Original Paper

Reversal of Metabolic Syndrome Characteristics

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ABSTRACT

Background: Metabolic syndrome (MetS) is a constellation of three or more clinical health abnormalities from a list of five and, therefore, can vary significantly in its profile. Successful intervention strategies for preventing or resolving individuals' MetS may benefit from better understanding how specific risk factor profiles influence improvement in syndrome status.

Methods: A retrospective analysis of clinical records for members participating in a university-based health assessment/fitness center between 1978 and 2003 was undertaken in 2005. First-year and second-year measures of body mass index, triglycerides, high-density lipoproteins, fasting blood glucose, and blood pressure were compared. Prevalence of individual MetS risk markers, as well as deviation from cut-point levels, were compared in members with and without the syndrome and in subgroups of those whose MetS status changed between the two examinations.

Results: Of the 878 members analyzed, 133 (15%) presented with metabolic syndrome at first visit. Within 2 years of participating in a health assessment/fitness center, 42% of the members resolved their MetS status. Elevated triglycerides differentially characterized those participants who did not improve their MetS status, since that risk marker was not prevalent in the reversal group, but was 86% prevalent in the nonreversal group. For those who resolved their MetS status, there was a 33% improvement in triglycerides level.

Conclusions: While MetS resolution was achieved within 2 years for many participants in this study, it is likely that customized treatment interventions are necessary for those individuals with elevated triglycerides, the chief abnormality for those who did not resolve.

INTRODUCTION

THE METABOLIC SYNDROM (MetS) is characterized by a cluster of risk factors that place people at high risk for type 2 diabetes, cardiovascular disease (CVD), stroke and high rates of mortality.¹⁻⁴ Recognizing the significant negative health impact of MetS, the scientific community has undertaken an intense effort to estimate the extent to which people display the characteristics of MetS.²⁻¹⁴ Studies suggest that 30% of all overweight Americans exhibit the syndrome,¹¹ and prevalence in U.S. adults over 65 approaches 50%.¹⁵

In an effort to design appropriate intervention strategies for MetS patients, longitudinal studies have begun to focus on select community populations in which specific characterization of MetS is a priority while development patterns and reversal trends are carefully analyzed. For instance, in a study recently published by Tankó et al.,¹⁶ a sample of postmenopausal women living in Copenhagen was followed-up for an average 8.5 years to assess the role of a number of metabolic risk factors in the pathogenesis of CVD. Their work illustrated that enlarged waist combined with elevated triglycerides may be the best yardstick of increased risk for fatal cardiovascular events in that population. The 2005 CASTEL (CARDIOVASCULAR STUDY in the ELderly) study of Italian seniors followed-up its participants for 12 years to investigate the relationship between triglycerides and high-density lipoprotein cholesterol (HDL-C) levels, as well as other metabolic risk factors, and the development of coronary heart disease (CHD). Results demonstrated that high triglycerides and low HDL-C levels were independent predictors of increased CHD mortality in women; in fact, the combination of those two markers nearly quadrupled their risk.¹⁷

Other research has focused on the therapeutic implications of MetS diagnoses, and many studies have investigated the utility of lifestyle changes (especially improved exercise and diet) in treating the underlying causes of metabolic syndrome.¹⁸ For example, studies have already shown that the risk of developing MetS is lower for moderately-to-highly fit individuals, and that persons with the condition at baseline can reverse their MetS status within 6 months of

starting an exercise program.^{19,20} It is reasonable to inquire, however, whether all MetS risk factor profiles can be so readily resolved.

Accordingly, the purpose of the present retrospective study was to analyze the dynamic nature of MetS in members of a health assessment/fitness center in order to determine whether MetS profiles with differing risk marker composition were more likely to resolve over a 2-year period. Of course, it is acknowledged that individuals may not permanently "resolve" or "reverse" their MetS condition by temporarily improving their measures on a number of clinical risk factors; perhaps "remission" conveys their MetS status more accurately. In any case, this research focused on specific MetS abnormalities to determine which characteristics were most responsive to improvement versus those that were resistant to correction.

RESEARCH DESIGN AND METHODS

Study participants

The data from which this study is derived are physiologic, blood laboratory, and maximal stress-testing measures obtained from members of a health assessment/fitness center (located on the campus of Oakland University in Rochester, Michigan) between the years 1978 and 2003. The total member population of 4,666 comprised southeast Michigan residents who responded to the center's outreach efforts seeking adults who wished to maintain or improve their health status. These members underwent one or more comprehensive wellness assessments at this health enhancement institute, and approximately 12,000 visits or medical examinations occurred over a 25-year period. All participants provided written informed consent for their data to be included in subsequent research. The present study of this archived clinical information was conducted in 2005 and was approved by the University's Institutional Review Board.

Based on initial interviews, most members participated out of interest in making positive lifestyle changes to enhance their well-being. Following a full physical examination (blood and urine specimens obtained), body weight

and height were measured to calculate body mass index (BMI), and a treadmill maximal stress test was administered. Members received a comprehensive consultation with the institute's senior staff at a later date where each finding was discussed, and recommendations aimed at behavioral changes encouraging health enhancement were presented.

The sample for this study was a subset ($n = 878$) of members who had successive health exams over a 2-year period, with each examination resulting in a set of measures related to the clinical abnormalities comprising MetS. Inclusion criteria included participants being over 18 with a signed consent for clinical examination and participation. Exclusion criteria excluded those who had missing data relevant to establishing the presence or absence of metabolic syndrome. Individuals were not excluded on the basis of presenting with diabetes or cardiovascular disease. Participants' age ranged from 20–80 years, with a mean age of 45.2 (± 11.0) and a median age of 45.0 years.

In the current study, National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines^{1,18} for the operational definition of the syndrome were adopted. However, because measures of waist circumference and body fat percentage were not consistently obtained from members of this institute, the gauge of obesity was taken as the BMI value defined as body weight in kilograms divided by squared height in meters. While BMI may be a fair-to-poor predictor of an individual's body fatness (especially abdominal adiposity), it does correlate with increased risk of chronic disease due to obesity, and has been a criterion used by the World Health Organization in its determination of metabolic syndrome.¹ Thus, in the current study, MetS is defined as having at least three of the following five metabolic abnormalities: BMI ≥ 30 kg/m²; sitting systolic blood pressure ≥ 130 mm Hg or diastolic ≥ 85 mm Hg; HDL < 1.04 mmol/L (40 mg/dL) for men, < 1.30 mmol/L (50 mg/dL) for women; triglycerides ≥ 1.69 mmol/L (150 mg/dL); and fasting blood glucose ≥ 6.10 mmol/L (110 mg/dL). It should be noted that the threshold for elevated glucose was revised downward to 5.55 mmol/L (100 mg/dL) in late 2005 by health organizations. However, the prior standard was operational

for much of the time frame covered by this retrospective study, as well as other studies cited in this manuscript, so the higher level of fasting blood glucose was retained in defining MetS for the present research.

All statistical analyses were performed using SPSS version 13.0 (SPSS, Inc., Chicago, IL). Logistic regression was used to identify which factors had the most influence on the resolution or development of MetS. Differences between groups were evaluated using independent sample *t* tests.

RESULTS

Table 1 presents baseline MetS information for the 878 members who had two comprehensive health assessments over a 2-year period and who presented with ($n = 133$) or without ($n = 745$) MetS.

It is noteworthy that only 15% of these people were found to have MetS ($n = 133$) at their initial exam. While this prevalence was far lower than the 24% of the U.S. adult population of a comparable age estimated to currently exhibit MetS according to the NCEP ATP III definition,¹¹ it was also found in the larger population of the institute's members ($n = 4,666$). As seen in Table 1, elevated triglycerides was the number one abnormality by prevalence (86.3%) in participants with MetS. By contrast, in the MetS-free individuals, only 14.6% had the triglycerides abnormality, a six-fold difference. An abnormally low HDL was the second most frequent marker among individuals with MetS, present in 75% of these participants, compared to its 17% presence in MetS-free individuals. Hypertension was observed twice as frequently in the MetS group versus those without MetS. Interestingly, elevated glucose was not particularly frequent in participants with MetS, being present in only 38% of this group; but it was found in just 4% of the MetS-free group, resulting in nearly a 10-fold difference between the MetS and MetS-free groups. Therefore, glucose level may also qualify as a likely predictor of MetS.

To assess changes in health status of the 133 individuals who presented with MetS on their first visit, mean values of each abnormality for

TABLE 1. BASELINE (FIRST-VISIT) METS CHARACTERISTICS FOR FIRST-TIMERS AS A GROUP AND AS SUBGROUPS OF THOSE PRESENTING WITH METS OR WITHOUT (METS-FREE)

<i>First-timer characteristics</i>	<i>Total (n = 878)</i>	<i>MetS (n = 133)</i>	<i>MetS-free (n = 745)</i>	<i>MetS vs. MetS-free</i>
Mean age (years; +/-SD)	45.2 (11.0)	48.3 (10.1)	44.6 (11.0)	3.7 ^a
% Male	77.0%	85.7%	75.4%	10.3% ^a
% Female	23.0%	14.3%	24.6%	-10.3% ^a
% With:				
Systolic BP $\geq$ 130 mm Hg	38.8%	72.8%	32.8%	40.0% ^a
Diastolic BP $\geq$ 85 mm Hg	43.0%	72.8%	37.7%	35.1% ^a
Triglycerides $\geq$ 1.69 mmol/L [150 mg/dL]	25.3%	86.3%	14.6%	71.7% ^a
HDL $<$ 1.04 (M) or 1.30 (F) mmol/L [40 (M) or 50 (F) mg/dL]	25.7%	75.2%	16.8%	58.4% ^a
BMI $\geq$ 30 kg/m ²	15.5%	63.9%	6.9%	57.0% ^a
Glucose $\geq$ 6.11 mmol/L [110 mg/dL]	8.9%	37.5%	3.9%	33.6% ^a
MetS	15.1%	100%	0%	100.0% ^a
0 or 1 risk marker	63.9%	0%	75.0%	-75.0% ^a
No. of risk markers	1.3	3.5	0.9	2.6 ^a

^a $p < 0.01$

MetS, metabolic syndrome; SD, standard deviation; BP, blood pressure; HDL, high-density lipoproteins; BMI, body mass index.

the first and second visits within 2 years were compared (Table 2). The results showed that 56 people (42%) reversed their MetS status within this two-year period, while 77 people (58%) did not reverse. At the second visit or exam, mean age of individuals who reversed their MetS status was 47.5 ($\pm$ 11.1) years compared to 51.1 ($\pm$ 9.0) years for those who did not

reverse. While this difference was statistically significant ($p < 0.05$), age-matched analysis does not explain why 42% successfully reversed their MetS condition.

The results in Table 2 show that the most dramatic difference between the individuals with MetS who reversed and those who did not was the initial-visit triglycerides level.

TABLE 2. MEAN VALUES OF METS MARKERS FOR 133 PARTICIPANTS WITH METS ON FIRST VISIT, COMPARING THOSE WHO BECAME METS-FREE AND THOSE WHO CONTINUED TO HAVE METS

<i>MetS Risk Marker</i>	<i>Mean clinical values and percent change</i>					
	<i>1st Visit</i>	<i>2nd Visit</i>		<i>1st Visit</i>	<i>2nd Visit</i>	
	<i>MetS</i>	<i>MetS-Free</i>	<i>% Chg.</i>	<i>MetS</i>	<i>Still MetS</i>	<i>% Chg.</i>
Systolic BP (mm Hg)	134.1	127.0	-5.3***	137.0	134.9	-1.5
Diastolic BP (mm Hg)	89.8	83.4	-7.0***	89.6	88.8	-0.9
Triglycerides (mmol/L)	2.34	1.56	33.1***	2.67	2.68	0.6
[mg/dL]	[207.4]	[138.7]		[236.3]	[237.7]	
HDL (mmol/L)	1.03	1.14	10.6***	0.98	0.97	-0.2
[mg/dL]	[39.8]	[44.0]			[37.7]	[37.6]
BMI (kg/m ²)	30.6	29.3	-4.2***	32.6	32.2	-1.4*
Glucose (mmol/L)	5.58	5.23	-6.1**	6.73	6.70	-0.5
[mg/dL]	[100.4]	[94.2]		[121.2]	[120.6]	
Number of risk markers	3.3	1.5	-54.7***	3.6	3.5	1.7
Number of Subjects		<i>n = 56</i>			<i>n = 77</i>	
Mean (yrs. +/-SD)		47.5 (11.1)			51.1 (9.0)	
age @ 2nd Visit						

* $p < 0.10$; ** $p < 0.05$; *** $p < 0.01$.

MetS, metabolic syndrome; BP, blood pressure; HDL, high-density lipoproteins; BMI, body mass index; SD, standard deviation.

Mean triglycerides was 207.4 mg/dL in the reversal group, compared to 236.3 mg/dL in the nonreversal group, a 14% difference observed at the first visit. Second-visit triglycerides data showed a more pronounced difference. The reversal group demonstrated a 33% improvement, while no improvement was noted in those who did not reverse their status. The second-leading marker in terms of improvement over the two-year period was the HDL level, showing an 11% change in the group who reversed their MetS status.

BMI changes were less pronounced, declining by 4.2% between visits among individuals whose MetS condition resolved.

Not presented in Table 2 are prevalence data describing the percentage of people with each abnormality, of interest because this shows how the MetS profile changed during participants' memberships. The top three risk markers observed in the reversal group after two years of participation (at second visit) were hypertension (43%), HDL (34%), and BMI (34%). In contrast, for the nonreversal individuals, the profile was relatively unchanged with hypertension (91%), triglycerides (86%), and HDL (76%) still predominant. The most significant difference in the risk marker rankings at the second examination was that triglycerides was a top-ranking abnormality only in the nonreversal group.

To quantify how sensitive MetS status is to changes in levels of risk factors comprising the profile, logistic regression analyses were

performed using data for the participants who either reversed the condition ($n = 56$) or developed it ($n = 38$) during the time frame of this study. Specifically, the difference between those individuals' first- and second-visit clinical measures on each abnormality was examined to determine how the odds of resolving versus developing MetS changed as one specific abnormality changed, controlling for the other abnormalities. Categorical factors, such as gender and age ranges, proved to be non-significant and were not included. Interestingly, the regression coefficients for BMI and systolic blood pressure measures (data not shown) also proved to not be significant in the logistic regression model. Variables that contributed significantly to the final logistic regression model were the triglycerides, HDL, and glucose blood value changes over time. Table 3 presents the results, which again illustrates the relevance of these abnormalities (especially the predominance of dyslipidemia) in affecting MetS status.

For example, considering the effect of changes in triglycerides level, the model for resolving MetS indicated an odds ratio (OR) of 0.98 for that difference variable; therefore, each unit (0.01 mmol/L or 1 mg/dL) increase in triglycerides reduces the odds of resolving MetS by a multiple of 0.98, or by -2%, controlling for other variables. Increasing triglycerides by a more meaningful 101 mg/dL (equivalent to a one-standard deviation change

TABLE 3. PERCENT CHANGE IN METS STATUS ODDS AS A FUNCTION OF CHANGE IN CLINICAL MEASURES FOR SELECTED RISK FACTORS

Difference Variable	% Change in MetS odds per change in variable					
	Clinical status: resolve MetS			Clinical status: develop MetS		
	OR ^a	1-Unit Chg. ^b	1-SD Chg. ^c	OR ^a	1-Unit Chg. ^b	1-SD Chg. ^c
TG	0.980	-2.0%	-87.0%	1.020	2.0%	639.0%
HDL	1.200	20.0%	416.0%	0.834	-16.6%	-80.5%
GLU	0.930	-7.0%	-63.8%	1.075	7.5%	175.2%

Notes. Data are for the subsample of 94 individuals (56 + 38) who exhibited a change in MetS status.

^aOR = Odds ratio; each significant @ $p < 0.03$.

^bRead as: For each +1-unit (0.01 mmol/L or 1 mg/dL) change in the clinical measure over time, the odds of resolving (or developing) MetS change by the indicated percentage, controlling for other variables in the model.

^cChange equivalent to +1 standard deviation (SD) in the variable for the subsample, where: SD of TAG difference ~ 1.14 mmol/L (101 mg/dL); SD of HDL difference ~ 0.23 mmol/L (9 mg/dL); SD of GLU difference ~ 0.77 mmol/L (14 mg/dL).

MetS, metabolic syndrome; TG, triglycerides; HDL, high-density lipoproteins; GLU, glucose.

as evidenced by the clinical data for the subsample) reduces the odds of resolving MetS by 87%. Viewed from the opposite perspective, that same increase of 101 mg/dL in triglycerides leads to a 639% increase in the odds of developing MetS. On the other hand, a one-standard deviation increase (9 mg/dL) in HDL level improves the odds of reversing MetS by over 400%, and also decreases the odds of developing the condition by 80%.

DISCUSSION

One of the more significant findings in this retrospective, longitudinal study of health assessment/fitness center participants is that MetS was resolved within a time frame of only 2 years in 42% of the individuals who presented with MetS. These results from middle-aged men and women are not unlike the results of a Johns Hopkins study²⁰ of senior citizens (ages 55–75) in which 42% had MetS, with approximately 43% reversing their MetS status within 6 months of exercise intervention. Similarly, the HERITAGE study²¹ designed to assess exercise intervention over a 20-week period found that of the 105 participants with the metabolic syndrome at baseline, 30.5% reversed their MetS status after the exercise training.

Perhaps more significant in the present study is the finding that elevated triglyceride level significantly differentiated those who resolved their MetS status from those who did not. As noted in the Results, the triglycerides marker is not in the top three in the reversal group, but is the second-leading marker in the nonreversal group. Moreover, the data showed that of all the improvements evident in the MetS reversal group, triglycerides reduction of 33% was the largest, followed by an 11% improvement in HDL levels. Results from logistic regression analyses confirmed these observations or trends.

Thus, triglycerides elevation appears to be an especially effective indicator for identifying individuals who will exhibit changes in the five components of MetS criteria sufficient to exceed, or fall below, risk thresholds for the condition. This observation is in agreement with results from a 2-year (2003–2004) analysis

of the clinical characteristics of MetS in Korean men and women over 40 years of age that also demonstrated hypertriglyceridemia to be well correlated with prevalence of metabolic syndrome.²² The present findings are also in accord with results from a long-term prospective study of postmenopausal Danish women¹⁶ that assessed the independent contribution of individual components of MetS to the risk of fatal cardiovascular events. The Danish research showed that, among the array of MetS criteria, elevated triglycerides was associated with the highest hazard ratios for all-cause and CVD-related death. Furthermore, the study detected that elevated triglycerides along with enlarged waist had an additive impact on cardiovascular risk; since that composite trait is concordant with a relative distribution of more central versus peripheral fat, which is a recognized predictor of atherogenesis and CVD.^{23,24} Likewise, a 2003 study²⁵ of National Health and Nutrition Survey (NHANES III) data implicated elevated triacylglycerols and enlarged waist with increased “metabolic risk” and accelerated mortality after middle age in both genders due to a syndrome of lipid over-accumulation. Even adolescents with the “hypertriglyceridemic waist” phenotype have been shown to exhibit greater risk of metabolic syndrome.²⁶

The absence of a control group was a limitation of the current retrospective study. Since this investigation was not a treatment study and logs concerning members’ dietary habits and exercise regimen were not available within the archived records examined in this research, it was not possible to ascertain the precise roles nutritional changes and fitness training may have played in resolving participants’ MetS condition. However, the influence of medications was analyzed using records on hand from both visits concerning participants’ hypertension, cholesterol, diabetes, or diet medications routine. χ^2 analysis revealed no difference in prescription drug usage between those who improved and those who did not; thus, medication use was not a confounding variable.

This study’s adoption of the unrevised hyperglycemia level (110 mg/dL) from the NCEP ATP III MetS definition^{1,18} was inconsequential. A separate analysis showed that in spite of more

participants naturally exhibiting “elevated glucose” using the newer 100 mg/dL threshold, that risk factor was still subordinate to levels of blood lipids in explaining resolution of MetS.

Finally, although the sample of individuals whose records were examined in this research included both genders and was comprised of a broad range of ages and fitness levels, the results may not be generalizable to other populations beyond members of a health assessment/fitness center. Furthermore, the people used in this study were those who completed two physical examinations within 2 years; therefore, they may have been more motivated than the overall fitness center population. In spite of the imperfections inherent to a retrospective research design, this study’s results reinforce findings published elsewhere, especially concerning the role of hypertriglyceridemia in the development or reversal of metabolic syndrome. In fact, the data suggest that MetS individuals with elevated triglycerides are less likely to resolve in such a short time span and might require additional, customized treatment interventions.

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REFERENCES

- Hunt KJ, Resendez RG, Williams K, Haffner SM, Stern MP. National Cholesterol Education Program versus World Health Organization metabolic syndrome in relation to all-cause and cardiovascular mortality in the San Antonio Heart Study. *Circulation* 2004;110:1251–1257.
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998;15:539–553.
- Sattar N, Gaw A, Scherbakova O, Ford I, O’Reilly DS, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. *Circulation* 2003;108:414–419.
- Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio Heart Study. *Diabetes Care* 2003;26:3153–3159.
- Villegas R, Perry IJ, Creagh D, Hinchion R, O’Halloran D. Prevalence of the metabolic syndrome in middle-aged men and women. *Diabetes Care* 2003;26:3198–3199.
- Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Bonadonna RC, Muggeo M; Bruneck study. Carotid atherosclerosis and coronary heart disease in the metabolic syndrome: prospective data from the Bruneck study. *Diabetes Care* 2003;26:1251–1257.
- McNeill AM, Rosamond WD, Gorman CJ, Heiss G, Golden SH, Duncan BB, East HE, Ballantyne C. Prevalence of coronary heart disease and carotid arterial thickening in patients with the metabolic syndrome (the ARIC Study). *Am J Cardiol* 2004;94:1249–1254.
- Resnick HE, Jones K, Ruotolo G, Jain AK, Henderson J, Lu W, Howard BV; Strong Heart Study. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians: the Strong Heart Study. *Diabetes Care* 2003;26:861–867.
- Katzmarzyk PT, Church TS, Blair SN. Cardiorespiratory fitness attenuates the effects of the metabolic syndrome on all-cause and cardiovascular disease mortality in men. *Arch Intern Med* 2004;164:1092–1097.
- Palaniappan L, Carnethon MR, Wang Y, Hanley AJ, Fortmann SP, Haffner SM, Wagenknecht L; Insulin Resistance Atherosclerosis Study. Predictors of the incident metabolic syndrome in adults: The Insulin Resistance Atherosclerosis Study. *Diabetes Care* 2004;27:788–793.
- Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among U.S. adults: Findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002;287:356–359.
- Jurca R, Lamonte MJ, Church TS, Earnest CP, Fitzgerald SJ, Barlow CE, Jordan AN, Kampert JB, Blair SN. Associations of muscle strength and aerobic fitness with metabolic syndrome in men. *Med Sci Sports Exerc* 2004;36:1301–1307.
- 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;27:2222–2228.
- Pitsavos D, Panagiotakos DB, Chrysohou C, Papaioannou I, Papadimitriou L, Tousoulis D, Stefanadis C, Toutouzias P. The adoption of Mediterranean diet attenuates the development of acute coronary syndromes in people with metabolic syndrome. *Nutr J*. 2003;2:1.
- Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. *Diabetes Care* 2004;27:2444–2449.
- Tankó LB, Bagger YZ, Qin G, Alexandersen P, Larsen PJ, Christiansen C. Enlarged waist combined with

- elevated triglycerides is a strong predictor of accelerated atherogenesis and related cardiovascular mortality in postmenopausal women. *Circulation*. 2005;111:1883–1890.
17. Mazza A, Tikhonoff V, Schiavon L, Casiglia E. Triglycerides + high-density-lipoprotein-cholesterol dyslipidaemia, a coronary risk factor in elderly women: The Cardiovascular Study in the Elderly. *Intern Med J* 2005;35:604–610.
 18. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486–2497.
 19. Stewart KJ, Bacher AC, Turner K, Lim JG, Hees PS, Shapiro EP, Tayback M, Ouyang P. Exercise and risk factors associated with metabolic syndrome in older adults. *Am J Prev Med* 2005;28:9–18.
 20. LaMonte MJ, Barlow CE, Jurca R, Kampert JB, Church TS, Blair SN. Cardiorespiratory fitness is inversely associated with the incidence of metabolic syndrome: A prospective study of men and women. *Circulation* 2005;112:505–512.
 21. Katzmarzyk PT, Leon AS, Wilmore JH, Skinner JS, Rao DC, Rankinen T, Bouchard C. Targeting the metabolic syndrome with exercise: Evidence from the HERITAGE Family Study. *Med Sci Sports Exerc* 2003;35:1703–1709.
 22. Kwon HS, Park YM, Lee HJ, Lee JH, Choi YH, Ko SH, Lee JM, Kim SR, Kang SY, Lee WC, Ahn MS, Noh JH, Kang JM, Kim DS, Yoon KH, Cha BY, Lee KW, Kang SK, Son HY. Prevalence and clinical characteristics of the metabolic syndrome in middle-aged Korean adults. *Korean J Intern Med* 2005;20:310–316.
 23. Tankó LB, Bruun JM, Alexandersen P, Bagger YZ, Richelsen B, Christiansen C, Larsen PJ. Novel associations between bioavailable estradiol and adipokines in elderly women with different phenotypes of obesity: implications for atherogenesis. *Circulation* 2004;110:2246–2252.
 24. Carr DB, Utzschneider KM, Hull RL, Kodama K, Retzlaff BM, Brunzell JD, Shofer JB, Fish BE, Knopp RH, Kahn SE. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. *Diabetes* 2004;53:2087–2094.
 25. Kahn HS, Valdez R. Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration. *Am J Clin Nutr* 2003;78:928–934.
 26. Esmailzadeh A, Mirmiran P, Azizi F. Clustering of metabolic abnormalities in adolescents with the hypertriglyceridemic waist phenotype. *Am J Clin Nutr* 2006;83:36–46.

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