The Value of the Metabolic Syndrome Concept in Elderly Adults: Is It Worth Less Than the Sum of Its Parts?

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OBJECTIVES: To determine whether the metabolic syndrome (MetS) or its components were more closely associated with disease states and inflammation in elderly adults.

DESIGN: Sydney Memory and Ageing Study. Cross-sectional, observational cohort.

SETTING: Population-derived, community-dwelling elderly adults.

PARTICIPANTS: Nine hundred thirty individuals aged 70 to 90.

MEASUREMENTS: Age- and sex-adjusted odds ratios (ORs) for disease states; fasting circulating inflammatory markers and oxidative metabolism byproducts.

RESULTS: MetS was associated with diabetes mellitus (OR = 4.1, $P < .001$) and bowel cancer (OR = 9.1, $P = .03$) but not in analyses that controlled for component conditions. Models containing component conditions had the strongest associations with heart disease. Disease associations were improved after addition of component conditions to the MetS model. The reverse did not hold: disease associations were not improved when MetS was added to the components model. Low high-density lipoprotein cholesterol (HDL-C) was independently associated with myocardial infarction (OR = 2.32) and angina pectoris (OR = 2.59) (both $P < .008$). Waist circumference was independently associated with cancer (OR = 1.82, $P = .008$). Although MetS was associated with higher C-reactive protein, vascular cell adhesion molecule, interleukin-6, amyloid A, homocysteine, and malondialdehyde, it explained less than half of the variance of models containing its components.

CONCLUSION: The observation that MetS is associated with disease states and markers of circulating inflammation in the elderly is explained mainly by abdominal obesity and low HDL-C. Longitudinal data will further clarify these cross-sectional findings that MetS appears to be less than the sum of its parts in elderly adults. **J Am Geriatr Soc 60:1734–1741, 2012.**

Key words: metabolic syndrome; diabetes mellitus; obesity; lipids; inflammation

Life expectancy has progressively increased over recent decades, as has the prevalence of age-related diseases, including heart disease, diabetes mellitus (DM), and cancer. Abdominal obesity, a core feature of metabolic syndrome (MetS), which is defined as abdominal obesity with at least two of four other conditions [high glucose, high triglycerides, high blood pressure, and low high-density lipoprotein cholesterol (HDL-C)] increases the risk of these diseases.[1] The hypothesis supporting a diagnosis of MetS is that it has additive or even multiplicative weight over its components in predicting disease.[2]

MetS is associated with risk of cardiovascular disease (CVD), DM,[3–7] myocardial infarction (MI), and stroke[8] and thus is of interest in geriatric medicine. MetS plus DM is associated with four times greater cardiac mortality in men and 14 times greater in women.[9] MetS in elderly adults is associated with mortality, explained by the independent effects of glucose and lipid subfractions.[10] Other studies also support superiority of component conditions over MetS—fasting glucose better predicted CVD and DM,[11] and the Framingham Risk Score better predicted

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CVD[12]—but MetS is also reported to have predictive value equivalent to its components.[13–15] The clinical value of MetS remains subject to intense international debate.[16] The hazard in clinical application of MetS is that important, validated risk factors may be undertreated if the syndrome is not present.

Half of the U.S. population aged 60 and older meet MetS criteria,[17] yet its utility in elderly adults remains unclear. Component conditions are (cross-sectionally) independently associated with CVD but not MetS.[18] Longitudinal studies show that MetS does not predict incident stroke or MI.[19,20] Associations with specific component conditions may explain the association between MetS and mortality.[9] Further studies are necessary to dissect the associations between MetS and major diseases and metabolic measures and to discern whether the syndrome itself, or its components, identify people with disease or disease risk.

In addition to traditional risk factors, inflammation and oxidative stress are putative intermediaries in the pathogenesis of diseases associated with MetS and aging, with few published data examining these in elderly adults.

Thus, a large cohort of community-dwelling, nondemented elderly adults were examined to determine whether MetS was associated with disease states and circulating markers of inflammation and oxidative metabolism. Whether MetS better explained associations with disease states in elderly adults than its component conditions was evaluated.

METHODS

Participants

Participants were drawn from the Sydney Memory and Ageing Study,[21] a population-derived cohort of 1,037 nondemented adults in eastern Sydney aged 70 to 90, recruited through the mandatory electoral roll and examined between 2007 and 2009. Data on 930 participants permitted MetS classification, with complete components data on 920. Exclusion criteria were insufficient English, major neurological disease (dementia, developmental disability, multiple sclerosis, motor neuron disease), severe psychiatric disease, progressive malignancy, and baseline Mini-Mental State Examination[22] score less than 24. The University of New South Wales and South-Eastern Illawarra Area Health Service–Eastern Sector Human Research and Ethics Committees (05037) approved the protocol. Participants provided written informed consent.

Participants completed a medical and lifestyle history questionnaire, including current medications. The medical questionnaire captured a variety of diseases and cancers (bowel, lung, breast, uterine, ovarian, prostate, stomach, kidney, liver, skin, and blood). Weight and height were measured with participants barefoot in light street clothes, body mass index (BMI) was calculated (weight/height^2), and the waist was measured (0.01 m) at the narrowest point between the ribcage and the anterior superior iliac crest.

MetS was determined using the International Diabetes Federation criteria:[2] large waist circumference plus two or more of high blood pressure, high triglyceride, or high glucose levels, or low HDL-C, with sex- and race-specific waist cutoffs (women > 80 cm; men, European > 94 cm, Asian > 90 cm). The presence of components was determined for blood pressure (taking antihypertensive medications, systolic blood pressure $\geq$ 130 mmHg, or diastolic blood pressure $\geq$ 85 mmHg), glucose (diagnosed DM or fasting glucose $\geq$ 5.6 mmol/L), lipids [lipid-lowering therapy, fasting triglycerides $\geq$ 1.6 mmol/L or low HDL-C (men < 1.03 mmol/L, women < 1.29 mmol/L)]. Impaired fasting glucose was defined as 5.6 to 6.9 mmol/L.[23]

Metabolic Measures and Circulating Markers of Inflammation

Blood was collected after a 10-hour overnight fast, and samples were frozen at −80°C. Assay measurements were plasma glucose using the glucose oxidase method (Beckman Coulter, Fullerton, CA); total cholesterol, HDL-C, triglycerides, and urate using the timed-endpoint method (Beckman Coulter); low-density lipoprotein cholesterol (LDL-C) estimated using the Friedewald equation; homocysteine using reverse-phase high-performance liquid chromatography (HPLC; BioRad, Munich, Germany); malondialdehyde (MDA) using reverse-phase HPLC with ultraviolet detection [coefficient of variation (CV) = 6% at 12.1 umol/L, 7% at 19.7 umol/L]; serum insulin (in duplicate) using radioimmunoassay (Linco, St. Charles, MO) (CV < 4%); cortisol, thyroid-stimulating hormone, B12, and folic acid levels using chemiluminescent immunoassays (Access Immunoassay Systems, Beckmann Coulter); serum cytokine levels using cytometric bead array for interleukin (IL)-1ß, IL-6, IL-8, IL-10, IL-12p70, and tumor necrosis factor alpha (TNF-α; BD Biosciences, San Jose, CA);[24] for vascular cell adhesion molecule-1 (VCAM-1) and plasminogen activator inhibitor-1 (PAI-1) and serum amyloid A (United States Biological, Marblehead, MA) using sandwich enzyme-linked immunosorbent assays (Bender Medsystems GmbH, Vienna, Austria); and high-sensitivity C-reactive protein (hsCRP) using near-infrared particle immunoassay rate (Synchron LXi, Beckman Coulter).

Statistical Analyses

Comparisons between participants with and without MetS for disease states were examined using contingency tables and chi-square tests. Normally distributed biochemical parameters were compared using *t*-tests. Nonnormally distributed parameters (insulin, insulin resistance, all inflammatory markers, and hsCRP) were compared using Mann–Whitney tests.

Analysis of covariance (ANCOVA) was used to control for age and sex; for lipids and inflammation markers, ANCOVA also included lipid-lowering therapy use. In ANCOVA, insulin, insulin resistance, triglycerides, CRP, IL-8, IL-10, IL-12p70, serum amyloid A, PAI-1, urate, B12, homocysteine, and creatinine were logarithmically transformed. Glucose, serum VCAM (sVCAM), malondialdehyde (MDA), IL-1ß, IL-6, and TMF-α, were normalized according to rank-order scores.[25]

Hierarchical regression analyses examined whether MetS or its components had stronger relationships with diseases (logistic regression) and inflammatory measures [ordinary least squares (OLS) regression]. In logistic regression, the significance of changes in model fit

produced by adding variables to the model was assessed according to the change in the −2 log likelihood values using the chi-square distribution, with degrees of freedom equal to the number of newly introduced variables. For the hierarchical OLS regressions, the statistical significance of change in coefficient of determination (R^2) values was obtained using the *F* statistic. Regression models examined 920 participants with complete components data with MetS as a single predictor variable, with the five component conditions as predictor variables, and with MetS plus components as predictor variables. A variance inflation factor score of less than 5 indicated lack of multicollinearity. Analyses were performed using PASW Statistics 18.0 (SPSS, Inc., Chicago, IL).

RESULTS

Participant Demographics

Mean participant age was 78.6 ± 0.2, and mean BMI was 27.2 ± 0.2 kg/m^2 (range 15.7–41.3 kg/m^2). Self-reported rates of ever smoking were 54%, diagnosed heart disease 12%, diagnosed DM 12%, hypertension 61%, and lipid-lowering therapy 62%. Participants were predominantly Caucasian (99%); 1% were Asian. Most were born in Australia (72%), Europe (22%), and Asia (3%), and 94% mainly spoke English. In education, 44% had not completed high school, and 42% had a post-secondary education.

The prevalence of MetS was 54.4%. Comparisons of those with and without MetS are shown in Table 1. Participants with MetS more frequently lived with others and were twice as likely to use a cane to assist walking but were similar in use of other aids, including hearing aids, walkers, and motorized wheelchairs (data not shown).

Disease Prevalence in MetS

Cardiovascular Disease

MetS was associated with heart disease and angina pectoris but not after adjustment for sex and age. After sex and age adjustment, MetS was associated with a higher prevalence of hyperlipidemia [OR = 1.44, 95% confidence interval (CI) = 1.10–1.88, *P* = .009], hypertension (OR = 2.58, 95% CI = 1.96–3.38, *P* < .001), and longer duration of lipid-lowering (10.0 ± 0.7 vs 8.1 ± 0.5 years, *P* = .009) and antihypertensive (13.1 ± 0.5 vs 10.0 ± 0.7 years, *P* = .007) therapy. The prevalence of stroke, transient ischemic attack (TIA; Table 1), claudication, aortic aneurysm, atrial fibrillation, and other cardiac arrhythmias was similar (data not shown).

Diabetes Mellitus

DM prevalence was higher in MetS (age- and sex-adjusted OR = 4.1, 95% CI = 2.47–6.81, *P* < .001). Participants with DM plus MetS received antiglycemic medications more frequently (75% vs 50%, *P* = .02) and rated their glucose control as adequate less frequently (53% vs 75%, *P* = .04) than those with DM alone. Only 18% of participants with MetS had normal fasting glucose, compared with 75% of those without MetS.

MetS was present in 87% of participants with DM and 78% of participants with impaired fasting glucose. Only 22% of participants with normal fasting glucose had MetS.

Other Disease States and Malignancies

The prevalence of bowel cancer was 10 times as high in participants with MetS (age- and sex-adjusted OR = 9.3, 95% CI = 1.18–73.7, *P* = .03). MetS was associated with a higher rate of arthritis (OR = 1.35, 95% CI = 1.04–1.76, *P* = .02) and lower rates of chronic obstructive pulmonary disease (OR = 0.34, 95% CI = 0.12–0.99, *P* = .046) and osteoporosis (OR = 0.64, 95% CI = 0.45–0.90, *P* = .007). Rates of renal disease, urinary tract infection, depression, Parkinson's disease, sleep apnea, and other cancers were similar (data not shown).

Metabolic and Inflammatory Markers in MetS

Fasting insulin and insulin resistance were higher in MetS, remaining so after adjustment for age and sex. Total cholesterol and LDL-C were lower in MetS; total cholesterol remained so after adjusting for age, sex, and lipid-lowering therapy.

MetS was associated with higher serum creatinine, hsCRP, VCAM-1, amyloid, IL-6, and oxidative byproducts (homocysteine, MDA, and urate). After adjustment for age, sex, and lipid-lowering therapy use, hsCRP, sVCAM, MDA, and urate remained significantly higher in MetS. Vitamin B12 was lower in MetS; serum cortisol (an index of pituitary–adrenal activation) and thyroid-stimulating hormone levels were similar (data not shown).

Model Comparisons: MetS Against and with Its Component Parts

The independent associations between MetS and its components were examined in logistic regression against heart disease, MI, angina pectoris, cerebrovascular accident (CVA), TIA, and all cancers. MetS and its components were entered simultaneously as independent variables (Table 2). For all diseases, there were significant independent associations with at least one component but not with MetS. Independent associations for cardiac disease were found with low HDL-C, high glucose, and high blood pressure. Low HDL-C had independent associations with acute MI, angina pectoris, and TIA and high triglycerides with CVA. High waist circumference was independently associated with cancer.

Hierarchical logistic regression examined the increase in model associations with disease, first, by inclusion of components in the model of MetS and, second, by inclusion of MetS in the components model. Results were consistent with those above. For all diseases examined, components introduction into the MetS model improved the level of association; the increase in the Nagelkerke R^2 was greater than that produced by the introduction of MetS into the components models. Statistically significant increases in the level of association were produced by components inclusion into the MetS model for cardiac disease

Table 1. The Sydney Memory and Ageing Study: Demographics and Prevalence of Disease States and Metabolic, Hormonal and Inflammatory Parameters in Participants with and without Metabolic Syndrome (MetS) n = 930

Factor	No MetS, n = 424	MetS, n = 506	*P*-Value	*P*-Value[a]
Age, mean (SEM)	78.4 (0.2)	78.8 (0.2)		
Male, n/N (%)	169/424 (39)	264/506 (53)	<.001	
Weight, mean (SEM)	66.4 (0.7)	77.6 (0.6)	<.001	
Body mass index, kg/m^2, mean (SEM)	25.1 (0.2)	28.7 (0.2)	<.001	
Systolic blood pressure, mmHg, mean (SEM)	141 (1)	148 (1)	<.001	
Diastolic blood pressure, mmHg, mean (SEM)	81 (1)	83 (1)	.005	
Ever smoked, n/N (%)	224/424 (52)	285/505 (56)	.08	
Accommodation status, n				
Living in community alone	222	215		
Living in community with spouse	160	213		
Living in community with other	51	64		
Living in retirement home or other	7	14	.02	
Access to a pet to talk to or touch, n/N	88/424	80/506	.93	
Cane use, n/N (%)	23/400 (5.8)	46/401 (11.5)	.01	
Comorbidities, n/N (%)				
Heart disease[b]	126/424 (29.7)	189/504 (37.5)	.004	.08
Acute myocardial infarction	42/424 (9.9)	67/502 (13.3)	.06	.07
Angina pectoris	43/424 (10)	76/498 (15.3)	.01	.07
Cerebrovascular accident	15/424 (3.5)	19/500 (3.8)	.76	
Transient ischemic attack	26/424 (6.1)	30/492 (6.1)	.85	
Hyperlipidemia	247/424 (58.3)	325/506 (64.4)	.01	.009
Hypertension	214/424 (50.5)	356/506 (70.3)	<.001	<.001
Diagnosis diabetes mellitus	20/424 (4.7)	88/502 (17.5)	<.001	<.001
Arthritis	218/424 (51.4)	286/501 (57)	.04	.02
Osteoporosis	113/424 (26.6)	79/481 (16)	.000	.007
Chronic obstructive pulmonary disease	12/424 (3)	5/504 (1)	.04	.046
Bowel cancer	1/424 (0.2)	10/506 (2)	.006	.03
Metabolic and hormonal measures, mean (SEM)				
Glucose, mmol/L	5.4 (0.04)	6.3 (0.06)	<.001	<.001
Total cholesterol, mmol/L	4.9 (0.04)	4.6 (0.04)	<.001	<.001[c]
High-density lipoprotein cholesterol, mmol/L	1.6 (0.02)	1.3 (0.02)	<.001	<.001[c]
Low-density lipoprotein cholesterol, mmol/L	2.9 (0.04)	2.8 (0.03)	.04	.26[c]
Triglycerides, μm/L	0.9 (0.02)	1.3 (0.03)	<.001	<.001[c]
Insulin, μU/mL	13.2 (0.3)	17.5 (0.4)	<.001	<.001
Homeostasis model assessment of insulin resistance[26]	3.22 (0.08)	5.00 (0.15)	<.001	<.001
Creatinine, μm/L	87 (2.0)	91 (1.0)	.04	.39
Uric acid, mmol/L	0.32 (0.00)	0.35 (0.00)	<.001	<.001[c]
Malondialdehyde, μm/L	13.0 (0.1)	14.0 (0.2)	<.001	<.001[c]
Homocysteine, μm/L	11.0 (0.2)	11.8 (0.2)	.003	.06[c]
Vitamin B12, pg/mL	242 (21.0)	187 (8.0)	.01	.02
Inflammatory biomarkers, mean (SEM)				
Plasminogen activator inhibitor-1, ng/mL	81 (1.0)	82 (1.0)	.30	.18
C-reactive protein, mg/L	2.7 (0.3)	3.2 (0.2)	<.001	<.001[c]
Serum vascular cell adhesion molecule-1, ng/mL	1,025 (25.0)	1,155 (39.0)	.004	<.001[c]
Tumor necrosis factor alpha, pg/mL	3.1 (0.9)	2.5 (0.2)	.76	–
IL-1β, pg/mL	3.4 (0.4)	3.1 (0.2)	.52	–
IL-6, pg/mL	6.5 (0.5)	6.7 (0.3)	.01	.13[c]
IL-8, pg/mL	19.3 (0.5)	20.7 (0.7)	.35	–
IL-10, pg/mL	2.5 (0.1)	2.8 (0.1)	.15	–
IL-12p70, pg/mL	3.0 (0.1)	3.2 (0.1)	.64	–
Serum amyloid A, μg/mL	57.8 (7.8)	57.6 (8.9)	.04	.13[c]

[a] Adjusted for age and sex.
[b] Acute myocardial infarction, angina pectoris, and chronic heart failure.
[c] Adjusted for age, sex, and lipid-lowering therapy use.
SEM = standard error of the mean; IL = interleukin.

[Δ−2LogL=−16.68, degrees of freedom (*df*) = 5, *P* = .005], acute MI (Δ−2LogL = −11.66, *df* = 5, *P* = .04), angina pectoris (Δ−2LogL = −15.66, *df* = 5, *P* = .03), and TIA (Δ−2LogL = −11.55, *df* = 5, *P* = .04). MetS introduction into the components model had no effect on model association for each disease examined.

Similar results were found when examining relationships between MetS and components and biochemical measures. Table 3 shows regression analyses for models with inflammatory and metabolic parameters as the dependent variables and MetS and its components as independent variables. Creatinine levels were independently

Table 2. Sydney Memory and Ageing Study: Logistic Regression Analysis of Disease States Against Metabolic Syndrome (MetS) and Its Component Conditions

Disease Outcome	Independent Variable[a]	Wald	Odds Ratio (95% Confidence Interval)	*P*-Value
Cardiac disease[b]	Age	13.046	1.06 (1.03–1.09)	<.001
	Sex	41.698	0.38 (0.28–0.51)	<.001
	High waist	0.464	1.18 (0.73–1.92)	.50
	High triglycerides	0.004	0.99 (0.61–1.58)	.95
	Low HDL-C	6.077	1.60 (1.10–2.32)	.01
	High glucose	8.696	1.81 (1.22–2.68)	.003
	High blood pressure	7.920	2.08 (1.25–3.45)	.005
	MetS	2.808	0.64 (0.38–1.08)	.09
Acute myocardial infarction	Age	12.193	1.08 (1.36–1.13)	<.001
	Sex	31.926	0.25 (0.16–0.41)	<.001
	High waist	0.535	1.32 (0.63–2.78)	.46
	High triglycerides	0.587	1.29 (0.67–2.47)	.44
	Low HDL-C	9.861	2.25 (1.36–3.73)	.002
	High glucose	1.447	1.46 (0.84–2.54)	.23
	High blood pressure	1.796	1.69 (0.78–3.63)	.18
	MetS	1.900	0.58 (0.27–1.26)	.17
Angina pectoris	Age	14.780	1.09 (1.04–1.14)	<.001
	Sex	13.309	0.45 (0.29–0.69)	<.001
	High waist	1.160	1.51 (0.71–3.21)	.28
	High triglycerides	2.563	0.55 (0.27–1.14)	.11
	Low HDL-C	12.885	2.49 (1.51–4.11)	<.001
	High glucose	2.282	1.54 (0.88–2.69)	.13
	High blood pressure	1.428	1.57 (0.75–3.31)	.23
	MetS	0.755	0.71 (0.33–1.53)	.38
Transient ischemic attack	Age	1.889	1.04 (0.98–1.10)	.17
	Sex	3.685	1.78 (0.99–3.20)	.05
	High waist	0.812	0.67 (0.28–1.61)	.37
	High triglycerides	1.384	0.55 (0.20–1.49)	.24
	Low HDL-C	6.060	2.44 (1.20–4.97)	.01
	High glucose	0.518	1.30 (0.63–2.70)	.47
	High blood pressure	3.10	2.68 (0.89–8.06)	.08
	MetS	0.399	0.72 (0.26–2.01)	.53
Cerebrovascular accident	Age	0.318	1.02 (0.95–1.10)	.57
	Sex	9.374	1.30 (0.14–1.65)	.002
	High waist	0.242	0.76 (0.26–2.27)	.62
	High triglycerides	7.191	3.56 (1.41–9.00)	.007
	Low HDL-C	0.004	1.03 (0.44–2.42)	.95
	High glucose	0.807	0.68 (0.30–1.57)	.37
	High blood pressure	0.026	1.10 (0.35–3.41)	.87
	MetS	0.061	0.86 (0.26–2.89)	.80
All cancers	Age	2.419	1.02 (0.99–1.05)	.12
	Sex	6.660	0.70 (0.53–0.92)	.01
	High waist	6.903	1.82 (1.16–2.84)	.009
	High triglycerides	0.021	0.96 (0.62–1.50)	.88
	Low HDL-C	0.005	1.01 (0.71–1.44)	.95
	High glucose	1.797	1.28 (0.89–1.85)	.18
	High blood pressure	0.012	1.02 (0.67–1.57)	.91
	MetS	0.926	0.79 (0.49–1.28)	.34

[a] Independent variables (components of MetS) are defined according to the International Diabetes Federation classification.[1]
[b] Acute myocardial infarction, angina pectoris, and chronic heart failure.
HDL-C = high-density lipoprotein cholesterol.

associated with triglycerides; hsCRP with waist and low HDL-C; VCAM and IL-6 levels with low HDL-C; MDA with triglycerides and glucose; and serum amyloid A with waist circumference, glucose, and low HDL-C. There were no independent associations with MetS in any analyses.

Hierarchical regression examined whether associations between biochemical measures and MetS were improved by including components in the MetS model or by including MetS in the components models. Significant increases in statistical association were produced by components inclusion in MetS models for hsCRP ($\Delta R^2 = 0.038$, $P < .001$), sVCAM ($\Delta R^2 = 0.031$, $P < .001$), MDA ($\Delta R^2 = 0.050$, $P < .001$), and amyloid A ($\Delta R^2 = 0.018$, $P = .005$). In contrast, the introduction of MetS into components models did not improve the R^2.

DISCUSSION

MetS is a composite constructed from clinical and biochemical measures, ostensibly to identify individuals at risk

Table 3. Sydney Memory and Ageing Study: Contribution of Component Conditions and Metabolic Syndrome to Variance of Renal Function and Markers of Inflammation and Oxidative Metabolism

Variable	Independent Variable[a]	ß	*t*	*P*-Value
Creatinine	Age	0.210	7.399	<.001
	Sex	−0.466	−16.149	<.001
	High waist	0.018	0.517	.60
	High triglycerides	0.081	2.694	.007
	Low HDL-C	0.010	0.309	.76
	High glucose	0.002	0.045	.96
	High blood pressure	0.054	1.728	.08
	MetS	−0.020	−0.405	.69
C-reactive protein	Age	0.046	1.415	.16
	Sex	0.062	1.893	.06
	High waist	0.180	4.642	<.001
	High triglycerides	0.020	0.580	.56
	Low HDL-C	0.123	3.313	.001
	High glucose	0.022	0.523	.60
	High blood pressure	−0.047	−1.321	.19
	MetS	0.004	0.074	.94
Serum vascular cell adhesion molecule-1	Age	0.176	5.420	<.001
	Sex	−0.036	−1.094	.27
	High waist	0.014	0.347	.73
	High triglycerides	0.032	0.934	.35
	Low HDL-C	0.188	5.028	<.001
	High glucose	0.006	0.140	.89
	High blood pressure	−0.005	−0.145	.88
	MetS	−0.008	−0.133	.89
Interleukin-6	Age	0.110	3.308	.001
	Sex	−0.100	−2.957	.003
	High waist	0.011	0.271	.79
	High triglycerides	−0.021	−0.610	.54
	Low HDL-C	0.093	2.451	.01
	High glucose	0.018	0.405	.69
	High blood pressure	−0.001	−0.023	.98
	MetS	0.019	0.325	.74
Homocysteine	Age	0.263	8.410	<.001
	Sex	−0.212	−6.681	<.001
	High waist	0.006	0.163	.87
	High triglycerides	0.027	0.812	.42
	Low HDL-C	0.048	1.346	.18
	High glucose	0.004	0.087	.93
	High blood pressure	0.059	1.729	.08
	MetS	0.003	0.167	.87
Malondialdehyde	Age	0.064	2.014	.04
	Sex	−0.017	−0.540	.59
	High waist	0.073	1.910	.06
	High triglycerides	0.067	1.997	.046
	Low HDL-C	0.050	1.386	.17
	High glucose	0.293	7.007	<.001
	High blood pressure	0.075	2.144	.03
	MetS	−0.041	−0.723	.47
Serum amyloid A	Age	0.082	2.507	.01
	Sex	0.212	6.414	<.001
	High waist	0.136	3.457	.001
	High triglycerides	−0.037	−1.075	.28
	Low HDL-C	0.080	2.140	.03
	High glucose	0.085	1.983	.048
	High blood pressure	0.026	0.739	.46
	MetS	−0.068	−1.218	.22

[a] Independent variables (components of MetS) are defined according to the International Diabetes Federation classification.[1]
HDL-C = high-density lipoprotein cholesterol.

of CVD, DM, and, perhaps, other diseases. Its merit is that this one composite alerts clinicians to screen for and manage its components. A major controversy in the MetS debate is whether it confers risk above that of its individual components. The utility of MetS has not been extensively interrogated in elderly adults. In this study,

associations between MetS and disease and biochemical parameters in elderly adults were examined to determine whether MetS or its individual components better explained such associations.

It was found that elderly adults with MetS had higher rates of cardiac disease, angina pectoris, bowel cancer, and metabolic diseases, but (notably) not TIA or CVA. Regression model analyses found that these disease associations were with components of MetS rather than MetS itself. Forcing MetS into the component models did not strengthen associations. In contrast, adding components to the MetS models consistently strengthened the statistical association with each disease. Analyses testing the independence of components and MetS found that specific components (waist and lipid fractions) explained the disease associations; MetS held no independent associations. Furthermore, the expected associations between TIA, CVA, and MetS were absent, yet independent associations with lipids were evident, indicating that MetS in elderly adults was less sensitive at identifying individuals with important and common geriatric diseases than traditional risk factors. These findings suggest that, in elderly adults, MetS appears to be less than the sum of its components in explaining associations with CVD and cancer.

MetS was found to be associated with higher levels of CRP, sVCAM, IL-6, and serum amyloid A. To the knowledge of the authors, this is the first study to report serum amyloid A and sVCAM levels in advanced age, although multivariate analyses revealed that components models explained a greater variance for each of these inflammatory markers than MetS. Furthermore, in model analysis, each inflammatory marker was associated independently with low HDL-C but not the construct of MetS. These findings suggest that the higher inflammatory markers observed in MetS are due to relationships between inflammation and low HDL-C rather than with MetS. Higher hsCRP and sVCAM have been reported in elderly adults, but independence from component conditions was not examined.[27]

MetS was also associated with higher products of oxidative metabolism but not independently of component conditions. Higher homocysteine levels[28] and indices of oxidative stress[29] are reported in MetS but dependent on DM and hypertension, suggesting that coexisting disease may explain relationships. In the current study, impaired fasting glucose or DM and central obesity were independently associated with higher oxidative marker levels, and B12 levels were lower in MetS, perhaps explained by the higher prevalence of DM and its treatment.

Strengths of this study include detailed evaluation in a large cohort with comprehensive inflammatory and oxidative measures. Potential confounders (education, smoking, ethanol, depression, and use of physical aids for independent living) were examined to ensure that participants with MetS were similar to those without. Limitations include cross-sectional design; disease states were self-reported, but rigorous ascertainment may have underreported diseases. Selection and survivor biases are probable in healthy, community-dwelling participants.

These findings suggest a lack of clinical utility for MetS in elderly adults. The absence of the syndrome may lead to undertreatment of known disease risk factors in elderly adults; instead clinicians should continue to seek and treat cardiometabolic risk factors. These findings suggest that MetS may not be useful in elderly adults as a means of stratification of disease risk. Longitudinal studies will inform whether MetS identification has greater value in predicting incident health outcomes in elderly adults than specific disease risk factors.

In conclusion, the construct of MetS in advanced age appears to be less than the sum of its parts in explaining associations with cardiac and other disease states and circulating inflammation. Established risk factors that are components of MetS are the important correlates of disease and disease intermediates rather than MetS itself.

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Conflict of Interest: There are no conflicts to declare. Samaras has received honoraria for seminars and teaching on obesity and type 2 DM (MSD, Janssen, AstraZeneca) and is on an advisory board (MSD, for sitagliptin). She receives royalties on a book on DM that she has coauthored (*Fast Facts Diabetes*, Health Press Limited, Abingdon, Oxfordshire, UK).

Brodaty has received honoraria, been a sponsored speaker, is on an advisory board, and has been or is an investigator with regards to dementia and Alzheimer's disease Pfizer, Novartis, Janssen, Lundbeck, Lilly, Sanofi, Servier, Merck, Baxter, and Wyeth. Sachdev has received honoraria for teaching and leading seminars on neurocognitive disorders.

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