ECHOCARDIOGRAPHIC AND CARDIAC SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY PREDICTORS OF LEFT VENTRICLE REVERSE REMODELING AFTER SURGICAL REVASCULARIZATION IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND LEFT VENTRICLE SYSTOLIC DYSFUNCTION

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Background: The extent of scar or viable hypocontractile myocardial tissue determines postinfarction left ventricle remodeling. The aim of this pilot study was to evaluate the revascularization effect in a group of patients with ischemic cardiomyopathy and LV systolic dysfunction indicated for surgical revascularization, based on evidence for multivessel disease on coronarography and viable myocardium (CMR, SPECT).

Aims: To evaluate the revascularization effect in patients with ischemic LV systolic dysfunction and to find preoperative predictors of revascularization effect.

Methods: 33 patients (64±11 years) with baseline LVEF 34.9±9.3 % were included in the study. After a follow-up of 10.7±1.2 months, ECHO and SPECT were performed again. The whole group of patients was divided according to revascularization effect (↑ LVEF > 5 % and ↓ LVESV > 5 % compared with baseline) into revascularization responders (R, n = 22) and nonresponders (NR, n = 11).

Results: At baseline there was no difference between the subgroups in LVEF (R = 35.7±11.0 % vs. NR = 34.3±8.2 %), EDV (R = 183.6±43.2 vs. NR = 180.2±80.5 ml), ESV (R = 118.5±40.4 vs. NR = 119.7±55.2 ml).

The responders showed in a revascularization effect subanalysis differences in the values of LVEF (+9.8±8.1 %, p < 0.009), reduction of EDV (–39.9±50.9 ml, p = 0.05) and ESV (–35.4±42.6 ml, p = 0,002) compared with baseline.

The only preoperative parameters predicting LV reverse remodeling were the T_{E-Em} (R = –10.6±44.1 vs. NR = 29.7±43.7 ms, p = 0.037) and the size of fixed perfusion defect (FPD) (R = 11.9±13.5 vs. NR = 22.9±15.3 % of LV, p = 0.044).

Conclusions: Patients with ischemic LV systolic dysfunction with a preoperatively determined myocardial viability develop LV reverse remodeling. The only preoperative parameters predicting LV reverse remodeling were echocardiographic T_{E-Em} and FPD on SPECT.

INTRODUCTION

Chronic heart failure is a clinical syndrome that in United States alone affects about 5 million patients per year. It is responsible for approximately 1,000,000 hospitalizations and 300,000 deaths[1.] The most common cause of chronic left-sided heart failure in developed countries is ischemic heart disease (IHD) (ref.[2, 3]).

One prognostic factor emerging from a number of laboratories, clinical and functional tests, is the ejection fraction of the left ventricle (LVEF) (ref.[4]). Endsystolic and enddiastolic LV volumes are the basic measured parameters from which LVEF can be assessed using a simple calculation. A single evaluation of enddiastolic or endsystolic volume produces quantitative information about the level of LV remodeling/ the possibility of its reversibility after the start of particular myocardial treatment. LV volume assessment also provides important

prognostic information after myocardial infarction and after surgical correction for valvular diseases[5-7].

IHD plays a role in triggering heart failure by a number of mechanisms. These can be divided into two groups according to possible therapeutic intervention. The first group of probably irreversible processes includes primarily myocardial necrosis with subsequent development of scar leading to LV remodeling which depends on the extent of the infarction. As potentially curable causes of heart failure, can be considered, stunning and hibernation of myocardium which represent a functional adaptation state to acute or chronic myocardial ischemia[8].

Currently, there are available a number of imaging methods with high diagnostic accuracy for revealing the presence of viable myocardium or nonviable scar. Routinely used radionuclide methods such as single photon emission tomography (SPECT) using perfusion radiopharmacs ([201]thalium, [99m]technecium-MIBI) and positron

emission tomography (PET) with a metabolic radiopharmaceutical (^{18}F-deoxyglucose) have higher sensitivity and slightly lower specificity in viable myocardium detection than stress echocardiography[8].

The correct selection of patients for surgery with an extensive hibernating myocardium mass before revascularization is pivotal from the viewpoint of assessment of revascularization effects apropos the relatively high periprocedural risk attending the surgical revascularization of the myocardium. The problem is the coexistence of scar and other individual ischemic substrates (hibernation and stunning respectively) that can be, to varying extent present in the same patient. Another no less important factor is the duration of LV remodeling and its severity. Presently there are limited data on predictors of revascularization in terms of reverse remodeling onset and systolic and diastolic function improvement as pivotal markers of the prognostic benefits to revascularized patients. The amount of viable myocardium or the ratio of hibernating healthy myocardium and nonviable myocardium needed for optimal revascularization so that the outcome of revascularization outweighs its risk is not definitely known. What level of LV remodeling is an irreversible phase of cardiomyopathy remains another question[9].

The aim of this pilot study was to evaluate the revascularization effect in a group of patients with ischemic cardiomyopathy and LV systolic dysfunction indicated for surgical revascularization, based on evidence of multivessel disease on coronarography and viable myocardium. Another aim was to find pre-operative predictors of revascularization effects in terms of LV reverse remodeling induction.

Patient group

A total of 33 consecutive patients aged 63.7±11.7 years were included in the study. All were examined within the frame of prospective follow-up of patients with ischemic cardiomyopathy based on coronarography and viability of myocardium from other examinations (cardiac gated SPECT, cardiac magnetic resonance imaging) for surgical revascularization of myocardium. Patients with acute coronary syndrome in the preceding three months were excluded.

The basic clinical characteristics and results of evaluated parameters for the whole group and subgroups of responders and nonresponders of revascularization at baseline are depicted in Table 1.

After an average length of follow-up of 10.7±1.2 months after surgery and 11.6±1 month after preoperative selection, all patients were regularly examined clinically, echocardiographically and by cardiac gated-SPECT. The whole patient group (n = 33) was then divided into 2 subgroups: revascularization responders (n = 22) and revascularization nonresponders (n = 11). The selection was made according to the onset of reverse remodeling assessed from results of the control cardiac gated-SPECT (as higher SPECT reproducibility of selected parameters compared with echocardiography), whilst the criterion for inclusion in the responder group was a postoperative

increase by >5 % and reduction of LVESV > 5 % compared to preoperative baseline values of the given patient[9].

All patients had optimized treatment for ischemic heart disease and heart failure comparable for responders and nonresponders; all were in the NYHA class I-III. All patients were part of a complex LV myocardium viability and function assessment and after signing written consent examined echocardiographically, by cardiac gated-SPECT. All examinations were performed in tight sequence during one day in one center and were evaluated double-blind.

Echocardiography

Echocardiographic examinations were performed on GE Ultrasound Vivid 7 (GE Healthcare Technologies, Waukesha, Wisconsin, USA) equipped with a multifrequency ultrasound probe. The evaluation of echocardiographic findings was performed off-line in an environment of archival program EchoPAC 7 Option (version BT 06) blindly without knowledge of clinical status or results of other examinations. The resting examination with synchronous registration of 1 ECG lead was performed standardly from parasternal projections on the long and short axis of LV and from apical 2, 3 and 4 chamber projections. Endsystolic and enddiastolic volumes were assessed from 2-dimensional images (B-mode) – endsysto-
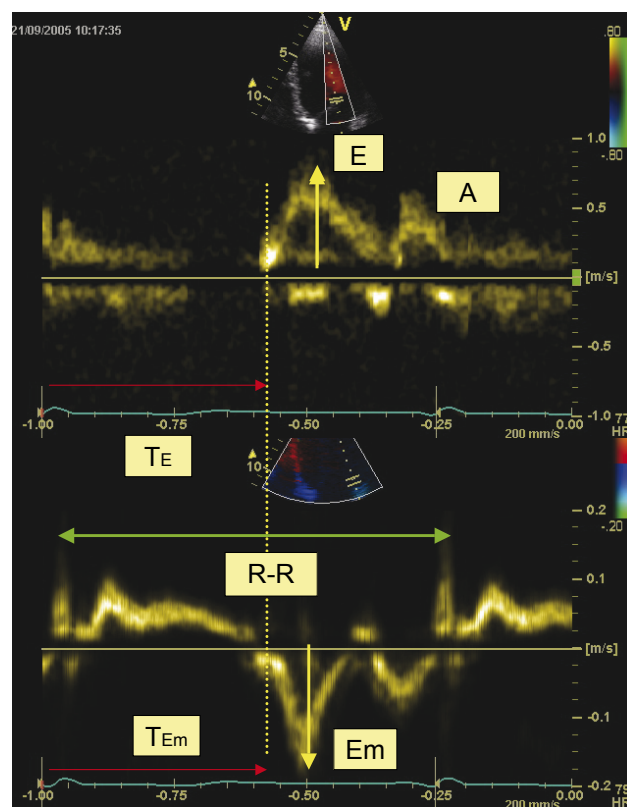
Fig. 1. Measured echocardiographic parameters from PWD of transmitral flow (upper part) and PW-TDE of mitral annulus (lower part). (Early diastolic transmitral flow velocity E, diastolic mitral annular velocities Em, time interval between onset of early transmitral flow and early annular mitral motion T_{E-Em}).

Table 1. Baseline clinical characteristics of the whole group and revascularization responders and nonresponders subgroups.

	whole group (n=33)	nonresponders (n=11)	responders (n=22)
Men/women	(21/12)	(7/4)	(14/8)
Mean age (yr)	63.7±11.7	62.6±12	64.1±11.2
Myocardial infarction in history (n)	28 (85%)	11 (100%)	17 (78%)
Chest pain - AP (CCS class)	1.2±1.27	1.22±1.3	1.04±1.1
NYHA (class)	2.2±1.8	2.3±1.9	2.13±2
Type 2 DM (n)	13 (39%)	6 (54%)	7 (32%)
Hypertension (n)	24 (73%)	11 (100%)	13 (59%)
Stroke in history (n)	6 (18%)	3 (27%)	3 (14%)
Smokers (n)	14 (42%)	3 (27%)	11 (55%)
Atrial fibrillation (n)	7 (21%)	3 (27%)	4 (18%)
2-vessel disease (n)	12 (36%)	4 (36%)	8 (36%)
3-vessel disease (n)	21 (64%)	7 (63%)	14 (63%)
LMCA disease (n)	10 (30%)	5 (50%)	5 (23%)
LAD disease (n)	31 (94%)	10 (91%)	21 (95%)
Bypass number (n)	3.3±0.92	3.3±0.82	3.28±0.96

p = NS (responders vs. nonresponders in individual parameters)

Table 2. Baseline values of evaluated echocardiographic and gated-SPECT parameters of the whole group, revascularization responders and nonresponders subgroups before surgery.

	whole group (n=33)	nonresponders (n=11)	responders (n=22)
LVEF ECHO biplane (%)	34.9±9.3	35.7±11	34.3±8.2
LVEF gated SPECT (%)	34.7±9.4	34.9±11.1	34.6±8.4
EDV ECHO biplane (ml)	181.6±66.3	183.5±43.2	180.2±80.5
EDV gated SPECT (ml)	204.9±71.7	198.5±60.4	208.2±78.2
ESV ECHO biplane (ml)	119 ±56.2	118.5±40.4	120.6±65.3
ESV gated SPECT (ml)	138.1±62.6	133.5±56.9	140.6±66.6
Total perfusion defect- PD (% LV)	37.1±16.5	39.5±18.9	38±35.8
Fixed perf. defect- FPD (% LV)	15.7±14.9	22.9±15.3	11.9±13.5*
PD-FPD (% LV)	21.2±13.2	16.6±12.5	23.5±13.3
PD/FPD ratio	2.36±1.89	1.72±1.3	3.2±2.1*
E (cm/s)	76.9±25.1	71.4±25.2	80.8±25.2
A (cm/s)	67.5±28.7	67.8±30.2	67.3±28.9
E/A	1.4±0.9	1.3±0.8	1.5±1
Sm (cm/s)	3.4±1.2	3.3±1.2	3.5±1.3
Em (cm/s)	3.4±1.1	3.3±1.4	3.4±0.8
T_{E-Em} (ms)	6.2±47.4	29.7±43.6	-10.6±44.1*

* p < 0.05 (responder vs. nonresponders)
(E – early transmitral flow velocity, A – late transmitral flow velocity, E/A ratio, Sm – average systolic mitral annular velocity, Em – average early diastolic mitral annular velocity, T_{E-Em} – time interval between onset of early transmitral flow and early annular mitral motion)

lic and enddiastolic planimetry of endocardial border of LV were performed in the undermentioned echocardiographic projections[10]. LV volumes and EF were assessed using Simpson's disc method from 2 apical projections on LV long axis, apical 4-chamber projection first followed by apical 2-chamber projection. All parameters were assessed as averages of 3 measures of 1-cycle recordings during stable sinus rhythm. In case of atrial fibrillation (n = 7, 21% of patients) the particular parameters were obtained by averaging from heart cycles with identical R-R intervals (differences between evaluated R-R intervals < 5 ms). Two investigators without knowledge of clinical, gated SPECT, MRI and angiographic data, performed off-line analysis of the echocardiograms. Disagreements in interpretation were resolved by consensus.

The measured echocardiographic parameters were LV volumes and LVEF evaluated using biplanar echocardiographic approach (apical 2-chamber and apical 4-chamber projections), transmitral flow velocities E, A, E/A ratio, systolic mitral annular velocity Sm, diastolic mitral annular velocities Em, Am, time interval between onset of early transmitral flow and early annular mitral motion T_{E-Em}, which was chosen in a post-hoc analysis. (Fig. 1)

Gated technetium-99m sestamibi (MIBI) single photon emission computed tomography
Rest Imaging after Nitrate Administration

All patients underwent 1-day rest imaging with nitrate administration: 8 mCi (296 MBq) ^{99m}technecium-MIBI was injected at rest, with SPECT imaging performed 1 hour after injection. Three hours later, 24 mCi (888 MBq) ^{99m}technecium-MIBI was injected after sublingual nitrate administration 1 hour before SPECT imaging.

Scintigraphy

Gated SPECT imaging (64 projections from the 45° right anterior oblique projection to the 45° left posterior oblique projection, 8 frames/cycle) was performed using a 2-detector gamma camera (ecam, Siemens, Erlangen, Germany) equipped with a low-energy, high-resolution parallel-hole collimators. Myocardial perfusion images were analyzed visually and quantitatively on computer-generated polar maps using automated, commercially available software 4D-MSPECT package (University of Michigan, Ann Arbor, MI, USA). Gated single photon emission computed tomography rest left ventricular ejection fractions (LVEF) and left ventricular enddiastolic/endsystolic volumes (EDV/ESV) were obtained using software 4D-MSPECT.

For further analysis, the values of resting cardiac gated-SPECT were used, i.e. resting perfusion defect size (deterioration of 2.5 SD compared to normal database, expressed as % of total LV), nonviable myocardium (fixed perfusion defect with an accumulation below 50 % of maximum, expressed as % of total LV) and resting values of LVEF, EDV and ESV.

Statistical analysis

Statistical analysis was performed on statistical software SPSS for Windows 12.0 (SPSS Inc., Chicago, USA).

Paired t-tests for dependent samples were used for statistical evaluation of differences between individual subgroups at baseline and after revascularization of myocardium. Receiver operating curve (ROC) analysis was used for assessment of sensitivity and specificity of individual parameters for presurgical prediction of LV reverse remodeling. p≤0.05 was the chosen level of significance.

RESULTS

1. Characteristics of the whole group, subgroup of responders and nonresponders of revascularization at baseline.

Baseline values of evaluated echocardiographic and gated-SPECT parameters of the whole group, revascularization responders and nonresponders subgroups before surgery are depicted in Table 2.

The differences in the measurements of LVEF between biplane echocardiography and cardiac gated SPECT were not statistically significant. However from the statistics there was a significant difference between enddiastolic and endsystolic volumes that were systematically underestimated by echocardiography. The values from the gated-SPECT of myocardium were reliable and accurate 10.7 months after surgery in terms of the ability to divide the whole group into responders and nonresponders subgroups.

From the statistical analysis of revascularization responder and nonresponder subgroups differences existed in the number of patients with fixed perfusion defect (responders 61 % vs. nonresponders 47 %). The presence of a nonviable myocardium (fixed perfusion defect) in each particular coronary artery area was no different in the areas of left anterior descending artery anterior, circumflex artery or right coronary artery. There were no differences in localization of hemodynamically significant coronary artery stenoses, completeness of surgical revascularization (responders 80 % vs. 61 % nonresponders).

2. Influence of cardiovascular revascularization on monitored parameters of the whole group and subgroups of responders and nonresponders of revascularization.

After an average duration of 10.7±1.2 months after surgical revascularization, the echocardiography and gated-SPECT of myocardium were checked.

The influence of surgical revascularization on LVEF (%), ESV (ml) and EDV (ml) in the whole group, revascularization responder and nonresponder subgroups after surgery evaluated by echocardiography and cardiac gated-SPECT are depicted in Figures 2, 3, 4.

For other examined parameters in the whole group there was a significant reduction in resting perfusion defect from baseline values of 37.1±16.5 to 30.2±22.5 % of LV, p = 0.029. In the responder subgroup the value of total perfusion defect decreased after revascularization from baseline values of 35.8±15.5 to 23.8±22 % of LV, p ≤ 0.05. In the nonresponder subgroup, the total perfusion defect remained stable after revascularization with the entry values of 39.5±18.9 and control values of 42.4±18.6 % of LV, p ≤ NS. Values of the other parameters (fixed perfusion

defect, E, A, E/A, Sm, Em, T_{E-Em}) remained unchanged after surgical revascularization

3. Preoperative predictors of revascularization in relation to reverse remodeling onset.

In a retrospective analysis of revascularization of myocardium responder and nonresponder subgroups in terms of a possible preoperative prediction of myocardial revascularization, the result apropos LV reverse remodeling onset (post-operative increase of LVEF ≥ 5 % and a simultaneous decrease of LV endsystolic volume ≥ 5 % compared to baseline values) statistically significant differences were found in two examined parameters. The first parameter in which both subgroups had a preoperative difference was the range of a fixed perfusion defect measured by gated-SPECT of myocardium (responders 11.9±13.5 %
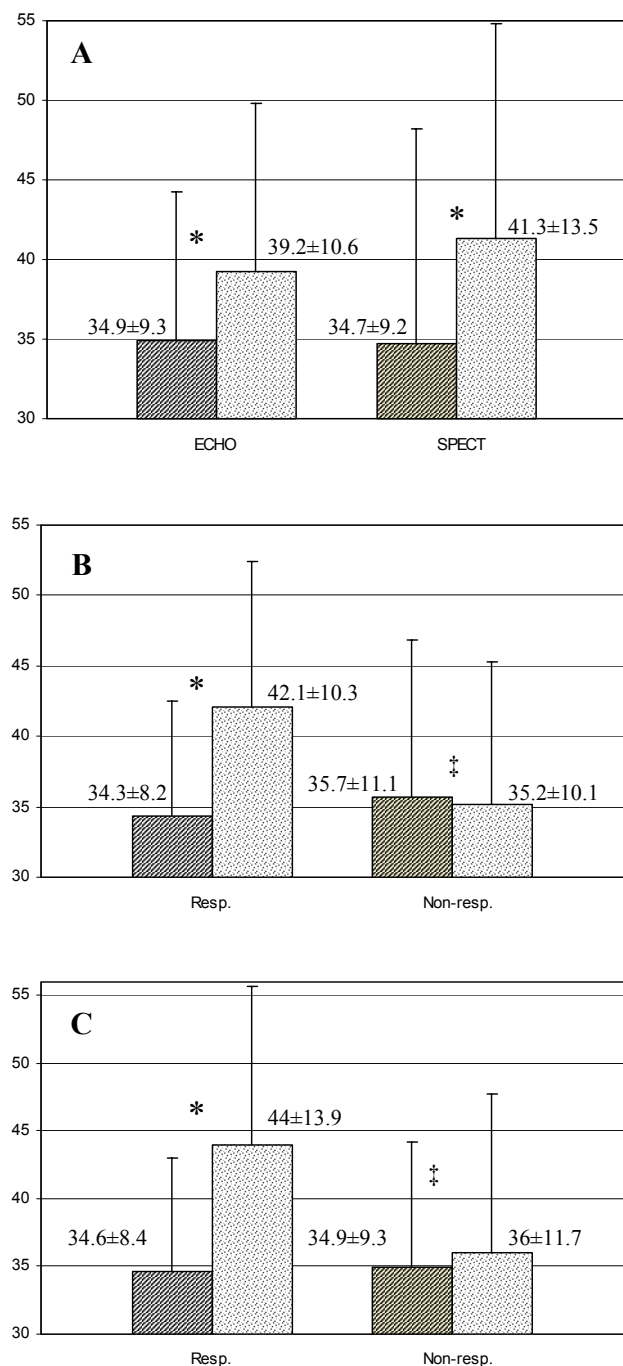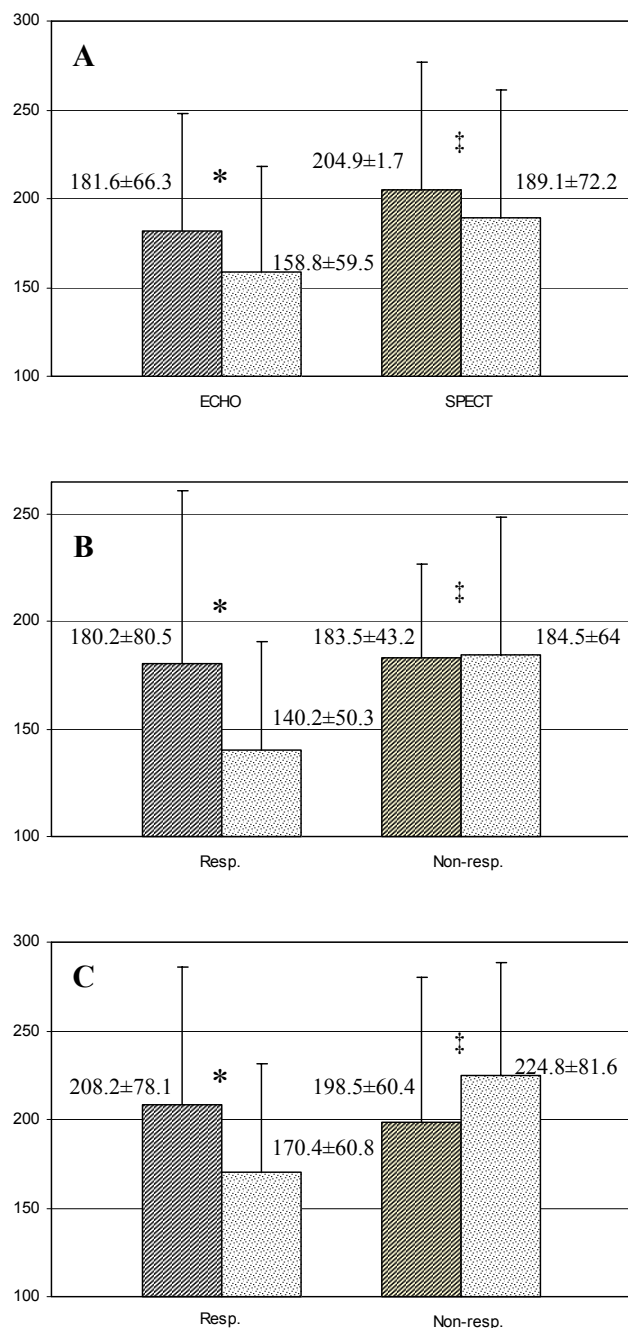

Fig. 2. Influence of surgical revascularization on LVEF (%) in the whole group **(A)**, revascularization responders and nonresponders subgroups 10.7 months after surgery evaluated by echocardiography **(B)** and cardiac gated-SPECT **(C)**. (*p≤0.05, ‡p =NS).
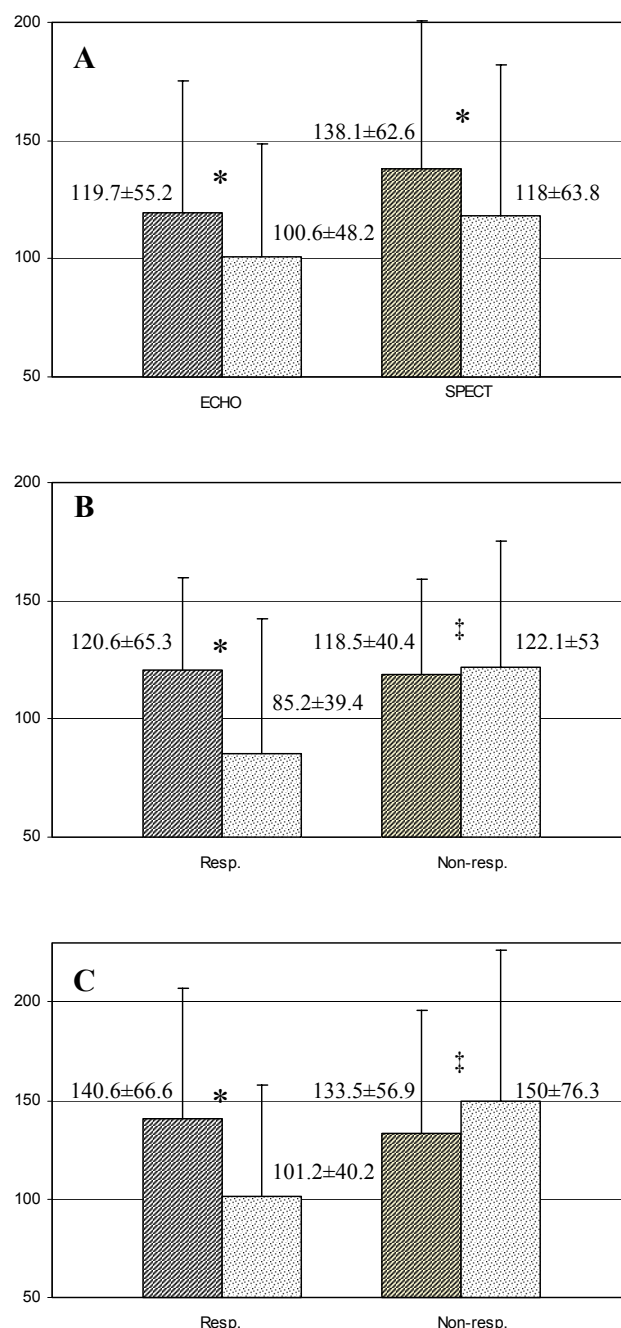
Fig. 3. Influence of surgical revascularization on ESV of LV (ml) in the whole group **(A)**, revascularization responders and nonresponders subgroups 10.7 months after surgery evaluated by echocardiography **(B)** and cardiac gated SPECT **(C)**. (*p≤0.05, ‡p =NS).

LV vs. nonresponders 22.9±15.3, p=0.044). Cut-off value <15 % of LV predicts LV reverse remodeling with sensitivity of 72 % and specificity of 73 %. (Fig. 5)

Another parameter in which both subgroups differed significantly was an entry value of echocardiographic parameter T_{E-Em}, which was significantly different in the responder subgroup (-10.6±44.1 compared to 29.7±43.7 ms in nonresponder subgroup, p = 0.037).

Receiver operating curve (ROC) showed that a cut-off value of T_{E-Em} <13 ms predicts reverse remodeling of LV after revascularization with a sensitivity 78 % and specificity 78 %. (Fig. 6)

Pre-operative results of other examined parameters (LVEF, EDV, ESV, E, A, E/A, Em, total perfusion defect) were not significantly different.
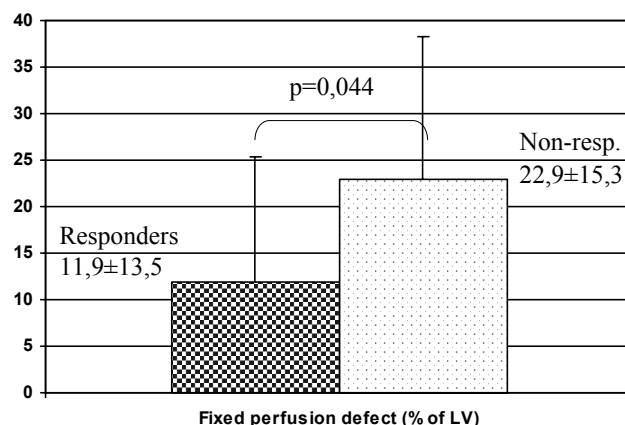
Fig. 5. Preoperative values of fixed perfusion defect assessed by cardiac gated SPECT (responders 11.9±13.5 % LV vs. nonresponders 22.9±15.3, p = 0.044). Cut-off <15 % of LV in ROC analysis predicts LV reverse remodeling with sensitivity of 72 % and specificity of 73 %.

Fig. 6. Preoperative values of T_{E-Em} by echocardiography with a statistically significant difference in the responders subgroup -10.6±44.1 compared to nonresponders subgroup 29.7±43.7 ms, p = 0.037. Receiver operating curve (ROC) showed that a cut-off value of T_{E-Em} <13 ms predicts LV reverse remodeling after revascularization with a sensitivity 78 % and specificity 78 %.
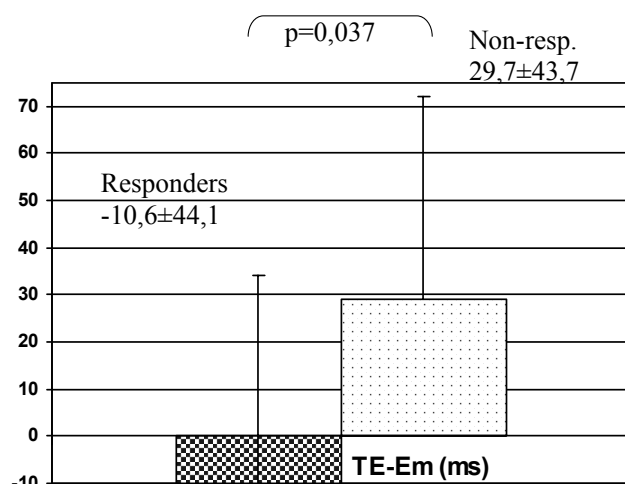

Fig. 4. Influence of surgical revascularization on EDV of LV (ml) in the whole group **(A)**, revascularization responders and nonresponders subgroups 10.7 months after surgery evaluated by echocardiography **(B)** and cardiac gated SPECT **(C)**. (*p ≤ 0.05, ‡p = NS).

DISCUSSION

Revascularization of myocardium represents a way of treating patients with ischemic cardiomyopathy mainly with systolic LV dysfunction. Patients with preoperative evidence of a significant mass of viable myocardium and multivessel disease have significant benefit from this procedure[11]. A relatively high periprocedural risk needs to be considered in patients with systolic LV dysfunction. Perioperative mortality of aorto-coronary bypass surgery in this specific group ranges according to several reports from approximately 5 % in younger adults and up to 30 % in older adults with more severe LV systolic dysfunction and depending on its severity, age, sex, surgery urgency, severity of coronary arteries affection, complicating factors, co-morbidities and other factors[8].

A preoperative finding of a significant mass of hibernating myocardium before surgery is fundamental for clinical management and selection of patients for revascularization. The outcome of revascularization can be significantly affected by coexistence of a scar tissue and individual ischemic substrates (hibernation, stunning) in one patient, severity and length of lasting of LV remodeling. It is necessary to emphasize that the aim of revascularization is not only an amelioration of the symptoms of heart failure but also increased survival, onset of LV reverse remodeling and prevention of its progression caused by a deterioration of LV systolic and diastolic function and prevention of myocardium infarction and sudden cardiac death rate by elimination of arrhythmogenic substrates[8] Considering the revascularization of myocardium effect in our study there was an evident postoperative reduction of LV volumes and increase in LVEF after revascularization in the whole patient group but mainly in the revascularization responder subgroup. This finding is in a good agreement with a number of other studies published in this area[8, 9, 11, 13, 14]. A postoperative statistically significant reduction of total perfusion defect extent on SPECT and a stationary extent of a fixed perfusion defect representing nonviable myocardial scar tissue was also evident. We found a statistically significant difference in extent of nonviable myocardium by SPECT at baseline between the responders and nonresponders of the revascularization subgroups. Presently there are limited data on predictors of revascularization in terms of reverse remodeling onset and systolic and diastolic function improvement, which are considered to be the fundamental markers of prognostic benefit of revascularized patients with proven hibernating myocardium. Regression of heart failure symptoms, improvement in exercise capacity and a level of LV reverse remodeling directly in the majority of studies correlated with the preoperative extent of a presumably viable myocardium. Lombardo et al. found that a preoperative documentation of viable myocardium of at least 13 % of LV by dobutamine echocardiography is needed for a reverse LV remodeling from 36 to 41 %[12]. Ragosta et al. showed that a preoperative extent of viable myocardium of at least 53 % assessed using [201]thalium-SPECT is needed for a statistically significant postoperative increase in LV from 29 % to 41 %[13]. According to various studies using mostly radionuclide methods, this value ranges from 8 to 67 % of LV[8, 14]. The extent of viable myocardium assessed using gate-SPECT of myocardium ranging from 25 to 30 % of LV can be considered a reasonable cut-off value for a relatively accurate prediction of reverse LV remodeling onset (postoperative increase of LVEF >5 %) assessed using receiver operating curve (ROC) analysis[9].

To date, there is one study in which patients with substantial nonviable myocardium on ^{18}F-FDG/SPECT are predicted to have a poor early functional outcome[26]. Based on this finding we tested a fixed perfusion defect parameter assessed using gated-SPECT of myocardium as a marker of a nonviable myocardial scar tissue in the light of reverse LV remodeling prediction defined as a simultaneous increase of LVEF of at least 5 % and decrease of EDV of at least 5 % evaluated after 11 months from revascularization, which we consider a long enough time interval for an onset of a functional recovery of hibernating regions of myocardium after coronary revascularization. Gated-SPECT of myocardium was considered a reference method for evaluation of LV reverse remodeling. It is a clinically robust method, highly reproducible and relatively independent of the examiner. In the responder subgroup we reported an LVEF increase of 9.8 %, EDV reduction of 40 ml and ESV reduction of 35.4 ml compared to baseline values. The only statistically significant gated-SPECT predictor of revascularization result in terms of reverse remodeling onset in our study was surprisingly not baseline preoperative value of total extent of perfusion defect but a value of fixed perfusion defect (infarct size). This parameter can be considered a marker of scar tissue after myocardial infarction. There is a close association between fibrosis in human hearts and infarct size assessed by sestamibi gated SPECT. Sestamibi infarct size has been quantified using a standardized approach based on cardiac phantom studies[25]. The presence and extent of nonviable myocardium is a very strong mortality predictor in patients with ischemic heart disease[15.] Cut-off values of this parameter (fixed perfusion defect) below 15 % of LV had in our study a relatively high sensitivity and specificity in LV reverse remodeling after revascularization. We can presume that for a reverse LV remodeling it is necessary to show a preoperative mass of viable myocardium of at least 85 % of LV. It is a relatively higher value than in available studies using radionuclide methods in patients with LV systolic dysfunction[8, 13, 14]. However, for this result we needed to take into account preoperative LV systolic function, rate of LV remodeling and patient's co-morbidities. All patients in the revascularization nonresponder subgroup had a history of myocardial infarction compared to only 71 % of patients after myocardial infarction in the responder subgroup. This difference was not statistically significant. Another fact that has to be mentioned is a larger number of patients with a nonviable myocardium in revascularization responders subgroup compared to nonresponders subgroup (61 vs. 41 %). That means that not every patient after myocardial infarction had an evident fixed perfusion defect on gated-SPECT of myocardium. The above-men-

tioned number of patients with a nonviable myocardium is nevertheless larger than for instance the patient group of Hoilund-Carlsen et al. (8 % of 168 revascularized patients with a stable angina pectoris)[16]. This fact is in our study caused by a selection of patients with a systolic LV dysfunction with a large number of patients after myocardial infarction. An absolute value of fixed perfusion defect in our patient group (12 % of LV in responders vs. 23 % in nonresponders) demonstrates a larger extent of nonviable myocardial tissue in the revascularization nonresponders subgroup. We found no correlation between localization of nonviable myocardium in individual coronary artery perfusion areas and revascularization outcome. Thus, the only preoperative predictor of revascularization in terms of reverse LV remodeling onset in patients with ischemic cardiomyopathy is extent of nonviable myocardium.

We found a statistically significant difference in values of T_{E-Em} between revascularization responders and nonresponders subgroups. Patients in the responder subgroup had a negative value of T_{E-Em}. This means that an average annular motion velocity T_E lags behind the onset of transmitral flow E wave. Patients in the nonresponder subgroup had positive values of $T_{E-Em.}$ That means that the early annular motion velocities preceded onset of transmitral flow. The lag of onset of early annular mitral motion behind the beginning of diastolic LV filling was for the first time described by Garcia et al. in patients with restrictive cardiomyopathy, whilst in a group of healthy control subjects Em preceded E wave[17]. Hasegawa et al. found in another experimental work a relationship between time interval T_{E-Em} and diastolic relaxation constant tau assessed using catheterization a progressive decrease of peak mitral annular velocity Em and its lag behind the beginning of wave E of transmitral flow[18]. Rivas-Gotz et al. in an experimental model of acute ischemia of myocardium demonstrated a relationship between T_{E-Em}, deterioration of LV diastolic function and a subsequent increase of LV filling pressures during acute myocardial ischemia[19].

Diwan et al. confirmed these results in a clinical study demonstrating a significant inverse correlation of invasively measured LV filling pressures and time interval T_{E-Em} (ref.[20]). However, correlation of the time interval T_{E-Em} needs to be considered an academic demonstration of a narrow pathophysiologic connection between ischemia of LV myocardium and an early phase of diastole. A concept of myocardial ischemia inducing a lag of an early annular mitral motion can generally be proposed. Myocardial relaxation in early phase of diastole is energetically very demanding[22-24]. It leads to a diastolic LV dysfunction with increased enddiastolic LV pressures. Correlation of T_{E-Em} to the invasively measured LV filling pressures is however very loose. This is in an agreement with a study published by Guron et al.[21]. Presently there is no study available describing a correlation of T_{E-Em} and an improvement in systolic LV function after revascularization of myocardium. An interpretation of such a relationship is not easy, but in the light of experimental and clinical studies considering hemodynamics and diastolic function of LV, it seams that T_{E-Em} is an indirect echocardiographic marker of hibernating myocardial tissue extent. A viable myocardium

is partially able to adaptively react to a chronic coronary hypoperfusion state with inhibition of not only an active contraction of the given hibernating segment but also of an energetically demanding early diastolic relaxation of myocardium in the particular region[22-24]. From this point of view T_{E-Em} is in our study a single echocardiographic parameter predicting revascularization result in terms of reverse LV remodeling onset. It can also be considered an indirect marker of hibernating tissue extent. T_{E-Em} has in prediction of LV reverse remodeling in our study sensitivity 78 % and specificity 78 %. However, this parameter has to be validated mainly according to reproducibility, which is relatively favorable in our study (T_{E-Em} interobserver and intraobserver coefficient of variation 7 % and 5 % respectively). Another weak point of this parameter is the presence of atrial fibrillation leading to an inhomogeneity of individual heart cycle lengths. This particular problem can be partly solved by measuring T_{E-Em} after a selection of heart cycles with identical R-R interval. A small number of patients with atrial fibrillation in our study do probably not distort results of this parameter measurement.

Limitations

The mentioned results need to be verified on a larger number of patients in a similarly designed multicentric study, which definitely proves or refutes advisability of measuring some baseline parameters in term of selection of an optimal treatment strategy in a group of patients with ischemic cardiomyopathy and LV systolic dysfunction.

CONCLUSIONS

After 11 moths from revascularization in patients with a preoperative documentation of viability of myocardium, there is an increase in LVEF, decrease in EDV and ESV. From echocardiographic parameters, T_{E-Em} is potentially usable. This parameter solely predicts reverse LV remodeling after revascularization of myocardium. Values of T_{E-Em} can be an indirect marker of a nonviable hibernating myocardial tissue extent. Fixed perfusion defect extent representing a nonviable myocardial tissue assessed using gated-SPECT of myocardium is an important preoperative predictor of LV function improvement after revascularization. It is necessary to approve results of this study concerning revascularization outcome prediction on a larger amount of patients in a similarly designed multicentric study.

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