

Does Prevalence of the Metabolic Syndrome in Women with Coronary Artery Disease Differ by the ATP III and IDF Criteria?

TODD M. BROWN, M.D.,^{1,2} DHANANJAY VAIDYA, M.B.B.S., Ph.D.,³
WILLIAM J. ROGERS, M.D.,² DAVID D. WATERS, M.D.,⁴ BARBARA V. HOWARD, Ph.D.,⁵
JEAN-CLAUDE TARDIF, M.D.,⁶ and VERA BITTNER, M.D., M.S.P.H.²

ABSTRACT

Background: The definition and prognostic utility of the metabolic syndrome remain controversial. Analyses in predominantly healthy populations suggest that the International Diabetes Federation (IDF) definition identifies more men with metabolic syndrome than the Adult Treatment Panel III (ATP III) criteria, with little difference among women. Whether the IDF definition identifies a greater prevalence of the metabolic syndrome than the ATP III definition in women with coronary artery disease (CAD) is unknown.

Methods: We compared the prevalence and prognostic utility of both definitions of the metabolic syndrome in postmenopausal women with angiographic CAD enrolled in the Women's Angiographic Vitamin and Estrogen Trial (WAVE). We excluded 51 of 423 women enrolled (12%) who had missing data for components of the metabolic syndrome.

Results: Mean age was 65.3 ± 8.4 years, 70% were white, mean body mass index (BMI) was 30.5 ± 6.0 kg/m², mean waist circumference was 96.2 ± 12.9 cm, 89% had hypertension by history or elevated blood pressure, 58% had diabetes or hyperglycemia, 54% had low high-density lipoprotein cholesterol (HDL-C), and 44% had hypertriglyceridemia. Metabolic syndrome prevalence was 70% and 74% by ATP III and IDF criteria, respectively; 68% met criteria for both definitions. Classification between the two criteria was not affected by ethnicity or age. Incident cardiovascular events were similar in both metabolic syndrome classifications.

Conclusions: Among postmenopausal women with angiographic CAD, the metabolic syndrome is very prevalent. The IDF modification of the ATP III definition only identifies a small additional number of women as having metabolic syndrome, independent of ethnicity or age, and provides little additional prognostic information.

¹Health Services Research Training Program, and ²Division of Cardiovascular Diseases, University of Alabama at Birmingham, Birmingham, Alabama.

³Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, Maryland.

⁴Division of Cardiology, University of California, San Francisco, San Francisco, California.

⁵MedStar Research Institute, Hyattsville, Maryland.

⁶Department of Medicine, Montreal Heart Institute, Montreal, Canada.

T.M.B.'s position is supported in part by grant number 5 T32 HS013852 from the Agency for Healthcare Research and Quality, Rockville, Maryland.

INTRODUCTION

THE METABOLIC SYNDROME is highly prevalent and associated with increased risk for cardiovascular disease and stroke.¹⁻⁴ In 2002, The National Cholesterol Education Program Adult Treatment Panel III (ATP III) categorized the metabolic syndrome as a constellation of hypertension, hyperglycemia, dyslipidemia, and increased waist circumference as a measure of visceral adiposity.¹ Recently, the International Diabetes Federation (IDF) redefined the metabolic syndrome.⁵ Their new definition varies from that of the ATP III in two fundamental ways. First, the IDF has adopted cutoff points to define elevated waist circumference that are lower than the traditional ATP III waist circumference cutoff points for women. Second, the IDF has made central obesity a requirement in their definition of the metabolic syndrome, mandating that a person meet the waist circumference criterion and also two of the other four traditional criteria (increased triglycerides, low high density lipoprotein cholesterol [HDL-C], elevated blood pressure, or elevated fasting glucose).

Several published reports have compared the prevalence of the metabolic syndrome based on the ATP III and IDF definitions.⁶⁻¹⁴ In these studies, there has been only slight variability between these two definitions in the number of people identified as having the metabolic syndrome, especially in women. However, all these studies have looked at populations with a low overall prevalence of coronary artery disease (CAD) and have not focused on postmenopausal women. Identification of the metabolic syndrome in patients with established CAD is important. Patients with metabolic syndrome have increased operative mortality following coronary artery bypass graft surgery,¹⁵ and the metabolic syndrome is an independent predictor of mortality among women with stable CAD.¹⁶ Furthermore, the metabolic syndrome is one of four criteria qualifying patients with CAD for an optional low-density lipoprotein cholesterol (LDL-C) goal of <70 mg/dL.² It is unknown if the IDF definition, when applied to a population of postmenopausal women with CAD, would identify more women as having the metabolic syndrome and potentially increased cardiovascular risk than the ATP III definition.

The Women's Angiographic Vitamin and Estrogen trial (WAVE) was a trial of estrogens and

antioxidant vitamins in women with CAD.¹⁷ A previous analysis from this dataset found an association between the metabolic syndrome defined by ATP III criteria and subsequent clinical events but no independent association with CAD progression measured by serial angiography.¹⁸ In the current analysis, we have compared the prevalence of the metabolic syndrome as defined by the ATP III and IDF criteria and compared the prognostic utility of the two definitions.

MATERIALS AND METHODS

Study population

The WAVE trial enrolled 423 postmenopausal women with angiographically documented CAD and randomized them in a 2 × 2 factorial design, between hormone replacement therapy (HRT) and placebo and between antioxidant vitamins and placebo.¹⁹ For the present analysis, we used the deidentified public access dataset obtained from the Coordinating Center of the WAVE study. This dataset is available through the National Heart, Lung and Blood Institute (NHLBI) website www.nhlbi.nih.gov/resources/decade/descriptions/wave.htm. We excluded 51 of the 423 women (12%) for this analysis who had missing data for components of the metabolic syndrome. Of the 51 women with missing data, waist circumference values were missing from 44, triglycerides and HDL-C from 16, fasting blood glucoses from 15, and blood pressure readings from 6. In the remaining 372 women, we compared the prevalence of the metabolic syndrome and its individual components using the ATP III and IDF definitions.

Metabolic syndrome definitions

For the ATP III definition, we characterized these women as having the metabolic syndrome if they met any three of the following criteria: (1) waist circumference > 88 cm, (2) triglycerides ≥ 150 mg/dL, (3) HDL-C < 50 mg/dL, (4) systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg or history of hypertension, (5) fasting blood glucose ≥ 100 mg/dL or history of diabetes mellitus or taking antidiabetic medications (Table 1).

For the IDF definition, we characterized these women as having the metabolic syndrome if they had a waist circumference ≥ 80 cm and two of

TABLE 1. METABOLIC SYNDROME CLASSIFICATIONS

<i>Adult Treatment Panel III</i>	<i>International Diabetes Federation</i>
Any three of the following: 1. Waist circumference > 88 cm 2. Triglycerides ≥ 150 mg/dL 3. HDL-C ^a < 50 mg/dL 4. Systolic blood pressure ≥ 130 mmHg <i>or</i> Diastolic blood pressure ≥ 85 mmHg <i>or</i> History of hypertension 5. Fasting blood glucose ≥ 100 mg/dL <i>or</i> History of diabetes mellitus <i>or</i> Taking antidiabetic medications	1. Waist circumference ≥ 80 cm and 2. Any two of the following: a) Triglycerides ≥ 150 mg/dL b) HDL-C < 50 mg/dL c) Systolic blood pressure ≥ 130 mmHg <i>or</i> Diastolic blood pressure ≥ 85 mmHg <i>or</i> History of hypertension d) Fasting blood glucose ≥ 100 mg/dL <i>or</i> History of diabetes mellitus <i>or</i> Taking antidiabetic medications

^aHDL-C, high-density lipoprotein cholesterol.

the other four criteria listed for the ATP III definition (Table 1). For women designated non-white, the public use dataset does not report any additional information on ethnicity. However, the IDF recommends a waist circumference criterion of >80 cm for women of all ethnicities.

Clinical outcomes

In the deidentified public access dataset made available through the NHLBI, clinical end points are grouped into the following composite outcomes: (1) cardiovascular death or nonfatal myocardial infarction (MI), (2) coronary artery bypass grafting or percutaneous coronary intervention, and (3) MI, stroke, or congestive heart failure (CHF). Therefore, we compared the number of events occurring in each of these composite outcomes during the follow-up period of the study among women who met the ATP III and IDF definitions of the metabolic syndrome, respectively.

Statistical analyses

In order to compare differences between these two different definitions, we grouped the women into four categories: those who met only the IDF definition, those who met only the ATP III definition, those who met both definitions, and those who met neither definition. We compared baseline characteristics among the four groups using standard descriptive statistics. We also compared the prevalence of the individual components of the metabolic syndrome between these groups and tabulated the number of clinical events during follow-up for each group. *t* Tests were used to compare continuous variables, and chi-square was used for categorical data. For all analyses, a

two-tailed alpha of 0.05 was used to determine statistical significance.

RESULTS

Baseline characteristics of the 372 women are displayed in Table 2. Overall, 70% were white, with a mean age of 65.3 (±8.4) years and a mean body mass index (BMI) of 30.5 (±6.0) kg/m². Metabolic syndrome as defined by both ATP III and IDF criteria was present in 253 women, and 90 women did not meet criteria for either definition. Only 29 women were categorized differently by the two definitions, resulting in 92.2% agreement between the two definitions (kappa 0.81, *p* < 0.001). Additionally, there were no differences in agreement between the two metabolic syndrome definitions based on race or age subgroups (Table 3).

Of the 29 women who were categorized differently by the two definitions, the 7 women who met criteria only for the ATP III definition of the metabolic syndrome had lower mean BMI and waist circumference, as expected. They also had lower HDL-C levels but higher systolic and diastolic blood pressures than the 22 women who met criteria only for the IDF definition (Table 2). Thus, women who met only the ATP III criteria tended to meet metabolic syndrome criteria more often because of an elevated triglyceride level and a low HDL-C level and less often because of an elevated waist circumference than the women who met only the IDF definition (Table 4).

Table 5 lists the clinical events by metabolic syndrome category. Women with metabolic syndrome were more likely to have a cardiovascular event

TABLE 2. BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS GROUPED BY METABOLIC SYNDROME CATEGORY^{a,b,c}

	Classifications agree			Classifications disagree		p value ^d
	Overall (n = 372)	MS by both (n = 253)	No MS (n = 90)	MS by IDF only (n = 22)	MS by ATP III only (n = 7)	
Age	65.3 (8.4)	64.9 (8.1)	65.9 (9.0)	64.7 (9.1)	70.5 (8.9)	NS
Race						
White	70%	70%	67%	73%	86%	NS
BMI	30.5 (6.0)	32.1 (5.5)	27.7 (5.9)	26.5 (2.8)	22.4 (1.0)	<0.001
WC	96.2 (12.9)	100.7 (10.9)	88.2 (12.8)	85.3 (2.3)	73.6 (2.9)	<0.001
FBG	124.4 (58.5)	138.3 (62.6)	88.5 (9.7)	122.2 (68.8)	91.1 (9.3)	NS ^e
A1C	6.5 (1.6)	6.9 (1.7)	5.5 (0.5)	6.7 (2.6)	5.7 (0.7)	NS
Lipids						
TChol	200.2 (41.1)	198.1 (41.2)	202.6 (41.3)	204.6 (38.8)	232.6 (33.9)	NS
HDL-C	50.3 (12.9)	46.1 (10.2)	60.6 (13.3)	58.0 (13.3)	41.8 (5.8)	0.004
TG	162.0 (87.5)	183.3 (91.5)	105.9 (40.5)	142.1 (89.1)	172.4 (37.1)	NS
LDL-C	117.9 (36.6)	116.1 (35.8)	120.0 (39.0)	117.8 (33.6)	154.0 (29.5)	0.017
Blood pressure						
SBP	139.4 (20.0)	141.2 (19.6)	136.1 (21.6)	129.9 (11.4)	144.6 (23.3)	0.031
DBP	75.6 (10.3)	75.4 (10.2)	76.5 (10.6)	71.3 (7.7)	83.1 (10.8)	0.003

^aWomen were grouped into four categories: those who met both definitions ($n = 253$), those who met neither definition ($n = 90$), those who met only the IDF definition ($n = 22$), and those who met only the ATP III definition ($n = 7$). Statistical comparison was performed only for those groups that had mutually exclusive definitions of the metabolic syndrome, that is, the group of women who met only IDF criteria and the group of women who met only ATP III criteria.

^bAll values expressed as mean (standard deviation) or %.

^cA1C, hemoglobin A1C; ATP III, Adult Treatment Panel III; BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; LDL-C, low-density lipoprotein cholesterol; MS, metabolic syndrome; TChol, total cholesterol; TG, triglycerides; SBP, systolic blood pressure; WC, waist circumference

^dFor comparison between MS-IDF only and MS-ATP III only categories.

^eStatistical testing done using log-transformed values as these values were not normally distributed.

during the study than those without metabolic syndrome. Overall, 40 of the 282 women (14%) classified as having metabolic syndrome by one or both definitions and only 5 of the 90 women (6%) with-

out metabolic syndrome had a cardiovascular event during follow-up ($p = 0.045$). Of these 40 women, 38 (95%) met criteria for both the ATP III and IDF classifications of the metabolic syndrome.

TABLE 3. NUMBER AND PERCENT OF WOMEN IN EACH OF THE METABOLIC SYNDROME CATEGORIES IN OVERALL POPULATION AND BY RACE AND AGE SUBGROUPS^a

	Classifications agree		Classifications disagree		Chi-square ^b
	MS by both n (%)	No MS n (%)	MS by IDF only n (%)	MS by ATP III only n (%)	
All women ($n = 372$)	253 (68)	90 (24)	22 (6)	7 (2)	
Race					
White ($n = 260$)	178 (69)	60 (23)	16 (6)	6 (2)	Chi-square = 1.388 $p = 0.969$
Non-white ($n = 112$)	75 (67)	30 (27)	6 (5)	1 (1)	
Age, years					
<65 ($n = 178$)	124 (70)	41 (23)	12 (7)	1 (1)	Chi-square = 3.882 $p = 0.369$
≥65 ($n = 194$)	129 (67)	49 (25)	10 (5)	6 (3)	

^aATP III, Adult Treatment Panel III; IDF, International Diabetes Federation; MS, metabolic syndrome.

^bChi-square tests performed to assess for variation in the distribution of women among the four metabolic syndrome categories for race and age subgroups.

TABLE 4. NUMBER AND PERCENT OF WOMEN MEETING EACH OF THE INDIVIDUAL METABOLIC SYNDROME COMPONENTS GROUPED BY METABOLIC SYNDROME CATEGORY^{a,b}

	Overall (n = 372)	Classifications agree		Classifications disagree		p value ^c
		MS by both (n = 253)	No MS (n = 90)	MS by IDF only (n = 22)	MS by ATP III only (n = 7)	
WC						
ATP III	274 (74)	230 (91)	44 (49)	0 (0)	0 (0)	
IDF	337 (91)	253 (100)	62 (69)	22 (100)	0 (0)	
TG	162 (44)	142 (56)	7 (8)	7 (32)	6 (86)	0.039
HDL	199 (54)	178 (70)	9 (10)	5 (23)	7 (100)	0.001
BP	331 (89)	237 (94)	67 (74)	20 (91)	7 (100)	NS
GLU	216 (58)	198 (78)	4 (4)	12 (55)	2 (29)	NS

^aWomen were grouped into four categories: those who met both definitions (n = 253), those who met neither definition (n = 90), those who met only the IDF definition (n = 22), and those who met only the ATP III definition (n = 7). We compared the proportion of women meeting each of the metabolic syndrome components among those classified differently by the two definitions in order to explore how these definitions differ.

^bATP III, Adult Treatment Panel III; BP, blood pressure; GLU, glucose; HDL, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; MS, metabolic syndrome; TG, triglycerides; WC, waist circumference.

^cFor comparison between MS-IDF only and MS-ATP III only categories. p values were not calculated for waist circumference, as by definition, women in the ATP III only group do not meet either waist circumference criterion, and women in the IDF only group meet only the IDF waist circumference criterion.

DISCUSSION

In our analysis of postmenopausal women with angiographically documented CAD, there was very high agreement between the ATP III and IDF definitions for metabolic syndrome. Overall, the two definitions were concordant in 92.2% of these women, and 38 of 45 clinical events occurred among women who met both definitions of the metabolic syndrome. Only 29 of the 372 women met criteria for one definition of the metabolic syndrome but not the other. The lack of a significant difference in prevalence of the metabolic syndrome between the two definitions and lack of difference in prognostic utility appear

to result from the overall high prevalence of the metabolic syndrome (68% by both definitions) and the high prevalence of pronounced central obesity in this cohort. The mean BMI was 30.5, and 74% of these women met the more stringent ATP III criterion for elevated waist circumference. As a result, the less stringent IDF waist circumference criterion did not result in a substantial increase in the number of women meeting criteria for the metabolic syndrome.

In previous comparisons of the ATP III and IDF definitions in relatively healthy populations, the IDF definition has defined a slightly larger population of people as having the metabolic syndrome.⁶⁻¹⁴ These additional individuals catego-

TABLE 5. NUMBER AND PERCENT OF CLINICAL CARDIOVASCULAR EVENTS GROUPED BY METABOLIC SYNDROME CATEGORY^a

	Overall (n = 372)	Classifications agree		Classifications disagree	
		MS by both (n = 253)	No MS (n = 90)	MS by IDF only (n = 22)	MS by ATP III only (n = 7)
CV death or MI	15 (4)	12 (5)	1 (1)	1 (5)	1 (14)
CABG or PCI	15 (4)	13 (5)	2 (2)	0 (0)	0 (0)
MI, stroke, or CHF	24 (7)	20 (8)	3 (3)	1 (5)	0 (0)
Combined CV end point ^b	45 (12)	38 (15)	5 (6)	1 (5)	1 (14)

^aATP III, Adult Treatment Panel III; CABG, coronary artery bypass grafting; CHF, congestive heart failure; CV, cardiovascular; IDF, International Diabetes Federation; MI, myocardial infarction; MS, metabolic syndrome; PCI, percutaneous coronary intervention.

alized by the IDF and not the ATP III tended to be younger and more obese and to have less prevalent cardiovascular disease. Additionally, this increase in prevalence associated with the IDF definition was more pronounced in men than in women. The results of our analysis seem to align with these previously published reports. We studied an older female population with documented coronary heart disease. Given the very high prevalence of obesity and the metabolic syndrome in this population, there is very little variation in these two definitions.

Since the publication of the IDF definition for the metabolic syndrome in 2005, there has been a great deal of speculation about whether the IDF or ATP III definition would be better at predicting cardiovascular events. With the exception of one report in which the IDF was a better predictor of carotid atherosclerosis in women,²⁰ the ATP III definition has been associated with a higher prevalence of cardiovascular disease and has been a better predictor of incident cardiovascular events than the IDF definition.²¹⁻²⁴ In populations such as ours with a high prevalence of obesity, including pronounced central obesity, and with underlying coronary heart disease, the majority of individuals will meet criteria for both metabolic syndrome definitions, and the majority of events will occur among individuals who meet criteria for both definitions.

Our study has a number of limitations. First, we only studied postmenopausal women with angiographically documented CAD. Although this limits our ability to extrapolate these findings to other populations, it represents a unique population that has not been studied previously with respect to this clinical question. Second, as only 29 of the 372 women (7.8%) were differentially classified by the two definitions and there were few cardiovascular events overall, we are unable to draw firm conclusions about differences in the clinical characteristics or risk for cardiovascular clinical outcomes between these two definitions in this population, but our analyses suggest that either definition can be used for classification and prognostication. Third, the public use dataset does not specify the proportion of nonwhite women who were of African American, Hispanic, or Asian origin. As the IDF recommends a waist circumference criterion of >80 cm for women of all ethnicities, our inability to analyze different nonwhite ethnicities does not result in misclassification.

CONCLUSIONS

Among postmenopausal women with angiographic coronary artery disease and a high prevalence of obesity, both MS definitions successfully identify a subset of women at high risk for future cardiovascular events. Further studies in younger populations without cardiovascular disease and with more divergence in the categorization of the study participants between these two definitions will be needed to elucidate whether either definition is a better predictor of cardiovascular events than the other.

DISCLOSURE STATEMENT

No competing financial interests exist.

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Address reprint requests to:

Todd M. Brown, M.D.

UAB Division of Cardiovascular Diseases

LHRB 306

701 19th Street South

Birmingham, AL 35294

E-mail: tmbrown@uab.edu