

Usefulness of early dobutamine stress echocardiography for the assessment of risk of restenosis after percutaneous coronary interventions

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Abstract

Background: The increasing role of percutaneous coronary interventions (PCI) in the treatment of coronary artery disease and relatively high restenosis rate following PCI require the introduction of available, easy to perform and cost-effective tests that would enable detection of restenosis after PTCA and identification of patients at particularly high risk of restenosis.

Aim: To estimate the predictive value of early dobutamine stress echocardiography (DSE) for the assessment of risk of coronary restenosis.

Methods: Thirty-nine patients with a single coronary vessel disease after PCI were enrolled in this study. DSE was performed twice – 2 to 3 days after the procedure and repeated after 8 to 12 months. All patients underwent coronary angiography after one-year follow-up.

Results: Data analysis of direct pre- and postprocedural echocardiography showed that the wall motion score index decreased significantly ($p < 0.0001$), whereas ejection fraction increased significantly after the intervention when compared with baseline ($p < 0.0001$). Restenosis was detected in 8 out of 10 subjects with positive DSE test and in 3 out of 29 subjects with negative DSE test.

In a group of 11 patients with restenosis confirmed in the coronary angiography, one-year follow-up DSE was found positive in 9 patients (80% test sensitivity) but in two cases results were false negative. Negative test was observed in 27 out of 28 individuals without restenosis (90% test specificity).

Conclusions: DSE is highly sensitive and specific in prediction and detection of restenosis after PCI. DSE performed early after PCI is safe.

Key words: dobutamine stress echocardiography, restenosis, percutaneous coronary intervention

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Introduction

In spite of cutting-edge technologies (drug eluting stents) introduced to interventional cardiology, restenosis after percutaneous coronary interventions (PCI) remains a serious clinical problem. The probability of restenosis ranges from 8 to 60% and depends on a combination of such risk factors as diabetes mellitus, arterial hypertension, smoking, hyperlipidaemia, gender, history of coronary artery disease (CAD), stenosis characteristics (site of coronary lesion, stenosis length, reference vessel diameter) and type of coronary intervention (angioplasty

with or without stent implantation, atherectomy, employment of coated stents, brachytherapy) [1, 2]. Analysing data from large clinical trials such as BENESTENT I, BENESTENT II, MUSIC, WEST 1, DUET, FINISS 2, FLARE, SOPHOS and ROSE³, a marked difference is observed with respect to the rate of coronary interventions for restenosis between patients undergoing mandatory control angiography at 6th month of follow-up and those with control coronary angiography for clinical indications [3]. In more than 50% of patients, restenosis is not accompanied by any symptoms, but this does not mean that it does not pose a threat to the patient.

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Because electrocardiographic stress test, performed particularly in subjects after coronary revascularisation or with a single vessel disease, has a poor sensitivity (approximately 40 to 55%) in detection of restenosis, other methods, especially echocardiographic stress examination or stress scintigraphy, are currently employed [4]. Dobutamine stress echocardiography (DSE) is currently the most extensively used test due to its high precision, availability and relative cost-effectiveness. A negative result of stress echocardiography predicts a low risk of cardiologic events within the next 4 to 5 years [5] (i.e. <1%) with the exception of diabetic and renal failure patients who present significantly accelerated course and progression of atherosclerosis. A positive test is associated with 10 to 30% probability of cardiac events within the next 3 to 5 years [6].

The purpose of this study was to estimate the prognostic value of DSE performed soon after PCI for risk assessment of coronary restenosis.

Methods

Study groups

This study involved 39 patients admitted to our department between 2001 and 2003. There were 32 male and 7 female patients. In all patients, CAD was diagnosed based on clinical presentation and coronary angiography. At that moment patients were selected for PCI. Individuals with significant valvular disease, dilated cardiomyopathy, left ventricular (LV) myocardial hypertrophy or unstable CAD were excluded. Inclusion study criterion was a single-vessel disease involving any large epicardial vessel. All patients were readmitted to hospital and underwent control examinations after 8 to 12 months.

Coronary angiography, PCI

Coronary lesions were assessed with respect to localisation and degree of lumen reduction according to the AHA criteria, defining stenosis $\geq 50\%$ of vessel lumen area as significant. PCI was performed according to the commonly accepted standards [7] and in 33 (85%) patients intracoronary stents were implanted. In all patients repeat coronary angiography was carried out after 8 to 12 months of follow-up.

Stress echocardiography

Stress echocardiography was performed according to current standards [8, 9]. This examination was performed twice, 2 to 3 days after PCI and after 8 to 12 months of follow-up.

Restenosis diagnosis

Based on the results of the control (after 8 to 12 months) coronary angiography, patients were divided into

two groups: a group with coronary restenosis (R) and a group without restenosis (NR). Restenosis was diagnosed if the control coronary angiography revealed recurrence of stenosis exceeding 50% at the site of previous angioplasty or a loss of more than 50% of regained vessel diameter. No patients demonstrated any symptoms of CAD instability that would be an indication for premature control coronary angiography during 8-12 month follow-up.

Statistical analysis

Data were analysed using computer STATISTICA 6.0 PL software. Examined parameters were analysed by means of Student's t-test and χ^2 test. Results are expressed as mean \pm standard deviation. A p value <0.05 was considered statistically significant.

Results

Group R comprised 11 subjects – 10 men (26%) and 1 woman (3%), while group NR included 28 individuals – 22 male (56%) and 6 females (15%). Prevalence of overweight or obesity, diabetes mellitus and smoking was much higher in the group of patients with coronary restenosis. Additionally, disturbances of lipid metabolism were noted more frequently in the group of patients with restenosis at follow-up angiography. Overall clinical characteristics and prevalence of risk factors in group R and group NR are outlined in Table I.

Symptoms associated with CAD, assessed according to the Canadian Cardiovascular Society (CCS) criteria in the consecutive stages of follow-up, are presented in Table II. At baseline, the mean CCS class was similar in both groups, however, it progressively deteriorated during follow-up in patients from group R.

Left ventricular contractility at rest was compared before and 2 to 3 days after PCI. In total, 624 echocardiographic segments of LV were analysed. Prior to PCI, 458 of them (R:135 + NR:323) were identified as normokinetic, 144 (R:36 + NR:108) as hypokinetic, 21 (R:4 + NR:17) as akinetic and 1 segment as dyskinetic (R). In the echocardiographic assessment performed soon after PCI, the number of normokinetic segments increased to 536 (R:146 + NR:390) but hypokinetic segments decreased to 77 (R:48 + NR:29) and akinetic to 11 (R:1 + NR:10). No dyskinetic segments were recorded at that time. The average number of hypokinetic segments in group NR decreased much more than in group R ($p=0.009$). The number of normokinetic segments increased in both groups, although this increase was markedly higher in group NR ($p=0.005$) (Figure 1).

Intracoronary stents were implanted during 33 (85%) PCI procedures, and 6 (15%) procedures were performed using balloon catheters (POBA) without stent implantation. In group R, in 8 cases stents were implanted while 3 procedures were carried out without

Table I. Clinical characteristics and prevalence of selected risk factors in patients with (R) or without restenosis (NR)

Parameter		Group R n=11	Group NR n=28	p
Age [years]		58.7±7.3	53.5±8.1	NS
Weight [kg]		89±12.4	74.3±11.6	<0.05
Height [m]		1.73±0.07	1.7±0.07	NS
BMI [kg/m ²]		29.5±3.2	25.8±3.6	<0.05
Prior to PCI	Total cholesterol [mg/dL]	269±71	208±42	<0.05
	HDL-cholesterol [mg/dL]	38±8	53±13	<0.05
	LDL-cholesterol [mg/dL]	188±52	115±25	<0.05
	Triglycerides [mg/dL]	140±85	146±65	NS
8-12 months after PCI	Total cholesterol [mg/dL]	194±54	206±51	NS
	HDL-cholesterol [mg/dL]	45±9	55±14	NS
	LDL-cholesterol [mg/dL]	111±34	107±21	NS
	Triglycerides [mg/dL]	135±27	112±46	NS
Previous myocardial infarction		5 (9%)	9 (23%)	NS
Diabetes mellitus		7 (18%)	3 (7%)	<0.05
Smoking		9 (23%)	5 (13%)	<0.05
Arterial hypertension		8 (20%)	14 (36%)	NS
Gender	Men	10 (26%)	22 (56%)	NS
	Women	1 (3%)	6 (15%)	
Family history of CAD		6 (15%)	5 (13%)	NS

Abbreviations: BMI – body mass index, PCI – percutaneous coronary intervention, CAD – coronary artery disease

Table II. Severity of angina complaints according to the mean CCS class prior to PCI, 2 to 3 days following PCI, 8 to 12 months after PCI

	Prior to PCI		After PCI		8-12 months of follow-up	
	CCS class	min-max	CCS class	min-max	CCS class	min-max
Group R (n=11)	2.6±0.7	1-4	1.3±0.5	1-2	2.5±0.5	2-3
Group NR (n=28)	2.2±0.6	1-3	1.7±0.5	1-2	1.3±0.5	1-3
p	NS		<0.02		<0.0001	

stents. In group NR, in 25 individuals intracoronary stents were employed whereas in 3 subjects only balloon catheters were used (NS). The groups differed significantly with respect to the length of implanted stents – in group R they were markedly longer than in NR patients (18.5±3.38 vs. 12.9±3.8 mm, p=0.0008). In all patients enrolled in the study, PCI was considered successful (defined as residual stenosis <30%).

Among 29 individuals with a negative early DSE test, restenosis was detected only in three cases while among 10 patients with a positive test, restenosis after 8 to 12 months was diagnosed in 8 of them. The prognostic value of early negative DSE for evaluation of freedom from restenosis (specificity) was 90%, while

that of positive DSE with respect to restenosis occurrence (sensitivity) was 80%.

Of note is also the presence of a correlation between the result of early DSE and changes of LV ejection fraction and wall motion score index (WMSI) that are outlined in Table III. After 8 to 12 months, the WMSI was significantly higher in patients with restenosis but ejection fraction was markedly lower in comparison with group NR (p=0.001 and p=0.0005, respectively).

Discussion

The results of our study indicate that DSE performed soon after PCI is helpful in the estimation of restenosis

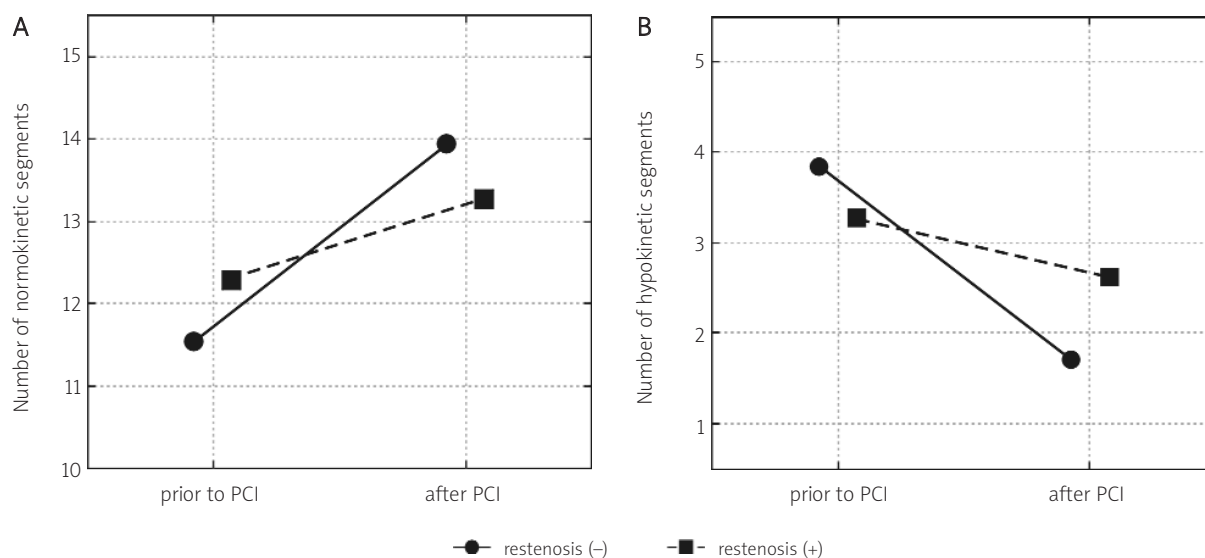


Figure 1. PCI-induced changes in the averaged number of normokinetic (A) and hypokinetic (B) segments in groups with or without restenosis

risk. Early assessment of restenosis risk is of paramount importance. Owing to this, we are able to decide how aggressively the treatment should be applied and which scheme of control (diagnostic tests) should be chosen in on individual patient to detect restenosis most effectively. According to published data, diabetes mellitus is one the most important risk factors of atherosclerosis development [1, 10, 11]. The results presented herein confirm that in diabetic patients restenosis in the control follow-up coronary angiography was much more frequent ($p=0.018$), as was the case with new lesions in other coronary vessels (in 2 out of 7 patients). Based on data analysis, an increased rate of repeat interventional coronary procedures was also shown in the smokers. A similar relationship was also found in the previously published reports [12, 13].

A correlation between positive early DSE test and restenosis occurrence or absence is not completely clear. There is still a search for a factor responsible for ischaemia provocation just after the successful PCI. A potential explanation may be the existence of impaired coronary flow reserve (CFR) that in spite of successful PCI

does not return back to normal value and which identifies patients vulnerable to restenosis development [14, 15]. Dissection occurrence, impaired laminar blood flow within the artery and an insufficient increase in vessel lumen at the site of PCI, which were not observed in our group, may also preclude CRF normalisation.

The presence of previously diagnosed myocardial dysfunction may also be associated with changes within the microcirculation. It is explained to be a result of microembolisation during PCI due to mobilisation of the embolic material and responsive vasospasm of microvasculature following stent implantation, not visualised in the coronary angiography [16].

Rodes-Cabau et al. [17] employed perfusion scintigraphy for the assessment of ischaemia inducibility 3 to 7 days following PCI. Their study involved 30 patients with a single-vessel disease who underwent PCI. They showed that in spite of angiographic success of the procedure, in 5 (17%) patients an impaired accumulation of radionuclide in the PCI-related area was detected. During follow-up examination of 4 patients, who underwent control coronary angiography, 3 of them had

Table III. Relationship between result of early dobutamine stress echocardiography and EF or WMSI values

	Prior to PCI		2-3 days after PCI		8-12 months after PCI	
	EF [%]	WMSI	EF [%]	WMSI	EF [%]	WMSI
DSE (+)	51.5±6.3	1.337±0.305	53±6.3	1.218±0.225	43±8.6	1.375±0.354
DSE (-)	48.6±4.9	1.295±0.114	55±4.6	1.019±0.114	55.9±7	1.088±0.101
p	NS	NS	NS	NS	0.0005	0.001

Abbreviations: EF – ejection fraction, WMSI – wall motion score index, DSE (+) – patients with positive result of early dobutamine stress echocardiography, DSE (-) – patients with negative early dobutamine stress echocardiography

restenosis confirmed on angiography. Among patients without any ischaemia in the radionuclide study, 19 subjects had control coronary angiography after 8 to 11 months. Only in 3 of them was restenosis noted. The prognostic value of the positive test for the development of restenosis was 75% and for negative test result – 84%.

Similar results were demonstrated in the study published in 1997 by Dagianti et al. [18]. Patients after PCI with echocardiographic stress examination before and 1 to 2 days after the procedure were enrolled. It was shown that in 22 (29%) of 76 patients exercise contractility abnormalities were provoked during early stress examination. Follow-up examination was performed 6 months later. An assessment of clinical status and second echocardiographic stress test were carried out at that time. Based on clinical symptoms and the results of the stress test, control coronary angiography was performed in 47 patients and restenosis was seen in 18 (82%) out of 22 subjects with positive early stress echocardiographic test. Meanwhile, restenosis in the group of patients with negative test results was found in 7 (13%) subjects.

Although the vast majority of published reports documented DSE safety, some studies revealed adverse effects related to DSE performed very early after an invasive coronary intervention. Pressman [19] reported a case of myocardial infarction induced by dobutamine test in a patient after PCI involving the left anterior descending artery. However, our report confirmed the safety of the stress echocardiographic examination performed early (2 to 3 days) after PCI.

To date, no obvious risk factors predisposing patients to coronary restenosis development and also efficacious methods of its prevention have been established. Due to the high rate of stenosis recurrence at the site of previous PCI, early identification of particularly predisposed patients is of clinical significance. Data published in this study confirmed that DSE was very helpful to identify such high risk patients.

Conclusions

1. Dobutamine stress echocardiography carried out just after PCI has a high prognostic value in predicting restenosis at 8 to 12 months of follow-up.
2. Early dobutamine test is safe.

References

1. West NE, Ruygrok PN, Disco CM, et al. Clinical and angiographic predictors of restenosis after stent deployment in diabetic patients. *Circulation* 2004; 109: 867-73.
2. Cutlip DE, Chhabra AG, Baim DS, et al. Beyond restenosis: five-year clinical outcomes from second-generation coronary stent trials. *Circulation* 2004; 110: 1226-30.
3. Ruygrok P, Webster M, de Valk V, et al. Clinical and angiographic factors associated with asymptomatic restenosis after percutaneous coronary intervention. *Circulation* 2001; 104: 2289-94.
4. Marwick TH. Stress echocardiography. *Heart* 2003; 89: 113-8.
5. Dhond MR, Donnell K, Singh S, et al. Value of negative dobutamine stress echocardiography in predicting long-term cardiac events. *J Am Soc Echocardiogr* 1999; 12: 471-5.
6. Poldermans D, Fioretti PM, Boersma E, et al. Long-term prognostic value of dobutamine-atropine stress echocardiography in 1737 patients with known or suspected coronary artery disease: A single-center experience. *Circulation* 1999; 99: 757-62.
7. Smith SC Jr, Dove JT, Jacobs AK, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines) – executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 2001; 37: 2215-39.
8. Płońska E. Echokardiografia obciążeniowa. Standardowa metoda nieinwazyjna w diagnostyce choroby wieńcowej. *Ultrasonografia* 2002; 9: 49-51.
9. Lewandowski M, Szwed H, Płońska E, et al. Wartość diagnostyczna echokardiograficznej próby dobutaminowej w rozpoznawaniu stabilnej choroby wieńcowej. *Pol Arch Med Wewn* 2003; 110: 1405-14.
10. Mathew V, Gersh BJ, Williams BA, et al. Outcomes in patients with diabetes mellitus undergoing percutaneous coronary intervention in the current era: a report from the Prevention of REStenosis with Tranilast and its Outcomes (PRESTO) trial. *Circulation* 2004; 109: 476-80.
11. Chaves AJ, Sousa A, Mattos LA, et al. Volumetric analysis of in-stent intimal hyperplasia in diabetic patients treated with or without abciximab: results of the Diabetes Abciximab steNT Evaluation (DANTE) randomized trial. *Circulation* 2004; 109: 861-6.
12. Violaris AG, Thury A, Regar E, et al. Influence of a history of smoking on short term (six month) clinical and angiographic outcome after successful coronary angioplasty. *Heart* 2000; 84: 299-306.
13. Howard G, Wagenknecht LE, Burke GL, et al. Cigarette smoking and progression of atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study. *JAMA* 1998; 279: 119-24.
14. Di Mario C, Moses JW, Anderson TJ, et al. Randomized comparison of elective stent implantation and coronary balloon angioplasty guided by online quantitative angiography and intracoronary Doppler. DESTINI Study Group (Doppler Endpoint STenting INternational Investigation). *Circulation* 2000; 102: 2938-44.
15. Dupouy P, Aptekar E, Pelle G, et al. Early changes in coronary flow physiology after balloon angioplasty or stenting: a 24-hour Doppler flow velocity study. *Catheter Cardiovasc Interv* 2002; 57: 191-8.
16. El-Tamimi H, Davies GJ, Sritara P, et al. Inappropriate constriction of small coronary vessels as a possible cause of a positive exercise test early after successful coronary angioplasty. *Circulation* 1991; 84: 2307-12.
17. Rodes-Cabau J, Candell-Riera J, Domingo E, et al. Frequency and clinical significance of myocardial ischemia detected early after coronary stent implantation. *J Nucl Med* 2001; 42: 1768-72.
18. Dagianti A, Rosanio S, Penco M, et al. Clinical and prognostic usefulness of supine bicycle exercise echocardiography in the functional evaluation of patients undergoing elective percutaneous transluminal coronary angioplasty. *Circulation* 1997; 95: 1176-84.
19. Pressman GS. Acute infarction of a previously stented coronary artery precipitated by dobutamine stress echocardiography. *J Am Soc Echocardiogr* 2000; 13: 150-1.

Przydatność wczesnej echokardiograficznej próby dobutaminowej po zabiegu przezskórnej interwencji wieńcowej dla oceny ryzyka restenozy

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Streszczenie

Wstęp: Wzrastająca rola przezskórnych interwencji wieńcowych (PCI) w leczeniu choroby wieńcowej, a także stosunkowo częste występowanie powtórnego zwężenia wymagają wprowadzenia dostępnych, łatwych do wykonania i tanich testów pozwalających wykryć restenozę po PCI, a także wyodrębnić grupę pacjentów szczególnie narażonych na jej wystąpienie.

Cel: Określenie wartości prognostycznej wczesnej echokardiograficznej próby obciążeniowej z użyciem dobutaminy (DSE) dla wystąpienia restenozy.

Metodyka: Do badania włączono 39 pacjentów z jednoznaczniową chorobą wieńcową po zabiegu PCI. DSE wykonano 2-krotnie, 2–3 dni po zabiegu i w odstępie 8–12 mies. U wszystkich pacjentów wykonano koronarografię w trakcie badania kontrolnego po roku.

Wyniki: Analiza danych z badania ultrasonograficznego przed i wkrótce po zabiegu potwierdziła, że wartość wskaźnika WMSI istotnie się obniżyła ($p < 0,0001$). Wartość frakcji wyrzutowej istotnie wzrosła w porównaniu z wartością przed zabiegiem ($p < 0,0001$). Restenozę rozpoznano u 8 z 10 osób, u których uzyskano dodatni wynik DSE, i u 3 z 29 osób z wynikiem ujemnym.

W grupie 11 osób z potwierdzoną angiograficznie restenozą, DSE w kontroli po roku zakończyła się wynikiem dodatnim u 9 pacjentów (czułość testu 80%), w 2 przypadkach wynik okazał się fałszywie ujemny. Ujemny wynik testu zanotowano u 27 spośród 28 osób bez restenozy (swoistość 90%).

Wnioski: Echokardiografia obciążeniowa z użyciem dobutaminy ma dużą czułość i swoistość w prognozowaniu i rozpoznawaniu restenozy po zabiegu PCI. Wykonana wcześniej po PCI jest badaniem bezpiecznym.

Słowa kluczowe: echokardiograficzny test dobutaminowy, restenozą, przezskórna interwencja wieńcowa

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