

Value of transesophageal dobutamine stress echocardiography for selection of the type of cardiac surgery in significant ischaemic mitral insufficiency

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Abstract

Background: Ischaemic mitral regurgitation (IMR) may be surgically treated by isolated myocardial revascularisation or in combination with valve repair. Dobutamine stress echocardiography (DSE) may be helpful in selecting an optimal surgical strategy.

Aim: To develop the optimal surgical approach to patients (pts) with significant ($ERO \geq 0.2 \text{ cm}^2$) IMR on the basis of TEE-DSE. An attempt was undertaken to select patients in whom coronary revascularisation should be performed alone or in combination with reconstruction of mitral apparatus.

Methods: The study group comprised 212 pts (M/F – 134/78; mean age 65 ± 10 years) with a history of Q-wave myocardial infarction qualified to elective surgical revascularisation on the basis of coronary angiography. In 25 pts with significant IMR (ejection fraction $< 40\%$, wall motion score index 1.8 ± 0.3) TEE-DSE was performed. Based on TEE-DSE results pts were divided into the following groups: Group I – 7 pts with significant reduction of MR and improvement of left ventricular contractility following dobutamine infusion and qualified to CABG; and Group II (n=18) without significant changes of IMR (9 pts) or with significant reduction of IMR without significant influence on WMSI (9 pts) who were qualified to CABG with mitral valve surgery.

Results: In 4 pts from Group II valve replacement was performed and the remaining 14 pts had mitral annuloplasty. Echocardiographic assessments performed 2-7 days, 6 months and 12 months following the surgical procedure revealed IMR intensity as follows (number of patients is given): Group I – small 5/4/4, moderate 2/2/2, severe 0/0/0, Group II – small 15/14/13, moderate 2/3/3, severe 0/0/0.

Conclusions: TEE-DSE seems to be a useful tool for optimal selection of surgical treatment in patients with significant IMR and qualification for CABG.

Key words: ischaemic mitral regurgitation, echocardiography, transesophageal dobutamine stress echocardiography

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Introduction

Ischaemic mitral regurgitation (IMR) is a common complication of coronary artery disease (CAD) and is associated with poor outcome [1-3]. Studies carried out so far have shown that IMR is an independent and unfavourable risk factor significantly influencing one-year and 5-year mortality [2, 4]. The complex pathomechanisms of IMR are responsible for difficulties in development of effective treatment. Investigators are

still discussing the advantages of isolated myocardial reperfusion over myocardial revascularisation combined with mitral valve repair [5-8].

Reversibility of IMR, considering the extent of myocardial perfusion damage, may be evaluated with dobutamine stress echocardiography (DSE) [9]. On the other hand, reliable assessment of morphological details of mitral apparatus is possible with the use of transesophageal echocardiography (TEE). It is particularly

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important to perform this examination prior to elective coronary artery bypass surgery (CABG) to allow cardiac surgeons to evaluate intraoperative strategy. In order to improve the diagnostic power of TEE we extended it by the functional protocol, i.e. TEE-DSE.

In this study we attempted to develop a management strategy based on the results of TEE-DSE for patients with significant IMR who were selected for CABG due to CAD [10-13].

Methods

Study group

The study involved patients aged 18-75 years with a history of Q-wave myocardial infarction (MI) and CAD confirmed on coronary angiography, who were selected for CABG, and in whom echocardiography revealed significant IMR. The IMR was diagnosed if functional regurgitation was secondary to CAD (primarily MI) and without organic lesions of the leaflets, tendinous chords or papillary muscles, excluding mechanical complications of MI. Exclusion criteria were as follows: organic lesions of mitral valvular apparatus, prosthetic heart valve, haemodynamically significant non-mitral valvular disease, past CABG, acute myocarditis, hypertrophic cardiomyopathy, systemic diseases, liver impairment, renal impairment, impairment of central nervous system, cancer, alcoholism, severe COPD, other diseases with poor prognosis, predicted low patient compliance and lack of patient's written consent to participate. The study protocol was approved by the Ethics Committee at the University of Medical Sciences in Warsaw.

Echocardiography

Echocardiographic examinations were performed in every patient 2-3 days before the scheduled CABG and included transthoracic echocardiography (TTE), TEE and TEE-DSE. Follow-up TTE was carried out on day 2-7 and at 6 and 12 months after CABG; TEE was performed if the visualisation was poor. Studies were carried out with either a Sonos 5500, 2500 or Philips E 33 and a 2.5-3.5 MHz transthoracic and Omniplane II and III multiplane transesophageal probes. Each examination was recorded on a magneto-optical drive or S-VHS tape and then evaluated by two independent cardiologists.

Transthoracic echocardiography (TTE)

Before TEE, every patient underwent full TTE according to current medical standards [14]. Left ventricular (LV) contractility was analysed according to the guidelines of the American Society of Echocardiography using the 16-segment model [15]. Left ventricular ejection

fraction (LVEF) was calculated with the modified Simpson method. Wall motion score index (WMSI) was additionally calculated in every subject. Severity of mitral regurgitation was assessed using the following methods:

1. semi-quantitative method: 0 to 4+ scale;
2. assessment of pulmonary venous flow;
3. evaluation of the proximal jet width within the left atrium (width of vena contracta) (16): severe regurgitation >8 mm;
4. measurement of proximal isovelocity surface area (PISA) [17];
5. calculation of the effective regurgitant orifice area (ERO) [18]: significant regurgitation ≥ 20 mm² [2].

Transesophageal echocardiography (TEE)

Prior to TEE-DSE, complete TEE was performed with particular stress on the morphological evaluation of the mitral apparatus, determination of the degree of mitral regurgitation (the same methods as for TTE) and contractility of each segment of LV.

Transesophageal dobutamine stress echocardiography (TEE-DSE)

The examination was performed in order to evaluate LV viability and detailed analysis of dynamics of significant IMR confirmed on TTE during dobutamine infusion. Dobutamine was initially administered at the rate of 5 μ g/kg of body weight/min which was increased in 5 μ g increments every 3 min up to a maximal dose of 20 μ g/kg of body weight/min. Contractility of every segment of LV as well as heart rate were monitored beat-to-beat on ultrasonography. At the beginning of each dose and 60 seconds prior to dose increase echocardiographic assessment of LV function was carried out using substernal view – short axis at the level of the papillary muscles and mitral leaflets, and then through transthoracic view – long axis four chamber and two chamber views. The viability test was found positive if improvement of contractility of at least two LV segments was observed during dobutamine infusion by at least one class.

Surgical treatment

All patients were previously selected to for CABG. After determining with TEE-DSE the group of subjects requiring surgery for IMR, patients were assigned to the appropriate method of cardiosurgical treatment. The main purpose of the procedure was mitral annuloplasty. If preoperative echocardiography or intraoperative revision of the valve revealed features preventing effective annuloplasty, the valve was replaced with a biological or mechanical prosthesis while the subvalvular apparatus remained untouched as far as

Table I. Clinical and echocardiographic characteristics of the study patients

Parameter	All group (n=212) number (n)/percent (%)	Group with severe IMR (n=25) number (n)/percent (%)
Gender (F/M)	78 (37%)/134 (63%)	8 (32%)/17 (68%)
Mean age (years)	65±10	63±10
Location of myocardial infarction:		
Anterolateral	101 (47.6%)	16 (64%)
Inferior	111 (52.4%)	9 (36%)
Coronary angiography:		
Single vessel disease	125 (59%)	0 (0.0%)
Multi-vessel disease	87 (41%)	25 (100.0%)
Treatment:		
Thrombolytic treatment	67 (31.6%)	14 (56%)
Coronary angioplasty	108 (51%)	6 (24%)
Comorbidities:		
Arterial hypertension	134 (63%)	20 (80%)
Diabetes mellitus	52 (24.5%)	12 (48%)
Heart failure (NYHA class III/IV)	48 (22.6%)	13 (52%)
Hypercholesterolaemia	123 (58%)	23 (92%)
Family history of coronary artery disease	143 (67%)	23 (92%)
Smoking	151 (71%)	20 (80%)
Pharmacological treatment:		
Angiotensin-converting enzyme inhibitors (ACE-I)	176 (83%)	21 (84%)
β-blockers	195 (92%)	21 (84%)
Statins	197 (93%)	25 (100%)
Nitrates	49 (23%)	17 (68%)
Acetylsalicylic acid	204 (96%)	25 (100%)
Echocardiographic parameters:		
End-diastolic left ventricular diameter	55±7 mm	5.8±0.4 cm
Ejection fraction	42±12%	34±5%
Left ventricular wall motion score index	1.6±0.5	1.8±0.3
Mitral regurgitations small/moderate/severe	40 (19%)/33 (15.5%)/25 (12%)	0 (0.0%)/0 (0.0%)/25 (100.0%)

possible. The undersizing annuloplasty was the method of choice in all subjects. The following cardiosurgical procedures were planned for treatment of dysfunction of other components of mitral apparatus: rupture or significant prolongation of the tendinous chords – implantation of artificial tendinous chords; incomplete valvular repair with annuloplasty was followed by Alfieri edge-to-edge mitral repair [19].

Statistical analysis

The results are presented as mean ± standard deviation for continuous variables or numbers and percentages for categorical variables.

Results

Characteristics of the study group

The study enrolled 212 individuals (M/F–134/78; mean age 65±10 years). Clinical and echocardiographic characteristics of the whole study group are presented in Table I. Patients with significant IMR confirmed on echocardiography comprised 12% of the whole study group, i.e. 25 subjects. Clinical and echocardiographic characteristics of the IMR patients are included in Table I. Patients were divided into two groups on the basis of dynamics of changes of the mitral regurgitant jet during infusions of small doses of dobutamine.

Table II. Influence of TEE-DSE in mitral regurgitation size and left ventricular wall motion score index in study patients with significant IMR

	Group of patients with significant IMR (n=25)		
	Number of patients	IMR	WMSI
Group I	7	↓	↓
Group II	9	↓	No changes
	9	No changes	↓

Group I comprised 7 subjects in whom significant reduction of the mitral regurgitation jet and improvement of LV contractility were found during TEE-DSE. The suggested strategy of treatment in these patients was isolated coronary revascularization without mitral repair.

Group II consisted of the remaining 18 patients in whom administration of dobutamine did not affect IMR degree (9 subjects) or caused considerable reduction of IMR but without significant improvement of WMSI (9 patients). These subjects were qualified for both CABG and mitral annuloplasty or mitral replacement therapy.

Table II shows the effects of dobutamine infusion on IMR intensity.

Results of surgical treatment

All patients underwent surgical myocardial revascularisation. Mean graft number was 2.5. A biological valve was implanted in 2 subjects with preserved subvalvular apparatus; in 2 patients a Medtronic Hall 29 mm mechanical heart valve was implanted in the mitral position without removing the subvalvular apparatus. In 14 other subjects intraoperative conditions allowed for insertion of an undersizing annuloplasty ring and 8 of them underwent additional valvular repair: in 4 patients Alfieri stitch technique was used, whereas the other 4 had artificial tendinous chords implanted due to the rupture of a single chord or prolongation of the papillary muscle. None of the patients had indications for left ventriculoplasty.

All patients from Group I and 17 subjects from Group II survived the perioperative period. One patient from Group II died on the 2nd day post surgery – CABG with insertion of biological valve. Hospitalisation at the postoperative intensive care unit was extended to

a mean duration of 3.2 days (from 2 to 8 days). In 6 patients an intraaortic balloon pump was applied due to low output syndrome: in 2 subjects directly before the surgery, in 4 subjects during or immediately after the procedure. Respiratory failure lasting for several days and requiring ventilatory support occurred in 3 patients.

During long-term follow-up one patient from Group I died (sudden cardiac death before 6 months of follow-up) and one subject from Group II died (before 12 months of follow-up).

Echocardiographic assessment of procedure outcome

Results of the analysis of MR immediately after as well as 6 and 12 months after the surgery are shown in Table III. None of the operated patients, regardless of chosen method of treatment and time of echocardiographic evaluation, had MR greater than moderate.

Discussion

The results of our studies clearly show that there is a group of patients with remote MI in whom the presence of significant IMR results directly from reversible LV dysfunction. Restoration of normal contractility within the affected area by means of revascularisation significantly reduced IMR and allowed surgical repair of the mitral valve to be avoided. In addition to the postprocedural evaluation, our results apply to the long-term follow-up.

Ischaemic MR as a complication of MI remains a short- and long-term predictor of poor outcome [2, 4]. Severity of IMR significantly influences mortality rate due to MI. Analysis of the CADILAC trial (patients treated with coronary angioplasty) shows that the more severe the IMR – the higher the mortality rate, both during 30-day and one-year follow-up periods in subjects with ST-segment elevation acute coronary syndrome [4]. Studies assessing the use of thrombolytic therapy for acute MI also indicate considerable increase of one-year mortality rate related to the severity of IMR. A review of the SAVE trial unambiguously shows negative prognostic value of IMR in subjects with small or moderate IMR. In 727 patients after MI within the last 16 days and LVEF

Table III. Severity of mitral regurgitation directly after, and 6 as well as 12 months after surgery

Time after surgery	2-7 days			6 months			12 months		
	small	moderate	severe	small	moderate	severe	small	moderate	severe
Group I	5	2	0	4	2	0	4	2	0
Group II	15	2	0	14	3	0	13	3	0

$\leq 40\%$, MR of 1st and 2nd degree was found on ventriculography in 106 and 33 subjects respectively. Multifactorial analysis revealed that 1st and 2nd+ degree mitral regurgitation appeared to be an independent unfavourable predictor of death (relative risk 2.0; $p < 0.002$) [1].

Ischaemic MR is an independent predictor of cardiovascular death in patients with remote MI (multiplies the relative risk by 1.88 times) and increases mortality rate twice during 5-year follow-up (patients with IMR: $62 \pm 5\%$, without IMR: $39 \pm 6\%$, $p < 0.001$) [2].

According to various reports, DSE cannot be performed in 5 to 20% of patients due to an inadequate acoustic window on TTE [10]. In such patients, TEE-DSE was proven to be a good solution.

There are no data in literature evaluating the effects of TEE-DSE on IMR. It is however known, that TEE-DSE is a very accurate tool for the evaluation of presence of CAD [10, 12]. The examination is safe and, most importantly, feasible and clinically reliable practically in every patient [10, 11]. Mazeika et al. showed that occurrence of new MR during diagnostic DSE increases sensitivity of this method (from 78% to 81%) without decreasing its specificity for diagnosis of CAD [20].

Our analysis deals primarily with the evaluation of dynamics of IMR changes during TEE-DSE combined with accurate assessment of LV contractility and, mainly, its viability despite selective appraisal of IMR alone. We assumed that patients, in whom significant (at least by 2+) reduction of IMR with simultaneous considerable improvement of WMSI (improvement of contractility within at least 2 segments) is observed during evaluation of LV myocardial viability, will be qualified for CABG alone. The reduction of the mitral regurgitant jet without parallel significant improvement of WMSI observed in some patients was probably caused by the influence of dobutamine on the pressures within the cardiac chambers (IMR is a dynamic condition which may decrease after administration of positive inotropic agents) and/or decrease of the mitral ring area in response to dobutamine infusion rather than being confirmation of the presence of viable LV myocardium. In our opinion, such patients should be treated with coronary revascularisation with additional mitral valve repair, i.e. annuloplasty or valve replacement. In patients in whom IMR did not change during TEE-DSE (no reduction), we also performed CABG combined with mitral valve surgery.

Maximal dobutamine infusion rate was $20 \mu\text{g}/\text{kg}$ of body weight/min. In other studies evaluating the effects of dobutamine on the MR of various aetiology the doses of dopamine were far higher (up to $40 \mu\text{g}$), which

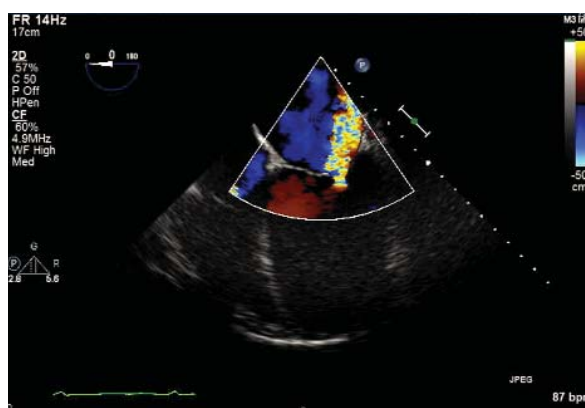


Figure 1. Severe mitral regurgitation; TEE-DSE before administration of dobutamine

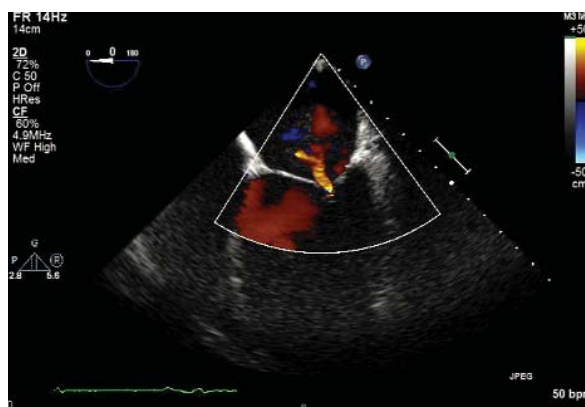


Figure 2. Small mitral regurgitation; TEE-DSE, dobutamine infusion rate $20 \mu\text{g}/\text{kg}$ of body weight/min



Figure 3. Moderate mitral regurgitation in a patient after isolated CABG; transthoracic echocardiography, 4-chamber apical view

certainly significantly influenced the haemodynamic effect of dobutamine as well as mitral ring size, and finally the severity of MR (primarily its reduction) [9]. Decrease of the regurgitant jet was independent of the dobutamine effect on myocardial viability and in consequence did not favourably influence LV geometry. We assumed rigorous criteria for the evaluation of IMR reduction (at least by 2+) and the appraisal was made dependent, first of all, on significant influence on the viability of LV myocardium (within at least 2 segments).

In our study we analysed a selected group of patients with significant IMR previously qualified to CABG, on the basis of coronary angiography and clinical picture. Fortunately, it is usually a small group of subjects (12% in our report), however, with high risk of death. The risk evidently remains in close relationship with MR severity.

An enormous problem in the treatment of IMR is still the high intraoperative mortality, from 3% for mitral annuloplasty, to 6.4% for single valve replacement, and up to 15.3% for complex procedures [21]. Therefore, it is extremely important to select even a small group of IMR patients in whom valvular repair may be avoided during CABG.

Management of IMR is still controversial. Debates are carried out as to whether better therapeutic effects can be obtained with isolated revascularisation or revascularisation combined with valvular surgery [5-8]. Opinions on isolated revascularisation are constantly divided. In 2001 Aklog et al. reported that in patients after CABG significant IMR persisted in 77% of subjects, whereas Tolis et al. in their study from 2002 showed that CABG alone produced desired therapeutic outcome in patients with severe ischaemic cardiomyopathy [5, 6].

The complex pathomechanisms of IMR are responsible for difficulties in development of effective treatment methods. Our clinical analysis aimed to reliably evaluate the severity of IMR, to reveal mechanisms responsible for development of IMR in individual patients, and to assess possible reversibility of IMR without the need for surgical repair of the mitral valve. It is imperative to identify patients with severe IMR in whom revascularisation alone (CABG or PCI) would be a sufficient method to restore normal function of the mitral valve. We found that TEE-DSE is the most reliable diagnostic tool, not only due to very good visualisation, which is particularly important during DSE, but also because of its better possibilities of evaluation of cardiac anatomy.

Recently, investigators have paid particular attention to the possibility of three-dimensional visualisation of MR. Three-dimensional reconstruction enables precise determination of IMR severity and clearly shows the real mechanisms leading to MR in individual patients [22, 23].

This method allows one to authentically reconstruct the mitral apparatus, according to its pathomechanism, which is responsible for the development of IMR in individuals [24, 25].

Conclusions

TEE-DSE seems to be a useful tool for optimal selection of surgical treatment in patients with significant IMR and qualification for CABG. On the basis of dynamic changes in mitral regurgitation severity, qualification of patients to surgical revascularisation alone or to bypass surgery plus surgical valvular repair seems to be justified. However, this method needs further evaluation in a larger population of patients with severe postinfarction ischaemic MR.

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Znaczenie echokardiograficznej przezprzelykowej próby dobutaminowej w ustaleniu optymalnej strategii leczenia operacyjnego u chorych z istotną niedokrwieną niedomykalnością mitralną zakwalifikowanych do pomostowania aortalno-wieńcowego

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Streszczenie

Wstęp: Niedokrwieną niedomykalność mitralną (NNM) może być leczona chirurgicznie poprzez wykonanie samej rewaskularyzacji lub w połączeniu z operacją naprawczą zastawki. Przezprzelykowa echokardiograficzna próba dobutaminowa (TEE-DSE) może być użyteczną metodą w ustaleniu optymalnej strategii leczenia.

Cel: Opracowanie optymalnej chirurgicznej strategii postępowania u chorych z istotną pozawałową NNM na podstawie TEE-DSE. Podjęto próbę oceny, u których chorych wykonać izolowaną rewaskularyzację, a u których, oprócz rewaskularyzacji wieńcowej, również interwencję chirurgiczną w obrębie aparatu zastawki dwudzielnej.

Metodyka: Grupę badaną stanowiło 212 chorych (134 mężczyzn i 78 kobiet; średnia wieku 65±10 lat) po przebytych zawałach mięśnia serca z wytworzeniem załamka Q, zakwalifikowanych na podstawie angiograficznej oceny naczyń wieńcowych do leczenia chirurgicznego. U 25 (12%) chorych ze stwierdzoną istotną NNM (EF <40%, WMSI 1,8±0,3) wykonywano TEE-DSE. Grupę I stanowili chorzy, u których stwierdzano istotne zmniejszenie wielkości fali zwrotnej oraz poprawę kurczliwości lewej komory (7 osób) i których zakwalifikowano do izolowanego zabiegu CABG; grupę II – 18 chorych zakwalifikowanych do CABG w połączeniu z plastyką aparatu zastawki dwudzielnej lub wymianą zastawki, u których TEE-DSE nie miało istotnego wpływu na wielkość NNM (9 chorych) lub dochodziło do istotnego zmniejszenia NNM, lecz bez istotnej poprawy w zakresie WMSI (9 chorych).

Wyniki: W grupie II u 4 chorych dokonano wymiany zastawki, u 14 wykonano plastykę mitralną. Analiza echokardiograficzna wykonana w 2.–7. dobie po zabiegu, w 6. oraz 12. mies. wykazała odpowiednio w poszczególnych grupach: grupa I – NNM mała 5/4/4, umiarkowana 2/2/2, duża 0/0/0; grupa II – NNM mała 15/14/13, umiarkowana 2/3/3, duża 0/0/0.

Wnioski: TEE-DSE wydaje się przydatną metodą, pozwalającą na optymalny wybór zakresu leczenia chirurgicznego u chorych z istotną NNM kwalifikowanych do zabiegu CABG.

Słowa kluczowe: niedokrwieną niedomykalność zastawki mitralnej, echokardiograficzna przezprzelykowa próba dobutaminowa

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