Original Article

Accuracy of Dobutamine Stress Echocardiography in Detecting Recovery of Contractile Reserve after Revascularization of Ischemic Myocardium

Hakimeh Sadeghian, MD[1], Masoumeh Lotfi-Tokaldany, MD[1*], Nader Fallah, PhD[1]
Seyed Hesameddin Abbasi, MD[1], Seyed Hossin Ahmadi, MD[1], Abas Ali karimi, MD[1]
Mojtaba Salarifar, MD[1], Salehi Rezvanyieh, MD[2]

[1] *Tehran Heart Center, Medical Sciences/University of Tehran, Tehran, Iran.*
[2] *Cardiology Department, Tabriz University of Medical Sciences, Tabriz, Iran.*

Received 9 May 2007; Accepted 21 July 2007

Abstract

Background: *This study was designed to investigate the accuracy of dobutamine stress echocardiography (DSE) in detecting the post-revascularization recovery rate of contractile reserve (CR) in ischemic myocardium.*

Methods: *A total of 112 segments from seven patients with low ejection fraction (<35%) and coronary artery disease were evaluated with DSE one week before and 12 weeks after coronary artery bypass graft surgery (CABG). Sensitivity, specificity, and positive and negative predictive values of DSE for detecting the recovery rate of CR were calculated based upon their standard definition and were presented with 95% confidence intervals (CI).*

Results: *The mean baseline left ventricular ejection fraction was 31±4%, which reached 35±7% after CABG unremarkably. The recovery rates of resting function and CR were 18.2% and 50% for hypokinetic and 15.6% and 24.1 for akinetic segments respectively. Specificity, sensitivity, and positive and negative predictive values of DSE for detecting the recovery of CR were 83% (CI=69-97), 89% (CI=83-96), 94% (CI = 88-99), and 73 % (CI = 55-88), respectively.*

Conclusion: *Despite acceptable sensitivity, specificity, and positive predictive value, DSE has a relatively lower negative predictive value for detecting the recovery of CR in ischemic myocardium and, consequently, the full extent of myocardial viability. Further sensitive techniques may, therefore, be needed to provide complementary information regarding long-term functional outcome.*

J Teh Univ Heart Ctr 4 (2007) 223-228

Keywords: *Echocardiography • Dobutamine • Myocardial ischemia*

Introduction

Hibernating myocardium defines the reversible contractile function of dysfunctional left ventricular (LV) segments subtended by stenotic coronary arteries in patients with chronic coronary artery disease following revascularization.[1-4] Detection of the contractile reserve (CR) of hibernating myocardium by noninvasive testing currently helps make clinical decisions regarding recommendation for revascularization in patients with severe ischemic LV dysfunction.[5]

Among different noninvasive imaging techniques, dobutamine stress echocardiography (DSE) is usually the initial approach for detecting hibernating myocardium

[*]**Corresponding Author:** ***Masoumeh Lotfi-Tokaldany,*** *Research Department, Tehran Heart Center, North Kargar Street, Tehran, Iran. 1411713138. Tel: +98-21-88029257. Fax: +98-21-88029256. E-mail: lotfi21366@yahoo.co.uk.*

because it is inexpensive, widely available, and has a good predictive value.[6] It is now becoming increasingly clear that certain myocardial segments are resistant to dobutamine stimulation but eventually show recovery of function after revascularization and, hence, are defined as hibernating.[7] It has been suggested that the recovery of resting function may be an inappropriate standard viability assessment and that improvement in CR is even more important in terms of functional capacity, preventing LV remodeling, and long-term prognosis.[4,8]

Improvement in left ventricular ejection fraction (LVEF) and heart failure symptoms after revascularization is associated with the presence of CR in a substantial number of segments in DSE; therefore, findings of DSE may guide therapeutic management in patients with severely ischemic LV dysfunction. We investigated the diagnostic accuracy of DSE to predict the degree of recovery in CR after surgical revascularization of the ischemic myocardium.

Methods

The study population comprised 7 patients with chronic coronary artery disease and severe LV dysfunction (EF<35) who underwent coronary artery bypass grafting (CABG). Patients with a recent acute myocardial infarction, significant valve disease, or inadequate image quality were not included. All the patients underwent DSE one week before intervention and repeated DSE at 3 months post-CABG. All the studies were observed by two independent experienced observers. The study findings were analyzed using the rest and dobutamine echocardiography report. The study was approved by the Ethics Committee of the hospital.

Dobutamine stress echocardiography

Echocardiography was performed with a 2.5-MHz transducer, Toshiba, version 5000, under resting conditions and during each dobutamine infusion step. Beta-blockers, calcium antagonists, and nitrates were discontinued in patients at least 2 days before DSE.

After baseline echocardiography, dobutamine infusion was initiated using a mechanical pump. Dobutamine was delivered intravenously beginning at 5 μ/kg/min for three minutes and increased by 5 μ/kg/min increments every three minutes to 15 μ/kg/min, at which dose it was administered for an additional three minutes. Blood pressure was measured periodically. 12-lead ECG was continuously monitored throughout the study and during the recovery phase. Infusion was terminated when severe hypotensive or hypertensive response, significant arrhythmias, prolonged angina, significant electrocardiographic changes, appearance of new wall motion abnormalities in at least two segments, or completion of the protocol was observed. Echocardiographic images were analyzed off-line using a 16-segment model.[7] Segmental wall motion was scored on a four-point scale: 1; normal, 2; hypokinetic (severely reduced wall thickening and inward wall motion), 3; akinetic (absence of systolic thickening and wall motion), and 4; aneurismal (dyskinetic regions with a diastolic contour abnormality). Regional LV function was assessed by resting and dobutamine echocardiography one week before and 3 months after intervention. A regional wall motion score index (WMSI) was quantified by summing the grades for each segment and dividing it by the total number of segments analyzed for each patient.

Demonstration of wall thickening in a previously akinetic segment or normalization of thickening in a previously hypokinetic segment was considered as criteria for myocardial viability. Improvement in segmental wall motion at stress by at least one grade compared with the baseline rest study was considered as recovery of CR in the follow-up study. Recovery of resting function in the follow-up studies was expressed by improvement on resting segmental wall motion after CABG at least one grade or more compared with the baseline rest study before CABG.

Left ventricular ejection fraction was measured at baseline, and peak dobutamine dosage was determined using an available software program that applied Simpson's rule on the apical two-chamber and four-chamber views.

CABG

Surgery was performed by cardiac surgeons using cardiopulmonary bypass and mild hypothermia (32-34 ºC). Every effort for complete revascularization was made during the operation to graft all epicardial vessels with significant stenosis. The median number of grafts was three (range 1-5); the cardiopulmonary bypass time was 64 minutes and the aortic clamp time 41 minutes.

Statistical analysis

Recovery rates at rest and stress are given with 95% confidence interval (CI). Continuous data are expressed as mean±SD and compared using the Student’s t-test for paired and unpaired data when appropriate. Univariate analysis for categorical variables was performed using the chi-square test. Sensitivity, specificity, and positive and negative predictive values (PPV & NPV) are based upon their standard definition and presented with their 95% CI. A p value<0.05 was considered significant.

Results

In all, 7 patients (mean age of 51.6±8.9 years, one woman), were enrolled in the study. There was no death or ischemic event during surgery or follow-up period. The mean baseline

LVEF of all the patients was 31±3.7%. Clinical, laboratory, and operative characteristics are shown in Table 1.

Table 1. Clinical, angiographic and operative data of study patients (n = 7)

variables	No of patients
EF 25-30%	1
EF 30-35%	6
History of myocardial infarction	6
Stable angina	7
Dyspnea (NYHA I-II)	7
Previous CABG	0
Diabetes	2
Hypertension	3
Dyslipidemia	5
Smoking	2
2-vessel disease	1
3-vessel disease	6
Number of distal coronary anastomoses	
2	1
3	1
4	4
5	1

EF, Ejection fraction; NYHA, New York heart association classification; CABG, Coronary artery bypass grafting

DSE before surgery

A total of 112 myocardial segments were analyzed (16 segments per patient), of which 76 (68%) had baseline wall motion abnormalities: 44 (39%) were hypokinetic and 32 (29%) akinetic. The responses of the 76 dysfunctional segments to dobutamine were as follows: continuous improvement in 43 segments (56.5%) and no change in 33 (43.4%). Evidence of CR was demonstrated in 9.4% (3/32) of the akinetic segments, while there was no CR in 90.6% (29/32) of them. Evidence of CR was demonstrated in 90.9% (40/44) of the hypokinetic segments, while there was no CR in 9.1% (4/44) of them. Thus, myocardial viability was detected more frequently in hypokinetic than in akinetic segments (P<0.0001).

After dobutamine injection, CR was presented in 79 (70.5%) of 112 segments and absent in 33 (29.5%). Wall motion score index was 1.96 at rest and decreased to 1.71 when stressed.

The mean baseline LVEF of all the patients was 31±3.7%, which reached 43.6±10% after dobutamine infusion.

Effect of coronary revascularization on LV function

Mean LVEF at rest increased insignificantly from 32±4% preoperatively to 35±7% post surgery. Wall motion score index at rest decreased from 1.96 preoperatively to 1.89 at follow-up insignificantly. Recovery of resting function was evident in 18% of hypokinetic and 15.6% of akinetic segments, whereas recovery in CR was evident in 50% of hypokinetic and 24.1% of akinetic segments.

Accuracy of DSE in predicting the recovery of CR after revascularization

Main findings are summarized in Table 2, Table 3 and Figure 1 Calculated sensitivity and specificity of DSE in detecting the recovery of CR in all segments were 89.2% (95%CI, 83-96) and 82.8% (95%CI, 69-97), respectively. The PPV of DSE for detecting CR was 93.7% (95%CI, 88-99) and NPV was 72.7% (95%CI, 57-88). From 33/112 segments without CR before surgery, 9 (27.3%) presented CR and 27(72.7%) showed no CR after CABG. From 79/112 segments with CR before CABG, 74 (93.5%) showed CR while 5 (6.5%) did not show CR after surgery.

Results of DSE before and after surgical intervention are depicted in Table 2.

Table 2. Comparison of myocardial segments with different function in terms of the presence of CR, detected by DSE, before and after CABG in 112 segments

Wall motion	Before CABG			After CABG		
	With CR N (%)	Without CR N (%)	Total N	With CR N (%)	Without CR N (%)	Total N
Normal	36 (100)	0	36	47 (100)	0	47
Hypokinetic	40 (91)	4 (9)	44	31 (94)	2 (6)	33
Akinetic	3 (9)	29 (91)	32	5 (16)	27 (84)	32
Total	79 (71)	33 (29)	112	83 (74)	29 (26)	112

CR, Contractile reserve; DSE, Dobutamine stress echocardiography; CABG, Coronary artery bypass grafting; N, Number

Of 29/32 akinetic segments without CR before CABG, 7/29 had CR after CABG, and 5/7 of them recovered resting function while 22/29 had neither recovery of CR nor recovery of resting function after CABG. All 3/32 akinetic segments with CR before surgery showed CR after surgery, but none of them recovered resting function.

From 40/44 hypokinetic segments with CR before surgery, 36/40 had CR after surgery and 8/36 of them recovered resting function while 4/40 had neither recovery of CR nor recovery of resting function after CABG. From 4/44 hypokinetic segments without CR before surgery, 2/4 had CR after surgery and 2/4 did not, while none of them had recovered resting function.

Outcome of wall motion at baseline (resting function) in 112 left ventricular segments is demonstrated in Figure1.

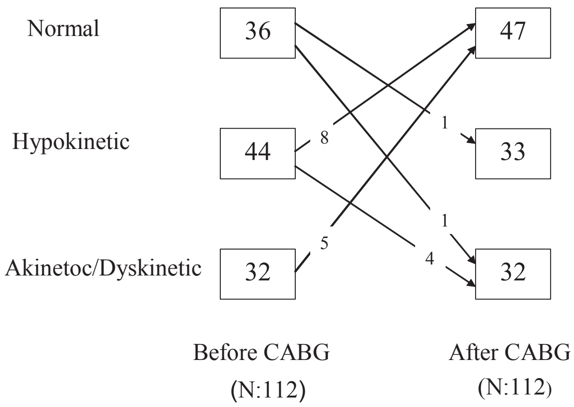

Figure1: Outcome of wall motion at baseline in 112 left ventricular segments after revascularization. The numbers in the boxes show the number of normal, hypokinetic, and akinetic/dyskinetic segments. The numbers on the arrows indicate the number of segments showing wall motion changes after coronary artery bypass grafting (CABG)

Table 3. Accuracy of dobutamine stress echocardiography for recovery of contractile reserve in 112 segments at 3 months after coronary artery bypass grafting

Accuracy	% (95%CI)
Recovery rate	27.3 (12-43)
Sensitivity	89.2 (83-96)
Specificity	82.8 (69-97)
PPV	93.7 (88-99)
NPV	72.7 (57-88)

CI, Confidence interval; NPV, Negative predictive value; PPV, Positive predictive value

Discussion

In agreement with previous reports[4,8,9] this study provides evidence to confirm high sensitivity and specificity of DSE to detect the recovery of CR in ischemic myocardium after revascularization.

It has been reported that CR is present more frequently in hypokinetic than in akinetic segments.[4] In line with this report, in our study, 90.9% of hypokinetic segments demonstrated CR before CABG and 86.4% of them showed CR after CABG. In contrast, among akinetic regions, 9.4% showed CR before CABG and 31.3% showed CR after CABG respectively.

The results of this study also indicate that the recovery rate of resting function is quite low (18%) for hypokinetic segments. This indicates that low-dose DSE is less effective in identifying improvement of resting function in hypokinetic segments that will improve function after revascularization. Possible reasons for this judgment have been explained previously.[10,11] Hypokinetic segments may contain a mixture of a considerable amount of scar tissue and some normal myocardium.[11] In this case, inotropic stimulation may provoke hypercontraction of normally perfused myocardium, thus showing a positive response. This, however, would not translate into an improvement of function after revascularization. In addition, in our study the recovery rate of akinetic segments was 15.6% and the amounts of increase in EF and decrease in WMSI were insignificant. Zaglavara et al. reported recovery rate of 52% in hypokinetic and 39% in akinetic segments and significant increase in EF (10%) 6 months after CABG. Also, they reported a significant decrease in WMSI at 6 weeks after CABG.[4] The possible reasons for these different results may be firstly, longer follow-up time of their study, and secondly, relatively long waiting list of CABG in our center (mean of 6 months). A reduction in myocardial contractility in hibernating myocardium conserves metabolic demand and may be protective, but prolonged and severe hibernation may lead to severe ultrastructural abnormalities, irreversible loss of contractile units, and apoptosis.[12]

Apparently, a relatively intact contractile apparatus is required for the demonstration of CR, and myocardial segments with advanced ultrastructural changes may not respond to dobutamine despite the presence of other markers of viability such as preserved metabolism or membrane function.[13,14] On the basis of these observations, it has been suggested that nuclear imaging may be more suitable than DSE for the assessment of myocardial viability in patients with depressed LV function and presumably more advanced myocardial ultrastructural damage.

Being able to predict early recovery in CR is of major clinical importance, particularly in patients with severely depressed LV function, because it can give an estimate of myocardial response to inotropes during the early postoperative period and, thus, an indication of early postoperative and in-hospital morbidity and mortality.[15]

Severely depressed LV ejection fraction and worse functional status independently increase the risk of CABG.[16] In these patients, the decision for CABG must balance the perioperative risk against the benefit of long-term functional improvement in the presence of myocardial viability. It seems that more than one method for viability detection is necessary to make the correct treatment decision in such cases. DSE may be valuable for the prediction of the early response of the hibernating myocardium to revascularization, whereas other more sensitive techniques may provide complementary information regarding long-term functional outcome. Using nuclear techniques (known to be more sensitive but less specific than DSE) in conjunction can be helpful in detecting the recovery of CR as an end point.

Conclusion

Despite acceptable sensitivity, specificity, and positive predictive value, DSE has a relatively lower negative predictive value for detecting the recovery of CR and, consequently, full extent of myocardial viability in ischemic myocardium. Further sensitive techniques like nuclear techniques may, therefore, be required to provide complementary information on long-term functional outcome.

This Study had the following limitation. We only indicated patients with severe LV impairment so that despite the relatively small number of patients, the number of dysfunctional segments was adequate to give statistical significance to the results. Because of the low percentage of women, findings may not fully apply to women, who are reported to have worse outcomes after CABG compared with men.[17]

Acknowledgment

This study was supported by Tehran Heart Center, University of Medical Sciences. We thank Dr. Mahmood Sheikh Fathollahi, for assistance with analysis; and Dr. Sirous Jahangiri and Dr. Mohammad Majd For data collection.

References

1. Diamond G, Forrester J, deLuz P, Wyatt HL, Swan HJC. Post-extrasystolic potentiation of ischemic cardiomyopathy by atrial stimulation. Am Heart J 1978;95:204-209.
2. Rahimtoola Sh. Coronary bypass surgery for chronic angina-1981: a perspective. Circulation 1982;65:225-241.
3. Rahimtoola Sh. The hibernating myocardium. Am Heart J 1989;117:211-221.
4. Zaglavara T, Karvounis HI, Haverstad R, Hasan A, Parharidis GE, Louridas GE, Dark JH, Kenny A. Dobutamine stress echocardiography is highly accurate for the prediction of contractile reserve in the early postoperative period, but may underestimate late recovery in contractile reserve after revascularization of the hibernating myocardium. J Am Soc Echocardiogr 2006;19:300-306.
5. Pasquet A, Robert A, D Hondt AM, Dion R, Melin Ja, vanoverschelde JL. Prognostic value of myocardial ischemia and viability in patients with chronic left ventricular dysfunction. Circulation 1999;100:141-148.
6. Bonow R. Identification of viable myocardium. Circulation 1996;94:2674-2678.
7. La canna G, Alfieri O, Giubbini R, Gargano M, Ferrari R, Visioli O. Echocardiography during infusion if dobutamine for identification of reversible dysfunction in patients with chronic coronary artery disease. J Am Coll Cardiol 1994;23:617-626.
8. Lombardo A, Loperfido F, Trani C, Pennestri F, Rossi E, Giordano A, Possati G, Maseri A. Contractile reserve of dysfunctional myocardium after revascularization: a dobutamine stress echocardiography study. J Am Coll Cardiol 1997;30:633-640.
9. Elhendy A Cornel JH, Van Domburg RT, Bax JJ, Roelandt JRTC. Effect of coronary artery bypass surgery on myocardial perfusion and ejection response to inotropic stimulation in patients without improvement in resting ejection fraction. Am J Cardiol 2000;86:490-494.
10. Pace L, Filardi PP, Cuocolo A, Prastaro M, Acampa W, Dellegrottaglie S, Storto G, Della Mortre AM, Piscione F, Chiariello M, Salvatore M. Diagnostic accuracy of low-dose dobutamine echocardiography in predicting post-revascularisatin recovery of fnction in patients with chronic coronary artery disease: relationship to thallium-201 uptake. Eur J Nucl Med 2001;28:1616-1622.
11. Cornel JH, Bax JJ, Elhendy A, Maat APWM, Kimman GJP. Geleijnse ML, Rambaldi R, Boersma E, Fiorettip PM. Biphasic Response to Dobutamine Predicts Improvement of Global Left Ventricular Function After Surgical Revascularization in Patients With Stable Coronary Artery Disease, Implications of Time Course of Recovery on Diagnostic Accuracy. J Am Coll Cardiol 1998;31:1002–1010.
12. Morrow DA, Gersh BJ, Braunwald E. Chronic coronary artery disease. In: Zipes DP, Libby P, Bonow RO, Braunwald E, eds. Braunwald's Heart Disease: a text book of cardiovascular medicine. 7th ed. Philadelphia: Elsevier Sanders; 2005. p. 1281-1335.
13. Camici PG, Wijns W, Borgers M, De Silva R, Ferrari R, Knuuti J, Lammertsma AA, Liedtke AJ, Paternostro G, and Vatner SF. Pathophysiological mechanisms of chronic reversible left ventriculay dysfunction due to coronary artery disease (hibernating myocardium). Circulation 1997;96:3205-3214.
14. Baumgartner H, Porenta G, Lau YK, Wutte M, Klaar U, Mehrabi M, Siegel RJ, Czernin J, Laufer G, Sochor H, Schelbert H, Fishbein MC, Maurer G. Assessment of myocardial viability by dobutamine echocardiography, positron emission tomography and thalium-201 SPECT: correlation with histopathology in expanded hearts. J Am Coll Cardiol 1998;32:1701-1708.
15. Redwod SR, Ferrari R, and Marber MS. Myocardial hibernation and stuning from physiological principles to clinical practice. Heart 1998;80:218-222.
16. Pagano D, Townend JN, and Bonser RS. What is the role of revascularization in ischemic heart failure? Heart 1999; 81: 8-9.
17. Pepine CJ. Ischemic heart disease in women: facts and wishful thinking. J Am Coll Cardiol 2004; 43:1727-1730.