Arch Iran Med. December 2018;21(12):572-577

http www.aimjournal.ir

ARCHIVES OF IRANIAN MEDICINE

Original Article

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Comparison of Lipid Ratios to Identify Metabolic Syndrome

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Abstract

Background: The objective of this study was to compare various lipid ratios for detection of metabolic syndrome (MetS) in the Iranian general population.

Methods: This cross-sectional study involved 5677 subjects aged ≥18 years from the general population in Kerman, Iran. Associations between lipid ratio quartiles and MetS were analyzed using logistic regression models. The areas under receiver operating characteristic (ROC) was calculated to determine the accuracy of lipid ratios in predicting MetS.

Results: The adjusted chance of having MetS across quartiles of all lipid ratios had an increasing significant pattern ($P < 0.0001$). The area under the curves of triglyceride/high-density-lipoprotein-cholesterol (TG/HDL-C) ratio was 0.85 (95% CI = 0.84–0.87) in men and 0.85 (95% CI = 0.84–0.86) in women, of total cholesterol (TC)/HDL-C ratio was 0.79 (95% CI = 0.77–0.81) in men and 0.79 (95% CI = 0.77–0.81) in women and of low-density-lipoprotein cholesterol (LDL-C)/HDL-C ratio was 0.73 (95% CI = 0.71–0.75) in men and 0.74 (95% CI = 0.72–0.76) in women.

Conclusion: Our results indicate that the TG/HDL-C Ratio is a better marker than the LDL-C/HDL-C ratio and the TC/HDL-C ratio for identifying MetS in the Iranian population and could be used in clinical practice.

Keywords: Area under the curve, Lipid ratios, Metabolic syndrome

Cite this article as: Rezapour M, Shahesmaeili A, Hossinzadeh A, Zahedi R, Najafipour H, Gozashti MH. Comparison of lipid ratios to identify metabolic syndrome. Arch Iran Med. 2018;21(12):572–577.

Received: March 28, 2018, Accepted: October 28, 2018, ePublished: December 1, 2018

Introduction

Metabolic syndrome (MetS), which is characterized by a collection of interrelated disorders such as abdominal obesity, hypertension, dyslipidemia and hyperglycemia, has had an increasing pattern of growth during recent years.[1] It is estimated that 20%–25% of the adult population around the world suffer from MetS[2] and the prevalence varies between <10% to 84% depending on the population and the MetS definition criteria.[3] The results of a population-based cohort study in Iran indicates that the pattern is also increasing (35.6% in 2001 vs. 42.5% in 2013) in this country.[4] Various factors such as sedentary life style, urbanization, higher level of income and obesity have been associated with MetS.[2,5,6] The evidence indicate that individuals with MetS are at higher risk of getting diabetes type 2, chronic kidney diseases, and cognitive impairment.[7-11] Growing body of evidence indicates that MetS increase risk of morbidities such as cardiovascular diseases, diabetes mellitus cardiovascular mortality and all-cause mortality.[12-14]

As the early diagnosis and treatment of MetS may prevent its progress to unwanted complications, identifying appropriate criteria that accurately differentiate patients from healthy subjects may be beneficial from the clinical point of view. The NCEP ATP III is one of the most widely used criteria for diagnosis of MetS[15] but it requires measurement of waist circumference (WC) which is not measured routinely by health care providers[16] and this consequently postpones early diagnosis of the affected population. Recently, indices of lipid ratios such as total cholesterol/high-density lipoprotein cholesterol (TC/HDL-C), triglyceride (TG)/HDL-C and low-density lipoprotein cholesterol (LDL-C)/ HDL-C has been suggested as alternatives for diagnosis of MetS.[1,16-19] It seems that clinical usefulness of lipid ratios (that simultaneously use serum levels of two lipids) to identify MetS are better than individual lipids[16,20-22] but research on accuracy of this approach in diagnosis of this Mets is limited and restricted to specific populations.[16,23-25]

While the criteria for diagnosis of MetS may vary based on differences in definition of its components in different populations, specific studies on specifying the diagnostic criteria are needed. In the Iranian population, only limited number of studies have been conducted on the accuracy of lipid ratios in diagnosis of MetS.[26] Thus, the objective of this study was to compare the discriminative ability of lipid ratios (TC/HDL-C, TG/HDL-C and LDL-C/HDL-C) to identify men and women with MetS and to determine their relevant optimal cut-offs in Iranian adults. We also compared the results obtained from the NCEP ATP III criteria to those from the Iranian-adapted criteria.

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Materials and Methods

Recruitment and Data Collection

In this cross-sectional study, we analysed the baseline data of 5679 individuals aged 18–87 years, who participated in this study from September 2009 to September 2011 in the KERCADRS (Kerman Coronary Artery Disease Risk Factor Study) population-based cohort study. The study profile has been reported in detail previously.[27]

After obtaining informed consent, 10 mL venous fasting blood sample was derived from each participant to measure serum lipids and fasting blood sugar using enzymatic methods. All participants underwent a structured face-to-face interview to collect demographic and behavioral/life-style related variable data. Physical examination was done to obtain anthropometric measures and blood pressure. Weight was measured without shoes and extra clothing by an error of ±100 g. Height was measured from heel to the top of head in standing position without shoes using tape measure ± 0.5 cm error. WC was measured in standing position with 20–30 cm distance between feet, and between the last rib and pelvic crest. Blood pressure was taken according to the World Health Organization (WHO) standards after 10 minutes. rest twice using the right arm in sitting position, and the average was recorded. MetS was defined based on both NCEP ATP III and KERCARD[28] criteria. The NCEP ATP III criteria consists of having high blood pressure (BP > 130/80), high triglyceride (TG >150), high glucose (FBG <100, or those with diabetes), low HDL (HDL <40 in men and HDL <50 in women) and high waist circumference (>88 cm in women, >102 cm in men). If the patient had three or more criteria, he/she was considered as having MetS. The KERCARD criteria were similar to NCEP ATP III except that the cut-off point for WC was more than 86 cm for women and 98 cm for men.[28]

All participants were categorized into quartiles based on their lipid ratios (TC/HDL-C ratio, LDL-C/HDL-C ratio and TG/HDL-C ratio), and biochemical characteristics of the population were compared across the lipid ratio quartiles.

Statistical Analysis

Statistical analysis was performed using State version 11 for Windows (Stata Corp., College Station, TX, USA). Lipid measures and the clinical variables were compared between participants with and without MetS in men and women separately using the Mann-Whitney test. One-way ANOVA and Bonferroni post hoc tests were applied for comparison of variables across lipid ratio quartiles. After adjustment for age, gender, body mass index, hypertension and diabetes, association between lipid ratio quartiles (independent variable) and MetS (binary dependent variable) was examined by logistic regression analysis. To compare the discriminative ability of lipid ratios as markers for MetS (both based on the NCEP ATPIII criteria and the proposed criterion by the KERCADRS study in Kerman), sex-specific receiver operating characteristic (ROC) curves were drawn and areas under the curve (AUC) were calculated. A *P* value of 0.05 for the two-tailed test was considered as statistically significant.

Results

In total, 1984 (34%) out of 5679 studied participants were diagnosed with MetS based on the ATP III criteria. People who had MetS were significantly older that MetS-free individuals. Body mass index (BMI), WC and blood pressure were significantly higher in MetS patients than healthy individuals. Furthermore, the fasting blood sugar and serum lipids (except HDL) in MetS was significantly increased compared to MetS-free participants while the HDL significantly decreased. This pattern was in the same direction in both men and women (Table 1).

The mean level of WC, BMI, TC, LDL, TG, systolic and diastolic blood pressure and fasting glucose across quartiles

Table 1. Demographic Characteristics (mean±SD) of Participants With and Without MetS

N = 5679	Total		Men (2546)			Women (3133)		
	MetS -	MetS+	MetS -	MetS+	*P* Value	MetS -	MetS+	*P* Value
	3695 (65%)	1984 (35%)	1764 (69%)	782 (31%)		1931 (62%)	1202 (38%)	
Age	44.1 (17.2)	53.3 (12.8)	43.0 (16.5)	52.8 (14.4)	<0.0001	38.4 (14.3)	53.6 (11.7)	<0.0001
BMI	24.4 (5.1)	28.6 (4.5)	23.6 (4.3)	27.4 (4.4)	<0.0001	25.0 (4.8)	29.5 (4.5)	<0.0001
WC (cm)	85.3 (11.3)	93.9 (10.8)	83.8 (10.8)	95.8 (10.9)	<0.0001	78.1 (10.5)	92.6 (10.6)	<0.0001
FBS (mmol/L)	102.4 (23.7)	124.4 (51.1)	95.6 (25.7)	122.3 (45.0)	<0.0001	90.1 (22.7)	125.9 (54.6)	<0.0001
TG (mmol/L)	148.1 (78.7)	209.0 (115.6)	126.5 (93.8)	216.6 (115.1)	<0.0001	107.2 (55.5)	204.1 (115.8)	<0.0001
SBP (mm Hg)	119.3 (21.7)	129.6 (21.6)	115.9 (16.6)	131.2 (20.4)	<0.0001	107.9 (17.0)	128.6 (22.3)	<0.0001
DBP (mm Hg)	76.8 (12.1)	82.6 (11.1)	76.8 (9.3)	84.1 (10.9)	<0.0001	73.2 (8.8)	81.6 (11.0)	<0.0001
TC (mmol/L)	189.4 (32.4)	210.0 (45.3)	183.2 (42.9)	199.1 (41.1)	<0.0001	186.4 (40.1)	217.2 (46.5)	<0.0001
HDL-C (mmol/L)	38.6 (10.2)	34.3 (8.2)	37.8 (9.1)	30.8 (6.4)	<0.0001	42.7 (9.7)	36.7 (8.5)	<0.0001
LDL-C (mmol/L)	118.5 (33.3)	135.2 (38.0)	120.4 (35.4)	126.7 (34.6)	<0.0001	122.4 (33.9)	140.6 (39.1)	<0.0001
TC/HDL-C ratio	4.8 (1.4)	6.3 (1.9)	5.1 (1.6)	6.7 (2.0)	<0.0001	4.5 (1.3)	6.2 (1.9)	<0.0001
TG/HDL-C ratio	3.2 (2.8)	6.8 (6.1)	3.7 (3.4)	7.7 (5.9)	<0.0001	2.8 (2.1)	6.2 (6.1)	<0.0001
LDL-C/HDL-C ratio	3.1 (1.1)	4.0 (1.2)	3.3 (1.2)	4.1 (1.3)	<0.0001	2.9 (1.0)	3.9 (1.2)	<0.0001

Abbreviations: BMI, body mass index; WC, waist circumference; FBS, fasting blood sugar; TGs, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

of lipid ratios (Quartiles of TC/HDL-C Ratio, LDL-C/HDL-C Ratio and TG/HDL-C Ratio) showed a rising trend (*P*-trend < 0.0001) whereas a significant decrease in the level of HDL was observed across quartiles of all lipid ratios (*P*-trend < 0.0001) (Table 2).

The chance of having MetS across quartiles of all lipid ratios had an increasing significant pattern (Table 3). The odds ratios (ORs) were significantly greater in the higher levels compared to the lower levels of lipid ratios quartiles in both men and women. The increase in ORs had a statistically significant uniform trend across quartiles of all lipid ratios in both women and men (*P*-trend < 0.0001).

The AUC of lipid ratios for diagnosis of MetS based on KERCARD criteria in women ranged from 0.74 for LDL-C/HDL-C to 0.85 for TG/HDL-C ratio and approximately the same findings were seen when the NCEP ATP III criteria was used (Figure 1B and 1D).

When we used KERCARD criteria, a nearly similar pattern to women was seen for men. The AUC was a bit lower when NCEP ATP III criteria were used (ranged from 0.69 for LDL-C/HDL-C to 0.83 for TG/HDL-C ratio) (Figure 1A and 1C).

Discussion

In this study, the accuracy of lipid ratios for diagnosis of MetS was examined. The area under the curve for lipid ratios was somehow the same for men and women. Furthermore, the chance of having MetS showed an increasing trend across quartiles of all lipid ratios, both in men and women. The TG/HDL-C was the best ratio to discriminate individuals with and without MetS both based on NCEP ATP III and KERCARD criteria.

The usefulness of TG/HDL-C ratio for diagnosis of MetS has been addressed in variety of studies including studies

Table 2. Biomarkers and Components of MetS Across Quartiles of Lipid Ratios.

Quartiles of TC/HDL-C Ratio	**Q1 (< 4.05)**		**Q2 (4.05–5.05)**		**Q3 (5.05–6.25)**		**Q4 (>6.25)**		
N = 5677	**1364 (24%)**		**1424 (25%)**		**1436 (25%)**		**1453 (26%)**		***P*-trend**
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
WC (cm)	77.82	12.6	83.9	12.1	88.1	11.8	90.3	10.9	<0.0001
BMI	23.29	5.0	25.6	5.4	26.7	4.7	27.2	4.5	<0.0001
TC (mmol/L)	158.47	33.3	183.3	33.5	201.9	36.0	226.8	43.7	<0.0001
HDL-C (mmol/L)	46.53	9.5	40.4	7.4	36.1	6.5	30.1	6.4	<0.0001
LDL-C (mmol/L)	95.44	26.2	120.0	26.3	135.4	30.1	152.6	36.4	<0.0001
TG (mmol/L)	83.64	35.8	114.3	44.2	153.6	59.6	238.2	145.2	<0.0001
SBP (mm Hg)	110.71	18.5	115.7	20.2	120.8	20.5	123.5	21.1	<0.0001
DBP (mm Hg)	73.89	9.6	76.7	10.3	79.2	10.4	80.1	10.9	<0.0001
FBS (mg/dL)	94.74	30.0	100.3	35.1	104.5	35.6	114.2	48.4	<0.0001
Quartiles of LDL-C/HDL-C Ratio	**Q1 (<2.5)**		**Q2 (2.53–3.28)**		**Q3(3.28–4.13)**		**Q4 (>4.13)**		
N = 5548	**1339 (24%)**		**1383 (25%)**		**1404 (25%)**		**1422 (26%)**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
WC (cm)	78.6	12.9	84.2	12.8	87.2	11.6	89.4	11.2	<0.0001
BMI	23.5	5.0	25.7	5.4	26.5	4.8	27.0	4.5	<0.0001
TC (mmol/L)	155.9	32.5	181.8	31.9	201.2	33.4	226.7	39.2	<0.0001
HDL-C (mmol/L)	45.6	10.1	40.4	8.1	36.5	6.9	31.5	6.5	<0.0001
LDL-C (mmol/L)	91.3	24.8	117.4	23.8	134.4	25.6	158.1	33.2	<0.0001
TG (mmol/L)	94.4	49.8	120.5	55.2	151.5	66.2	187.0	70.5	<0.0001
SBP (mm Hg)	112.1	19.0	115.5	20.3	119.9	20.7	122.7	21.3	<0.0001
DBP (mm Hg)	74.4	9.7	76.5	10.2	78.9	10.6	79.8	11.0	<0.0001
FBS (mg/dL)	96.5	32.7	100.9	36.8	104.4	36.5	109.2	42.3	<0.0001
Quartiles of TG/HDL-C Ratio	**Q1 (<2.11)**		**Q2(2.11 – 3.31)**		**Q3(3.31 – 5.28)**		**Q4 (>5.28)**		
N = 5679	**1383(24%)**		**1419(25%)**		**1434(25%)**		**1443(26%)**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
WC (cm)	77.2	11.9	83.6	11.9	88.3	11.7	91.1	11.1	<0.0001
BMI	23.3	4.9	25.4	5.3	26.7	4.8	27.4	4.5	<0.0001
TC (mmol/L)	172.3	38.1	186.8	41.2	198.3	41.0	213.0	47.1	<0.0001
HDL-C (mmol/L)	46.8	9.0	40.4	7.6	35.9	6.3	29.9	6.5	<0.0001
LDL-C (mmol/L)	111.7	32.6	124.9	35.4	132.5	35.7	132.9	38.0	<0.0001
TG (mmol/L)	69.8	18.1	107.4	22.4	149.6	29.3	263.1	136.4	<0.0001
SBP (mm Hg)	109.8	18.4	117.0	20.3	120.3	20.6	123.6	20.9	<0.0001
DBP (mm Hg)	73.8	9.4	77.2	10.7	78.9	10.7	80.0	10.4	<0.0001
FBS (mg/dL)	93.0	26.0	98.9	32.0	104.5	36.7	117.4	50.9	<0.0001

Abbreviations: BMI, body mass index; WC, waist circumference; FBS, fasting blood sugar; TGs, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

Table 3. The Associations Between Lipids Ratio and Odds of MetS (Adjusted ORs 95% CI)

		OR	CI	OR	CI	OR	CI	P-trend
Quartiles of TC/HDL-C Ratio								
	Q1 (< 4.05)	Q2 (4.05 – 5.05)		Q3 (5.05 – 6.25)		Q4 (>6.25)		
Total[a]	Reference	2.81	2.11 – 3.76	8.57	6.47 – 11.37	26.39	19.81 – 35.17	<0.0001
Men[b]	Reference	1.98	1.21 –3.24	6.36	4.01 – 10.10	20.01	12.68 – 31.58	<0.0001
Women[b]	Reference	3.46	2.41 – 4.99	10.35	7.19 – 14.89	29.36	20.09 – 42.91	<0.0001
Quartiles of TG/HDL-C Ratio								
	Q1 (<2.11)	Q2 (2.11- 3.31)		Q3 (3.31 – 5.28)		Q4 (>5.28)		
Total[a]	Reference	4.20	2.93 – 6.01	18.56	13.09 – 26.32	89.93	62.62 – 129.13	<0.0001
Men[b]	Reference	2.82	1.46 – 5.44	12.49	6.71 – 23.28	68.58	36.71 – 128.15	<0.0001
Women[b]	Reference	5.25	3.38 – 8.12	24.80	15.96 – 38.53	97.21	60.95 – 155.04	<0.0001
Quartiles of LDL-C/HDL-C Ratio								
	Q1 (<2.5)	Q2 (2.53- 3.28)		Q3 (3.28 – 4.13)		Q4 (>4.13)		
Total[a]	Reference	1.85	1.43 – 2.39	3.90	3.05 – 4.98	9.29	7.27 – 11.89	<0.0001
Men[b]	Reference	1.26	0.83 – 1.91	2.58	1.76 – 3.77	6.54	4.53 – 9.46	<0.0001
Women[b]	Reference	2.32	1.67 – 3.23	5.12	3.70 – 7.09	10.99	7.87– 15.35	<0.0001

Abbreviations: TGs, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol;
[a]Adjusted by age, gender, BMI, HTN, DM.
[b]Adjusted by age, BMI, HTN, DM.

in Spain,[17] Korea,[25] and Ghana.[29] In addition, some studies in children confirmed the usefulness of this ratio compared to other lipid ratios for diagnosis of MetS. The AUC for TG/HDL-C ratio in our study was similar to studies in Spain[19] and China.[18] The superiority of TG/HDL-C ratio for diagnosis of Mets compared to other ratios maybe as a result of the fact that in TG/HDL-C, 2 components of MetS (TG and HDL-C) are considered simultaneously, while in other ratios (TC/HDL-C and LDL-C/HDL-C) just one component of MetS is used. Although for diagnosis of MetS

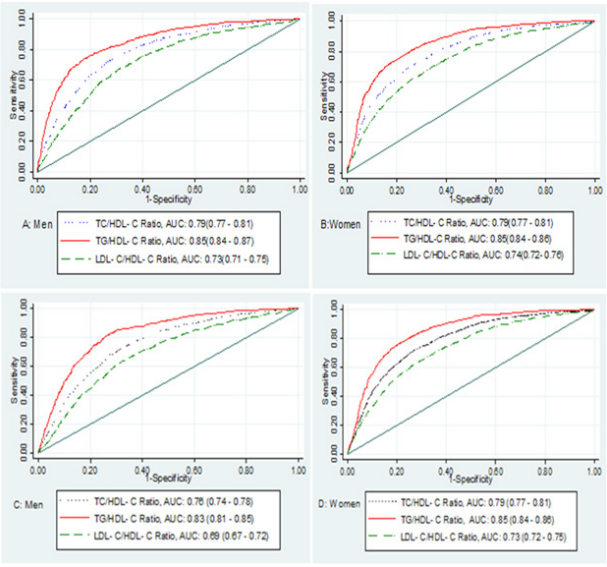

Figure 1. Recevier Operating Charecteristic (ROC) Curves of Lipid Ratios to Identify Men (A) and Women (B) with MetS Based on the KERCARD Criteria and Men (C) and Women (D) Based on the NCEP ATP III Criteria. TG/HDL-C, triglyceride/high-density lipoproteion cholesterol, TC/HDL-C, total cholesterol/high-density lipoproteion cholesterol, LDL-C/HDL-C, low-density lipoprotein cholesterol/high-density lipoproteion cholesterol.

an overview of the patient condition and measurement of WC are needed, WC usually is not measured in clinics. It is reported that only 6% of family physicians perform the measurements.[30] Therefore, measuring TG/HDL-C ratio, which is a simpler method for physicians, may be helpful in diagnosis and treatment of patients with MetS. Since most levels of blood fats such as triglycerides and HDL are measured routinely and TG/HDL ratio can be easily calculated, use of this ratio may be an effective strategy in early detection of MetS patients which are at the risk of cardio-vascular diseases.

Insulin resistance in MetS patients is the main risk factor of developing cardiovascular diseases.[31] Insulin resistance is usually evaluated by two methods including the measurement of WC and laboratory methods. The inaccessibility of laboratory methods for insulin resistance evaluation in various settings always limits its usefulness.[30] We did not study the usefulness of lipid ratios in diagnosis of insulin resistance, but regarding the fact that most MetS patients have some degrees of insulin resistance, our results may be suggestive of the potential utility of TG/HDL-C ratio in diagnosis of insulin resistance in this population. However, to prove this idea, the validity of lipid ratios (which are usually more accessible and cheaper than insulin resistance tests) for diagnosis of insulin resistance should be carefully investigated in future studies.

Although we did not study the validity of lipid ratios in prediction of CVDs, a growing body of evidence suggest that MetS has a strong relationship with ischemic heart disease.[14] The TG/HDL-C ratio has been reported as an independent factor related to ischemic heart diseases in some research.[32] As TG/HDL-C ratio increases, LDL with smaller size (LDL particle) and more density[33] will become more athrogenic. The higher level of TG/HDL-C has a higher correlation with the risk of developing IHD, insulin resistance and

athrogenic mechanism of LDL even when LDL level is in the normal range.[34] Even in one study among young people, use of this ratio identified more people at risk of IHD than use of MetS criteria.[35] Other studies also confirmed that lipid ratios are important predictive factors of IHD.[34,36] Although LDL is still the main goal of treatment in lipid disorders for prevention of CHD in some studies, high TG and low HLD have also been associated with increased risk of cardiac ischemia.[37] Addressing the usefulness of lipid ratios in prediction of MetS and cardio-vascular disease in future prospective studies may open a new window toward the applicability of lipid ratios in clinical decision making and management of patients.

The result of the present study does not mean that MetS criteria should be replaced by TG/HDL ratio. Instead, the data can be used as a simple tool for assessment and management of patients with MetS who may be missed by just relying on physical examination in over-crowded clinical settings.

We would like to acknowledge the limitations of this study. Due to the cross-sectional nature of the data, the results need to be confirmed by long-term prospective studies which address the stability of the relationship between TG/HDL ratio and MetS and also aging. In addition, intra-subject variability of serum lipids may result in non-differential classification of study participants.

In conclusion, our results suggest that the TG/HDL-C ratio is a better marker than the LDL-C/HDL-C and TC/HDL-C ratios for identifying MetS in Kerman, Iran. Also we have shown that AUCs of lipid ratios can be used to identify MetS with the application of ATP III and KERCARD criteria which we found to be similar. The results of the present study may be beneficial in clinical management of patients. Undoubtedly, high quality prospective studies in different settings are needed.

Authors' Contribution

MHG and AS contributed to conception or design. MR and AS contributed to acquisition, analysis, or interpretation. MR and AS drafted the manuscript. AH, RZ, HN, MHZ critically revised the manuscript.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

This study was approved by the Research Review Board of the Kerman University of Medical Sciences (Ethic No. 88-110KA).

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