METABOLIC SYNDROME: CRITERIA VALIDATION IN THE ELDERLY

Stefania Maggi, M.D., Marianna Noale, Sc.D., and Gaetano Crepaldi, M.D., Center on Aging, National Research Council, Padova, Italy

Please address correspondence to:
Stefania Maggi, M.D., Ph.D.
CNR Center on Aging
Via Giustiniani,2
35128 Padova, Italy
Email: Stefania.maggi@in.cnr.it

Introduction

The metabolic syndrome (MetS) is the term used to describe a clustering of metabolic and physiologic risk factors for both type 2 diabetes mellitus and atherosclerotic cardiovascular diseases first described about 40 years ago [1]. Despite an increasing number of works in the literature dedicated to MetS, its underlying mechanism is still not completely understood. Many studies have shown that four of its components – obesity (especially central obesity), impaired glucose tolerance, atherogenic dyslipidemia (high levels of triglycerides; small, dense low-density lipoproteins; and low levels of high density lipoprotein cholesterol), and hypertension ─ coexist in the population to a greater degree than could be expected by chance alone [2]. The first issue that needs to be addressed with regards to MetS is that the prevalence rates and the interactions between these components are probably different across sexes, age, and ethnic groups. Moreover, the definition of MetS is itself unclear, as its components are continuous variables, implying that cut-off values are needed. As yet there is no consensus as to the specific threshold to be used for each component [3]. Very few studies have, moreover, specifically focused on the validity of these criteria in the elderly (age > 65 yrs).

In 2001, the National Cholesterol Education Program - Third Adult Treatment Panel III (ATP III) proposed a series of criteria similar to those of the WHO [4], except for the fact that the key component was visceral obesity and not insulin resistance. The ATP III did not find enough evidence to recommend the routine measurement of insulin sensitivity or the 2-hour post-challenge glucose test but simply included a fasting glucose assessment. The ATP III criteria have recently been further revised [5] and the new definition recommends that at least 3 of the following 5 elements should be present: increased waist circumference (≥ 102 cm in men and ≥ 88 cm in women), hypertriglyceridemia (≥ 150 mg/dl or on drug treatment), low HDL cholesterol (< 40 mg/dl in men and < 50 mg/dl in women or on drug treatment), hypertension (≥ 130 mmHg systolic and ≥ 85 mmHg diastolic or on drug treatment), and a fasting glucose ≥ 100 mg/dL or on drug treatment. However, as the NCEP – ATP III criteria and cut-off values represent experts' consensus and not evidence-based findings, their validity in different age groups needs to be verified.

Criteria Validation in the Elderly

The Italian Longitudinal Study on Aging (ILSA), an epidemiological study conducted in Italy in a random sample of 5,632 individuals aged 65-84 years [6], reported a prevalence rate of 31.3%

in men and 59.4% in women, with consistently higher rates in women in each age group [7]. The prevalence rates of the individual components of Mets are outlined in Figure 1.

Low HDL-Ch and abdominal obesity were extremely frequent findings in older women and significantly more so than in men. Based on this observation, it was hypothesized that the cut off values utilized for these variables might not be appropriate in elderly females. Using receiver-operating characteristics analysis (ROC curve analysis) we were able to identify the cut off values for these variables that best predicted their clustering and the risk of MetS is presented in the Table 1.

Table 1. Odds ratio (confidence interval) for HDL-Ch and waist circumference (ATP III criteria), by gender. ILSA study, weighted data.

	Males OR (95% CI)	Females OR (95% CI)
HDL cholesterol (< 40 mg/dl males, < 50 mg/dl females)	8.85 (5.71-13.71)	5.52 (3.87-7.87)
Waist circumference (> 102 cm males, > 88 cm females)	4.72 (3.09-7.22)	7.21 (4.61-11.27)

The association of these components at the cut offs proposed by the ATP III panel with at least two others was significant in both men and women. In particular, with regards to women, the risk of MetS was more than 5 times higher in those with low HDL cholesterol and more than 7 times higher in those with abdominal obesity.

Using the ROC curves, the cut off levels suggested for both men and women by the ATP III panel indicate that there is a significant association with MetS for all the components, except for blood pressure, that had the best cut off at 145/95 for men and at 135/90 for women [8]. In order to interpret these results correctly, it must be emphasized that blood pressure's ability to identify older individuals with or without MetS is quite poor and, thus, its intrinsic value alone in predicting MetS is debatable, as suggested by previous analyses [9].

The odd ratios for MetS, according to gender and quartiles of waist circumference and BMI are outlined in Figures 2 and 3. In these models, the cut off levels suggested for both men and women by the ATP III panel indicate that there is a significant association with MetS for waist circumference. Interestingly, waist circumference was significantly associated to MetS and did not lose its significance even after adjustment for BMI (Figure 3). On the contrary, BMI is significantly associated to MetS, but after adjustment for waist circumference the association continues to significant in women only for BMI > 30 Kg/m^2 (Figure 4).

Discussion

The ATP III cut-off values are clinically relevant and applicable in a population of elderly Caucasians. Using these criteria, some of the components of MetS are extremely frequent in our population; nonetheless they represent a significant risk of developing MetS. Our data support the hypothesis that BMI, except for the > 30 kg/m2 level in women, is not predictive of MetS, while waist circumference is strongly associated to its risk, independently of BMI. This is in agreement with previous data showing that BMI is not a good predictor of cardiovascular risk as body composition changes with age (e.g. loss of free fatty mass, decrease in height) [10]. In previous reports [7,11] we have demonstrated that MetS is a strong predictor of the development of diabetes and of CVD mortality in a 4-year follow-up. It is our conviction that MetS, which is present in epidemic proportions among the elderly, represents one of the major threats to longevity and healthy aging.

References

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Figure 1. Prevalence rates (%) of the individual components of the metabolic syndrome, by gender. ILSA Study.

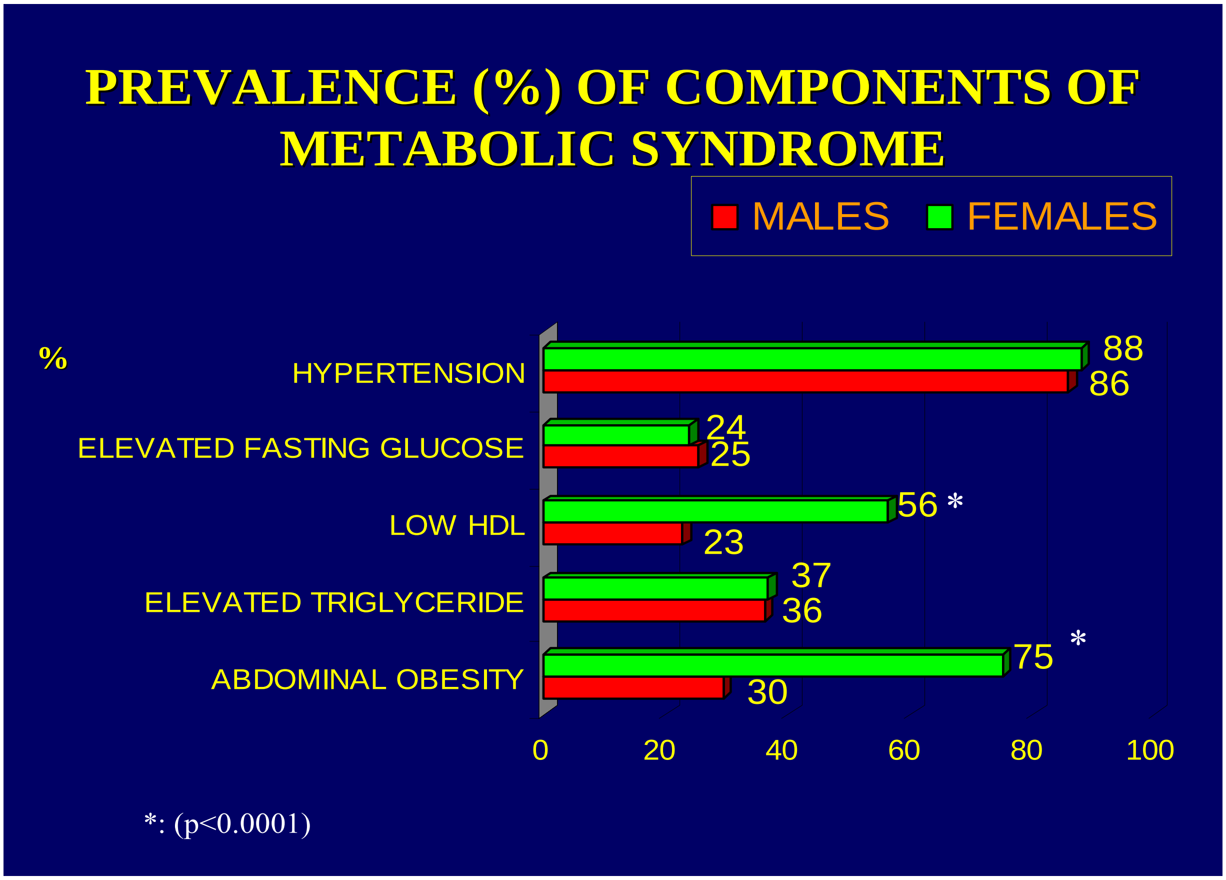
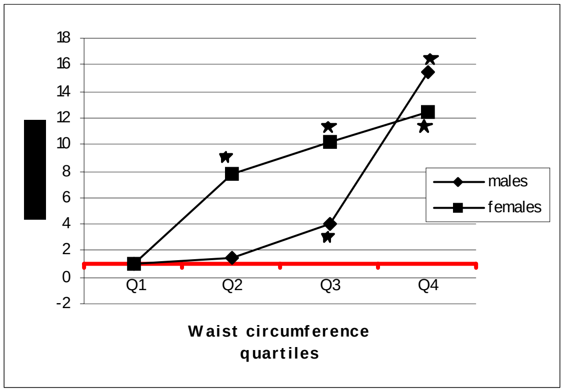
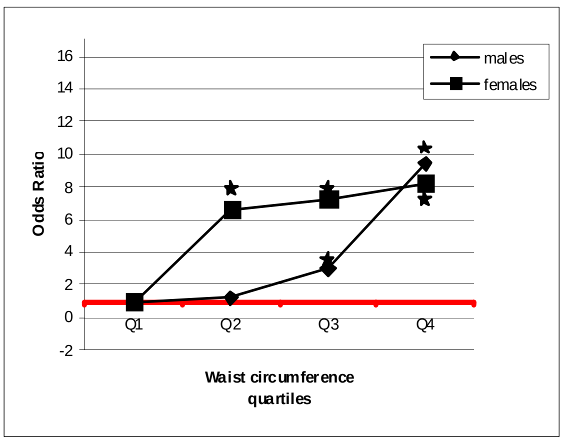


Figure 2. Odds ratios for MetS, by gender and waist circumference quartiles. ILSA study, weighted data.



Quartiles WC:

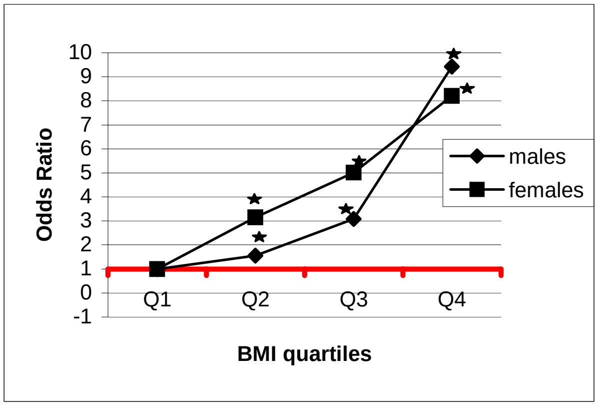
		OR	95% CI	p-value
males	Q1<91	1.00		
	Q2 91-97	1.47	0.94-2.28	0.09
	Q3 97-104	*3.99*	*2.70-5.89*	*<0.0001*
	Q4>104	15.39	10.33-22.92	<0.0001
females	Q1<89	1.00		
	Q2 89-97	7.74	5.74-10.45	<0.0001
	Q3 97-106	10.16	7.52-13.75	<0.0001
	Q4 >106	12.46	9.01-17.25	<0.0001



WC after controlling for BMI:

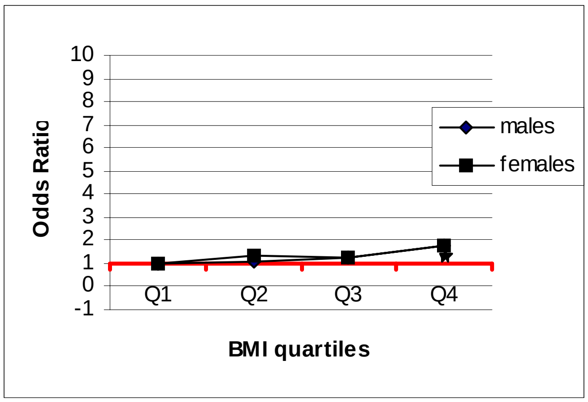
		OR	95% CI	p-value
males	Q1<91	1.00		
	Q2 91-97	1.25	0.75-2.06	0.39
	Q3 97-104	*3.01*	*1.80-5.02*	*<0.0001*
	Q4>104	9.40	5.28-16.74	<0.0001
females	Q1<89	1.00		
	Q2 89-97	6.59	4.67-9.34	<0.0001
	Q3 97-106	7.86	5.30-11.67	<0.0001
	Q4 >106	8.21	5.10-13.22	<0.0001

Figure 3. Odds ratios for MetS, by gender and BMI quartiles. ILSA study, weighted data.



BMI:

		OR	95% CI	p-value
males	Q1<23.9	1.00		
	Q2 23.9-26.2	1.55	1.02-2.37	0.04
	Q3 26.2-28.5	3.09	2.06-4.61	<0.0001
	Q4>28.5	9.43	6.38-13.90	<0.0001
females	Q1<24.1	1.00		
	Q2 24.1-27.1	3.15	2.35-4.20	<0.0001
	Q3 27.1-30.4	5.01	3.71-6.78	<0.0001
	Q4 >30.4	8.21	5.96-11.31	<0.0001



BMI after controlling for WC:

		OR	95% CI	p-value
males	Q1<23.9	1.00		
	Q2 23.9-26.2	1.06	0.65-1.72	0.81
	Q3 26.2-28.5	1.25	0.74-2.12	0.41
	Q4>28.5	1.78	1.01-3.15	0.05
females	Q1<24.1	1.00		
	Q2 24.1-27.1	1.30	0.92-1.85	0.14
	Q3 27.1-30.4	1.25	0.84-1.87	0.28
	Q4 >30.4	1.73	1.07-2.77	0.02