Prognostic Value of TIMI Frame Count in Patients with Metabolic Syndrome

Metabolik Sendromlu Hastalarda TIMI Kare Sayısının Prognostik Değeri

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Abstract

Background: The aim of our study was to determine the coronary angiographic distribution and frequency of atherosclerotic lesions in the coronary arteries in patients with stable angina and metabolic syndrome (MS) as well as to assess the association of these lesions with TIMI frame count and combinations of MS criteria.

Methods: Two hundred sixty-one patients aged 61.8±1.4 years were included in the study. All subjects were divided into three large groups: group 1 - patients with significant coronary artery stenosis and with MS (n=148), group 2 - patients with significant coronary artery stenosis and without MS (n=75), and group 3 - patients without significant coronary artery stenosis and without MS (n=38). At the same time, the patients in group 1 were again divided into 3 subgroups based on the number of MS criteria. Arterial blood pressure (BP), waist circumference (WC), and levels of fasting glucose (FG), triglycerides (TG) and high-density lipoproteins (HDL) were measured in all patients. All subjects underwent coronary angiography and TIMI frame count was calculated.

Results: According to the results in patients with stable angina with 5 criteria of MS, the TIMI frame count was significantly greater than in patients with stable angina with 3 and 4 criteria of MS. While in the group of patients with stable angina with 3 criteria of MS, the most frequent combination found was BP +WC + FG (28.3±6.2%), in patients with stable angina with 4 MS criteria, it was BP + WC + FG + HDL combination (48.0±7.1%).

Conclusions: The TIMI frame count method is simple, inexpensive and broadly applicable and plays role in the understanding of the physiology and pathophysiology of coronary artery blood flow in patients with stable angina and MS. For this reason, the calculation of TIMI frame count in patients with stable angina and MS has an important place in selecting the treatment options and determining the prognosis of the disease. *Turk Jem 2011; 15: 1-7*

Key words: Metabolic syndrome, stable angina, TIMI frame count

Özet

Amaç: Yapmış olduğumuz çalışmanın amacı metabolik sendromu (MS) olan stabil anginalı hastalarda aterosklerotik lezyonların koroner anjiyografik dağılımı ve sıklığının belirlenmesi ve aynı zamanda bu lezyonlarla TIMI kare sayısı ve MS kriter kombinasyonları arasında ilişkinin değerlendirilmesidir.

Materyel ve Metod: Çalışmaya ortalama yaşı 61.8±1.4 olan 261 hasta alındı.Tüm hastalar 3 büyük gruba ayrıldı. Grup 1`e MS ve koroner arterlerde anlamlı darlık olan 148 hasta, grup 2`e koroner arterlerde anlamlı darlık olan ve MS olmayan 75 hasta, grup 3`e MS ve koroner arterlerde anlamlı darlık olmayan 38 hasta alındı. Aynı zamanda grup 1`de olan hastalar MS kriter sayısına göre 3 alt gruba ayrıldı.Hastalarda arteryel kan basıncı (KB), bel çevresi (BÇ), açlık kan şekeri (AKŞ), trigliserid (TG) ve yüksek yoğunluklu kolesterol (HDL) değerleri ölçüldü. Hastalarda selektif koroner anjiyografi yapılarak TIMI kare sayısı hesaplandı.

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Bulgular: MS 5 kriteri bulunan stabil anginalı hastaların TIMI kare sayısı değerleri, MS 3 ve 4 kriteri bulunan stabil anginalı hastaların TIMI kare sayısı degerlerine göre anlamlı olarak daha fazla bulundu. MS 3 kriteri olan stabil anginalı hastalarda KB+BÇ+AKŞ (28,3±6,2%) kombinasyonu daha sık görüldü. MS 4 kriteri olan stabil anginalı hastalarda ise en sık KB+BÇ+AKŞ+HDL (48,0±7,1%) kombinasyonu görüldü.

Sonuç: TIMI kare sayısı basit, ucuz ve geniş uyğulanan metot olarak, MS ve stabil anginası olan hastalarda koroner kan akımının fizyolojisi ve patofizyolojisi ile ilgili önemli bilgiler verir. MS'i olan stabil anginalı hastalarda TIMI kare sayısının hesaplanması hastalığın prognozunun tayininde ve tedavi seçiminde önemli rolü olacaktır. *Türk Jem 2011; 15: 1-7*

Anahtar kelimeler: Metabolik sendrom, stabil angina,TIMI kare sayısı

Introduction

In 1988, a complex of symptoms involving hyperinsulinemia, impaired glucose tolerance, hypertriglyceridemia, arterial hypertension, and decreased high-density lipoprotein (HDL) cholesterol was defined as the metabolic syndrome (MS) by G. Reaven (1). G. Reaven was the first to demonstrate that this syndrome is in essence insulin-resistant and that it increases the risk of coronary artery disease. In 1989, J. Kaplan added abdominal obesity to this syndrome and called it the "fatal quartet" (2). According to statistical data, the frequency of MS ranges from 10 to 25% in the general population (3). Each of the MS criteria increases the risk of coronary artery disease by itself. This increased risk leads to the development and rapid progression of heart diseases at a younger age in the general population. An interaction of MS criteria also plays an important role in the rapid progression of heart diseases at a younger age. Consequently, all these risk factors create a vicious circle. The presence of abdominal obesity in patients with MS is one of the important factors in the increased risk of coronary artery disease (4). Studies dealing with this issue have demonstrated that over 50 years of age, 50% of the patients with abdominal obesity have arterial hypertension and ischemic heart disease and 30% of them have type 2 diabetes (5). Patients who have both abdominal obesity and impaired glucose tolerance have a 1.9- to 2.1-fold higher incidence of myocardial infarction (6,7). Abdominal obesity also triggers dyslipidemia leading to an elevation of atherogenic lipid levels in blood. Elevated atherogenic lipid levels and decreased anti-atherogenic lipid levels in blood result in accelerated formation of atherosclerotic lesions. Patients with MS usually have elevated TG and low-density lipoprotein (LDL) levels and decreased HDL levels (8). This triad is also referred as the atherogenic lipoprotein phenotype, which increases the risk of ischemic heart disease (9). It has been shown that the frequency of atherosclerosis accelerates at total cholesterol levels exceeding 150 mg/dl. Higher LDL cholesterol and lower HDL cholesterol levels are an important risk factor for atherosclerosis. Especially in patients with MS, a low level of HDL cholesterol has been shown to be highly important. More recently, the ratio of total cholesterol to HDL cholesterol has also been accepted as an important determinant of risk factors. If this ratio is greater than 6.4 in men, the risk is increased by 2 to 14% as compared with total and LDL cholesterol, whereas a ratio greater than 5.6 increases this risk by 25 to 45 percent (10). In patients with MS, several combinations of all these risk factors cause structural changes to occur in the intima and media of the arterial wall. These alterations occurring during adolescence evolve into yellowish-grayish fatty streaks containing smooth muscle cells and macrophages in the arteries. As the age increases, lipid particles begin to deposit on these fatty streaks, causing the lesions to develop. Continuing to grow over time, these lesions turn into plaques covered with fibrous cap and containing a large lipid core (11). In patients with MS, the plaques in the coronary arteries develop more rapidly, resulting in a serious decrease in blood flow through the coronary arteries. In stable angina patients with MS, the TIMI (thrombolysis in myocardial infarction) frame count plays an important role in the assessment of decreased coronary blood flow rate. Being an objective and simple method, the TIMI frame count was first introduced in 1990 to assess blood flow through coronary arteries (12). The TIMI frame count is calculated as the number of frames counted until the opaque substance travels from the coronary artery's ostium to pre-specified distal points (13). In individuals with coronary artery disease, the TIMI frame count objectively indicates coronary blood flow and plays an important role in the assessment of coronary microcirculation (13). In studies conducted by Sun and colleagues, the TIMI frame count was observed to significantly increase in coronary arteries, based on microvascular spasm with the effect of provocative factors (10,11). In stable angina patients with MS, the assessment of coronary blood flow by the TIMI frame count plays an important role in determining the prognosis as well. In studies conducted by Gibson and colleagues, a positive correlation between myocardial infarction and death has been shown by the TIMI frame count (12). The aim of our study was to determine the coronary angiographic distribution and frequency of atherosclerotic lesions in stable angina patients with MS as well as to assess the association of these lesions with TIMI frame count and combinations of MS criteria.

Materials and Methods

The study enrolled 261 patients (160 men and 101 women) with a mean age of 61.8±1.4 years. The study included those patients who had stable angina with clinically NYHA II-III functional capacity and who showed a coronary angiography indication as confirmed by non-invasive stress-test protocols. The subjects were assessed for coronary artery disease based on coronary angiography. Those cases that showed 75% or more lesions in coronary arteries were regarded to have significant coronary artery disease. Each patient was assigned to one of the 3 large groups: group 1 - patients with significant coronary artery stenosis and MS (n=148), group 2 - patients with significant coronary artery stenosis and without MS (n=75), and group 3 - patients without significant coronary artery stenosis and without MS (n=38). At the same time, the patients in group 1 were again divided into 3 subgroups based on the number of MS criteria. Table 1 shows the statistical data of the patients included in the study.

There was no significant difference in tobacco use between the groups. The diagnosis of MS was based on the presence of three of the following five criteria established by the National

Cholesterol Education Program -ATP III in 2001 (14).
1. A waist circumference (WC) of >102 cm in males and > 88 cm in females
2. A triglyceride (TG) level of ≥150 mg/dl
3. A high-density cholesterol (HDL) level of < 40 mg/dl in males and <50 mg/dl in females
4. Blood pressure (BP) of ≥130/85 mmHg
5. Fasting blood glucose (FBG) of ≥110 mg/dl

In all patients, arterial BP, anthropometric measurements, FBG, total cholesterol, TG and HDL levels were obtained. Blood values were measured with a ®Siemens Dimension maxÐ (Germany) biochemical analyzer. For all patients included in the study, the body mass index (BMI) was calculated with the following formula.

BMI=body weight (kg) / height (m^2)

Patients with coronary ectasia, anomalies, coronary vasospasms, non-selective coronary angiographies, cardiomyopathies, heart failure, and valvular or congenital heart disease, and those with arrhythmias which could induce hemodynamic changes likely to affect the TIMI frame count were excluded from the study. In the patients, coronary angiography was selectively performed through the right femoral artery and the right brachial artery using the Judkins technique. The results of coronary angiography were evaluated and reported by two experienced specialists who were blinded to the study. As diagnostic catheters, a 5F Judkins (Medtronic, Mexico) and a 5F brachial (Tiger Terumo, Belgium) catheter were used. An opaque medium containing lopromide was used to view coronary arteries (Ultravist-370 mgI/l, Germany). The coronary arteries were routinely viewed from the cranial and caudal angles in right and left oblique positions as described in previous studies (12). Coronary angiographies of the patients were taken using a ®GE HealthcareÐ (France) X-ray imaging device and ®Innova Biplane and Single-Plane X-ray SystemsÐ program. TIMI frame count calculations were performed using the "TIMI frame count" method applied by Gibson and colleagues (12). The first frame count was regarded as the point where the opaque substance covered 70% of the coronary artery lumen and continued to move forward. The last frame count was regarded as the frame where the opaque substance reached the distal standard points. The distal point was set as the first branch of the posterolateral artery for the right coronary artery (RCA), as the distal bifurcation or segment called the whale's tail for the left anterior descending (LAD) artery, and for the circumflex artery (Cx), it was the most distal segment of the obtuse marginal branch. The TIMI frame count was generally calculated based on the distance between two points from the right oblique cranial and caudal positions (RAO cranial, caudal) for LAD/Cx arteries and from the left oblique cranial (LAO cranial) position for RCA (12,13). Statistical calculations were performed using the SPSS computer program. The Student's t-test and Chi-square (X2) test were used to compare the data between the groups. A p-value below 0.05 was considered statistically significant.

Table 1. Group assignments of the patients based on the number of MS criteria and coronary artery disease

Groups		Number of criteria	Significant stenosis of 75% or more on coronary angiography
Group 1	(n=148)	≥3	+
Group 1a	(n=53)	3	+
Group 1b	(n=50)	4	+
Group 1c	(n=45)	5	+
Group 2	(n=75)	<3	+
Group 3	(n=38)	<3	-

Table 2. Distribution and mean ages of the patients

		Number of patients	Gender	Age
Total	261	M-160	F-101	
Group 1	56.7%	59.5%	40.5%	61.1±1.1
group 1a	35.8%	62.3%	37.7%	59.7±1.4
group 1b	33.8%	58.0%	42.0%	59.6±1.5
group 1c	30.4%	57.8%	42.2%	62.0±1.5
Group 2	28.7 %	62.7 %	37.3%	64.0±1.2
Group 3	14.6%	65.8 %	34.2%	60.2±1.7

Results

Of 261 study patients with stable angina, 223 were found to have 75% or more stenosis in their coronary arteries. Patients included in the groups showed no significant differences in terms of mean age. Table 2 shows the gender and age relationships of the patients included in the groups.

Systolic blood pressure (SBP) values of the patients included in group 1c (160.0±5.2, p1a =0.011, p2=0.0001, p3=0.00001) were found to be significantly higher than those in group 1a, group 2 and group 3. In group 1a, SBP values (142.9±4.0, p2=0.0001) were significantly higher than those in group 2. There were no significant differences in SBP values either between group 1a (142.9±4.0, p1b=0.215, p3=0.093) compared to group 1b (150.7±4.9) and group 3 (133.0±4.2), or between group 1b (150.7±4.9, p1c=0.198) and group 1c (160.0±5.2). The diastolic blood pressure (DBP) values of the patients included in group 1c (89.0±2.5, p2=0.01, p3=0.024) were found to be significantly higher than those in group 2 and group 3. Figure 1 shows BP values of the groups.

FBG values of the patients included in group 1c (180.7±26.3, p1a=0.001, p2=0.00001, p3=0.0001) were found to be significantly higher than those in group 1a (117.8±5.9), group 2 (95.7±1.7), and group 3 (101.2±2.4). There were no significant differences in FBG values between the patients in group 1c (180.7±26.3, p1b=0.353) and group 1b (152.9±15.9) and those in group 2 (95.7±1.7, p3=0.06) and group 3 (101.2±2.4). The patients in group 1c had significantly lower HDL values (34.2±2.1, p=0.001)

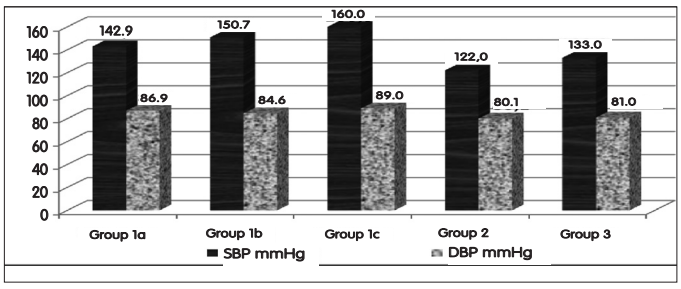

Figure 1. Blood pressure data of the groups

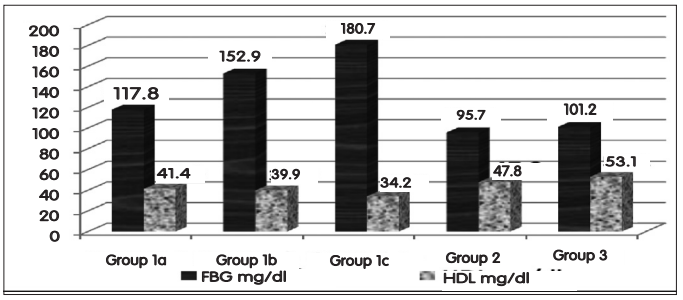

Figure 2. FBG and HDL data of the groups

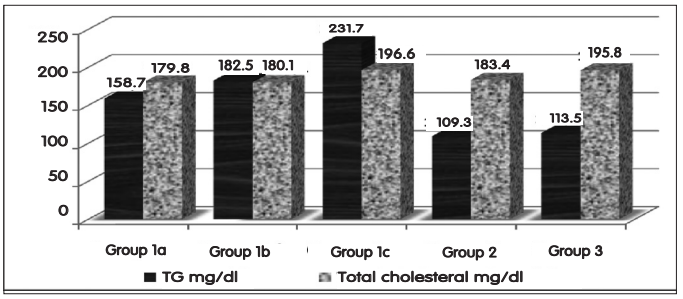

Figure 3. TG and total cholesterol data of the groups

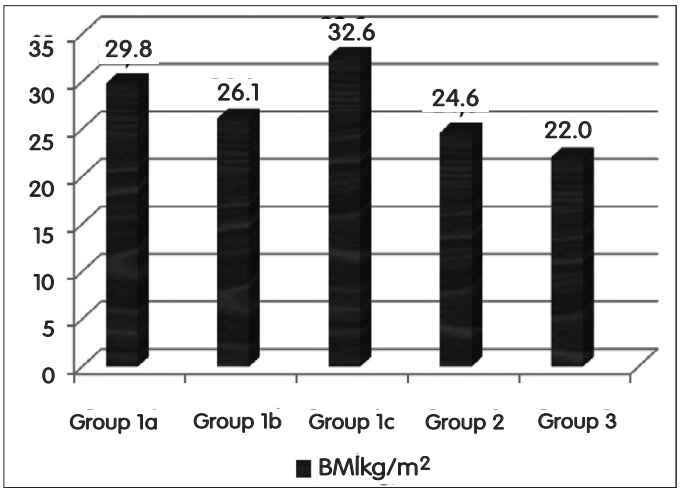

Figure 4a. BMI data of the groups

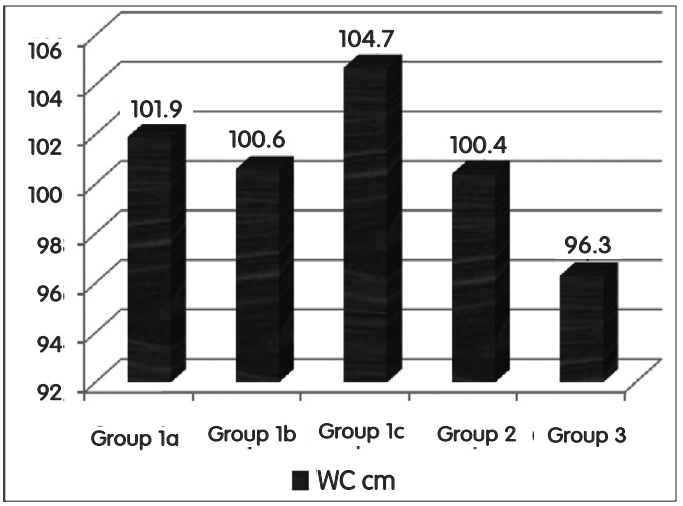

Figure 4b. WC data of the groups

than those in other groups. HDL values of the patients in group 1b (39.9±1.4, p2=0.02, p3=0.003) were found to be significantly lower than those in group 2 (47.8±1.7) and group 3 (53.1±2.2). The lowest HDL level was observed in group 1c (34.2±2.1) and the highest in group 3 (53.1±2.2). Figure 2 shows FBG and HDL values of the groups.

The study patients assigned to group 1c had significantly higher TG levels (TG 231.7±19.2, p1a=0.005, p2=0.00001, p3=0.0001) as compared with those in group 1a (TG 158.7±12.1), group 2 (TG 109.3±4.7), and group 3 (TG 113.5±5.7). And, TG levels of the patients in group 1b (182.5±25.1, p2=0.0001, p3=0.0001) were significantly higher than those in group 2 (TG 109.3±4.7) and group 3 (TG 113.5±5.7). No significant differences were seen between the patients in group 1a and group 1b, those in group 1b and group 1c and those in group 2 and group 3 in terms of TG values. No significant differences in total cholesterol were seen between the groups. Figure 3 shows TG and total cholesterol values of the groups.

The patients in group 1c had a significantly higher BMI (BMI 32.6±0.9, p1b=0.0001, p2=0.0001, p3=0.00001) when compared with those in group 1b (BMI 26.1±0.8), group 2 (BMI 24.6±0.7), and group 3 (BMI 22.0±0.6). The BMI in group 1a (BMI 29.8±0.9, p1b=0.007, p2=0.0001, p3=0.0001) was found to be significantly higher than that in group 1b (BMI 26.1±0.8), group 2 (BMI 24.6±0.7) and group 3 (BMI 22.0±0.6). No significant differences in BMI values were seen between either the patients in group 1a and group 1c or those in group 1b and group 2. The WC of the patients in group 1c (104.7±2.1, p3=0.011) was significantly higher than that of the patients in group 3 (WC 96.3±2.0). No significant differences in WC values were observed between the patients in group 1a and groups 1b, 1c, 2 and 3 and those in group 1b and group 3. Figure 4a and figure 4b present BMI and WC values of the groups.

In our study, the criterion of 75% or more lesions in LAD+ Cx+ RCA and RCA+LAD arteries was found to be significantly more frequent in the stable angina patients with MS in group 1 (group 1a, group 1b, group 1c) as compared to the stable angina patients without MS in group 2. However, single-vessel lesions (LAD, RCA) were significantly more frequently seen in the patients without MS in group 2. Moreover, the criterion of 50% or more lesions in the left main coronary artery (LMCA) was found to be more frequent in the patients in group 1 than in those in group 2. Figure 5 shows the comparison of angiographic data between the groups.

At the same time, the presence of lesions in multiple sites of a coronary artery (LAD, RCA, LMCA) was significantly more frequent in patients in group 1 than in those in group 2. Figure 6 show frequency data for angiographic lesions of the groups.

Among the patients enrolled in the study, the greatest TIMI frame

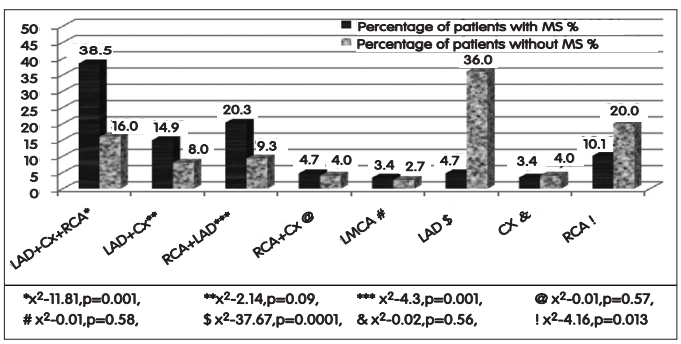

Figure 5. Comparison of angiographic data between the groups

count was observed in group 1c. The patients in group 3 however showed the lowest TIMI frame counts when compared with other groups. The RCA TIMI frame count (24.3±3.1, p1a=0.0122, p1b=0.021, p2=0.0014, p3= 0.0002) of the patients in group 1c was significantly higher than of those in group 1a

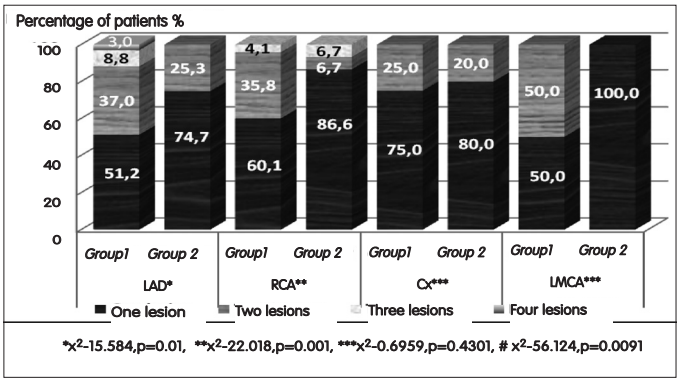

Figure 6. Frequency data for angiographic lesions in group 1 and group 2

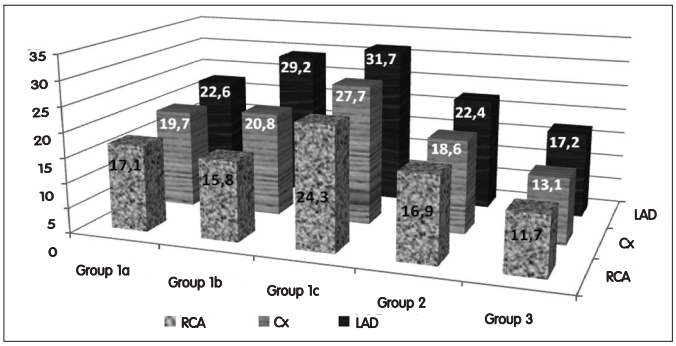

Figure 7. TIMI frame count data of the groups

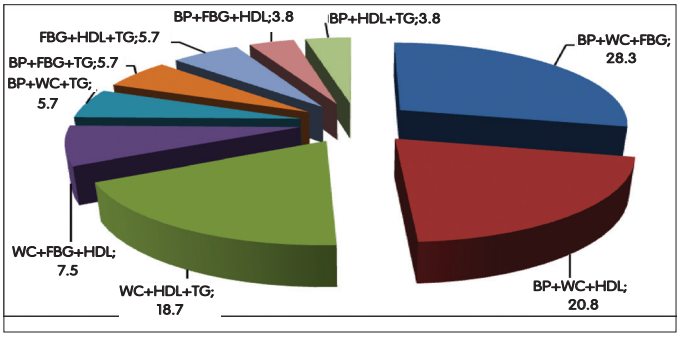

Figure 8. MS criteria combination data of the patients in group 1a

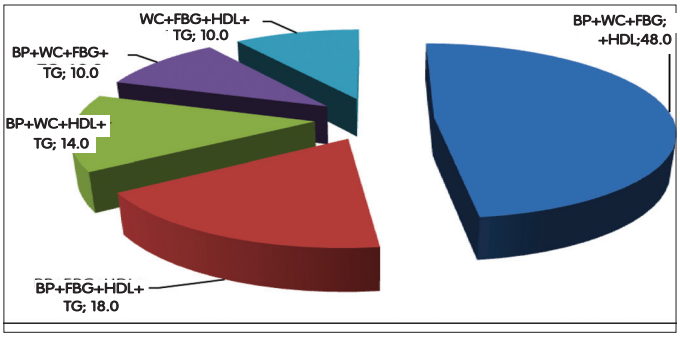

Figure 9. MS criteria combination data of the patients in group 1b

(TIMI frame count 17.1±1.2), group 1b (TIMI frame count 15.8±1.8), group 2 (TIMI frame count 16.9±0.7) and group 3 (TIMI frame count 11.7±0.7). The RCA TIMI frame counts of the patients in group 1a (17.1±1.2, p3=0.0099) and group 1b (15.8±1.8, p3=0.0461) were significantly higher than the RCA TIMI frame count of those in group 3 (11.7±0.7). The RCA TIMI frame count of the patients in group 1a was not significantly different than the RCA TIMI frame counts of the patients in groups 1b and 2. The LAD TIMI frame count of the patients in group 1c (31.7±1.7, p1a=0.002, p2=0.0013, p3=0.00001) was significantly higher than the LAD TIMI frame counts of the patients in groups 1a, 2 and 3. The LAD TIMI frame count of the patients in group 1b (29.2±2.4, p1a=0.0176, p2=0.0092, p3=0.0007) was significantly higher than the LAD TIMI frame counts of the patients in group 1a, group 2 and group 3. The LAD TIMI frame counts of the patients in group 1a (22.6±1.4, p3=0.041) and group 2 (22.4±0.9, p3=0.0429) were significantly higher than the LAD TIMI frame counts of the patients in group 3 (17.2±2.0). There were no significant differences between LAD TIMI frame count values of the patients in group 1a and group 2 and of those in groups 1b and 1c. The Cx TIMI frame count of the patients in group 1c (27.7±1.7, p1a=0.0005, p1b=0.019, p2=0.0001, p3=0.0001) was significantly higher than the Cx TIMI frame counts of the patients in all other groups. The Cx TIMI frame counts of the patients in group 1a (19.7±1.0,p3=0.0004), group 1b (20.8±2.0, p3=0.0011) and group 2 (18.6±0.7, p3=0.0026) were significantly higher than the Cx TIMI frame count of the patients in group 3 (13.1±0.6). There were no significant differences between Cx TIMI frame count values of the patients in group 1a and group 1b and those in group 1a and group 2. Figure 7 shows the comparison of TIMI frame count data of the groups.

In the patients in group 1a, the MS criteria combination of BP+WC+FBG was significantly more frequent (28.3±6.2%) than all other combinations. In addition, the criteria combinations of BP+WC+HDL (20.8±5.6%) and WC+HDL+TG (18.7±5.4%) were more frequent than the other 6 combinations. The least frequently seen MS criteria combinations were those of BP+FBG+HDL (3.8±2.6%) and BP+HDL+TG (3.8±2.6%). Figure 8 shows MS criteria combinations in group 1a.

In the patients in group 1b, the most frequently seen MS criteria combination was found to be BP+WC+FBG+HDL (48.0±7.1%). Other more frequently seen combinations were BP+FBG+HDL+TG (18.0±5.4%) and BP+WC+HDL+TG (14.0±4.9%). The least frequently seen combinations were BP+WC+FBG+TG(10.0±4.2%) and WC+FBG+HDL+TG(10.0±4.2%). Figure 9 shows MS criteria combinations in group 1b.

Discussion

In our study, lesions involving 2 and/or 3 vessels were significantly more frequently seen in stable angina patients with MS than in stable angina patients without MS. According to the available data, lesion distribution in stable angina patients showed the combinations of LAD+Cx+RCA and RCA+ LAD, respectively. However, single-vessel lesions were observed significantly more often in stable angina patients without MS. Single-vessel lesions were seen as LAD and RCA lesions. The results indicated that stable angina patients with MS showed a higher incidence of lesions on two or more sites of the same coronary artery. These lesions were seen in the LAD, RCA, and Cx arteries, respectively. MS patients with angiographically signifi-

cant stenosis had a higher TIMI frame count than non-MS patients with angiographically significant stenosis. A positive correlation was found between increasing number of MS criteria and TIMI frame count. Stable angina patients with 5 MS criteria had higher RCA, LAD and Cx TIMI frame counts than the stable angina patients with 3 MS criteria. The LAD TIMI frame count of the stable angina patients with 4 MS criteria was significantly higher than the LAD TIMI frame count of the patients with 3 MS criteria. Moreover, RCA and Cx TIMI frame counts of the stable angina patients with 4 MS criteria were significantly lower than TIMI frame counts of the patients with 5 MS criteria. And the most interesting aspect of our study was which criteria combinations were more frequently seen in the stable angina patients with 3 and 4 MS criteria. The results showed that the stable angina patients with 3 MS criteria had a higher frequency of the BP+WC+FBG combination (28.3±6.2%). Of the patients with a criteria combination of BP+WC+FBG, 50% were male and 50% were female patients. Moreover, though not significantly different within this group of patients, the combinations of BP+WC+HDL (20.8±5.6%) and WC+HDL+TG (18.7±5.4%) were significantly more frequent than in other groups. The combinations of BP+WC+HDL (males-87.5%, females-12.5%) and WC+HDL+TG (males - 71.4%, females - 28.6%) were more frequently seen in male patients. Based on this observation, it might be suggested that the MS criteria combination of BP+WC+FBG was the most effective one in affecting coronary blood flow in patients with 3 MS criteria. The results showed that the combination of BP+FBG+HDL and BP+HDL+TG was the least effective one in affecting coronary blood flow in patients with 3 MS criteria. In stable angina patients with 4 MS criteria, the combination of BP+WC+FBG+HDL (48.0±7.1%) was most frequently seen. The patients with this combination of criteria were all females. The second most frequently seen combination in stable angina patients with 4 MS criteria was BP+FBG+HDL+TG (18.0±5.4%). The patients with MS criteria combination of BP+FBG+HDL+TG were all males. The most rarely seen combinations in stable angina patients with 4 MS criteria were BP+WC+FBG+TG (10.0±4.2%) and WC+FBG+HDL+TG (10.0±4.2%). All these data suggest that stable angina patients with the MS criteria combination of BP+WC+FBG+HDL has a slower coronary blood flow. The results show that there is a positive correlation between increasing number of MS criteria and SBP, WC, BMI, FBG, and TG values in stable angina patients. In addition, a negative correlation was found between increasing number of criteria and HDL. However, no significant differences were detected in DBP and total cholesterol values. The fact that coronary atherosclerosis is widespread in patients with MS is associated with the endothelial dysfunction in this group of patients. With an increase in the synthesis of vasoconstructive substances on the vascular wall due to endothelial dysfunction in patients with MS, there also occurs an increase in susceptibility to these substances. At the same time, in patients with coronary artery disease, decreased fibrinolytic activity of the blood, increased microthrombosis, excessive synthesis of insulin-like growth factor (IGBF-1) in the liver and elevated atherogenic lipid levels in the blood result in more rapid growth of atherosclerotic lesions (15-19). An assessment of coronary blood flow in patients with MS and coronary artery disease has an important role in the long-term follow-up of coronary artery disease (20,21). Manginas and colleagues have shown that the measurement of TIMI frame count in patients with coronary artery disease is a relatively reliable, simple, and easy method (13). Factors affecting TIMI frame count in patients with coronary artery disease were specified as left ventricular hypertrophy, arterial blood pressure, heart rate, dyslipidemia, coronary vasospasm, microvascular dysfunction, microthrombosis in coronary arteries, and the coronary artery's lumen area (22-25). In their studies, Tanedo and colleagues have shown that there is a significant positive correlation between the coronary artery's lumen area and TIMI frame count (26). The presence of fixed lesions in coronary arteries of stable angina patients with MS leads to a hemodynamic decrease in the luminal area and also, to a decrease in coronary reserve (27). A study conducted in Finland and Switzerland with 4,483 diabetic patients examined the relationship between combinations of MS criteria and cardiovascular mortality (28). The results of this study demonstrated that the most frequently seen combinations of MS criteria in patients with MS were obesity+dyslipidemia, obesity+ hypertension, and obesity+hypertension+dyslipidemia. In another concomitant study, patients with MS had coronary artery disease (21.4%, p=0.001), myocardial infarction (9.0%,p=0.001), and stroke (4.8%, p=0.01) more frequently than those without MS. In this study, 10% of the patients with MS died during the 6.9 years of follow-up, 5.8% of deaths being due to a cardiovascular disease. As a comparison, 4.6% of the patients without MS died, 2.2% of deaths being due to a cardiovascular disease. Also, the DIG (Diabetes in Germany) study conducted in Germany in 4,020 diabetes patients has provided valuable information on combinations of MS criteria. Of the study patients with 3 MS criteria, 50.7% showed the criteria combination of BP+WC+FBG. But the patients with 4 MS criteria demonstrated the criteria combination of BP+WC+FBG+TG (31.9%) more frequently. All of the other combinations remained below 10 percent (29). Our results indicate that the MS criteria combinations of BP+WC+FBG and BP+WC+FBG+HDL increase the risk of coronary artery disease. These results have suggested that stable angina patients with MS would have more widespread coronary artery disease and a slower blood flow rate if they have the combinations of BP+WC+FBG and BP+WC+FBG+HDL. Timely detection of the patients with such a combination of MS criteria and calculation of TIMI frame counts following a coronary angiography should play an important role in the assessment of risks, estimation of prognosis, and selection of treatment modalities.

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