Relationship between metabolic syndrome and angiographic severity of coronary artery disease

Reza Miri[1], Amir Sajjadieh[2], Mohammad Parsamahjoob[1], Bahareh Hajibaratali[3], Masood Shekarchizadeh[4], Ali Asghar Kolahi[5], Mehran Sadeghi[6], Zahra Ahmadi[7], Hamedreza Farmanara[8], Mansoureh Shekarchizadeh-Esfahani[9]

Original Article

Abstract

BACKGROUND: There are a few literature data on the correlation between metabolic syndrome (MetS) and coronary disease among Iranian population. This study aimed to find relationship between MetS and severity of coronary artery disease (CAD) in presence of diabetes.

METHODS: Total of 192 patients were consecutively enrolled in the study who were admitted to coronary care unit because of acute coronary syndrome (ACS) and then underwent coronary angiography. MetS was defined by Iranian criteria. A coronary atherosclerosis score was used to quantify the extent of atherosclerotic involvement. The relationship between MetS and angiographic coronary artery disease (CAD) severity or clinical presentation was compared between them after adjusting for diabetes.

RESULTS: Individuals with MetS (n = 125) had a higher prevalence of ST-elevation myocardial infarction (71% vs 30%, P < 0.001), multi-vessel disease (50% vs 34%, P = 0.003), decreased ejection fraction (P = 0.001) and more severe angiographic stenosis based on both modified Gensini (P = 0.081) and syntax (P = 0.008) scores, compared to those without MetS. Syntax score showed statistically significant difference between two groups before (P = 0.021) and after adjustment for diabetes (P = 0.005).

CONCLUSION: MetS was related to the severity of CAD both clinically and by angiographic scores but diabetes was a challenging factor and may independently increase the severity of CAD.

Keywords: Metabolic Syndrome, Angiography, Severity, Coronary Artery Disease

Date of submission: 13 Jun 2015, ***Date of acceptance:*** 17 Aug 2016

Introduction

Metabolic syndrome (MetS) is considered a major health problem in recent years and recognized by a cluster of risk factors related to diabetes and amplified risk of coronary artery disease (CAD).[1,2] Previous studies have shown that Asians have additional risk for development of MetS since the prevalence of abdominal obesity and diabetes are greater among them.[3] Despite important controversy, the increased risk of cardiovascular diseases in subjects suffering from MetS has been established.[4,5] Recent epidemiological and clinical studies have confirmed the association between MetS and increased risk of CAD,[6,7] which is the leading cause of mortality. Morbidity and mortality from CAD are greater in patients with MetS; consequently, early evaluation of the risk of CAD in patients with MetS is necessary since it could lead to

1- Associate Professor, Department of Cardiology, Shahid Beheshti University of Medical Sciences AND Imam Hossein Hospital, Tehran, Iran
2- Associate Professor, Department of Cardiology, Isfahan University of Medical Sciences, Isfahan, Iran
3- Associate Professor, Department of Cardiology, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4- Internist, Fellow of Cardiology, Rajaei Cardiovascular Research Center AND Department of Cardiology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
5- Associate Professor, Social Determinants of Health Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran
6- Resident, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran
7- Resident, Department of Cardiology, Modarres Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
8- Resident, Department of Sports Medicine, Iran University of Medical Sciences, Tehran, Iran
9- Internist, Department of Internal Medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Correspondence to: Masood Shekarchizadeh, Email: masoodshekarchi@sbmu.ac.ir

change in lifestyle behavior and reducing CAD risk factors. Diabetes is considered as one of the complications of obesity and a strong risk factor for CAD.[8-10] There is evidence that shows the duration of diabetes is associated with greater risk of acute coronary syndrome (ACS) and CAD.[11-14] So this study was conducted to evaluate whether MetS could be associated with the coronary artery disease severity and to see whether the severity of coronary lesion was different in MetS patients with or without type 2 diabetes.

Materials and Methods

This cross-sectional study was done from February 2012 to March 2015 in Shahid Beheshti University of Medical Sciences, Tehran, Iran. Totally 192 patients were enrolled in the study, who were admitted to coronary care unit (CCU) due to chest pain, and subsequently underwent coronary angiography. Patients entered the study after obtaining written informed consent. Positive family history of coronary artery disease, current smoker or ex-smoker, subjects with high low-density lipoprotein-cholesterol (LDL-C) (LDL level > 160 mg/dl and or under treatment for high LDL) and prior coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) were considered as exclusion criteria. Data on social, demographic, personal and family medical history, and lifestyle (physical activity, smoking, alcohol intake, and diet) were obtained from either physical and laboratory examinations (anthropometric testing, blood sample laboratory analysis, and blood pressure measurements) or questionnaires. Triglyceride (TG), high-density lipoprotein-cholesterol (HDL-C) and fasting blood sugar (FBS) levels were measured by enzymatic methods (Pars Azmon commercial kits, Iran) based on previously published methods.[15]

Blood pressure was measured twice in sitting position after five minutes resting. Waist circumference was measured with a flexible tape placed on a horizontal plane at the level of the iliac crest as seen from the anterior view.[16]

Extent of coronary artery disease was assessed by modified Gensini and syntax scoring systems.

On quantitative analyses of coronary angiograms (Quantcor QCA, version 4.0; Pie Medical Imaging, Maastricht, The Netherlands), the presence of stenosis ≥ 50% in diameter of major epicardial vessels was characterized as CAD (Gensini score > 1).

The extent of CAD was quantified using the number of vessels with ≥ 50% stenosis and a coronary atherosclerosis score as mentioned below.[17,18]

The syntax score system used to show the severity of CAD quantitates the complexity and the extent of CAD to aid clinicians in assessing early and late outcomes of PCI and CABG in patients with multivessel CAD and has become the preferred risk assessment tool for grading lesion complexity.[19]

All statistical analyses were performed by SPSS (version 22.0, SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test and Q-Q plot were used to examine normality of data. Qualitative variables were expressed as numbers (percentages) and quantitative data was showed by mean and standard deviation (SD). Multiple logistic regression was used to compare the types of (ACS) and angiographic recommendations after adjustment for diabetes. P-values were considered significant at a level of < 0.05.

Results

Among 192 patients, 138 (71.9%) patients were male, and 125 (65%) patients fulfilled the criteria of MetS. Patients without MetS were significantly older than MetS group (P < 0.001). The prevalence of diabetes was 47%. Table 1 shows summary of clinical characteristics based on the presence of the MetS. Blood pressure, waist circumference, FBS, cholesterol (CHL), HDL-C, LDL-C, creatine phosphokinase-MB (CPK-MB) and troponin were significantly different in subjects with MetS compared to those free of MetS (P < 0.001). Table 2 shows among patients with MetS, low HDL-C (95%) was the most frequent component followed by increased waist circumference (82%), elevated FBS (76%), hypertension (HTN) (71%), and elevated TG (39%). The frequency of MetS components in all the subjects was as follows: Low HDL-C (80%), diabetes (70%), increased waist circumference (63%), HTN (50%), elevated TG (26%). Similar to the MetS group, low HDL-C was the most frequent finding (80%) in all the cases without MetS. Table 2 shows regardless of existing MetS, diabetic patients had significantly different Gensini scores (P < 0.001) and syntax scores (P = 0.007) compared to non-diabetic patients. Among hypertensive patients, only the syntax score was significantly different (P = 0.030) compared with normotensive patients while Gensini score (P = 0.900) showed no significant difference (data not shown).

Table 1. Demographic and biochemical parameters in the study patients

	Total	MetS		P
		Yes	No	
Number	192	125 (65.0)	67 (35.0)	
Age				
Mean ± SD	65.00 ± 11.00	63.0 ± 11.00	68.00 ± 10.00	0.007†
Median (range)	63 (44.00-85.00)	61 (44.00-85.00)	70 (46.00-82.00)	
Diastolic blood pressure				
Mean ± SD	81.00 ± 13.00	84.0 ± 14.00	75.00 ± 9.00	0.001†
Median (range)	80 (40.00-140.00)	80 (40.00-140.00)	80 (60.00-90.00)	
Waist Circumference				
Mean ± SD	98.00 ± 11.00	102.0 ± 10.00	92.00 ± 9.00	< 0.001†
Median (range)	98 (71.00-123.00)	102 (71.00-123.00)	89 (79.00-113.00)	
CPK				
Mean ± SD	1156.00 ± 1342.00	1509.0 ± 1462.00	499 ± 721	< 0.001‡
Median (range)	642 (46.00-6400.00)	1222 (57.00-6400.00)	250 (46.00-2982.00)	
CPK-MB				
Mean ± SD	137.00 ± 154.00	170.0 ± 161.00	75.00 ± 117.00	< 0.001‡
Median (range)	67 (15.00-696.00)	121 (20.00-696.00)	36 (15.00-510.00)	
Troponin				
Mean ± SD	0.96 ± 0.93	1.2 ± 0.92	0.51 ± 0.78	< 0.001‡
Median (range)	0.87 (0.02-3.16)	1.17 (0.02-3.16)	0.03 (0.02-2.48)	
Fasting blood pressure				
Mean ± SD	136.00 ± 63.00	141.0 ± 61.00	126.00 ± 66.00	0.003‡
Median (range)	118 (60.00-370.00)	129 (60.00-369.00)	101 (72.00-370.00)	
TG				
Mean ± SD	129 ± 75	147.0 ± 85.00	101.00 ± 38.00	< 0.001‡
Median (range)	105 (57.00-511.00)	121 (57.00-511.00)	91 (60.00-189)	
HDL-C				
Mean ± SD	36.00 ± 7.00	34.0 ± 7.00	39.00 ± 7.00	< 0.001†
Median (range)	36 (21.00-52.00)	35 (21.00-52.00)	41 (23.00-49.00)	
LDL-C				
Mean ± SD	97.00 ± 33.00	102.0 ± 33.00	88.00 ± 29.00	0.005†
Median (range)	94 (11.00-208.00)	97 (29.00-208.00)	89 (11.00-124.00)	
Systolic blood pressure				
Mean ± SD	134.00 ± 28.00	141.0 ± 29.00	121.00 ± 22.00	<0.001†
Median (range)	130 (70.00-240.00)	140 (70.00-240.00)	120 (85.00-190.00)	
Cholesterol				
Mean ± SD	162 ± 33	166.0 ± 38.00	154.00 ± 22.00	0.015†
Median (range)	161 (90.00-280.00)	171 (98.00-280.00)	157 (90.00-183.00)	
Acute coronary artery disease				
STEMI [n(%)]	109 (56.8)	89 (71.2)	20 (29.9)	< 0.001*
Non STEMI [n(%)]	16 (8.3)	16 (12.8)	0 (0.0)	
USA [n(%)]	67 (34.9)	20 (16.0)	47 (70.1)	
Diabetes				
Yes [n(%)]	91 (47.4)	71 (56.8)	20 (29.9)	< 0.001*
No [n(%)]	101 (52.6)	54 (43.2)	47 (70.1)	
Sex				
Male [n(%)]	138 (71.9)	79 (63.2)	59 (88.1)	< 0.001*
Female [n(%)]	54 (28.1)	46 (36.8)	8 (11.9)	
Hypertension				
Yes [n(%)]	97 (50.5)	89 (71.2)	8 (11.9)	< 0.001*
No [n(%)]	95 (49.5)	36 (28.8)	59 (88.1)	

* Based on chi-square test; † Based on Student's t-test; ‡ Based on Mann-Whitney test

MetS: Metabolic syndrome; STEMI: ST-elevation myocardial infarction; CPK: Creatine phosphokinase; TG: Triglyceride; LDL-C: Low-density lipoprotein-cholesterol; HDL-C: High-density lipoprotein-cholesterol; USA: Unstable angina

Table 2. Relationship between metabolic syndrome and angiographic severity of coronary artery disease

		Total	MetS		P	Model 1	Model 2
			Yes	No			
Gensini score	Mean ± SD	6.7 ± 2.8	7.1 ± 2.6	5.9 ± 2.9	0.004*	0.137£	0.081§
Syntax score	Mean ± SD	13.7 ± 7.7	14.9 ± 6.6	11.5 ± 8.9	0.008*	0.020£	0.005§
Ejection fraction	Mean ± SD	45.5 ± 8.7	44.6 ± 8.8	47.4 ± 8.4	0.032*	0.018£	0.002§
Angiographic results	SVD [n(%)]	26 (13.5)	10 (8.0)	16 (23.9)	< 0.001**	0.006£	0.003£
	2VD [n(%)]	77 (40.1)	53 (42.4)	24 (35.8)			
	3VD [n(%)]	85 (44.3)	62 (49.6)	23 (34.3)			
	LMS [n(%)]	4 (2.1)	0 (0.0)	4 (6.0)			
Medical treatment	Medical treatment [n(%)]	7 (3.6)	3 (2.4)	4 (6.0)	0.363**	0.101£	0.187£
	PCI [n(%)]	100 (52.1)	64 (51.2)	36 (53.7)			
	CABG [n(%)]	85 (44.3)	58 (46.4)	27 (40.3)			

Model 1: Adjusted for diabetes; Model 2: Adjusted for diabetes, age and sex; * Based on Student's t-test; ** Based on Fisher exact test; § Based on analysis of covariance; £ Based on multinomial logistic regression; MetS: Metabolic syndrome; SVD: Single-vessel disease; 2VD: Two-vessel disease; 3VD: Three-vessel disease; LMS: Left main stem; PCI: Percutaneous coronary angiography; CABG: Coronary artery bypass graft

ST-elevation myocardial infarction (STEMI) was more frequent in MetS group (P < 0.001). The frequency of multi-vessel disease was higher in patients with MetS compared to those without it (P < 0.001 and after adjustment P < 0.003).

However, syntax score showed statistically significant difference between two groups before (P = 0.008) and after adjustment for diabetes (P = 0.020) and age and sex (P = 0.005). Concerning the ejection fraction, the same result was observed after adjustment for diabetes status and age and sex (P = 0.032, P = 0.018, P = 0.002, respectively) (data not shown).

Discussion

This study showed significant relationship between MetS and CAD severity according to angiography documents in Iranian subjects. In addition, we showed that presence of diabetes has significant effect on the CAD severity among subjects with MetS.

Numerous studies have shown that MetS is able to predict cardiovascular events and diabetes, but there is argument about the role of MetS in cardiovascular risk among diabetic patients.[20-23] Yoon et al. showed there is no relationship between MetS and coronary atherosclerosis in diabetic subjects.[21] In addition, Won et al. showed among symptomatic Korean population, MetS was independently associated with the presence and severity of CVD only in the non-diabetic subjects, and there was no significant difference between MetS group and non-MetS group regarding their age.[24]

Similar to our results, Solymoss et al. showed that MetS was significantly related to more severe coronary angiographic alterations and higher frequencies of unstable angina, myocardial infarction, PCI, and CABG.[18] Another important finding in our study was the 1.5 to 3 fold increased risk of new onset CVD in patients with MetS without diabetes.[14]

In our study, there was significant difference between modified Gensini score and syntax score. This comparison showed that patients with MetS had more severe atherosclerosis in coronary arteries by both scores.

After adjusting the effect of diabetes, syntax score was significantly associated with MetS, however the modified Gensini score did not have any significant association with MetS. Another important point is the effect of age. Patients without MetS were significantly older than other group after adjusting for age; Gensini score had non-significant relationship with MetS whereas syntax score was significantly related to the MetS. So apparently modified Gensini score, which was used in this study, was a better predictor; also, the syntax score was more complete than modified Gensini score.[18]

The syntax index assigns a heavier weight to the more severe luminal narrowing. Weights are also assigned to each segment depending on vessel size and importance; segments serving larger regions of myocardium are more heavily weighted.[23] Another probable cause, as mentioned earlier, is a semantic argument about the effects of diabetes on metabolic syndrome, which might have affected our results.[23]

Also in MetS group, the patients had more multi-vessel disease and more acute events (STEMI versus unstable angina); although they were younger in comparison to MetS patients.

Conclusion

MetS is strongly related to the severity of ACS presentation, documented clinically and angiographically in younger subjects. As such, control of MetS components is necessary in Iranian population. We recommend more studies with more participants and multicenter design and evaluation of Iranian lifestyle and MetS components, also utilizing complete Gensini score and other angiographic scores[24-28] with larger samples.

Acknowledgments

We would like to acknowledge the patients for their participation and staffs of CCU centers. We also thank Mrs. Ghodsi Najjari nurse of Imam Hossein Hospital CCU, Dr. Alireza Ebadi Associate Professor of Endocrinology, and Dr. Mehdi Yaseri, Assistant Professor of Biostatistics for their cooperation.

Conflict of Interests

Authors have no conflict of interests.

References

1. Timoteo AT, Mota Carmo M, Cruz Ferreira R. Does metabolic syndrome predict significant angiographic coronary artery disease? Rev Port Cardiol 2012; 31(12): 769-78.
2. Richelsen B, Pedersen SB. Associations between different anthropometric measurements of fatness and metabolic risk parameters in non-obese healthy, middle-aged men. Int J Obes Relat Metab Disord 1995; 19(3): 169-74.
3. Koh KK, Han SH, Quon MJ. Inflammatory markers and the metabolic syndrome: insights from therapeutic interventions. J Am Coll Cardiol 2005; 46(11): 1978-85.
4. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991; 14(3): 173-94.
5. Lindsay RS, Howard BV. Cardiovascular risk associated with the metabolic syndrome. Curr Diab Rep 2004; 4(1): 63-8.
6. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes 1988; 37(12): 1595-607.
7. St-Onge MP, Janssen I, Heymsfield SB. Metabolic syndrome in normal-weight Americans: new definition of the metabolically obese, normal-weight individual. Diabetes Care 2004; 27(9): 2222-8.
8. Ruderman N, Chisholm D, Pi-Sunyer X, Schneider S. The metabolically obese, normal-weight individual revisited. Diabetes 1998; 47(5): 699-713.
9. Conus F, Allison DB, Rabasa-Lhoret R, St-Onge M, St-Pierre DH, Tremblay-Lebeau A, et al. Metabolic and behavioral characteristics of metabolically obese but normal-weight women. J Clin Endocrinol Metab 2004; 89(10): 5013-20.
10. Yang RF, Liu XY, Lin Z, Zhang G. Correlation study on waist circumference-triglyceride (WT) index and coronary artery scores in patients with coronary heart disease. Eur Rev Med Pharmacol Sci 2015; 19(1): 113-8.
11. Srinivasan MP, Kamath PK, Bhat NM, Pai ND, Bhat RU, Shah TD, et al. Severity of coronary artery disease in type 2 diabetes mellitus: Does the timing matter? Indian Heart J 2016; 68(2): 158-63.
12. Talaei M, Sadeghi M, Marshall T, Thomas GN, Kabiri P, Hoseini S, et al. Impact of metabolic syndrome on ischemic heart disease-a prospective cohort study in an Iranian adult population: Isfahan Cohort Study. Nutr Metab Cardiovasc Dis 2012; 22(5): 434-41.
13. Kasai T, Miyauchi K, Kubota N, Tamura H, Kojima T, Yokoyama K, et al. The relationship between the metabolic syndrome defined by various criteria and the extent of coronary artery disease. Atherosclerosis 2008; 197(2): 944-50.
14. Kasper DL, Fauci AS, Hauser S, Longo D, Jameson J, Loscalzo J. Harrison's Principles of Internal Medicine. 19th ed. Philadelphia, PA: McGraw Hill Professional; 2015. p. 2449-54.
15. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome--a new worldwide definition. Lancet 2005; 366(9491): 1059-62.
16. Delavari A, Forouzanfar MH, Alikhani S, Sharifian A, Kelishadi R. First nationwide study of the prevalence of the metabolic syndrome and optimal cutoff points of waist circumference in the Middle East: the national survey of risk factors for noncommunicable diseases of Iran. Diabetes Care 2009; 32(6): 1092-7.
17. Gharipour M, Sadeghi M, Dianatkhah M, Bidmeshgi S, Ahmadi A, Tahri M, et al. The cut-off values of anthropometric indices for identifying subjects at risk for metabolic syndrome in Iranian elderly men. J Obes 2014; 2014: 907149.
18. Solymoss BC, Bourassa MG, Campeau L, Sniderman A, Marcil M, Lesperance J, et al. Effect of increasing metabolic syndrome score on atherosclerotic risk profile and coronary artery disease angiographic severity. Am J Cardiol 2004; 93(2): 159-64.
19. Mann DL, Zipes DP, Braunwald E, Libby P, Bonow RO. Braunwald's heart disease: A textbook of cardiovascular medicine. 10th ed. Philadelphia, PA: Elsevier/Saunders; 2015.
20. Gharipour M, Sadeghi MM, Sadeghi M, Farhmand N, Sadeghi PM. Detrimental predictive effect of

metabolic syndrome on postoperative complications in patients who undergoing coronary artery bypass grafting. Acta Biomed 2015; 86(1): 86-91.

21. Yoon SE, Ahn SG, Kim JY, Park JS, Shin JH, Tahk SJ, et al. Differential relationship between metabolic syndrome score and severity of coronary atherosclerosis as assessed by angiography in a non-diabetic and diabetic Korean population. J Korean Med Sci 2011; 26(7): 900-5.

22. Gensini GG. Coronary arteriography. Austin, TX: Futura Pub. Co; 1975. p. 261.

23. Ringqvist I, Fisher LD, Mock M, Davis KB, Wedel H, Chaitman BR, et al. Prognostic value of angiographic indices of coronary artery disease from the Coronary Artery Surgery Study (CASS). J Clin Invest 1983; 71(6): 1854-66.

24. Won KB, Chang HJ, Sung J, Shin S, Cho IJ, Shim CY, et al. Differential association between metabolic syndrome and coronary artery disease evaluated with cardiac computed tomography according to the presence of diabetes in a symptomatic Korean population. BMC Cardiovasc Disord 2014; 14: 105.

25. Ertek S, Cicero AF, Cesur M, Akcil M, Altuner KT, Avcioglu U, et al. The severity of coronary atherosclerosis in diabetic and non-diabetic metabolic syndrome patients diagnosed according to different criteria and undergoing elective angiography. Acta Diabetol 2011; 48(1): 21-7.

26. Dai DF, Lin JW, Kao JH, Hsu CN, Chiang FT, Lin JL, et al. The effects of metabolic syndrome versus infectious burden on inflammation, severity of coronary atherosclerosis, and major adverse cardiovascular events. J Clin Endocrinol Metab 2007; 92(7): 2532-7.

27. Kim JY, Mun HS, Lee BK, Yoon SB, Choi EY, Min PK, et al. Impact of metabolic syndrome and its individual components on the presence and severity of angiographic coronary artery disease. Yonsei Med J 2010; 51(5): 676-82.

28. Srinivasan MP, Kamath PK, Manjrekar PA, Unnikrishnan B, Ullal A, Kotekar MF, et al. Correlation of severity of coronary artery disease with insulin resistance. N Am J Med Sci 2013; 5(10): 611-4.

How to cite this article: Miri R, Sajjadieh A, Parsamahjoob M, Hajibaratali B, Shekarchizadeh M, Kolahi AA, et al. **Relationship between metabolic syndrome and angiographic severity of coronary artery disease.** ARYA Atheroscler 2016; 12(5): 220-5.