Heart Mirror Journal
From Affiliated Egyptian Universities and Cardiology Centers

Vol. 3, No. 2, 2009
ISSN 1687-6652

ORIGINAL ARTICLE

Myocardial Perfusion in Patients With Total Occlusion of a Single Coronary Artery With and Without Collateral Circulation

Maged El-Gantiry[1]; Salah El-Din Hamdy Demerdash[2]; Mona Rayyan[2]; Ramy Raymond[2]; Wael El-Naggar[1]; Nabil Farag[2]; Mohamed El-Ramly[1]; Sameh Thabet[2] and Amr Hassan, MD.[3]

[1]Cardiology Department, Dar Al Fouad Hospital; [2]Cardiology Department, Ain Shams University Hospital and [3]Cardiology Department, Cairo University Hospital

Background Previous studies that investigated the effects of coronary collateral circulation on myocardial perfusion were compromised by inclusion of patients with multivessel coronary artery disease, incomplete occlusion, prior myocardial infarction, or a combination of these.

Methods In this study we will investigate the relationship between angiographic collateral circulation and myocardial perfusion in patients with total occlusion of a single coronary artery, in the absence of myocardial infarction or significant stenosis in the other coronary arteries supplying the same myocardial territory.

Results Forty patients underwent stress myocardial single photon emission computed tomography within 90 days of angiography. Collateral circulation was present in 24 patients (Group A) and absent in 16 patients (Group B). Reversible perfusion defects were present in 22 (91.7%) patients in group A and in 12 (75%) in group B, comparison between both groups came back statistically insignificant (p-value=NS). Group A included 4 (18.2%) patients with a small size defect (<5%), 9 (40.9%) patients with a moderate perfusion defect (5-10%) and 9 (40.9%) patients with a large perfusion defect (>10%); while group B had 2 (16.6%) patients with small perfusion defect, 5 (41.6%) patients with a moderate perfusion defect and also 5 (41.6%) patients with a large perfusion defect, comparison between both groups came back statistically insignificant (p-value=NS). The mean exercise time for patients in group A was 6.9±0.92 minutes and their mean achieved peak METs was 7.35±0.35 METs. On the other hand; the mean exercise time for patients in group B was 6.9±0.83 minutes and their mean peak METs was 7.23±0.25 METs. Comparison between both groups also appeared to be statistically insignificant (p-value=NS).

Conclusions In patients with a single-vessel total coronary occlusion and without myocardial infarction, stress-induced myocardial ischemia is almost always present, irrespective of presence or absence of angiographic collaterals. These data suggest that coronary collaterals do not appear to protect against stress-induced perfusion defects. Nevertheless collaterals in our study did not have any positive impact on the functional capacity of patients, predicted by the analysis of exercise duration and achieved peak METs.

Keywords Coronary artery total occlusion, Collateral circulation, Myocardial perfusion, CTO.
(Heart Mirror J 2009; 3(2): 80-85)

INTRODUCTION

Coronary collateral blood vessels mature and develop in response to the presence of severe coronary stenosis. It is known that collateral vessels may maintain normal resting myocardial blood flow. However, patients may still have angina pectoris, ischemic electrocardiographic changes, or abnormal exercise myocardial perfusion imaging results, despite the presence of collateral circulation. Previous clinical studies have demonstrated that patients with a single, complete occlusion of a coronary artery have excellent long-term survival rates (1, 2, 3). In contrast; recent findings have suggested that patients with a chronically occluded vessel treated medically have substantial ischemic cardiac event rates over the long-term follow-up (4).

Abbreviations and Acronyms

CTO	: Chronic total occlusion
METs	: Metabolic equivalents
MPS	: Myocardial perfusion study
PET	: Positron emission tomography
SPECT	:Single photon emission computed tomography
Tl	: Thallium
(X)	: Mean

Previous scintigraphic studies that investigated the effects of coronary collateral circulation on myocardial perfusion showed inconsistent findings. Inclusion of patients with multivessel coronary artery disease, incomplete coronary occlusion, prior myocardial infarction, or a combination of these complicated the interpretation of the findings of these studies (5). Accordingly, the aim of our study was to ascertain the relationship between coronary collateral circulation and myocardial perfusion only in patients with total occlusion of a single coronary artery, in the absence of both myocardial infarction and significant stenosis in the other coronary arteries.

PATIENTS AND METHOD

Study Population

The recruitement was started in June, 2007 until October, 2008 in Dar Al Fouad Hospital. Forty patients with chronic total occlusion (CTO) of a single coronary artery as diagnosed by coronary angiography were included. The patients were divided into 2 groups according to the presence (Group A) or absence (Group B) of coronary collateral circulation. The number of patients in group A was 24 patients and the number included in group B was 16 patients.

All forty patients underwent exercise stress myocardial single photon emission computed tomography (SPECT) within 90 days of angiography. The exclusion criteria included a prior myocardial infarction (MI) by history or ECG, previous bypass surgery and significant stenosis in other coronary arteries supplying the same myocardial territory.

Stress Myocardial Spect Imaging

Patients were asked to discontinue the use of beta blocker, calcium channel blocker (For 48 hours) and nitrates (For 24 hours) before stress testing. Stress myocardial single photon emission computed tomography (SPECT) was carried out for all patients within 90 days of angiography. Myocardial perfusion studies were done using a 1-day rest/stress imaging protocol. Myocardial perfusion imaging was done using technetium 99-m as the radiotracer and stress was done through exercise testing on a motor-driven treadmill using standard Bruce protocol. Low dose technetium 99-m radiotracer was injected at rest and distribution of sestamibi myocardial uptake was imaged using the gamma camera 30-60 minutes later.

The patients underwent treadmill exercise testing with the Bruce protocol. Heart rate, systolic and diastolic blood pressures, and 12-lead ECG were recorded before exercise and at 1-minute intervals during exercise, with continuous ECG monitoring throughout the test. At peak exercise, high dose technetium 99-m radiotracer was then injected intravenously and flushed with saline solution. Patients were then encouraged to exercise for an additional 30 to 60 seconds after tracer injection. Post stress images were taken 10-20 minutes after exercise. Tomographic images were performed over 180 degrees and analyzed in the short axis, vertical long axis and horizontal long axis.

Coronary Angiography

All patients of the study had a left sided cardiac catheterization with coronary angiography. Angiographic cine images were recorded on compact disks for subsequent interpretation and analysis of the following:

- The vessel with chronic total occlusion (CTO).
- Location of the chronic total occlusion (CTO) within the vessel (Proximal, mid or distal).
- Presence of coronary collaterals was noted and graded from 1 to 3 as follows:

1. Grade 1= filling of side branches only.
2. Grade 2= partial filling of the epicardial segment.
3. Grade 3= complete filling of epicardial segment (6).

Statistical Analysis

All data were all recorded on an investigative report form, transferred to an IBM compatible computer and then statistically using SPSS statistical software (Version 16) in order to obtain:

1. *Descriptive statistics:*
   - Mean (X) and standard deviation (SD) for quantitative data.
   - Frequency for qualitative data.
2. *Analytical statistics:*
   - Paired sample "t" test to compare between two variables' means for the same sample.
   - Chi square test for qualitative data analysis.
   - P value denoted level of significance were a p value <0.001 was considered as highly statistically significant, a p value <0.05 was considered as statistically significant whereas a p value >0.05 was considered to be non statistically significant.

RESULTS

Angiographic Results

All the forty patients included in the study had chronic total occlusion of a single coronary artery. None of the forty patients had total occlusion of the diagonal branch of LAD, the ramus artery, the PDA of the LCx or the posterolateral branch of RCA.

For statistical reasons concerning the relatively small sample number of patients, location of coronary occlusion was classified into three subsets; one including patients with CTO of LAD, the other subset includes patients with CTO of LCx or obtuse marginal branch of LCx and finally the third subset contains patients with CTO of RCA or PDA of RCA.

Patients with total occlusion of the LAD were 12 (50%) patients in group A and 7 (43.75%) patients in group B, those with total occlusion of the LCx or OM branch were 6 (25%) patients in group A and 4 (25%) patients in group B and finally total occlusion of the RCA or PDA branch of the RCA was found in 5 (31.25%) patients in group A and 6 (37.5%) patients in group B. Comparison between both groups regarding the site of coronary artery occlusion was statistically insignificant (p-value=NS).

Table 1: Comparison between both groups as regard to site of coronary artery occlusion:

	Group A n=24	Group B n=16	*p-value*
LAD	12 (50%)	7 (43.75%)	*NS*
LCx or OM branch	6 (25%)	4 (25%)	*NS*
RCA or PDA of RCA	6 (25%)	5 (31.25%)	*NS*

Exercise Test Results

Exercise Time

The duration of exercise was measured in all forty patients; the exercise time for patients in group A was ranging from 4 to 9.5 minutes with mean exercise time of 6.9±1.8 minutes. On the other hand the exercise time for patients in group B was ranging from 4 to 9 minutes with mean exercise time of 6.9±1.2 minutes. Comparison between the two groups regarding exercise time was statistically insignificant (p-value=NS).

Table 2: Comparison between both groups as regard to exercise time:

	Group A n=24	Group B n=16	*p-value*
Mean (SD)	6.9 (±1.8)	6.9 (±1.2)	*NS*

Peak Metabolic Equivalents (METs)

The achieved peak METs was recorded for all patients; it was ranging from 6.2 to 8.3 METs in group A patients, with mean value of 7.3±0.35 METs. On the other hand peak METs in group B patients ranged between 6.6 to 8.1 METs with mean value of 7.2±0.5 METs. Comparison between the two groups regarding the achieved peak METs was statistically insignificant (p-value=NS).

Table 3: Comparison between both groups as regard to exercise time:

	Group A n=24	Group B n=16	*p-value*
Mean (SD)	7.3 (±0.7)	7.2 (±0.5)	*NS*

Spect Results

Reversible Perfusion Defect:

Presence or absence of a reversible perfusion defect on myocardial perfusion imaging is considered the core of comparison between the two study groups. It was found that reversible perfusion defects were present in 22 (91.7%) patients in group A and in 12 (75%) in group B. Comparison between both groups regarding the presence of reversible perfusion defect was statistically insignificant (p-value=NS).

Table 4: Comparison between both groups as regard to presence of reversible perfusion defect:

	Group A n=24	Group B n=16	*p-value*
Reversible perfusion defect	22 (91.7 %)	12 (75 %)	*NS*

Size of perfusion defect

We compared the size of perfusion defect in all patients with positive reversible perfusion defect; which were 22 (91.7%) patients in group A and 12 (75%) patients in group B. We found that group A included 4 (18.2%) patients with a small size defect (<5%), 9 (40.9%) patients with a moderate perfusion defect (5-10%) and 9 (40.9%) patients with a large perfusion defect (>10%). On the other hand group B had 2 (16.6%) patients with small perfusion defect, 5 (41.6%) patients with a moderate perfusion defect and also 5 (41.6%) patients with a large perfusion defect. Comparison between both groups regarding the size of perfusion defect was statistically insignificant (p-value=NS).

Table 5: Comparison between both groups as regard to the size of perfusion defect:

	Group A n=22	Group B n=12	*p-value*
Small	4 (18.2%)	2 (16.6%)	*NS*
Moderate	9 (40.9%)	5 (41.6%)	*NS*
Large	9 (40.9%)	5 (41.6%)	*NS*

DISCUSSION

Several studies have investigated the effects of collateral circulation on myocardial perfusion during stress and at rest. In general, most of these studies have suggested that

HMJ Vol. 3, No. 2, 2009
Nov 2009: 80-85

collateral coronary vessels do not protect against stress-induced perfusion defects but that they may be important in preserving the resting myocardial blood flow to near-normal limits (7-9).

However, other investigators suggested that collateral circulation may prevent stress-induced myocardial ischemia (10-12).

With PET, several studies have suggested that coronary collaterals preserve resting myocardial flow but are inadequate to protect against reduced blood flow during hyperemic stress (7, 8).

In contrast, several studies with planar 201Tl scintigraphy suggested that coronary collaterals also prevent stress-induced ischemia (10-12). The reason for the discordance in these PET and planar 201Tl studies is unclear (9).

Regarding the occurrence of reversible perfusion defect during stress myocardial SPECT, we found that reversible perfusion defects were present in 22 (91.7%) patients in group A (With angiographic collaterals) and in 12 (75%) in group B (Without angiographic collaterals).

Comparison between both groups came back statistically insignificant (p-value>0.05). Therefore; we concluded that the presence of angiographic collateral vessels did not protect against occurrence of myocardial perfusion defects during exercise stress.

The results of our study were generally concordant with those from other studies that were carried out using stress myocardial SPECT and stress myocardial PET.

He, et al. demonstrated that in patients with single-vessel total coronary artery occlusion without MI, stress-induced myocardial ischemia is almost always present, irrespective to the presence or absence of angiographic collaterals. They did not assess resting perfusion findings, because 201Tl stress/redistribution SPECT (Without resting injection) was one of the many MPS protocols used (5).

Nevertheless; our results were also concordant to that given by Aboul Enein, et al. they found that patients with single-vessel CTO had severe and extensive stress-induced myocardial perfusion defects regardless of the grade of angiographic coronary collaterals (9).

Although we had concordant results with the previous two studies, we faced discordant results in studies that were carried out using planar 201-Tl scintigraphy.

Eng, et al. suggested that collateral perfusion was adequate during maximal exercise. Collateral function was determined by analysis of exercise thallium-201 myocardial perfusion images for 41 cases of a totally occluded vessel supplying a non infarct territory. They had 19 normally perfused patients, however 13 of them were associated with defects in other myocardial regions supplied by diseased vessels and were considered relatively negative since the defects didn't involve the region of total occlusion (12).

The inclusion of cases with multivessel affection and the lower specificity of the planar imaging were both considerable limitations for the study.

Rigo, et al. also used exercise MPI to study coronary collateral function during exercise. The study suggested a role of coronary collaterals in providing relative protection from stress-induced ischemia (10).

Their results were also discordant to ours; however in there study, a majority of the regions analyzed were infarcted rendering the interpretation of their results to be difficult and one might even say inaccurate. On the other hand, none of the forty patients included in our study had a single resting perfusion defect.

To summarize what we have discussed earlier; there was no statistical significance regarding occurrence of reversible perfusion defect between the two groups of patients, with and without collaterals. Our results were generally concordant with those studies that were carried out using stress myocardial SPECT and were generally discordant with studies that were carried out using planar 201-Tl scintigraphy. This discrepancy might be related to the lower specificity of planar imaging, rendering their results less reliable than those obtained using SPECT.

As mentioned above; group A had 22 (91.7%) patients with positive reversible perfusion defect while group B included 12 (75%) with positive reversible perfusion defect. In other words normal SPECT results occurred only in 2 (8.3%) patients group A and in 4 (25%) patients in group B.

Regarding the size of perfusion defect; there was no statistical significance between both groups. We found that group A included 4 (18.2%) patients with a small size defect (<5%), 9 (40.9%) patients with a moderate perfusion defect (5-10%) and 9 (40.9%) patients with a large perfusion defect (>10%). On the other hand group B had 2 (16.6%) patients with small perfusion defect, 5 (41.6%) patients with a moderate perfusion defect and also 5 (41.6%) patients with a large perfusion defect. Hence we concluded that presence of collaterals did not affect the extent of perfusion defect when present.

Several studies have compared the extent of myocardial perfusion defects in patients with collateral circulation and in those without it (10, 13).

Tubau, et al. in a series of 22 patients with no prior infarction observed that, myocardial perfusion defects detected by planar Tl-201 imaging were found to involve more myocardial segments in patients without collateral circulation than in those with it (11).

Iskandrian, et al. observed that the extent of perfusion defects, measured by quantitative analysis of planar Tl-201 imaging in patients with left anterior descending artery stenosis, was smaller in patients with collateral circulation than in those without it. The extent of perfusion defects in patients with either left circumflex or right coronary artery stenosis was, however, similar for patients with collateral circulation and those without it (13).

The results of those two studies were discordant with our results; they suggested that presence of collaterals may alter the extent of perfusion defects by decreasing there size. However we found no evidence of such finding in our results. The only explanation we could think of was also the lack of specificity of planar imaging since both studies were done using planar Tl-201 imaging.

Nevertheless the study done by Iskandrian, et al. was done on patients with 70% or greater diameter narrowing and not patients with complete arterial occlusion; this may not eliminate the effect of the antegrade flow present in the main diseased epicardial vessel. Although this antegrade flow is thought to be affected by the luminal narrowing of the artery, it can never be neglected.

In our study we were enthusiastic to analyze certain parameters related to the functional capacity of patients. Duration of exercise, achieved peak metabolic equivalents (METs) and symptoms during exercise can all provide useful information for assessment of functional capacity through exercise treadmill testing (14).

During exercise treadmill testing using Bruce protocol; there were 18 (75%) symptomatic patients in group A and 8 (50%) patients in group B. The mean exercise time was 6.9±1.82 minutes for group A patients and 6.9±1.42 minutes for group B patients. The mean achieved peak METS was 7.35±0.35 in group A patients and 7.23±0.25 in group B patients. However comparison between the two groups regarding all those three variables was statistically insignificant (p-value >0.05), suggesting that collaterals in our study did not have any positive impact on the functional capacity of patients.

There were early clinical investigations of collateral function that used exercise electrocardiography in patients with chronic total coronary occlusions. Actually these studies were quiet few in number, probably due to the inability of the exercise ECG to localize the lesion causing ischemia (15).

The investigators of those few studies didn't show interest in analyzing the data involving the patient's functional capacity; they focused more on the presence or absence of ischemic electrocardiographic changes during exercise and obviously didn't use these changes in the comparison between patients with and without collaterals; due to the lack of localization of the electrocardiographic changes and the higher sensitivity and regional specificity of MPI, permitting a better correlation of angiographically determined pathoanatomy with functional regional responses during exercise.

Limitations

Several limitations of this study should be pointed out. First the study was performed on a relatively small number of patients (40 patients). Second, although nearly all of our patients had perfusion defects, most patients underwent coronary angiography after the SPECT study. Thus a referral bias—through which patients with an abnormal SPECT result would be more likely to be referred to catheterization than those with a normal SPECT study—cannot be ruled out. Finally, none of the forty patients had grade 3 collateral filling, in which there is complete filling of epicardial segments according to Rentrop method of grading of collaterals (6).

Clinical Implications

Assessment of myocardial ischemia and viability can provide unique information in the management of patients with chronic total coronary occlusion, because these patients may still be at high risk for future ischemic cardiac events.

Corresponding Author
Dr. Maged El-Gantiry
Cardiology Department, Dar Al Fouad Hospital, Cairo, Egypt
E-mail: maged_1201@hotmail.com

REFERENCES

1. Califf RM, Harrell FE,Jr, Lee KL, et al. The evolution of medical and surgical therapy for coronary artery disease. A 15-year perspective. JAMA 1989; 261(14):2077-86.
2. Alderman EL, Bourassa MG, Cohen LS, et al. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990; 82(5):1629-46.
3. Mark DB, Nelson CL, Califf RM, et al. Continuing evolution of therapy for coronary artery disease. Initial results from the era of coronary angioplasty. Circulation 1994; 89(5):2015-25.
4. Puma JA, Sketch MH,Jr, Tcheng JE, et al. The natural history of single-vessel chronic coronary occlusion: A 25-year experience. Am Heart J 1997; 133(4):393-9.
5. He ZX, Mahmarian JJ, Verani MS. Myocardial perfusion in patients with total occlusion of a single coronary artery with and without collateral circulation. J Nucl Cardiol 2001; 8(4):452-7.
6. Rentrop KP, Cohen M, Blanke H, et al. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. J Am Coll Cardiol 1985; 5(3):587-92.
7. Demer LL, Gould KL, Goldstein RA, et al. Noninvasive assessment of coronary collaterals in man by PET perfusion imaging. J Nucl Med 1990; 31(3):259-70.
8. McFalls EO, Araujo LI, Lammertsma A, et al. Vasodilator reserve in collateral-dependent myocardium as measured by positron emission tomography. Eur Heart J 1993; 14(3):336-43.
9. Aboul Enein F, Kar S, Hayes SW, et al. Influence of angiographic collateral circulation on myocardial perfusion in patients with chronic total occlusion of a single coronary artery and no prior myocardial infarction. J Nucl Med 2004; 45(6):950-5.

HMJ Vol. 3, No. 2, 2009
Nov 2009: 80-85

10. Rigo P, Becker LC, Griffith LS, et al. Influence of coronary collateral vessels on the results of thallium-201 myocardial stress imaging. Am J Cardiol 1979; 44(3):452-8.
11. Tubau JF, Chaitman BR, Bourassa MG, et al. Importance of coronary collateral circulation in interpreting exercise test results. Am J Cardiol 1981; 47(1):27-32.
12. Eng C, Patterson RE, Horowitz SF, et al. Coronary collateral function during exercise. Circulation 1982; 66(2):309-16.
13. Iskandrian AS, Lichtenberg R, Segal BL, et al. Assessment of jeopardized myocardium in patients with one-vessel disease. Circulation 1982; 65(2):242-7.
14. Topol EJ, Califf RM, Isner J, et al. Textbook of cardiovascular medicine. 3rd ed.: Lippincott Williams & Wilkins; 2006.
15. Helfant RH, Vokonas PS, Gorlin R. Functional importance of the human coronary collateral circulation. N Engl J Med 1971; 284(23):1277-81.