Original Research

Comparison Between Dobutamine Stress Echocardiography and Myocardial Perfusion Scan to Detect Viable Myocardium in Patients with Coronary Artery Disease and Low Ejection Fraction

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Introduction: Dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) are commonly used to detect viable myocardium. We designed this study to compare the results of these two methods in detecting myocardial viability.

Methods: We studied 736 segments from 46 patients (42 men, mean age 56 years), with coronary artery disease and impaired left ventricular systolic function (ejection fraction <40%), using low-dose DSE and ^{99m}Tc-sestamibi MPS. The two methods were compared in the detection of viability, primarily in dysfunctional and secondarily, in different anatomical segments.

Results: Of the 736 segments, 397 (53.9%) were normal or mildly hypokinetic and 339 (46.1%) dysfunctional. Of 49 severely hypokinetic segments, 33 (67.4%) were viable and 1 (2%) nonviable according to both methods, while discordant results were found in 15 (30.6%). Among 274 akinetic segments, both methods were concordant in 148 (54%) nonviable and 15 (5.5%) viable regions, while 111 (40.5%) segments showed discordance. Of 16 aneurysmal segments, 7 were viable according to MPS, but none showed contractile reserve on DSE. The two methods were concordant in 14.2% viable, 46.6% nonviable and discordant in 39.2% of all dysfunctional segments. Eighty-seven percent (98/113) of akinetic and 20% (8/41) of hypokinetic segments had ^{99m}Tc-sestamibi uptake, but did not show contractile reserve. There was more than 75% agreement in lateral basal, anterior apical and inferior apical segments.

Conclusion: The proportion of segments showing a positive response to dobutamine is significantly lower than those with technetium uptake. This suggests that the cellular mechanisms responsible for a positive inotropic response to adrenergic stimulation required a higher degree of myocyte functional integrity than those responsible for ^{99m}Tc-sestamibi uptake.

Low dose dobutamine stress echocardiography (DSE) and the myocardial perfusion scan (MPS) have been used to identify viable dysfunctional myocardium in patients with coronary artery disease and a low ejection fraction.[1-5] Both techniques can detect coronary artery disease and provide prognostic information,[1-5] thus guiding patient management decisions.[6,7]

Schinkel et al reviewed 17 direct comparative studies with different settings that used stress echocardiography and perfusion imaging in the same patients.[8] The

study suggested that both techniques are useful in evaluating patients with chronic coronary artery disease, although small differences between their accuracy exist in different settings. To assess myocardial viability after acute infarction, the modalities seem to be equally sensitive, whereas stress echocardiography is the more specific test.[9-12] In patients with chronic ischemic ventricular dysfunction, nuclear imaging has a high sensitivity for the detection of viable myocardium and a low specificity, whereas the converse is true for stress echocardiography.[13-16]

The aim of this study was to assess the agreement and disagreement between the two methods in detecting viable myocardium, in either dysfunctional or different anatomical segments.

Methods

Forty-six consecutive patients (42 men, 4 women, mean age 56.39 ± 10.52 years) with chronic coronary artery disease (CAD) and impaired left ventricular systolic function (ejection fraction, EF <40% at rest) were evaluated by DSE and ^{99m}Tc-sestamibi tomography for the assessment of myocardial viability. All patients had CAD documented by angiography and the EF reported by angiography was used to select patients. The mean ejection fraction for the study group was 29 ± 9% (range 13-40%). The two studies were performed a maximum of 2 weeks apart.

Dobutamine stress echocardiography

Beta-blockers, calcium antagonists and nitrates were discontinued in patients at least 2 days before DSE. Echocardiography was performed with a 3.5 MHz transducer (VIVID 3 GE) under resting conditions and during each dobutamine infusion step. After baseline echocardiography, dobutamine infusion was administered using a mechanical pump. Dobutamine was delivered intravenously beginning at 5 μg/kg/min for three minutes, increasing by 5 μg/kg/min increments every three minutes until it reached 15 μg/kg/ min for an additional three minutes. Blood pressure was measured periodically, and the 12-lead ECG was continuously monitored throughout the study and during the recovery phase. Grounds for termination of the infusion were a severe hypotensive or hypertensive response, significant arrhythmias, prolonged angina, significant electrocardiographic changes, appearance of new wall motion abnormalities in at least two segments, achievement of 85% of the maximum age-predicted heart rate, or completion of the protocol. Echocardiographic images were analyzed off-line and a 16-segment model was used, as suggested by the American Society of Echocardiography.[17] The anatomical segments of the 16-segmental model are shown in Figure 1. Segmental wall motion at rest was scored on a four-point scale: 1. normal or mildly hypokinetic; 2. severely hypokinetic (decreased endocardial excursion and systolic wall thickening); 3. akinetic (absence of endocardial excursion and systolic wall thickening); and 4. dyskinetic or aneurysmal (paradoxical outward movement in systole).[18]

Demonstration of wall thickening in a previously akinetic segment or normalization of thickening in a previously hypokinetic segment were considered as criteria of myocardial viability.[19] A dysfunctional left ventricular segment was considered to have contractile reserve if infusion of dobutmine at 10 or 15 μg/kg/min resulted in an improvement in contractile function of at least one grade.

Myocardial perfusion scan

Myocardial single photon emission computed tomography (SPECT) was applied only at rest. After an overnight fast, patients underwent qualitative, semiquantitative and quantitative SPECT, following intravenous administration of 20 mCi ^{99m}Tc-sestamibi under resting condition. Two tablets of sublingual nitroglycerin (TNG) equal to 0.8 mg of TNG were taken by patients 5 minutes prior to ^{99m}Tc-sestamibi injection. Computed tomography images were acquired one hour after infusion of the radiotracer.

Image acquisition was achieved with an Adoc dual head gamma camera without attenuation or scatter correction, using a low energy, all-purpose collimator and applying 180° SPECT. Transaxial tomograms were reconstructed: for each patient, six short-axis, three horizontal and three vertical long-axis slices were analyzed. A total of 16 myocardial segments per patient were studied. These segments were matched with the 16 segments evaluated by DSE. Tomographic views were analyzed by an experienced observer, who was unaware of the clinical data and echocardiograms. In each patient, two consecutive slices from the short axis series and two from the horizontal and vertical long axis series were selected from each set of images for visual analysis. Segments with a severe reduction of ^{99m}Tc-sestamibi activity (uptake below 50% of maximum uptake) were considered nonviable and all other segments

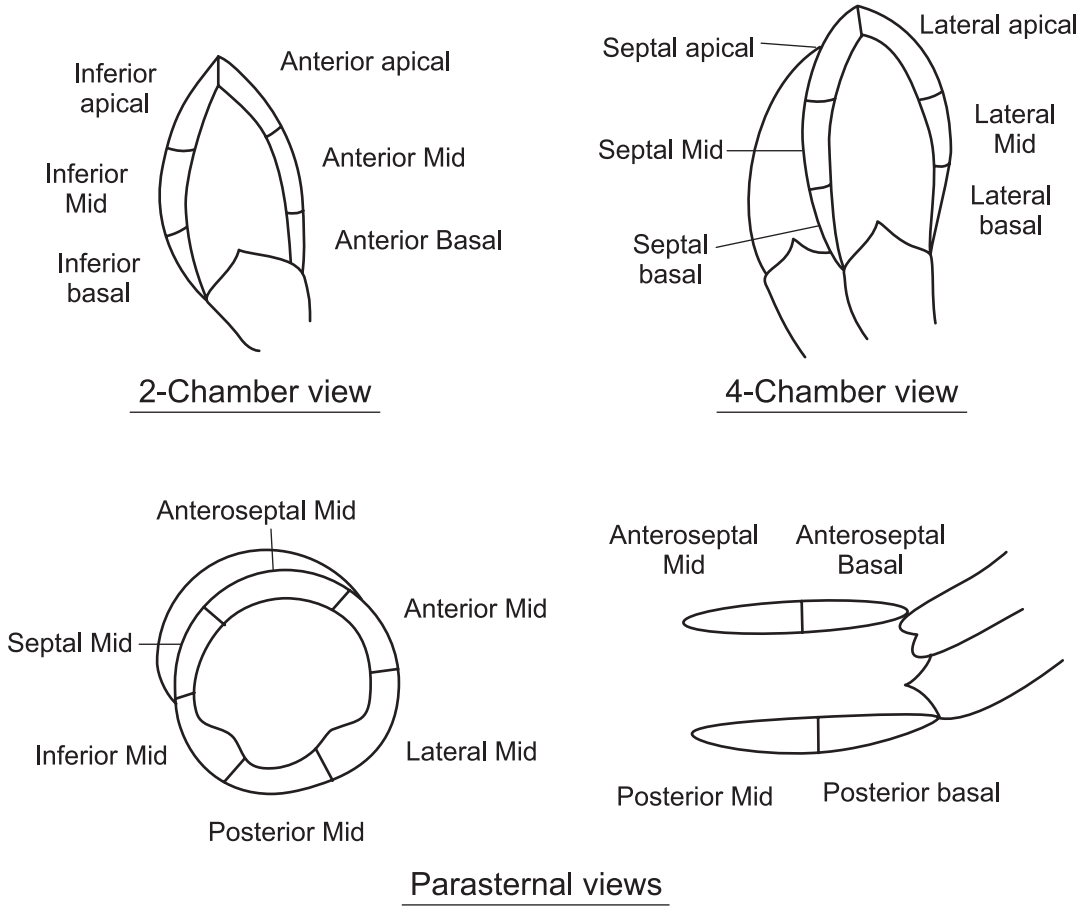

Figure 1. The anatomical segments in the 16-segmental model.

were considered viable. Uptake was measured semi-quantitatively based on the visual interpretation of color scale.

Statistical analysis

Continuous variables are expressed as mean ± SD. The Mc Nemar test was used in the analysis of discordant ^{99m}Tc-sestamibi tomography and DSE. The correlation between the two tests for the assessment of myocardial segment viability was expressed as percent agreement and value of Kappa (κ). We used the following grading system to evaluate agreement rate: poor agreement, a κ of 0.4 or less; moderate agreement, κ of 0.41 to 0.60; good agreement, κ of 0.61 to 0.80 and excellent agreement, κ greater than 0.80. If the value of κ was zero, we reported no agreement. A p-value <0.05 was considered statistically significant.

Results

A total of 736 myocardial segments from the 46 patients were evaluated. Regional contractile function, as assessed by resting two-dimensional echocardiography, demonstrated normal or mildly hypokinetic contraction in 397 (53.9%) segments and abnormal contraction in 339 (46.1%) segments. We excluded the 397 normal or mildly hypokinetic segments. The remaining 339 dysfunctional regions were included in further analysis. Of the 339 dysfunctional segments, 49 (6.7% of total) were severely hypokinetic at rest, 274 (37.2% of total) were akinetic, and 16 (2.2% of total) were aneurysmal.

Stress echocardiography findings

Of the 339 dysfunctional segments, 68 (20.1%) were viable and 271 (79.9%) nonviable by DSE. Viability was

found in 28/274 (10.2%) akinetic and 40/49 (81.6%) severely hypokinetic regions. All 16 aneurysmal segments were nonviable.

Perfusion scan findings

Of the 339 dysfunctional segments, 161 (47.5%) were viable and 178 (52.5%) nonviable. Results of resting two-dimensional echocardiography and MPS showed that 113/274 (41.2%) of akinetic, 41/49 (83.7%) of severely hypokinetic and 7/16 (43.8%) of aneurysmal regions were viable.

Concordance and discordance between methods

The two methods were concordant in 14.2% viable and 46.6% nonviable segments, and were discordant in detecting viability in 39.2% of segments. The Kappa value of 0.191 showed poor agreement between the two. Table 2 shows viability detected by DSE and MPS in hypokinetic, akinetic and aneurysmal segments. In the viability assessment of 49 severely hypokinetic segments, the two methods were concordant in 33 (67.4%) viable and 1 (2%) nonviable segments, whereas they were discordant in 15 (30.6%). Of 41 hypokinetic viable segments by MPS, 8 (20%) did not show contractile reserve by DSE. The agreement rate in these segments was 69.3%, $\varkappa$=0.060. In the detection of viability of 274 akinetic segments, both methods were concordant in 15 (5.52%) viable and 148 (54%) nonviable segments, but discordant in 111 (40.5%) segments. The number of segments with resting wall motion abnormality that were considered viable by ^{99m}Tc-sestamibi was significantly greater than the number of segments showing a contractile improvement in response to dobutamine (47.5% versus 20.1%, respectively; p<0.0001) (Table 1). Of 113 akinetic segments that were viable by MPS, 98 (87%) did not show contractile reserve by DSE. The agreement rate was also low among akinetic segments (59.3%, $\varkappa$=0.059). The agreement rate in detecting viability in 16 aneurysmal segments was 56.3% (all nonviable by DSE and 9 nonviable by MPS). A comparison between DSE and MPS in the detection of viability of different functioning segments is shown in Table 3. Of 40 hypokinetic segments with a positive response to dobutamine 17.5% (7/40) did not show ^{99m}Tc-sestamibi uptake, while of 28 akinetic segments with contractile reserve 46% (13/28) had no tracer uptake.

With respect to detecting viability in different anatomical segments, there was more than 75% agreement in lateral basal, anterior apical and inferior apical segments, but the value was lower in other anatomical segments.

Table 1. Viability detected by dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in all dysfunctional segments.

	DSE	MPS
Viability	68/339 (20.1%)	161/339 (47.5%)
Non viability	271/339 (79.9%)	178/339 (52.5%)

Table 2. Viability detected by dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in hypokinetic, akinetic and aneurysmal segments.

	Viable ratio (%)	
DSE akinetic	28/274	(10.2%)
DSE hypokinetic	40/49	(81.6%)
DSE aneurysmal	0/16	(0%)
MPS akinetic	113/274	(41.2%)
MPS hypokinetic	41/49	(83.7%)
MPS aneurysmal	7/16	(43.8%)

Discussion

In patients with severe CAD and a low EF, the assessment of residual viability in regions with chronic contractile dysfunction is important for predicting improvement of function after revascularization. This study focused on a direct comparison between two widely used methods: dobutamine stress echocardiography and ^{99m}Tc-sestamibi imaging for the assessment of viable myocardium.

In our study, a head-to-head comparison of the individual segments showed that the agreement rate between the two methods was 60.8%, with a disagreement

Table 3. Comparison between dobutamine stress echocardiography (DSE) and myocardial perfusion scan (MPS) in the detection of viability of different functioning segments.

		Agreement rate%		
Segments	Number	Viable	Non viable	Kappa
Severely hypokinetic	49	67.3	2.0	0.067
Akinetic	274	5.5	54.8	0.059
Aneurysmal	16	0	56.3	*

*Kappa was not calculated, because all aneurysmal segments were nonviable by DSE.

rate of 39.2%. Similar results have been reported previously.[18,20] Panza et al reported 68% agreement between DSE and thallium scan and Bax et al found 72% agreement between DSE and technetium scan.

We observed discordance between the two methods more frequently in akinetic segments that were viable by ^{99m}Tc-sestamibi imaging, but did not show contractile reserve by DSE (98/113 akinetic segments). Similar results were reported by Panza et al,[20] who compared ^{201}thallium imaging with dobutamine echocardiography and showed that a large number of segments demonstrated ^{201}thallium uptake but lacked contractile reserve. Of the 138 myocardial segments without contractile improvement shown by dobutamine, 95 (69%) had normal, or mildly to moderately reduced thallium uptake and were therefore considered viable by thallium imaging. The authors suggested that these findings emphasized the difference in the mechanisms involved in the identification of myocardial viability by the two techniques; the cellular processes responsible for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for thallium uptake.

Studies comparing metabolic imaging with FDG (fluorin-18 fluorodeoxyglucose) by dobutamine echocardiography[21-23] to assess contractile reserve have also shown compatible results. Baer et al[21] reported that dobutamine stimulation underestimates the number of segments with preserved FDG uptake. Sawada et al[23] also reported a substantial percentage of the segments with FDG uptake (19%) that did not exhibit contractile reserve; thus, the amount of viable tissue required to determine the presence of metabolic activity is likely to be less than that required for detection of contractile reserve. Bax et al[18] demonstrated that segments with both perfusion and contractile reserve have the least damage and fibrosis, while segments with perfusion but without contractile reserve have more damage/fibrosis, and segments lacking both perfusion and contractile reserve have the most severe damage/fibrosis. Our data confirm the fact that the number of akinetic segments considered viable by ^{99m}Tc-sestamibi under resting conditions is significantly greater than the number of those segments showing a contractile improvement in response to dobutamine.

We observed that 5.3% (20/374) of dysfunctional segments showed contractile reserve according to DSE, but did not show technetium uptake. Similarly, Panza et al reported 2% (6/311) of dysfunctional segments with similar presentation, but they explained this observation by the error inherent in the comparison of the two techniques, including poor anatomic correspondence of left ventricular segmentation in some patients. We think that this is more likely attributable to areas with non-transmural myocardial infarction, as explained by Armstrong.[24] He argued that at a threshold of infarction of ~20% transmurality, rest function could be anticipated to be markedly abnormal. However, as 80% of the wall thickness is viable (due to the hibernating or normal myocardium), augmentation with low-dose dobutamine would result in improved function in that region. On the other hand, because the spatial resolution of radionuclide imaging techniques is not sufficient to determine myocardial thickness accurately, non-transmural myocardial infarction cannot be reliably detected on the basis of scintigraphic anatomy. On the basis of assumed kinetics of thallium activity, non-transmural infarction should be manifest as reduced overall wall activity.[24] Discordance between the two methods in aneurysmal segments cannot be explained by this concept and could probably be attributed to the poor anatomic correspondence of left ventricular segmentation in some patients.

Although, at the moment, the most cost-effective imaging techniques to detect reversible contractile function are stress echocardiography and nuclear perfusion imaging, the use of newly developed echocardiography techniques such as tissue Doppler imaging during DSE has increased the sensitivity and specificity of echocardiography for detecting viability.[25]

The most important limitation of this study was that we could not follow our patients after coronary artery bypass surgery. Echocardiographic findings after revascularization could help us to determine the specificity and sensitivity of each method. A second limitation arises from the concept that, although a similar 16-segment model was used for DSE and SPECT data, misalignment may have influenced the results.

Conclusions

There is a relation between ^{99m}Tc-sestamibi uptake and the presence of contractile reserve on DSE in patients with chronic coronary artery disease and left ventricular dysfunction. However, the proportion of segments with preserved technetium uptake is significantly greater than those showing a positive re-

sponse to dobutamine. This suggests that the cellular mechanisms responsible for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for ^{99m}Tc-sestamibi uptake. The small number of segments with contractile reserve on DSE and without tracer uptake on perfusion scanning may be explained by the non-transmurality of myocardial infarction.

References

1. Pozzoli MMA, Fioretti PM, Salustri A, et al. Exercise echocardiography and technetium 99m MIBI single photon emission computed tomography in the detection of coronary artery disease. Am J Cardiol. 1991; 67: 350-355.
2. Günalp B, Dokumaci B, Uyan C, et al. Value of dobutamine technetium-99m-sestamibi SPECT and echocardiography in the detection of coronary artery disease compared with coronary angiography. J Nucl Med. 1993; 34: 889-894.
3. Amanullah AM, Bevegard S, Lindvall K, et al. Assessment of left ventricular wall motion in angina pectoris by two-dimensional echocardiography and myocardial perfusion by technetium-99m sestamibi tomography during adenosine-induced coronary vasodilatation and comparison with coronary angiography. Am J Cardiol. 1993; 72: 983-989.
4. Forster T, McNeill AJ, Salustri A, et al. Simultaneous dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computed tomography in patients with suspected coronary artery disease. J Am Coll Cardiol. 1993; 21: 1591-1596.
5. Senior R, Sridhara BS, Anagnostou E, et al. Synergistic value of simultaneous stress dobutamine sestamibi single-photon emission computerized tomography and echocardiography in the detection of coronary artery disease. Am Heart J. 1994; 128: 713-718.
6. Geleijnse ML, Elhendy A, Van Domburg RT, et al. Cardiac imaging for risk stratification with dobutamine atropine stress testing in patients with chest pain. Circulation. 1997; 96: 137-147.
7. Brown KA. Do stress echocardiography and myocardial perfusion imaging have the same ability to identify the low-risk patient with known or suspected coronary artery disease? Am J Cardiol. 1998; 81: 1050-1053.
8. Schinkela AFL, Bax JJ, Geleijnsea ML, et al. Noninvasive evaluation of ischaemic heart disease: myocardial perfusion imaging or stress echocardiography? Eur Heart J. 2003; 24: 789-800.
9. Elhendy A, Trocino G, Salustri A, et al. Low-dose dobutamine echocardiography and rest-redistribution thallium-201 tomography in the assessment of spontaneous recovery of left ventricular function after recent myocardial infarction. Am Heart J. 1996; 131: 1088-1096.
10. Le Feuvre C, Baubion N, Aubry N, et al. Assessment of reversible dyssynergic segments after acute myocardial infarction: dobutamine echocardiography versus thallium-201 single photon emission computed tomography. Am Heart J. 1996; 131: 668-675.
11. Smart SC, Stoiber T, Hellman R, et al. Low dose dobutamine echocardiography is more predictive of reversible dysfunction after acute myocardial infarction than resting single photon emission computed tomographic thallium-201 scintigraphy. Am Heart J. 1997; 133: 822-834.
12. Spinelli L, Petretta M, Cuocolo A, et al. Prediction of recovery of left ventricular dysfunction after acute myocardial infarction: comparison between 99mTc-sestamibi cardiac tomography and low-dose dobutamine echocardiography. J Nucl Med. 1999; 40: 1683-1692.
13. Sicari R, Varga A, Picano E, et al. Comparison of combination of dipyridamole and dobutamine during echocardiography with thallium scintigraphy to improve viability detection. Am J Cardiol. 1999; 83: 6-10.
14. Qureshi U, Nagueh SF, Afridi I, et al. Dobutamine echocardiography and quantitative rest-redistribution 201Tl tomography in myocardial hibernation. Relation of contractile reserve to 201Tl uptake and comparative prediction of recovery of function. Circulation. 1997; 95: 626-635.
15. Pagano D, Bonser RS, Townend JN, et al. Predictive value of dobutamine echocardiography and positron emission tomography in identifying hibernating myocardium in patients with postischaemic heart failure. Heart. 1998; 79: 281-288.
16. Kostopoulos KG, Kranidis AI, Bouki KP, et al. Detection of myocardial viability in the prediction of improvement of left ventricular function after successful coronary revascularization by using dobutamine stress echocardiography and quantitative SPECT rest-redistribution-reinjection 201Tl imaging after dipyridamole infusion. Angiology. 1996; 47: 1039-1046.
17. Schiller NB, Shah PM, Crawford M, et al. Recommendation for quantification of the ventricle by two-dimensional echocardiography. J Am Soc Echocardiogr 1989: 2; 358-367.
18. Bax JJ, Poldermans D, Schinkel AFL, et al. Perfusion and contractile reserve in chronic dysfunctional myocardium: relation to functional outcome after surgical revascularization. Circulation. 2002; 106 (suppl I): I14-I18.
19. Zaglavara T, Karvounis HI, Haverstad R, et al. 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.
20. Panza JA, Dilsizian V, Laurienzo JM, et al. Relation between thallium uptake and contractile response to dobutamine: implications regarding myocardial viability in patients with chronic coronary artery disease and left ventricular dysfunction. Circulation. 1995; 91: 990-998.
21. Baer FM, Voth E, Deutsch HJ, Schneider CA, Schicha H, Sechtem U. Assessment of myocardium by dobutamine transesophageal echocardiography and comparison with fluorin-18 fluorodeoxyglucose positron emission tomography. J Am Cardiol. 1994; 24: 343-353.
22. Sun KT, Czernin J, Krivokapich J, et al. Myocardial disease:

effects of dobutamine stimulation on myocardial blood flow, glucose metabolism, and wall motion in normal and dysfunctional myocardium. Circulation. 1996; 94: 3146-3154.
23. Sawada S, Elsner G, Segar DS, et al. Evaluation of patterns of perfusion and metabolism in dobutamine-responsive myocardium. J Am Coll Cardiol. 1997; 29: 55-61.
24. Armstrong WF. "Hibernating" myocardium: asleep or part dead? J Am Coll Cardiol. 1996; 28: 530-535.
25. Aggeli C, Giannopoulos G, Roussakis G, et al. Pre-ejection tissue-Doppler velocity changes during low dose dobutamine stress predict segmental myocardial viability. Hellenic J Cardiol. 2007; 48: 23-29.