison of cardiac event-free survival between group B patients with ≤ 5 scarred left ventricular segments and group A patients with > 5 scarred segments at preoperative echocardiography* (A)*, and between group B and group A patients after exclusion of 9 patients with moderate-severe mitral regurgitation* (B).

from the analysis of survival, the difference between group A and group B patients remained unchanged ($p < 0.004$).

When the inclusion in group A or B was entered into a multivariate logistic regression analysis with the presence/absence of ≥ 8 akinetic segments and the presence/absence of moderate-severe mitral regurgitation, the inclusion in group A or B was the only significant predictor of the post-surgical outcome (Wald 6.3, $p < 0.012$). In fact the two last variables did not satisfy the significance level ($p < 0.05$) required for inclusion in the model (akinesia: $p = 0.07$, mitral regurgitation: $p = 0.09$).

Left ventricular ejection fraction and mitral regurgitation changes. One year after surgical revascularization, the mean left ventricular ejection fraction in the population as a whole increased from 30 ± 4 to 32 ± 8%, but a significant improvement was observed only in group B patients (from 30 ± 4 to 34 ± 8 vs 30 ± 4 to 30 ± 6% in group A, $p < 0.03$).

Preoperative moderate or severe mitral regurgitation improved only in one group B patient (without events) and persisted unchanged in the remaining patients.

Discussion

The working hypothesis of the study was that in patients with severe chronic cardiomyopathy due to coronary artery disease, the extent of scarred myocardium is a crucial factor in obtaining clinical benefit from revascularization.

Histopathologic studies have found that scarred tissue in ischemic heart disease is related to previous myocardial infarction in 90% of cases and only rarely to the replacement of chronically hypoperfused territories by fibrosis[13,14]. Echocardiographic evidence of wall thinning and of replacement of the fine granular texture by highly reflective linear echoes in akinetic myocardial walls correspond to scarred tissue which cannot recover even after adequate revascularization[11,13].

More recently, Cwajg et al.[16] showed that the end-diastolic wall thickness of severely dysfunctional segments can predict the recovery of function after revascularization with the same accuracy as 201-thallium uptake: similar to segments with a 201-thallium uptake < 60%, 93% of severely dysfunctional segments with an end-diastolic thickness < 6 mm cannot recover after revascularization. On the other hand, only about 50% of severely dysfunctional segments with an adequate wall thickness or 201-thallium uptake may recover their function after revascularization.

The results of this study support the hypothesis that the benefits of surgical revascularization in patients with multivessel coronary disease and severe chronic ventricular dysfunction are related to the preoperative extent of scarred myocardium: patients with no more than 5/16 scarred segments, independently of their age or the main preoperative variables, have a good expected 2-year event-free survival which is significantly better than that of patients with more than 5/16 scarred segments, burdened by a 29% incidence of cardiac events. Furthermore, only in the former subgroup of patients does the ejection fraction significantly improve after revascularization. This indirectly confirms the preoperative presence of an adequate amount of viable myocardial tissue independently of the baseline number of akinetic segments. As would be expected, our results agree with those of previous studies that showed a relationship between the clinical benefits after myocardial revascularization and the preoperative amount of viable myocardium[3,4,7,8,10,17].

By means of low-dose dobutamine echocardiography, Meluzin et al.[17] showed that the presence of 6/16 or more dysfunctional but viable segments predicts a better outcome after revascularization compared to that of patients with a lesser amount of dysfunctional but viable myocardium (2 cardiac events/29 patients vs 35 cardiac events/104 patients). Using the same technique, Senior et al.[10] found that a good post-revascularization outcome may be expected in patients with at least 5/12 dysfunctional but viable segments (i.e., about 40% of the left ventricular wall) while the outcome of patients with lower viability is poorer. In our experience, resting echocardiography provided a simple method of prognostic stratification based on a cutoff (5/16 scarred segments) which had similar sensitivity and specificity in predicting the post-revascularization outcome.

In the present study, the preoperative left ventricular ejection fraction was not predictive of cardiac events. In patients with severe left ventricular dysfunction, the importance of the absolute value of the ejection fraction in influencing the outcome after coronary surgery is not well defined and the published data are contradictory[2,18]. Our results may depend on the small number of patients but also on the fact that we did not recruit subjects with an extremely poor myocardial function who, in our Institution, are preferably referred to heart transplantation or medical therapy.

Our data concerning mitral regurgitation are conflicting: although in this study, 40% of patients with preoperative moderate-severe mitral regurgitation did not benefit from coronary revascularization, multivariate analysis failed to confirm the independent predictive value of this variable. This finding can be explained by the small number of patients with significant mitral regurgitation in the present population but may also be attributable to the strong association we found between the severity of mitral dysfunction and the amount of scarred ventricular tissue. We were therefore unable to identify a subgroup of patients who might have benefited from mitral valve repair in adjunct to revascularization.

Study limitations and other considerations. This is a non-randomized prospective study in which the patients enrolled were scheduled for surgical revascularization on the basis of current criteria. Therefore those patients with more dilated ventricles, no viable myocardium at 201-thallium scintigraphy or low-dose dobutamine echocardiography or more advanced heart failure, in whom revascularization was not indicated, may have been excluded. Nevertheless, during the period of patient recruitment the concept that the extension of scar tissue as evaluated by means of resting echocardiography may influence the results of myocardial revascularization had not yet been introduced. Consequently, we retain that there was no such bias in patient selection. Furthermore, we excluded patients previously submitted to a coronary revascularization procedure and those in need of ventricular repair who have worse immediate and long-term results. Therefore, we do not know whether the method we used would maintain its predictive role when more extensively applied to the whole population of patients with chronic ischemic cardiomyopathy.

Secondly, in patients with a poor left ventricular function in whom the benefit of revascularization is generally proved[18], the cut-off of 5 scarred segments, although sensitive in identifying the post-revascularization events and with a high predictive negative power, was only moderately specific and had a low positive predictive value (29% of cardiac events in patients with > 5 scarred segments). In patients with > 5 scarred segments, more complex evaluation may be performed to predict the outcome after revascularization. Most of our patients underwent more complex viability tests, but dispersion of data does not allow us to evaluate the possible incremental value of these methods compared with resting echocardiography.

In conclusion, in patients with chronic ischemic cardiomyopathy and multivessel coronary artery disease, a correlation was observed between the extent of myocardial scar tissue and the clinical benefits of myocardial revascularization. Independently of other variables, patients with ≤ 5 scarred ventricular segments at preoperative resting echocardiography have a favorable post-surgical outcome: we feel that these patients, when their coronary anatomy is suitable for surgery, should undergo the operation without further viability evaluation. On the contrary, within 2 years of revascularization 80% of cardiac events occurred in patients with > 5 scarred segments at preoperative echocardiography: as some of the latter patients may still have a fairly good short- and mid-term outcome after bypass surgery, the choice of treatment should be guided by more complex preoperative evaluation. We feel that the incremental value of different viability tests and clinical variables such as the NYHA functional class, anginal symptoms and severity of mitral regurgitation should be tested on a larger patient population.

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