TORTUOSITY OF CORONARY ARTERIES : A NEW CAUSE OF MYOCARDIAL ISCHEMIA

Övsev DÖRTLEMEZ, M.D., Mehmet METİN, M.D., Atiye ÇENGEL, M.D., Mehmet ALKAN, M.D., Oğuz CAYMAZ, M.D., Halis DÖRTLEMEZ, M.D.

Gazi University, Faculty of Medicine, Department of Cardiology, Ankara, Turkey
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SUMMARY : 15 patients (8 women, 7 men) with evident tortuosity of coronary arteries and without any atherosclerotic lesions were selected. All of these patients had typical chest pain and their electrocardiograms (either at rest or during exercise) had ischemic pattern at various localizations. Myocardial thallium perfusion scintigraphies of all these patients also showed reversible ischemia. Proximal and distal blood flow velocities of these tortuose vessels were measured by the use of intracoronary Doppler-tipped guidewires. Coronary flow reserve was also evaluated by Papaverine in 5 of them. The parameters obtained by Doppler tipped guidewires in 15 patients and in the control group consisting of 10 patients with normal coronary angiograms and no tortuosity were : APV (average peak velocity), ADPV (average diastolic peak velocity), ASPV (average systolic peak velocity), DSPV (Diastolic/Systolic peak velocity ratio). Proximal APV/Distal APV ratio was significantly high in the study group ($p<0.001$). Distal ADPV which was significantly high when compared to proximal ADPV in the control group ($p<0.05$) was found to be lower than proximal values in the study group ($p<0.005$); ASPV and DSVR values of both groups showed no significant diffference.

We suggest that in patients with a suspicion of myocardial ischemia but with normal coronary angiograms, tortuosity of the coronary arteries can lead to ischemia by slowing down the velocity of blood in the distal parts of the vessel which can be shown by Doppler flow measurements.

Key Words : Myocardial Ischemia, Tortuosity, Intracoronary Doppler Tipped Guidewires, Coronary Flow Velocity.

INTRODUCTION

It is well known that coronary atherosclerosis is the major cause of myocardial ischemia but some other causes related to the coronary arteries such as congenital anomalies and Syndrome X can also result in myocardial ischemia.

It is also well known that some patients with typical histories of angina pectoris and evidence of myocardial ischemia at their electrocardiograms taken at rest or during exercise and with patterns of reversible ischemia during myocardial thallium perfusion scintigraphies have completely normal coronary angiograms. There are two main problems in these patients from the diagnostic standpoint. 1) Whether they really have myocardial ischemia, 2) If they have, what is the reason of myocardial ischemia since their angiograms are completely normal. It is observed during our studies in our hemodynamics laboratory that tortuosity or extreme

looping or kinking of the coronary arteries is a common finding in this type of patients. Many of them have coronary arteries with at least two proximal loops.

In the literature, it is stated that tortuosity of the carotid arteries can be a cause of cerebral ischemic attacks (3, 6) which led us to think that tortuosity or looping of the coronary arteries can be a cause of myocardial ischemia.

In order to see whether this kinking or looping of coronary arteries can result in myocardial ischemia, we decided to measure the velocity of intracoronary blood flow by Doppler Tipped Guidewires in the proximal and distal parts of these vessels. This method is helpful in the assessment of 1) Angiographically intermediate coronary artery stenosis, 2) The degree of residual stenosis during angioplasty and other coronary interventional procedures. The method is based on comparison of proximal and distal blood flow velocities (8, 11, 16, 18).

This study is designed to evaluate whether tortuosity of the coronary arteries can lead to myocardial ischemia in patients with typical chest pain and ischemic patterns at electrocardiograms (ECG) or thallium scintigraphies, and completely normal coronary angiograms. By the help of Doppler-tipped guidewires flow velocities in the proximal and distal parts of these tortuose vessels are measured. It is assumed that kinking of the vessels will slow down the blood flow in distal parts causing ischemia.

MATERIALS AND METHODS

The study was conducted at Gazi University Faculty of Medicine, Department of Cardiology during January and August 1993.

In our hemodynamics laboratory all patients with typical chest pain and ST segment depression (at least 1 mm. horizontal or down-slopping) during Treadmill exercise test underwent coronary angiograms performed by Judkins technique. 15 of them (8 women, 7 men, mean age : 54.3 ± 9.2) were selected for the purpose of this study due to the tortuosity of their left anterior descending (LAD) or circumflex (Cx) arteries. The criteria of tortousity was at least two loops to be present in the proximal part of the vessel. The coronary arteries of these 15 patients were completely normal except tortuosity. All of the patients had reversible perfusion defects during Thallium 201 myocardial scintigraphy.

In 6 of these 15 patients only circumflex artery was tortuose whereas in 9 of them both LAD and Cx were tortuose. Tortuosity of the right coronary artery was not studied because the guiding catheter would obstruct the right coronary ostium completely preventing correct recording of coronary blood flow sample.

None of our patients had any pathology that would disturb coronary blood flow samples and produce ischemic responses such as left ventricular hypertrophy, valvular heart disease or prolapse of mitral valve. Ergonovine positive patients were also excluded.

The control group consisted of 10 patients in the same age interval (52.3 ± 7.2), 7 women, 3 men who clinically had ischemic complaints and whose ECG's were considered to be ischemic but whose coronary angiograms revealed no pathology and no tortuosity.

Both in the study and the control group left guiding catheter was engaged to the left coronary ostium. Doppler Flowire, a 0.014 or 0.018 inch guidewire that has a 12-MHZ transducer at its distal tip (Flowire - Cardiometrics Inc. Mountain View CA) was advanced into the tortuose vessel from proximal to the distal parts. When adequate Doppler signals were obtained, flow velocity recordings were taken both from proximal and distal arteries with simultaneous ECG recordings.

The Doppler recordings obtained were :

APV : (Average peak velocity) in cm/sec.

ADPV : (Average diastolic peak velocity) cm/sec.

ASPV : (Average systolic peak velocity) cm/sec.

DSVR : (Diastolic/Systolic velocity ratio) cm/sec.

Proximal APV/Distal APV value was considered as the "Ratio". If the ratio was above 1.7, the presence of ischemia was accepted (7, 8, 15).

In 5 patients whose ratios were between 1.5 and 1.69, intracoronary Papaverine test was applied. After recording the distal blood flow, 12 mg. Papaverine was injected into the coronary artery and blood flow velocities were remeasured, thus coronary capillary flow reserve (CFR) was calculated. The ratio of the increase in distal APV (i.e, distal APV with papaverine/Distal APV before papaverine)

was calculated. If it was below 3, capillary flow reserve was accepted to be limited.

For statistical analysis, student's t-test was used.

RESULTS

All of the 15 patients with tortuosity had at least 1 mm. horizontal or down-slopping ST-segment depression during Treadmill exercise test. Ischemic changes occured in the inferior derivations at 8 of them and in the anterior derivations in 7 of them. Myocardial perfusion scintigraphies of the same patients revealed reversible ischemia in the inferior region in 3 patients, in the inferoposterior region in 4 patients, in inferolateral region in 4 patients, in the lateral region 3 patients and in the apical region in 1 patient.

Tortuosity of the vessel was present only in the circumflex artery in 6 of the patients and both in circumflex and left anterior descending artery in 9 of the patients (Fig 1, 2, 3, 4).

None of the patients had any history or sign of myocardial infarction. None of them had left ventricular hypertrophy, mitral valve prolapsus or valvular heart disease.

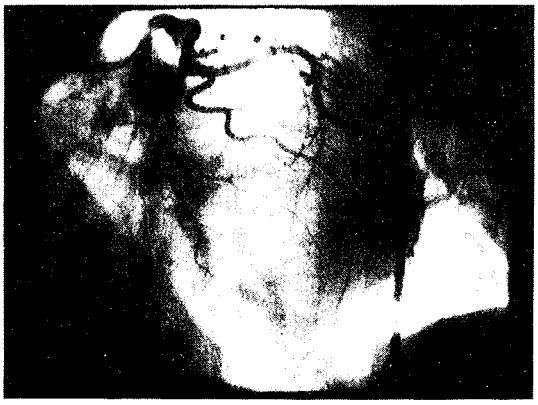

Fig - 1 : Coronary angiogram in left anterior oblique projection of a patient with tortuosity.

The results of the study and the control group are shown on Table 1 and 2.

When ratios (ratio of proximal APV to distal APV) of the study and control groups are compared, ratios of the study group are significantly higher than control group ($p<0.05$) Table 3.

In the study group ratios are between 0.9 and 3.6.5 of these patients have a ratio of 1.5 (Table 1). Since ratios between 1.5 and 1.69 are considered to be borderline values, papaverine test was used in these patients to measure blood flow reserve. The average increase in distal APV after papaverine was 2.42 which is considered low when compared to the 3-6 folds increase expected in normal coronary arteries (8, 16, 17) (Table 1).

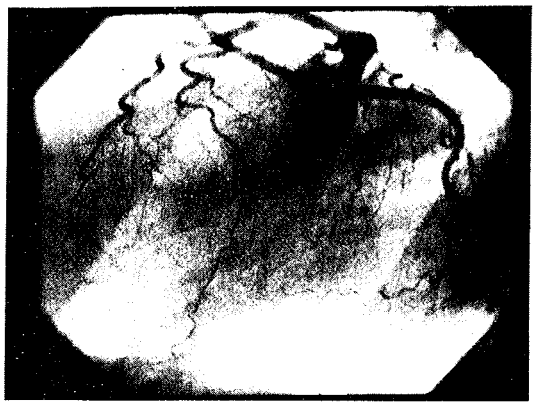

Fig - 2 : The same patient's coronary angiogram in left lateral projection.

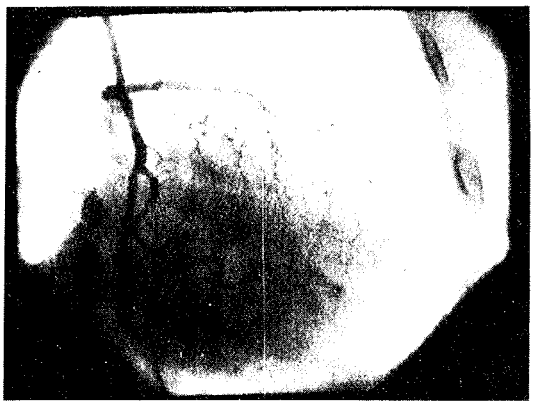

Fig - 3 : Another patient's coronary angiogram in right anterior obligue projection demonstrating.

The ratios of the control group are between 0.8 and 1.1 (Table 2). When proximal and distal ADPV's are compared, significant differences are found between the study and the control group. In the study group, expect 1 patient, all of the patients have greater proximal ADPV values than distal

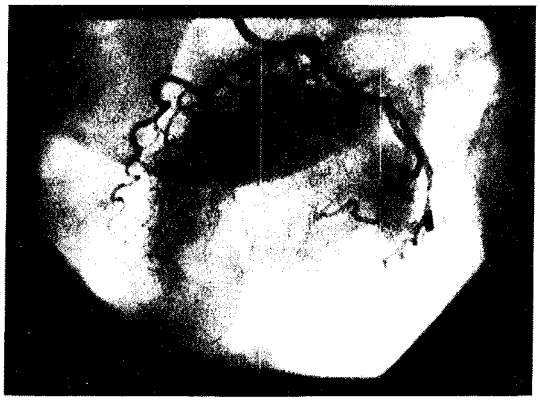

Fig - 4 : The same patient's coronary angiogram in left lateral projection.

ADPV values. Whereas in the control group distal ADPV values are greater than proximal ADPV values. The differences within both groups are statistically significant (Table 4).

The ASPV and DSVR values in the study and control groups are compared and no statistically significant difference is observed.

DISCUSSION

Although most of the time coronary artery disease can easily be diagnosed by clinical, electrocardiographic data, myocardial perfusion scintigraphy and coronary angiography; in the advanced technology era of modern times, even the gold standart of diagnosis : coronary angiography can be inadequate in some cases.

Between % 20 to % 30 of coronary angiograms performed on patients with chest pain show normal or near normal coronary arteries (9, 10). However angiographically finding coronary arteries as normal does not solve the diagnostic problem in some cases. Many investigators believe that a substantial percentage of patients who experience angina-like pain but who have angiographically normal coronary arteries may still have true myocardial ischemia (2, 4, 10, 14). Several mechanisms have been proposed as possible causes of myocardial ischemia in this group of patients such as abnormal affinity of red blood cells to hemoglobin, coronary arteriel disease of small vessels not visualized by coronary arteriography, abnormal neurohumoral regulation with abnormal vascular tone etc. (2). Considering these mechanisms, it appears most likely that an abnormal neurohumoral regulation of the small epicardial coronary arteries and the resistance vessels is responsible for the reduced dilator capacity in these patients (2).

In a previous preliminary study we noticed that in patients with chest pain and normal coronary angiograms, the frequency of tortuosity of coronary arteries especially in women was quite high (5). Whether this finding is related to the fact that "Syndrome X" is more common in women and whether tortuosity of the coronary arteries and Syndrome X are related conditions, remained questions to be solved by further metabolic, dynamic and intracoronary ultrasonographic investigations at the end of that preliminary study (5).

The relationship between carotid artery kinking and cerebral ischemic attacks (3, 6) tempted us to further investigate the linkage between coronary artery tortuosity and myocardial ischemia.

In the literature, Barilla et al indicated that tortuosity of circumflex artery could be the cause of myocardial ischemia in their 2 patients with chest pain and normal coronary angiograms (1). Although these 2 patients were ergonovine positive, the authors ignore vasospasm as the possible cause of myocardial ischemia and rather suggest the possible role of tortuosity. According to these authors, 2 mechanisms can cause myocardial ischemia in tortuose vessels: The first mechanism is axial kinking. During systol, kinking of the vessels leads to diminished blood flow beyond the point of kinking. The second mechanism suggested is increased reactivity of smooth muscle cells in the coronary arteries at the point of kinking (1).

In our study we measured intracoronary blood flow in these tortuose vessels by the help of Doppler-tipped guidewires. Doppler-tipped guidewires are believed to measure coronary blood flow velocity and coronary blood reserve quite satisfactorily (8, 16, 18). In patients with coronary artery stenosis if the ratio of the blood flow velocity between the proximal and distal parts of the lesion exceed 1.5-1.7, that lesion is accepted to be severe and the transstenotic gradient is greater than 30 mmHg in these cases (8). Coronary vasodilator reserve is also impaired in severe coronary artery disease.

Potent vasodilators like papaverine and adenosine increase coronary flow reserve up to 3-6 times of baseline in normal coronary arteries whereas it is

PATIENT GROUP							
CASE		APV	ADPV	ASPV	DSVR		RATIO
1	Distal	12.2	14.1	9.0	1.55		2
	Proximal	24.1	27.5	18.3	1.50		
2	Dist.	23.3	31.3	12.6	2.46		1.2
	Prox.	27.0	35.1	15.9	2.2		
3	Dist.	17.4	22.1	10.4	2.1		1.5
	Prox.	25.7	32.5	16.1	2.01		
+	Dist.	26.1	31.1	16.1	2.0	APV before P:1.5	2
Papaverine	Prox.	52.2	62.1	30.4	2.1	APV with P:2.0	
4	Dist.	33.0	40.4	19.8	2.03		1
	Prox.	34.1	38.2	26.9	1.42		
5	Dist.	26.3	31.4	14.2	2.1		2
	Prox.	52.1	65.6	31.6	2.07		
6	Dist.	23.3	27.8	15.8	1.75		1.2
	Prox.	28.4	33.5	19.9	1.7		
7	Dist.	24.8	31.0	15.9	1.94		1.5
	Prox.	37.3	42.1	17.4	2.4		
+	Dist.	52.1	65.2	33.0	2.0	APV before P:2.1	2.4
Papaverine	Prox.	126.8	143.1	55.6	2.6	APV with P:3.4	
8	Dist.	18.0	20.9	12.5	1.6		1.5
	Prox.	27.2	25.7	30.0	0.85		
+	Dist.	12.1	15.1	5.8	2.6	APV before P:0.7	3.6
Papaverine	Prox.	44.3	54.7	23.3	2.4	APV with P:1.6	
9	Dist.	17.8	20.2	13.1	1.5		1.5
	Prox.	26.9	32.2	15.2	2.12		
+	Dist.	24.1	28.3	14.20	2.0	APV before P:1.4	2.2
Papaverine	Prox.	53.0	57.4	27.6	2.07	APV with P:2.0	
10	Dist.	31.4	34.9	25.2	1.38		0.9
	Prox.	27.4	31.9	19.9	1.60		
11	Dist.	20.9	28.5	8.4	3.40		1.7
	Prox.	36.3	44.3	16.4	3.10		
12	Dist.	18.8	23.7	10.9	2.17		2.9
	Prox.	53.9	56.5	49.6	1.13		
13	Dist.	22.2	26.0	16.9	1.53		1.8
	Prox.	39.1	48.8	25.8	1.88		
14	Dist.	18.7	21.3	14.9	1.43		1.1
	Prox.	19.9	26.2	11.1	2.30		
15	Dist.	19.5	26.9	7.45	3.60		1.5
	Prox.	29.3	38.2	15.1	2.52		
+	Dist.	42.9	59.2	15.1	3.92	APV before P : 2.2	1.9
Papaverine	Prox.	81.5	112.5	21.2	5.30	APV with P : 2.8	

Table - 1

CONTROL GROUP						
CASE		APV	ADPV	ASPV	DSVR	RATIO
1	Distal	28.4	37.2	14.5	2.56	0.9
	Proximal	25.2	33.3	12.5	2.73	
2	Dist.	35.0	42.2	22.0	1.91	0.9
	Prox.	30.2	35.4	20.6	1.71	
3	Dist.	23.4	24.8	20.8	1.19	0.9
	Prox.	18.7	18.3	19.5	0.94	
4	Dist.	32.3	41.2	22.0	1.68	1.1
	Prox.	34.4	41.0	23.3	1.76	
5	Dist.	38.9	48.6	24.1	2.01	0.9
	Prox.	33.0	41.0	20.5	2.0	
6	Dist.	34.5	44.7	16.0	2.78	0.9
	Prox.	18.6	25.2	9.0	2.80	
7	Dist.	27.7	29.8	24.0	1.23	1.0
	Prox.	24.8	25.5	23.5	1.08	
8	Dist.	18.7	23.3	11.3	2.05	1.0
	Prox.	19.1	24.1	11.4	2.05	
9	Dist.	24.7	42.3	20.4	2.1	1.0
	Prox.	23.6	41.2	20.0	2.1	
10	Dist.	14.1	17.6	6.3	2.79	1.0
	Prox.	13.6	15.9	8.0	1.99	

Table - 2

RATIO : Prox APV/Distal APV
APV : Average peak velocity
ADPV : Average diastolic peak velocity
ASPV : Average systolic peak velocity
DSVR : Diastolic/systolic velocity ratio.
CFR : Coronary flow reserve

	Study Group	Control Group	P
$\frac{\text{Proximal AP}}{\text{Distal APV}}$ = Ratio :	1.54 ± 0.32	0.89 ± 0.09	0.001

Table - 3

	ADPV (proximal)	ADPV (Distal)	P
Study Group :	38.55 ± 11.34	26.70 ± 6.63	0.005
Control Group :	30.09 ± 9.95	35.07 ± 10.46	0.05

Table - 4

depressed in severe coronary stenosis (8, 16, 17).

In our study group proximal APV/Distal APV (ratio) was found to be 1.54 ± 0.32 and in our control group it was 0.89 ± 0.09 and the difference is statistically very significant ($p<0.001$). In the study group there were 5 intermediate patients whose ratios were 1.5. Coronary flow reserve was calculated by injection of intracoronary papaverine in this group with no significant rise in blood flow reserve.

The significantly high ratios in the study group, when compared to the control group and the impaired vasodilatory reserve in the 5 patients with borderline ratios in the study group can be accepted as evidence of myocardial ischemia in the patients with tortuose coronary vessels.

ADPV values in the proximal and distal parts of the vessel also showed significant differences between the study and the control grouup. In the study group distal ADPV values were significantly lower than the proximal values ($p<0.005$) whereas in the control group distal ADPV values were significantly higher than proximal values ($p<0.05$).

The significantly low ADPV values in the distal parts of the tortuose vessels resemble the ischemic pattern seen with severe coronary artery stenosis. In the patients without tortuosity distal ADPV values were greater than proximal ADPV values due to normal coronary blood flow velocity and normal coronary flow reserve in the distal parts of those vessels.

Although the measurement of intracoronary blood flow by Doppler-Flowire revealed some significant changes in tortuose vessels suggesting myocardial ischemia; the mechanism and the reason of this ischemia are not clear yet. It may well be due to axial torsion and kinking causing imparied blood flow or due to increased reactivity of smooth muscle cells as suggested in the literature (1) or it may occur as a result of some neurohumoral regulatory defect in these vessels.

In conclusion :Coronary arteries with tortuosity but without any atherosclerotic lesions can impair the kinetics of coronary blood flow and can cause myocardial ischemia. We suggest that measurement of coronary blood flow by Doppler-Flowire may bring some enlightment to the diagnostic problem of those patients whose clinical and non-invasive data resemble myocardial ischemia and whose coronary angiograms show normal but tortuose vessels. We also think it would better to consider these patients with distal flow impairment as patients with coronary heart disease and treat them likewise.

Correspondence to : Dr.Övsev DÖRTLEMEZ
Gazi Üniversitesi Tıp Fakültesi
Kardiyoloji Anabilim Dalı
Beşevler
06510 ANKARA - TÜRKİYE
Phone : 312 - 212 65 65 / 225

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