Effects of coronary collateral vessels in left ventricular segmental motions and myocardial viability using color kinesis dobutamine stress echocardiography

Ersan Tatli, MD, Huseyin Surucu, MD, Erkan Oztekin, MD, Abdullah Ulucay, MD, Fatih Ozcelik, MD, Orhan Ozer, MD, Meryem Aktoz, MD.

ABSTRACT

Objective: To detect the functional importance of coronary collaterals, which develop after acute myocardial infarctions (AMI).

Methods: Forty patients with acute AMI whose coronary angiography demonstrated a total occlusion of the left anterior descendant (LAD) artery were included in the study, between January 2003 and June 2004. All of the study patients underwent coronary angiography and left ventriculography using standard Judkins techniques (Phillips Integris-3000). Left ventricular (LV) free walls were divided into 5 segments, and all of these segments motions were evaluated then LV free wall motion score index (WMSI) was calculated. The study patients were divided into 2 groups: good (Rentrop 3; group I; n = 14) and poor coronary collateral circulation (Rentrop 0-2; group II; n = 26) according to the Rentrop grading. Then, color kinesis dobutamine stress echocardiography (CK-DSE) was performed to all patients with standard techniques 6 weeks after AMI.

Results: There were no significant differences for age, gender, risk factors for the coronary artery disease and use of the fibrinolytic therapy between the groups. There were no significant statistical differences for angiographic WMSI, left ventricular ejection fraction (LVEF), end-diastolic volume, end-systolic volume and end-diastolic pressures between the 2 groups. No difference was detected between Group I and II for initial EF, WMSI and peak dose WMSI in CK-DSE procedure. Viability was determined in all of the 14 patients in group I (100%) and 12 of 26 patients in group II (46%) (p=0.03).

Conclusion: In early periods of an AMI genesis of the coronary collateral circulation does not affect left ventricular global and regional systolic functions, but increase viability quite significantly. According to our findings early revascularization could be carried out in patients with good coronary collateral circulation without doing any test for viability.

Saudi Med J 2006; Vol. 27 (10): 1468-1472

In normal human being's heart there are plenty of small anastomotic vessels, which connect major coronary arteries to each other.[1] Much of them are intramural and subendocardial.[2] Because of their sizes (<200 microne) and the small amount of blood they carry they cannot be visible at coronary angiography in patients with mild coronary artery disease and normal coronary arteries. Physical causes (pressure gradient between open and occluded coronary arteries) such as coronary occlusion, anemia, chronic

From the Department of Cardiology, Trakya University School of Medicine, Edirne, *Turkey.*

Received 25th May 2006. Accepted for publication in final form 28th June 2006.

Address correspondence and reprint request to: Dr. Ersan Tatli, Department of Cardiology, Trakya University School of Medicine, Edirne, *Turkey.* E- mail: ersantatli@hotmail.com/ersantatli@yahoo.com

hypoxia, acute myocardial infarctions (AMI) and a series of chemical causes (myocardial cells those exposed to ischemia release angio-genetic and growth factors) result in the development of collateral vessels which can be visible angiographically.[3-8] The progress of coronary collateral circulation after an AMI is a process related to the time. Coronary collateral flow in first 6 hours of an AMI could be determined in only 16% of patients and only 5% of them are in sufficient degree. Collateral circulation could be determined in 62% of patients and only 38% of them are in adequate degree 1-13 days after AMI. These proportions are 85-95% and 75% respectively for the days 14-45. Coronary angiographies those performed after 45 days of AMI show similar results for collateral circulation.[9-11] It has been suggested in some studies that well developed coronary collateral circulation could decrease myocardial ischemia in the early period of AMI, protect left ventricular (LV) systolic function by limiting infarct extension, and reduce mortality. However, in another studies it has been suggested that well developed collateral circulation could have no effect on mortality and morbidity. Moreover, it may be increase mortality long term.[12-20] In our study, we aimed to study the effects of coronary collateral circulation's on LV global and regional systolic functions, and viability with coronary angiography, and color kinesis dobutamine stress echocardiography (CK-DSE) in patients with AMI.

Methods. Forty patients with acute anterior myocardial infarctions (MI) whose coronary angiography demonstrated total occlusion of the left anterior descendant (LAD) artery were included in the study, between January 2003 and June 2004. Patient with previous MI, permanent pacemaker, valve disease, cardiomyopathy, pre-excitation, intraventricular conduction delay, LV hypertrophy, rhythm disturbances, unstable angina pectoris, decompensated heart failure, severe hypertension and LV thrombus were excluded from the study. The diagnosis of AMI was defined as typical rise and fall of creatine kinase-MB (CK-MB), a biochemical markers of myocardial necrosis with symptoms of myocardial ischemia and ST segment elevation greater than 0.1 mV, in at least 2 contiguous leads, or new or presumably new left bundle branch block (LBBB) on the presenting electrocardiogram (ECG). Written informed consent was obtained from all study patients and the Local Ethics Committee approved the study protocol.

Angiography. Coronary angiography was performed in all study patients with standard Judkins techniques. This procedure was performed in an average of 14.3 days after AMI. The right anterior oblique view was used to assess the end-diastolic and end-systolic volumes, and left ventricular ejection fraction (LVEF) with digital marking technique. Ventriculography proceeded once a stable rhythm was present. Before ventriculography, LV end-diastolic pressure was obtained. Left ventricular wall on the ventriculography was divided into 5 segments digitally (anterobasal, anterolateral, apical, inferior and posterobasal) and segmental wall motions were assessed automatically. The points for each segment (normokinetic = 1, hypokinetic = 2, severe hypokinetic = 3, akinetic = 4, dyskinetic = 5, aneurysm = 6) were added and then divided into the number of segments. Thus, angiographic LV WMSI was calculated.[21] The study patients were divided into 2 groups: good (Rentrop 3 = group I; n = 14) and poor coronary collateral circulation (Rentrop 0-2; group II; n = 26) according to the Rentrop grading.[4] Color kinesis dobutamine stress echocardiography was performed to all patients after 6 weeks of AMI. We stopped the medications 5 days before the test for those patients affected with the test such as digitalis, nitrates, ß-blockers, and angiotensin converting enzyme inhibitors. Echocardiographic images were digitized at rest and at low dosage (5 to 10 μg kg/dk), peak dosage (5-40 μg kg/dk), and after the stress with the aid of Hewlett Packard Sonos-2500. End points included 85% of age predicted maximum heart rate (APMHR), angina, arrhythmias, marked hypertensive or hypotensive responses or development of large wall motion abnormality. Regional wall motions of the 9 segments of LAD territories were assessed with the 16 segment model outlined by the American Society of Echocardiography according to the principals of CK-DSE at rest, low dosage, peak dosage and after the stress by 2 different observers. According to the color histogram end-systolic with blue color was defined as normokinesia, green was hypokinesia, yellow or orange was akinesia, and red color was dyskinesia. Then, a score index was used from 1-4. Akinetic and dyskinetic segments were accepted as asynergic segments. Echocardiographic WMSI was calculated by adding the points for each segment divided by the numbers of segments. Improvement of a resting wall motion abnormality with low dose dobutamine was appreciated as viability. In some studies, it has been suggested that CK-DSE was superior to 2-dimensional echocardiography (lower interobserver variability and higher sensitivity and specificity) in evaluating wall motions.[22-24]

Statistical analysis. For interval variables, we used t test or Mann-Whitney U test to compare the frequencies between the groups using Chi-square

or Fischer test. A *p* value of <0.05 was considered statistically significant.

Results. There were no differences between the groups of coronary artery disease risk factors such as age, genders, hypertension, diabetes mellitus, cigarette smoking, family history of coronary artery disease, hyperlipidemia and usage of fibrinolytic agents. Preinfarction history of angina was present in 10 of 14 patients (71%) in group I and 12 of 26 patients (46%) in group II (p=0.003). There were no statistical differences between the groups for angiographic WMSI (2.3 ± 0.4, 2.5 ± 0.3; *p*>0.05), ejection fraction (EF) (41 ± 6%, 44 ± 5%; p>0.05), end-systolic volume (81±19, 82±15; *p*>0.05), end-diastolic volume (89 ± 19, 139 ± 17; *p*>0.05), end-diastolic pressures (21 ± 3, 27 ± 3; *p*>0.05) (**Table 1**). Before dobutamine infusion, in resting phase there were 39 dysfunctional and 24 normokinetic segments in group I, and 75 dysfunctional and 42 normokinetic segments in group II. There was no significant statistical difference between the 2 groups in resting phase (*p*>0.05). After low dose dobutamine infusion, 21 of 39 segments motion in group I and 20 of 72 segments motion in group II improved (viable segments). The proportion viable segment in group I was more than in group II, and that was statistically significant (*p*=0.01). After high dose dobutamine infusion, 3 of improved segments in group I and none of improved segments in group II became normogenetic (*p*>0.05). In other words, there were 3 stunned and 18 hibernating myocardial segments in group I, and no stunned segments in group II. In analysis of normokinetic segments, decreased myocardial function (severe ischemia) was seen in one of 24 segments in group I and 9 of 42 segments in group II after low dose dobutamine infusion (*p*>0.05). After a high dose dobutamine infusion, a decreased in myocardial function was seen in 21 of 24 segments in group I and all of the segments in group II (*p*>0.05). There was no significant statistical difference in groups for resting EF (39% versus 41%; *p*>0.05), resting WMSI (2.1±0.2 versus 2.1±0.1; *p*>0.05) and peak dose WMSI (2.4±0.1 versus 2.8±0.1; *p*>0.05). However, low dose WMSI was significantly lower in group I (1.5±0.1 versus 2.1±0.1; *p*=0.02). Viability

Table 1 - Angiographic parameters.

Angiographic parameters	Group I n =14	Group II n = 26	*P* value
Angiographic WMSI	2.3 ± 0.4	2.5 ± 0.3	NS
Ejection fraction (%)	41 ± 6	45 ± 4.8	NS
End-diastolic volume	90 ± 9	139 ± 17	NS
End-diastolic pressure	21 ± 3	27 ± 3	NS
End-systolic volume	81 ± 19	82 ± 15	NS

WMSI - wall motion score index, NS - not significant, Data are expressed as mean (±SD).

Table 2 - Results of echocardiography.

Echocardiographic parameters	Group I n = 14	Group II n = 26	*P* value
Resting ejection fraction (%)	39 ± 1.7	41 ± 1.3	NS
Patients (+) for viability	14/14 (100)	12/26 (46)	0.03
Mean viable segments number	4 ± 0.7	1.6 ± 0.4	0.01
Resting asynergic segments number	2.4 ± 0.9	3.1 ± 0.1	NS
Low dose asynergic segments number	1 ± 0.6	2.9 ± 0.6	0.05
Peak dose asynergic segments number	3.6 ± 0.8	5.5 ± 0.8	NS
Resting WMSI	2.1 ± 0.2	2.1 ± 0.1	NS
Low dose WMSI	1.6 ± 0.1	2.1 ± 0.1	0.02
Peak dose WMSI	2.4 ± 0.1	2.8 ± 0.1	NS

WMSI - Wall Motion Score Index, NS - not significant, Data are expressed as mean (±SD).

was positive for 12 of 26 patients in group II (46%) and all of 14 patients in group I (100%) (p=0.03). Viable segments mean was higher significantly in group I than group II (4 ±0.7 versus 1.6 ± 0.4; *p*=0.01). Resting (2.4 ± 0.9 versus 3.1±0.1; *p*>0.05) and peak dose (3.6 ± 0.8 versus 5.5 ± 0.8; *p*>0.05) asynergic segments mean was similar between groups. Results were summarized in **Table 2**.

Discussion. Fujita et al[10] and Schwarts et al[23] reported that development of sufficient coronary collateral flow was time dependent and in first 6 hours of AMI it could be determined in 5% of patients. For the days between 1 and 13, and after 14th day, the reported proportions were 38% and 56%. In the present study, coronary angiography was performed in the 14th day of AMI and good collateral flow was determined in 35% of patients. After the first 4 weeks of an acute coronary obstruction, the collateral resistance decrease quickly and collateral circulation reach to 90% of its maximum capacity.[24,25] Many studies reported that preinfarction angina induce collateral formation and in patients with preinfarction angina collateral formation is better.[26-28] In our study, preinfarction angina was present in 71% of patients with good collateral flow, and in 46% of patients with poor collateral flow. Several studies reported that improved collateral flow protects myocardium against risk of ischemia, limits infarction, and affects systolic functions positively in the early terms of AMI.[29-31] In the present study, angiographic global and regional systolic functions were better in patients with good collateral flow but there was no statistical difference between the groups. Some investigators have reported that collateral flow is not related to LV global and systolic functions.[3,16-18] Several methodologic studies have documented that LV wall motions could be evaluated quantitatively by Acoustic Quantification (AQ) color kinesis echocardiography method. This method reduces variations of interobserver evaluation and increases sensitivity and specificity according to the standard 2-dimensional echocardiographic method.[23-26,32-34] Acoustic Quantification color kinesis methods has been found superior to 2-dimensional echocardiography. We evaluated LV wall motions with the former method, which has not been used in any study before to evaluate the effects of coronary collateral flow on LV systolic functions and viability. Kodama et al[29] studied 21 patients with MI and found better systolic functions in patients with good collateral flow compared to patients with poor collateral flow at the end of the first month and second year. Boherer et al,[15] followed 146 patients for 3.5 years and couldn't find any difference in morbidity and mortality between patients with poor and good collateral flow. Gohle et al[19] and Jose Carlos et al,[20] reported that collateral flow has no effect on LV systolic functions. Mortality was found higher in patients with good collateral flow. They concluded that blood transported by collateral flow is not sufficient for metabolic requirements of myocytes and incapable of antegrade flow in patients with good collateral flow. They advocated that chronic ischemia persists in patients with good collateral flow and ischemic remodeling exists in these patients. In long term follow-up, there is an inverse relationship between the grade of antegrade flow and mortality and straight relationship between the grade of antegrade flow and collateral flow. In our study, to exclude the effect of the antegrade flow, only patients with total occlusions of the LAD were included in the study. The evaluation of CK-DSE at 6th week of AMI exposed higher numbers of ischemic segments of LV in patients with poor collateral flow but there was not significant difference between the groups. In both groups, global and regional systolic functions were similar. However, the mean number of viable segments, the number of patients with viability, and the sum number of viable segments was significantly higher in patients with good collateral flow. In our study, the number of patients with Reentrop 3 flow was 14 and the viability was positive in all of them. Only 12 of 26 patients whose Reentrop flow was below 3 were positive for viability. According to these findings, patients with good collateral flow may have good systolic functions in early terms of AMI but blood transmitted to LV by collaterals is not sufficient for myocytes metabolic requirements and LV functions may deteriorate because of ischemic remodeling in the course of time. However, blood transmitted by collaterals could be sufficient to maintain viability of hibernating myocardium. The major limitations of the present study are small number of subjects and short follow-up period. Subjects with total occlusion of LAD were included in the study; therefore, the number of subjects was limited. Additionally, we performed coronary angiography on the 14th day but CK-DSE was performed on the 6th week to minimize the possible effects of stunned myocardium on LV segmental motions.

Our findings suggest that collateral flow has no effect on LV global and regional systolic functions but increases viability considerably in early terms of MI. Acute myocardial infarctions patients with total occlusion and good collateral flow are positive for viability; as a result early revascularization could be performed in patients with good collateral flow without having any test for viability. Viability tests after AMI have to be preserved for patients with poor coronary flow, and decision making for revascularization could be performed, afterwards.

References

1. Levin DC. Pathways and functional significance of the coronary collateral circulation. ***Circulation*** 1974; 50: 831-833.
2. James TN. The delivery and distribution of coronary collateral circulation. ***Chest*** 1970; 58:183-204.
3. Elayda MA, Mather VS, Hall JR, Massumi GA, Garcia E, de Castro CM. Collateral circulation in coronary artery disease. ***Circulation*** 1985; 55: 58-60.
4. Rentrop KP, Cohen M, Blanke H, Phillips RA. Changes in collateral filling immediately after controlled coronary artery occlusion by angioplasty balloon in human. ***J Am Coll Cardiol*** 1985; 5: 587-592.
5. Zoll PM, Wessler S, Schlesinger MJ. Interarterial coronary anastomoses in the human heart, with particular reference to anemic and relative cardiac anoxia. ***Circulation*** 1951; 4: 797-815.
6. Lauries W, Woods J. Anastomosis in the coronary circulation. ***Lancet*** 1985; 2: 812-814.
7. Pepler W, Meyer B. Interarterial coronary anastomoses and coronary arterial pattern: a comparative study of South African Bantu and European hearts. ***Circulation*** 1976; 22: 1424-1426.
8. Eckstein R. Development of interarterial coronary anastomoses by chronic anemia. ***Circ Res*** 1995; 3: 306-310.
9. Schwartz H, Leiboff LH, Bren GH, Paya CH. Temporal evaluation of the human coronary collateral circulation after myocardial infarction. ***J Am Coll Cardiol*** 1996; 4: 1088-1093.
10. Fujita M, Sasayama S, Ohno A, Nakajima H, Asanoi H. Importance of angina for development of collateral circulation. ***Br Heart J*** 1987; 57: 139-143.
11. Cohen M, Rentrop KP. Limitation of myocardial ischemia by collateral circulation during sudden controlled coronary artery occlusion in human subjects. A prospective study. ***Circulation*** 1986; 74: 468-476.
12. Rogers WJ, Hood WP Jr, Mantle JA, Baxley WA, Kirklin JK, Zorn GL, et al. Return of left ventricular function after reperfusion in patients with myocardial infarction: importance of subtotal stenosis or intact collaterals. ***Circulation*** 1984; 69: 338-342.
13. Danchin N, Oswald T, Voiriot P, Juilliere Y, Cherrier F. Significance of spontaneous obstruction of high degree coronary artery stenoses between diagnostic angiography and later percutaneous transluminal coronary angioplasty. ***Am J Cardiol*** 1989; 63: 660-662.
14. Blanke H, Cohen M, Karsch KR, Fagerstrom R, Rentrop KP. Prevalence and significance of residual flow to the infarct zone during the acute phase of myocardial infarction. ***J Am Coll Cardiol*** 1985; 5: 587-592.
15. Boehrer JD, Lange RA, Willard JE, Hillis LD. Influence of collateral filling of the occluded infarct-related coronary artery on prognosis acute myocardial infarction. ***Am J Cardiol*** 1992; 69: 10-12.
16. Helfant RH, Kemp HG, Gorlin R. Coronary atherosclerosis, coronary collaterals and their relation to cardiac function. ***Ann Intern Med*** 1970; 73: 189-194.
17. Lavine P, Filip Z, Najmi M, Kimbiris D, Segal BL, Linhart JW. Clinical and hemodynamic evaluation of coronary collateral vessels in coronary artery disease. ***Am Heart J*** 1974; 84: 343-349.
18. Carroll R, Verani M, Falseth H. The effect of collateral circulation on segmental left ventricular contraction. ***Circulation*** 1974; 50:709-713.
19. Gohlke H, Heim E, Roskamm H. Prognostic importance of collateral flow and residual coronary stenosis of the myocardial infarct artery after anterior wall Q-wave acute myocardial infarction. ***Am J Cardiol*** 1991; 67: 1165-1169.
20. J. Carlos N, Paulo Roberto N, Macho P, Schwarze H, Sanchez G. Early infarct artery collateral flow does not improve long-term survival following thrombolytic therapy for acute myocardial infarction. ***Am J Cardiol*** 1999; 83: 21-26.
21. Braunwald E. Heart Disease. Vol. 1, 4th ed. Philadelphia: WB Saunders Company; 1992. p. 235-275.
22. Lau YS, Puryear JV, Gan SC, Fowler MB, Vagelos RH, Popp RL, et al. Assessment of left ventricular wall motion abnormalities with the use of color kinesis: A valuable visual and training aid. ***J Am Soc Echocardiogr*** 1997; 10: 665-672.
23. Schwartz SL, Cao QL, Vannan M, Pandian NG. Automatic backscatter analysis of regional left ventricular systolic function using color kinesis. ***Am J Cardiol*** 1996; 77: 1345-1350.
24. Lang RM, Vignon P, Weinert L, Bednarz J, Korcarz C, Sandelski J, et al. Echocardiographic quantitation of regional left ventricular wall motion using color kinesis. ***Circulation*** 1996; 93: 1877-1885.
25. Scaper W. The collateral circulation of the heart. New York: Elsevier; 1971.
26. Epstein SE. Influence of stenosis severity on coronary collateral development and importance of collaterals in maintaining left ventricular function during acute coronary occlusion. ***Am J Cardiol*** 1988; 61: 866-868.
27. Williams DO, Amsterdam EA, DeMaria AN, Miller RR, Mason DT. Functional significance of coronary collateral vessels in patients with acute myocardial infarction: relation to pump performance, cardiogenic shocks an survival. ***Am J Cardiol*** 1976; 18: 345-351.
28. Juilliere Y, Danchin N, Grentzinger A, Suty-Selton C, Lethor JP, Courtalon T, et al. Role of previous angina pectoris and collateral flow to preserve left ventricular function in the presence or absence of myocardial infarction in isolated total occlusion of the left anterior descending coronary artery. ***Am J Cardiol*** 1990; 65: 277-281.
29. Kodama K, Kusuoka H, Sakai A, Adachi T, Hasegawa S, Ueda Y, et al. Collateral channels that develop after an acute myocardial infarction prevent subsequent left ventricular dilatation. ***J Am Coll Cardiol*** 1996; 27: 1133-1139.
30. Visser RF, Van den Werff T, Ascoop CA, Bruschke AV. The influence of anatomic evolution of coronary artery disease on left ventricular contraction: an angiographic follow-up study of 300 non-operated patients. ***Am Heart J*** 1986; 112: 963-972.
31. Saito Y, Yasuno M, Ishida M, Suzuki K, Matoba Y, Emura M, et al. Importance of coronary collaterals for restoration of left ventricular function after intracoronary thrombolysis. ***Am J Cardiol*** 1985; 55: 1259-1263.
32. Lau YS, Puryear JV, Gan SC, Fowler MB, Vagelos RH, Popp RL, et al. Assessment of left ventricular wall motion abnormalities with the use of color kinesis: A value visual and training aid. ***J Am Soc Echocardiogr*** 1997; 10: 665-672.
33. Vitarelli A, Sciomer S, Schina M, Luzzi MF, Dagianti A. Detection of left ventricular systolic abnormalities in patient with coronary artery disease by color kinesis. ***Clin Cardiol*** 1997; 20: 927-993.
34. Vignon P, Mor-Avi V, Weinert L, Koch R, Spencer KT, Lang RM. Quantitative evaluation of global and regional left ventricular diastolic function with color kinesis. ***Circulation*** 1998; 97: 1053-1061.