

and the prognosis of anti-PL7 ASS under treatment were heterogeneous.

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# Obstructive sleep apnoea and metabolic syndrome in Mediterranean countries

To the Editors:

Obstructive sleep apnoea (OSA) is often associated with metabolic disturbances, including altered glucose metabolism and dyslipidaemia, which probably contribute to the increased cardiovascular risk in these patients [1]. The concept of the metabolic syndrome (MetS) as a cluster of cardiometabolic risk factors has gained popularity in recent years, and a much higher prevalence of the MetS has been found in OSA patients compared with the general population in several studies [1]. While the MetS largely reflects the effects of visceral obesity, environmental factors, *i.e.* the type of diet, could also play some role. The Mediterranean diet, rich in olive oil and fish, is protective against the MetS [2–4], but no study has examined the association of MetS and OSA in Mediterranean countries. We hypothesised that prevalence of the MetS might be lower in OSA patients living in the Mediterranean area compared with the prevalence values found in non-Mediterranean countries. Therefore, we retrospectively assessed the prevalence of the MetS according to the modified National Health and Nutrition Examination Survey Adult Treatment Panel (ATP) III criteria [5] in consecutive patients referred to sleep laboratories in Italy (n=107), Spain (n=138) and Greece (n=218).

Patients diagnosed with OSA in the period July 2007–September 2008 in Palermo, Italy (Respiratory Section, DIBIMIS, University of Palermo, and CNR Institute of Biomedicine and Molecular Immunology), Palma de Mallorca, Spain (Hospital Son Dureta) and Alexandroupolis, Greece (Sleep Unit, Medical School, Democritus University of Thrace), were evaluated in this study. All underwent clinical examination for clinical suspicion of OSA, and full polysomnography or nocturnal cardiorespiratory monitoring (eight channel) according to the American Academy of Sleep Medicine guidelines [6]. OSA was diagnosed when the apnoea/hypopnoea index (AHI) was  $>5$  events·h<sup>-1</sup>; mean lowest arterial oxygen saturation (Sa,O<sub>2</sub>) was recorded. Daytime sleepiness was subjectively assessed by the Epworth Sleepiness Score questionnaire. Body mass index (BMI) was defined as kg·m<sup>-2</sup>. Neck, waist and hip circumferences (cm) were measured. The MetS was diagnosed based on the presence of three or more of the following factors: waist circumference  $\geq 80$  cm in females and  $\geq 94$  cm in males; serum triglycerides  $\geq 150$  mg·dL<sup>-1</sup> or lipid-lowering treatment; high-density lipoprotein HDL cholesterol  $<40$  mg·dL<sup>-1</sup> in males and  $<50$  mg·dL<sup>-1</sup> in females or statin treatment; systemic hypertension (systolic blood pressure  $>135$  mmHg and/or diastolic blood pressure  $>85$  mmHg) or anti-hypertensive treatment; and fasting blood

glucose >100 mg·dL<sup>-1</sup> or anti-diabetic treatment [5]. Plasma glucose and lipids were analysed by standard laboratory methods in venous blood withdrawn in the morning in a fasting state. Treatment for hypertension (*i.e.* diuretics,  $\beta$ -blockers and angiotensin-converting enzyme (ACE) inhibitors, *etc.*), diabetes (*i.e.* oral antidiabetic drugs and insulin), or dyslipidaemia (*i.e.* statins and clofibrate, *etc.*) was recorded in all patients.

Data are reported as mean  $\pm$  SD for continuous variables, and percentage of positive subjects for categorical variables. Continuous variables in the three patients' samples were compared by one-way ANOVA with Bonferroni correction for multiple comparisons. The Chi-squared test was used to assess differences in the frequency of categorical variables. Variables significantly associated with MetS were tested by multiple logistic regression. Statistical analysis was performed by using the SPSS version 17 software (SPSS Inc., Chicago, IL, USA) and significance was at  $p < 0.05$  for all tests.

A total of 463 patients were diagnosed with OSA in the study period (107 in Palermo, 218 in Alexandroupolis and 138 in Palma de Mallorca), but 127 had to be excluded due to missing information (20, 98 and nine, from the respective samples), leaving 336 patients for analysis. Excluded patients did not show any significant difference compared to included ones for sex distribution, age, BMI or OSA severity (data not shown).

Table 1 summarises the anthropometric and clinical features of the samples. The percentage of female patients was similar in Italy and Spain (between 30% and 35%), and lowest in the Greek sample (19%). Age and AHI were similar in the three groups. Greek patients showed a significantly lower Sa<sub>a</sub>O<sub>2</sub> during sleep. Mean BMI and waist circumference were highest in the Greek patients, who also showed significantly higher treatment rates

for hypertension (ACE inhibitors 34.2%,  $\beta$ -blockers 11.7% and diuretics 19.2%), diabetes (oral hypoglycemic drugs 15.8%), or dyslipidaemia (29.2%) compared to Italian patients (ACE inhibitors 17.2%,  $\beta$ -blockers 8.0%, diuretics 6.9%, oral hypoglycemic drugs 3.4% and dyslipidaemia treatment 9.2%), or Spanish patients (ACE inhibitors 14.2%,  $\beta$ -blockers 7.4%, diuretics 16.8%, oral hypoglycemic drugs 7.4% and dyslipidaemia treatment 11.9%). Waist-to-hip ratio was lowest in Italian patients, intermediate in Greek patients and highest in Spanish patients.

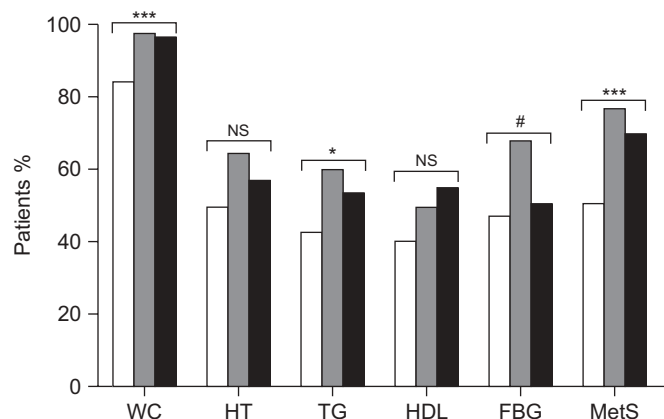
According to the National Cholesterol Education Program (NCEP)-ATP III definition, MetS was present in 67.3% of the patients of the entire cohort (fig. 1 and table 1), with the lowest prevalence in the Italian sample ( $p < 0.0001$  by Chi-squared test). Significant differences in the prevalence of single MetS components were found among the samples for waist circumference, triglycerides and fasting blood glucose, while prevalence of hypertension or low HDL-cholesterol was similar in the three samples. Logistic regression analysis in the entire sample identified age, BMI, male sex, lowest Sa<sub>a</sub>O<sub>2</sub> and presence of daytime sleepiness as significantly associated with MetS.

The results of this retrospective study do not support the hypothesis that patients with OSA from Mediterranean countries may be protected against MetS. Indeed, the prevalence rates observed were similar to those reported by other clinical studies in Western countries ranging between 30% and 87% [1]. Prevalence of MetS in Mediterranean OSA patients was at least twice as high as in the general population of the respective countries, which is rising and currently estimated to be between 22% and 25% [7–9]. The Greek sample showed the highest prevalence of markers of abdominal obesity, accounting

**TABLE 1** Characteristics of the patients

	All patients	Palermo, Italy	Alexandroupolis, Greece	Palma de Mallorca, Spain	p-value
<b>Patients n</b>	336	87	120	129	
<b>Males %</b>	72.3	65.5	80.8	69.0	<0.05
<b>Age yrs</b>	55.3 $\pm$ 12.3	54.3 $\pm$ 11.1	57.3 $\pm$ 12.8	54.2 $\pm$ 12.4	NS
<b>BMI kg·m<sup>-2</sup></b>	33.0 $\pm$ 7.2	33.0 $\pm$ 7.5	34.4 $\pm$ 6.4	31.7 $\pm$ 7.6	<0.01 <sup>#</sup>
<b>Neck circumference cm</b>	41.7 $\pm$ 4.6	40.0 $\pm$ 4.7	43.4 $\pm$ 3.8	40.9 $\pm$ 4.8	<0.0001 <sup>†</sup>
<b>AHI events·h<sup>-1</sup></b>	41.8 $\pm$ 28.1	44.2 $\pm$ 28.9	39.9 $\pm$ 27.2	42.1 $\pm$ 28.4	NS
<b>Lowest nocturnal Sa<sub>a</sub>O<sub>2</sub> %</b>	78.4 $\pm$ 11.7	81.9 $\pm$ 11.5	73.5 $\pm$ 12.6	80.3 $\pm$ 9.2	<0.001 <sup>†</sup>
<b>Epworth Sleepiness Scale score</b>	9.6 $\pm$ 5.4	9.9 $\pm$ 5.4	9.7 $\pm$ 5.7	9.4 $\pm$ 5.1	NS
<b>Waist-to-hip ratio</b>	1.00 $\pm$ 0.09	0.95 $\pm$ 0.07	1.00 $\pm$ 0.07	1.03 $\pm$ 0.10	<0.001 <sup>+</sup>
<b>Waist circumference cm</b>	112.0 $\pm$ 14.9	108.3 $\pm$ 16.2	117.6 $\pm$ 14.7	108.7 $\pm$ 12.7	<0.0001 <sup>†</sup>
<b>SBP mmHg</b>	130.9 $\pm$ 17.8	131.5 $\pm$ 18.6	129.7 $\pm$ 19.1	131.5 $\pm$ 16.4	NS
<b>DBP mmHg</b>	81.9 $\pm$ 10.6	84.7 $\pm$ 12.3	81.4 $\pm$ 8.2	81.1 $\pm$ 11.2	NS
<b>Cholesterol HDL mg·dL<sup>-1</sup></b>	47.7 $\pm$ 12.5	45.8 $\pm$ 12.2	47.9 $\pm$ 11.3	48.9 $\pm$ 13.6	NS
<b>Triglycerides mg·dL<sup>-1</sup></b>	165.0 $\pm$ 102.1	140.9 $\pm$ 78.4	168.7 $\pm$ 94.1	177.0 $\pm$ 119.6	<0.05 <sup>‡</sup>
<b>Fasting blood glucose mg·dL<sup>-1</sup></b>	109.7 $\pm$ 32.2	103.6 $\pm$ 30.3	112.2 $\pm$ 30.4	111.5 $\pm$ 34.5	NS
<b>Prevalence of MetS %</b>	67.3	50.6	76.7	69.8	<0.0001

Data are presented as mean  $\pm$  SD, unless otherwise stated. BMI: body mass index; AHI: apnoea/hypopnoea index; Sa<sub>a</sub>O<sub>2</sub>: arterial oxygen saturation; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high-density lipoprotein; MetS: metabolic syndrome; NS: nonsignificant. Results of multiple comparison testing: <sup>#</sup>: Greece > Spain; <sup>†</sup>: Greece > Italy and Spain; <sup>‡</sup>: Spain > Greece > Italy; <sup>§</sup>: Spain > Italy.



**FIGURE 1.** Metabolic syndrome (MetS) and its components. Significant differences in the prevalence of MetS were found among the samples for waist circumference (WC), triglycerides (TG) and fasting blood glucose (FBG). Hypertension (HT) and low high-density lipoprotein (HDL)-cholesterol were similar in the three samples. □: Italy; ■: Greece; ■: Spain. NS: nonsignificant. \*:  $p < 0.05$ ; \*\*\*:  $p < 0.001$ ; #:  $p < 0.005$ .

for the highest prevalence of MetS. The lowest prevalence of MetS was found in Southern Italy, together with the highest percentage of female patients and a relatively low waist-to-hip ratio. The Italian sample was quite similar to the Spanish one for percentage of females and waist circumference, but prevalence of MetS was almost 20% higher in Spain than in Italy. This finding leaves the possibility that some differences in diet may play a role, but we could not check for dietary composition in this retrospective study. Epidemiological data from Spain recently showed that prevalence of MetS in the general population by NCEP-ATP III criteria increased from 18% to 25% in a decade, especially in young subjects, in conjunction with a major shift from the Mediterranean diet towards the Western diet [10]. Our study suggests that such a change might have similarly occurred in patients with OSA, although significance of severity of hypoxaemia and sleepiness by logistic regression analysis confirms a possible role of intermittent hypoxia in the pathogenesis of metabolic disorders. In conclusion, prevalence of the MetS in patients with OSA was similar in Mediterranean and non-Mediterranean countries, suggesting that exposure to Mediterranean diet was either absent in these patients or insufficient to exert any protective effect. Studies on the dietary habits of OSA patients are warranted, especially regarding diet composition, as they may be useful in weight control and cardiovascular prevention programmes.

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