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The value of dobutamine stress echocardiography in predicting clinical improvement following coronary artery bypass grafting in patients with left ventricular systolic dysfunction

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Abstract

Background: *Recent years have seen an increasing number of patients with multivessel coronary artery disease and left ventricular systolic dysfunction being qualified for cardiac surgery. Identification of patients who are likely to benefit most from revascularisation procedures poses a considerable problem. The aim of the study was to assess the value of dobutamine stress echocardiography in predicting the clinical course following coronary artery bypass grafting (CABG) in patients with ischaemic left ventricular dysfunction.*

Methods: *Fifty patients with multivessel coronary artery disease and reduced left ventricular ejection fraction (LVEF < 40%) who were qualified for CABG were included in the study. Resting echocardiography and a small-dose (5–10 μg/kg/min) dobutamine test were performed before the procedure. Subsequent tests were repeated after the procedure and at 3.6 and 12 months. A combined endpoint of death, repeat hospitalisations, NYHA stage, severity of angina and left ventricular systolic function was evaluated.*

Results: *Two factors were found to affect the prognosis adversely following CABG in both univariate and multivariate analysis: a history of hypertension (p = 0.039, OR 4.9, 95% CI 1.4–17.1) and lack of improvement in contractility in at least 4 segments during the dobutamine test (p = 0.0003, OR 37.2, 95% CI 6.3–218.4). An improvement in contractility in at least 4 segments of the left ventricle is the most important prognostic factor.*

Conclusions: *The results of the dobutamine stress test have a more potent prognostic value than clinical or demographic parameters in predicting clinical improvement. Patients with negative results of the test represent the group with the gravest prognosis.* (Cardiol J 2007; 14: 174–179)

Key words: coronary artery bypass grafting, dobutamine stress echocardiography

Introduction

Surgical revascularisation has significantly improved the survival of patients with ischaemic heart damage by reducing mortality by 25% and the incidence of sudden cardiac death by half [1]. Left ventricular dysfunction is the most common consequence of coronary artery disease. In patients

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with areas of viable myocardium unfavourable left ventricular remodelling after revascularisation procedures occurs less frequently [2].

In coronary artery disease, ventricular dysfunction may be a consequence of both the permanent ventricular damage due to necrosis and fibrosis and the presence of damaged but viable stunned myocardium [3]. The term "myocardial hibernation" refers to a long-term impairment of contractility, most commonly as a result of chronic ischaemia. Blood flow is usually high enough to keep the myocytes alive but too low to meet fully the metabolic demands associated with the normal contraction of the heart muscle [4]. Evaluation of hibernated areas allows for a more precise stratification of the risks and benefits in patients with ischaemic heart failure undergoing coronary artery bypass grafting (CABG) [5]. The increased operative risk, which in patients with low ejection fraction ranges from 11% to 16%, is offset by the benefits resulting from the presence of viable myocardium in the area subjected to revascularisation [6]. It has been demonstrated that in patients with impaired left ventricular function but preserved viability the benefit of CABG is higher than the benefit of conservative treatment [7–10]. The diagnostic tests evaluating myocardial viability have therefore become a necessary element of qualification for revascularisation, especially in the case of patients with low left ventricular ejection fraction.

The aim of the study was to identify the demographic and clinical parameters affecting the clinical course in a one-year follow-up following CABG and to establish the value of dobutamine stress echocardiography in predicting postoperative clinical improvement.

Methods

Characteristics of the patient group

The study included 50 patients (42 men and 8 women with a mean age of 60 years) hospitalised at the Division of Cardiac Surgery of the Medical University of Białystok, Poland between May 2002 and February 2004. All the patients met the following inclusion criteria:

— chronic stable coronary artery disease;
— echocardiographically confirmed left ventricular systolic dysfunction: left ventricular ejection fraction (LVEF) below 40% (also confirmed in ventriculography);
— qualification of the patient for a revascularisation procedure (CABG);
— absence of haemodynamically significant valvular heart disease;
— the presence of appropriate technical conditions for the performance of stress tests.

Table 1. Patient characteristics.

Mean age (years)	60 ± 9 (39–75)
Body mass [kg]	82 ± 13
Height [cm]	171 ± 7
Body mass index	28 ± 4 (21–36)
Duration of CAD	6.5 years (3 months – 20 years)
A history of myocardial infarction	All the patients included in the study
Hypertension	20 (40%)
Diabetes mellitus	11 (22%)
Dyslipidaemia	36 (72%)
Smoking	24 (48%)
Family history of CAD	29 (58%)
NYHA class	Mean: III ± I
CCS class	Mean: 3 ± 1
Ejection fraction	34% ± 4%
Wall motion score index	2 ± 0,2
Number of affected coronary vessels	All patients: 3 vessels

CAD — coronary artery disease

The study was approved by the Bioethics Committee of the Medical University of Białystok, Poland.

The degree of heart failure was evaluated on the NYHA scale in accordance with the generally accepted criteria and the clinical severity of coronary artery disease was assessed according to the Canadian Cardiovascular Society (CCS). The basic demographic data and the characteristics of the study group are summarised in Table 1.

On the basis of the clinical picture the patients were qualified for coronary artery angiography combined with ventriculography and then underwent surgical revascularisation because of the presence of multivessel disease. All the patients underwent full coronary revascularisation and received typical treatment for ischaemic heart disease in accordance with current standards.

Course of the study

Resting echocardiography. Three to five days before CABG two-dimensional transthoracic echocardiography was performed in all the patients, during which the classical parameters were measured in line with the recommendations of the American Society of Echocardiography. Echocardiography was performed using the SONOS 5500 system (Philips) with the S-3 probe (frequency range: 1–3 MHz, ultraband). Left ventricular contractility

was evaluated by analysing the systolic increment of the thickness of its walls, adopting a division into 16 segments in line with the recommendations of the American Society of Echocardiography. During the test the wall motion score index (WMSI) was measured, assigning an appropriate score to each of the three segments of each of the left ventricular walls in accordance with the visual assessment [1 — normokinesis (normal contractility), 2 — hypokinesis (reduced systolic thickening of the wall), 3 — akinesis (no systolic thickening]. The WMSI was calculated by adding the scores assigned to specific segments and dividing them by their number. Measurements of the ejection fraction were performed in the two-dimensional mode, using the biplane Simpson's method and averaging the results from three subsequent cardiac cycles.

Both parameters were evaluated during both the resting tests and the stress test. Resting follow-up tests were performed one week after surgery and 3, 6 and 12 months after the procedure.

Echocardiography stress test. During the three days before the test none of the patients received drugs with a positive inotropic action. The test with low-dose dobutamine (5–10 μg/kg/min) was performed three or four days before CABG. After recording four standard views in the resting echo (long-axis parasternal view, short-axis parasternal view, four-chamber apical view and two-chamber apical view) an intravenous infusion of dobutamine was given. Six minutes after the infusion had begun recording on a magneto-optic disk was started. During the test and 10 minutes after its completion pulse and blood pressure were monitored. Discontinuation criteria were as follows: a blood pressure drop of over 10% of the baseline value, anginal pain, increasing dyspnoea and significant supraventricular and ventricular arrhythmias.

Contractility was evaluated by analysing the systolic increment of wall thickness and left ventricular ejection fraction. Both parameters were evaluated at rest and following dobutamine. Myocardial viability was defined as an improvement in wall contractility of at least 1 point on the 4-point scale of contractility. The test was considered positive if an improvement in contractility was achieved in at least 4 segments.

Baseline images recorded before CABG were compared with those recorded after the procedure and at 3, 6 and 12 months. During the follow-up visits the complications which made up the combined endpoint (death, exacerbation of heart failure, exacerbation of anginal symptoms and lack of improvement in left ventricular function) were evaluated.

Statistical methods

The analysis was performed using the t-test for matched and unmatched pairs or using the non-parametric Wilcoxon test at the significance level of < 0.05. Relative risk was defined as the incidence of events in the group with abnormal test results and the incidence of events in the group with normal test results. Multivariate logistic regression was performed using the MedCalc 8.1.0.0 software after the stepwise analysis had been established with the elimination of factors with statistical significance $p > 0.05$. The predictive value of each of the factors (clinical, demographic and echocardiographic) was analysed by the Kaplan-Meier method according to the Cox model, using the standard functions of the MedCalc 8.1.0.0 software. The statistical significance of the difference between the curves was evaluated with the log-rank test.

Results

During the 12-month clinical follow-up 4 out of 50 patients died (8%). The main contributing factor was the perioperative mortality of 6% (3 deaths during symptoms of increasing left ventricular failure and 1 death at 3 months following surgery owing to severe left ventricular failure). Complications occurred in 20 patients and included paroxysmal atrial fibrillation in 14 (28%) patients and exacerbation of heart failure requiring hospitalisation in 6 (12%) patients. During the follow-up none of the patients suffered myocardial reinfarction or required repeat revascularisation. One-year survival beyond the perioperative period reached 98%.

Before the procedure most of the patients had experienced anginal symptoms corresponding to CCS classes II and III. One year after the procedure 26 patients manifested anginal symptoms in CCS class I and 20 in CCS class II. None of the patients experienced CCS class III or IV symptoms (Fig. 1). At qualification for operation, 67% of the patients (31 patients) had been in NYHA class III. A year after revascularisation 17 patients were in NYHA class I and 21 in NYHA class III (82% of the study group). None of the patients in the study group manifested heart failure symptoms in NYHA class IV (Fig. 2).

No complications were observed during the dobutamine stress tests. None of the patients developed pain and no ECG changes were observed.

Univariate and multivariate analysis

The analysis took into account demographic (age and sex), clinical (the presence of coronary

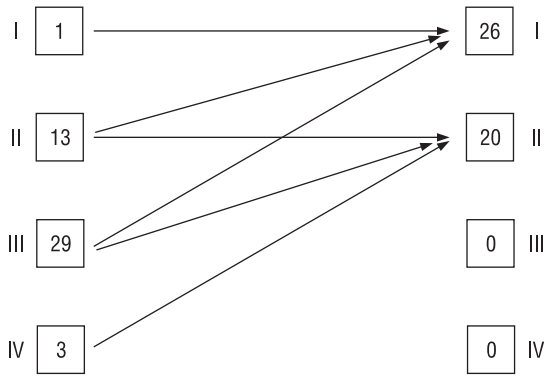

Figure 1. Change in CCS class from baseline at 1 year following CABG (patients who completed the one-year follow-up period are shown in the figure).

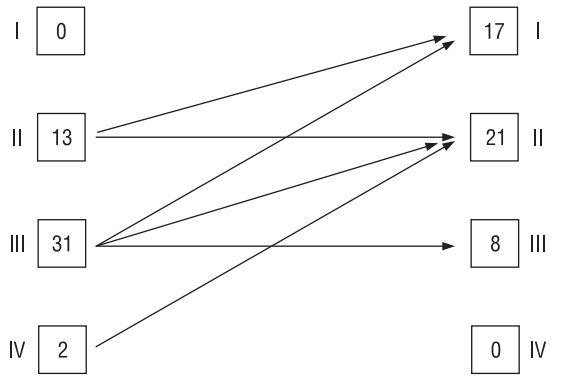

Figure 2. Change in NYHA class from baseline at 1 year following CABG (patients who completed the one-year follow-up period are shown in the figure).

artery disease risk factors described in Table 1, CCS class and NYHA class) and echocardiographic (LVEF, WMSI) factors.

Both univariate and multivariate analysis demonstrated that adverse prognosis following CABG was affected by the following:

— a history of hypertension (p = 0.039) associated with a 4.9-fold higher risk of complications (95% CI 1.4–17.1).

— lack of improvement in contractility in the dobutamine stress echo test (p = 0.0003). Patients in whom improvement during the stress test did not occur in at least 4 segments were at a 37.2-fold higher risk of complications (95% CI 6.3–218.4).

The survival curves for survival without complications with or without a history of hypertension

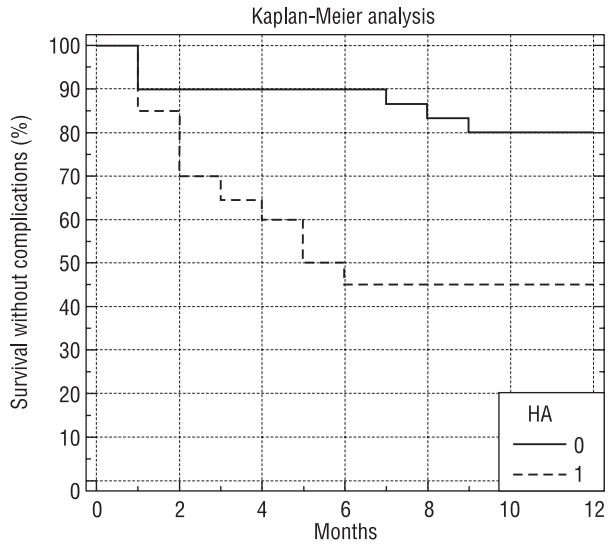

Figure 3. Survival without complications during the one--year follow-up in patients with and without a history of hypertension (HA), p = 0.039; a history of hypertension was associated with a 4.9-fold higher risk of complications (95% CI 1.4–17.1).

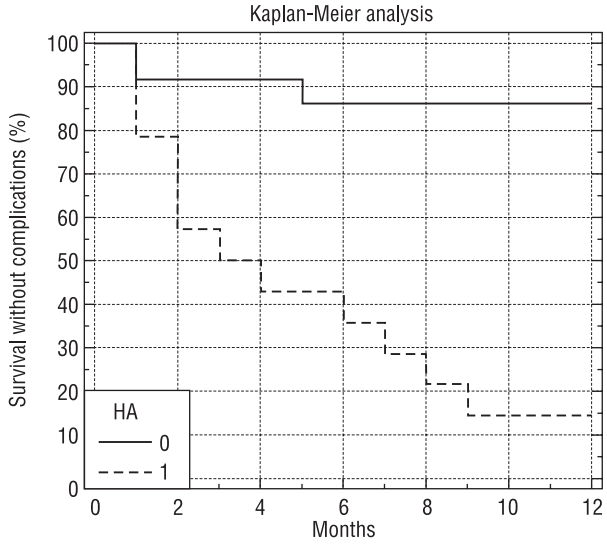

Figure 4. Kaplan-Meier survival curves for survival without complications over the one-year follow-up relative to the presence of viable myocardium in the dobutamine stress test (the solid line represents an improvement in contractility in at least 4 segments, while the dotted line represents no improvement in contractility); a 37.2-fold higher risk of complications (95% CI 6.3–218.4; p = 0.0003).

are presented in Figure 3, while Figure 4 shows survival relative to myocardial viability.

Discussion

An increasing number of patients with coronary heart disease and significant left ventricular dysfunction are being qualified for cardiac surgery. Revascularisation of viable myocardium is associated with a good prognosis for improved resting ejection fraction [9]. The literature offers publications assessing the value of the dobutamine test in predicting improvement in left ventricular function following CABG [9, 15]. There are, however, very few reports on the value of the test in predicting the clinical course, which was the subject of our study.

In our material the independent prognostic factors relating to the combined endpoint of death, necessity of hospitalisation, exacerbation of anginal symptoms and exacerbation of heart failure turned out to be the following: a history of hypertension and WMSI change following dobutamine. Our findings are consistent with those obtained by Bountioukos et al. [11], who found that hypertension, degree of contractility impairment during the dobutamine test and the severity of heart failure were independent prognostic factors for cardiac adverse events.

Rizzello et al. [12] considered the following to be independent prognostic factors: multivessel disease, WMSI change following dobutamine and left ventricular viability. Over the five-year follow-up, there were statistically less frequent cardiac deaths and three-year survival was 77%. Liao et al. [13] followed up for 2 years a group of 107 patients with significant left ventricular dysfunction who had undergone revascularisation following the stress tests. Mortality in the group of patients in whom no viable myocardium was found was significantly higher (83.5% *vs.* 57.2%, $p = 0.0037$). Another factor affecting poor prognosis was left ventricular end-systolic pressure, as emphasised by Schinkel et al. [14] and Afridi et al. [9]. In the latter study a cut-off point was also the demonstration of viability of 4 segments in which contractility had improved following dobutamine.

We found considerably fewer complications in patients in whom contractility improvement in a minimum of 4 segments was seen during the stress test. Bax et al. [15] also demonstrated that improvement in at least 4 segments reduced heart failure in further follow-up.

In a study by Williams et al. [16] the independent prognostic factors, in addition to WMSI, were age and baseline ejection fraction. According to Bouchart et al. [17], less favourable outcomes of surgical revascularisation were obtained in patients with left ventricular enlargement and a higher NYHA functional class. Chaudhry et al. [18] evaluated systolic reserve using a low-dose dobutamine stress test in patients with LVEF < 40%. In this study the NYHA class and systolic reserve independently affected cardiovascular mortality, while the left ventricular ejection fraction did not reach statistical significance. Pagano et al. [19] listed a low LVEF and a small number of viable segments as predictors of early cardiac death, with age, sex and NYHA class playing no predictive role. In our group of patients none of the parameters was found to be predictive for death in the peri- and postoperative periods. Owing to the small size of the group and the small overall number of deaths, we did not evaluate the effects of these parameters on mortality.

The small size of the study group, the observational nature of the study and the random selection of patients may be regarded as the limitations of the work presented above.

Conclusions

1. Results of dobutamine stress echocardiography in patients with a low left ventricular ejection fraction were more predictive for clinical improvement than clinical and demographic parameters.
2. Patients with a negative stress test represented the subgroup with the gravest prognosis.

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