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Original Study **OS 1 (1-9)**

Sleep duration, sleep quality and new markers of insulin resistance in obese subjects

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Abstract

Background: Sleep is an essential component of psychophysical well-being. Both insufficient duration and inadequate quality of sleep may increase the risk of diabetes mellitus, cardiovascular events and mortality. The relationship between short sleep duration and glucose disorders appears to be bidirectional. However, the link between duration, quality of sleep and new markers of insulin resistance (IR) in obesity is still unclear.
Aim: To evaluate sleep duration and quality in a group of overweight/obese subjects and their association with metabolic variables and IR markers.
Materials and methods: Anthropometric parameters, glycemic profile, biomarkers of IR were evaluated in adult patients with BMI >27 kg/m^2 without severe OSA (Obstructive Sleep Apnea Syndrome). Sleep duration and quality were assessed using the PSQI (Pittsburgh Sleep Quality Index) questionnaire. IR was estimated using HOMA-IR, TyG index (Triglycerides-Glucose Index) and Tg/HDL ratio (triglycerides/HDL-cholesterol).
Results: The 84 subjects included in the analysis (BMI 36.14 kg/m^2, waist circumference 110.42 cm) had a mean age of 54,65 years. The mean values of HOMA-IR (4.99±3.88), Tg/HDL (2.8±1.42) and TyG (4.74±0.25) were suggestive of a condition of insulin resistance. Nearly half of the patients (45%) had severe obesity and 84% had diabetes or IFG/IGT. The overall quality (total PSQI 7.63) and duration of sleep (5.76 hours) were not satisfactory and 59.5% of the patients had a total PSQI score >5, indicative of altered sleep quality.
When patients were divided according to the sleep quality, subjects with PSQI >5 (poor sleep quality) had higher values of BMI, waist circumference, and waist-to-height ratio, as compared to those with PSQI ≤5. Markers of IR, glycemic and lipid profile were similar in the two groups. Mean PSQI score and the percentage of subjects with poor sleep quality were significantly higher in patients with class II/III obesity, compared to those with BMI<35 Kg/m^2 (9.38 vs 6.02 respectively, p<0.001 and 77% vs 43% p 0.04).
Conclusions: In this group of overweight/obese patients without severe OSA, we did not observe any association of sleep quality and duration with markers of IR. Sleep duration and quality were inadequate, especially in subjects with more severe degrees of obesity, suggesting an inverse relationship between sleep quality and visceral obesity.

Key Word: insulin resistance; sleep quality; sleep duration; obesity

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Introduction

Sleep is an essential component of well-being. A sleep duration of 7-9 hours per day is considered appropriate for mental and physical health in adults (1). Sleep deprivation is a

common aspect of modern lifestyle, and in recent decades a reduction in sleep duration has been observed, with an increasing number of people reporting insufficient sleep (< 7 hours a night) (1). Some evidence suggests an association between short sleep duration and obesity, in both sexes (2,3). Furthermore, a sleep duration of less than 7 hours per night has been associated with adverse health outcomes, including hypertension, cardiovascular disease, and increased risk of death (4-8). Epidemiologic studies suggest that short sleep duration may also result in decreased glucose tolerance and increased risk of type 2 diabetes (9). A recent meta-analysis of prospective studies demonstrated a 9% increased risk of diabetes for each hour of sleep lost, compared to the optimal sleep duration of 7-8 hours per day (3). Unsatisfactory sleep has also been associated with a reduced quality of life (10).

Insufficient sleep induces complex hormonal changes and alters circulating levels of ghrelin, leptin and GLP1, resulting in increased hunger, daily caloric intake and body weight. In addition, short sleep duration induces chronic systemic inflammation, insulin resistance (IR) and reduction in pancreatic beta-cells activity. Inadequate sleep can activate the autonomic sympathetic system and dysregulate the hypothalamic-pituitary-adrenal axis, with increased evening cortisol levels and consequent IR and hyperglycemia. All these factors contribute to the risk of obesity and diabetes.

The link between sleep, obesity and glucose disorders seems to be bidirectional, as these metabolic conditions increase the risk of obstructive sleep apnea, nycturia, and neuropathic pain. Excess weight and an unhealthy lifestyle may therefore reduce sleep duration (11).

In addition to the importance of sleep duration, sleep quality also appears to influence cardio-metabolic health (1, 9, 11). Some data suggest a multifaceted relationship between poor sleep quality, cardiovascular health, obesity and diabetes risk (11).

However, the relationship of sleep duration and quality with more recently introduced IR surrogates in obesity, is still unclear.

Aim of the study

The aim of the study was to evaluate sleep duration and quality in a group of overweight/obese subjects without severe OSA and their association with metabolic variables and markers of insulin resistance.

Patients and methods

Patients

All adult patients consecutively attending the obesity clinic of the Endocrinology Unit at the University Hospital of Messina, Italy, in the period between 1 September and 30 November 2024 were included in the study. In this clinic, subjects with obesity (BMI>30 Kg/m^2) and patients with

excess weight (BMI>27 kg/m²) and metabolic complications, such as dyslipidemia and diabetes mellitus, are managed.

The exclusion criteria applied in the study were: age <18 years, pregnancy, type 1 diabetes mellitus, LADA, severe OSAS treatment with positive airway pressure (PAP), inability to answer the questionnaire, neoplasms and relevant acute pathological conditions.

Methods

For all subjects, clinical data, anthropometric parameters such as waist circumference, body weight, body mass index (BMI), and waist-to-height ratio (WHtR) and the following laboratory values were collected: fasting blood glucose, HbA1c, insulin, total cholesterol, HDL-cholesterol, triglycerides, creatinine, transaminases. LDL-cholesterol levels were calculated in mg/dl with the formula by Friedewald (12). Renal function was assessed by estimating glomerular filtration rate according to the CKD-EPI formula (ml/min/1.73m²) (13).

Insulin resistance was estimated by the HOMA-IR (Homeostatic model assessment), the Tryglycerides/glucose index (TyG) and the triglyceride-to-high-density lipoprotein cholesterol (Tg/HDL-C) ratio (14 - 16).

Assessment of sleep duration and quality

To assess sleep quality and duration, the Pittsburgh Sleep Quality Index (PSQI) was administered to all subjects participating in the study. The PSQI is a widely used self-report questionnaire that was validated across diverse contexts and populations.

The questionnaire provides a global and multidimensional assessment of sleep health and consists of 19 questions divided into 7 components, each component providing a score from 0 to 3. Higher scores indicate a greater severity of the problem. The total score is the sum of the 7 components. A $\leq$ 5 score suggests a good sleep quality, and a > 5 score indicates impaired sleep quality (17,18).

Evaluation of the presence of *Obstructive sleep apnea (OSA*)

As part of clinical management of obesity, all patients in our clinic undergo polysomnography to exclude the presence of OSA. Polysomnographic assessments (including AHI, blood oxygen saturation parameters, sleep architecture parameters and nocturnal heart rate) are performed using standard techniques. The mean number of apneas per hour of sleep (AHI) is used to classify OSA severity as mild ($5 \leq$ AHI <15 events/h), moderate ($15 \leq$ AHI <30 events/h), and severe (AHI $\geq$ 30 events/h) (19,20).

Statistical analysis

The numerical data were expressed as mean and standard deviations (SD) while the categorical variables as number and percentage. The Gaussian distribution of the study variables was

assessed through the Kolmogorov-Smirnov test and a parametric analysis was performed. A $p<0.050$ was considered statistically significant. Statistical analyses were performed using SPSS for Window-package.

Results

Clinical characteristics of the subjects participating in the study

Eighty-four subjects (24 men and 60 women; mean age 54.6 years) were consecutively recruited. Their clinical characteristics and anthropometric parameters are shown in **Table 1**. Study subjects had mean BMI (36.14 kg/m^2), waist circumference (110.42 cm), and WHtR (0.68) values indicative of visceral obesity. Approximately half of the patients (45.2%) had class-II or III obesity (BMI>35 Kg/m^2). Mean values of HOMA-IR (4.99±3.88), Tg/HDL (2.8±1.42) and TyG (4.74±0.25) were suggestive of insulin resistance. Prediabetes (IFG and/or IGT) was observed in the 34.5% of the study subjects and 42 patients (50%) were affected by type 2 diabetes. The mean value of eGFR was 82,96 ml/min. Transaminases values and lipid profile were within the normal ranges.

Table 1: Clinical characteristics of the subjects participating in the study

N	**84**
M/F	25/59
Age (years)	54.65±15.65
Smokers n (%)	12 (14.3%)
Weight (Kg)	95.84±22.84
BMI (Kg/m^2)	36.14±7.63
Waist circumference (cm)	110.42±15.88
Waist-to-height ratio	0.68±0.10
Class I obesity n (%)	32 (38.1%)
Class II or III obesity n (%)	38 (45.2%)
IFG and/or IGT n (%)	29 (34.5%)
Type 2 diabetes n (%)	42 (50%)
Fasting blood glucose (mg/dl)	113.65±30.11
HbA1c (%)	6.22±0.93
Fasting insulin (μU/ml)	21.27±15.48
HOMA-IR	4.99±3.88
TyG	4.74±0.25
TG/HDL	2.80±1.42
Total Cholesterol (mg/dl)	172.42±39.60
HDL Cholesterol (mg/dl)	49.87±11.77
LDL Cholesterol (mg/dl)	100.08±36.29
Triglycerides (mg/dl)	130.40±57.22
Creatinine (mg/dl)	0.91±0.34
eGFR (mL/min/1.73 m^2)	82.96±24.76
AST (U/L)	24.87±7.18
ALT (U/L)	30.64±19.08

Data are n, %, means and standard deviation.;eGFR: estimated Glomerular Filtration Rate; BMI: Body Mass Index:HbA1c: Glycated hemoglobin (expressed in %)IFG: Impaired fasting glucose;IGT: Impaired glucose tolerance

Pittsburgh Sleep Quality Index (PSQI) questionnaire scores

The PSQI scores of the subjects participating in the study are shown in **Table 2**. Both mean quality (PSQI score=7.63±4.77) and duration of sleep (5.76±1.49 hours) were unsatisfactory, and more than half of patients (59.5%) reported poor sleep quality (PSQI > 5).

Sleep efficiency was also below (C4 score 74%) the range of adequate quality (>85%). In contrast, the C1 score indicating the subjective assessment of sleep, suggested an inadequate perception of the problem by patients.

Table 2: Sleep quality of study subjects

Pittsburgh Sleep Quality Index scores	
C1-Subjective sleep assessment	1.33±0.85
C2-Sleep latency (minutes)	33.04±33.78
C3-Sleep duration (hours)	5.76±1.49
C4-Sleep efficiency (%)	74.6±14.01
C5-Sleep-disorders	1.39±0.76
C6-Sleep medications	0.13±0.55
C7-Daytime dysfunctions	1.07±0.79
C8-Total score	7.63±4.77
Subjects with total score > 5 n (%)	50 (59.5)

Pittsburgh Sleep Quality Index (PSQI):

- C1=Subjective sleep rating (0-3)
- C2=Sleep latency (minutes)
- C3=Sleep duration (hours)
- C4=Sleep efficiency (%)
- C5=Sleep disturbances (0-3)
- C6=Use of sleep medications (0-3)
- C7=Dysfunctions during the day (0-3)
- C8=Total score

C8> 5 = poor sleep quality

Clinical characteristics and anthropometric parameters of study subjects, stratified according to sleep quality, sex and degree of obesity

Clinical characteristics and anthropometric parameters of study subjects, stratified according to sleep quality are shown in **Table 3**. Subjects with PSQI > 5 (poor sleep quality) had significantly higher values of BMI, waist circumference, and WHtR compared to those with PSQI≤5. The percentage of subjects with class II or III obesity was higher in the group with worse sleep quality. Glycemic control, lipid profile and IR markers were similar in the two groups.

No differences in sleep quality scores were observed between men (PSQI score 6,19±4,58) and women (8,17±4,81), nor between subjects with and without alterations in glucose metabolism.

When patients were divided according to obesity degree, a significantly higher PSQI score was

observed in patients with II and III class obesity, as compared to those with BMI<35 Kg/m2 (9.38±4.92 *vs* 6.02±4.11 respectively, p<0.001); consistently, the percentage of subjects with poor sleep quality was higher in the subgroup with severe obesity (77% vs 43%, p=0.0425).

Table 3: Clinical characteristics and anthropometric parameters of study subjects, stratified according to sleep quality

	Subjects with poor sleep quality	**Subjects with good sleep quality**	**p**
N	50 (59.5%)	34 (40,5%)	
M/F	13/37	13/21	0.2780
Age (years)	54.54±13.79	53.77±18.08	0.6104
Smokers n (%)	9 (18%)	4 (11.7%)	0.4135
Weight (Kg)	99.82±24.22	90.20±19.31	0.0540
BMI (Kg/m2)	37.67±7.65	33.85±7.03	0.0217
Waist circumference (cm)	114.12±16.89	105.4±12.68	0.0115
Waist-to-height ratio	0.71±0.10	0.65±0.08	0.0066
Class I obesity n (%)	17 (34%)	15 (44%)	0.2898
Class II or III obesity n (%)	30 (60%)	8 (23%)	<0.001
IFG and/or IGT n (%)	17(34%)	12 (35%)	0.9695
Type 2 diabetes n (%)	23 (46%)	20 (59%)	0.3941
Fasting blood glucose (mg/dl)	110.86±30.12	118.47±29.8	0.2570
HbA1c (%)	6.07 ±0.90	6.45±0.95	0.0776
Fasting insulin (μU/ml)	24.49±17.72	15.64±8.46	0.1151
HOMA-IR	5.86±4.45	3.48±1.97	0.0892
TyG	4.73 ±0.25	4.76 ±0.26	0.6780
Tg/HDL	2,82 ±1,39	2,77±1,46	0.8714
Total Cholesterol (mg/dl)	178.82±42.97	161.03±33.10	0.0449
HDL Cholesterol (mg/dl)	49.96±12.04	49.3±11.59	0.8056
LDL Cholesterol (mg/dl)	104.11±40.03	92.39±29.66	0.1538
Triglycerides (mg/dl)	130.94±56.37	128.88±58.64	0.8729
Creatinine (mg/dl)	0.89±0.28	0.93±0.42	0.6059
eGFR (mL/min/1.73 m^2ml/min)	81.79±23.12	84.74±26.74	0.6059
AST (U/L)	24.85±7.36	24.58±7.18	0.8704
ALT (U/L)	32.83±21.16	27.09±15.09	0.1921

Data are n, %, means and standard deviation.

- eGFR: estimated Glomerular Filtration Rate
- BMI: Body Mass Index
- HbA1c: Glycated hemoglobin (expressed in %)
- IFG: Impaired fasting glucose
- IGT: Impaired glucose tolerance

Discussion

Sleep duration and quality are important aspects of mental and cardiometabolic health, with an impact on energy balance. Insufficient sleep duration and quality appear to be related to negative outcomes such as obesity, diabetes, cardiovascular disease, and all-cause mortality (21).

We evaluated sleep duration and quality in a group of overweight/obese subjects and their association

with metabolic variables and IR markers. To avoid the confounding effect of known pathological sleep disorders, patients with severe OSA were excluded from the analysis. In this group of subjects, we observed a high prevalence of insufficient duration and poor quality of sleep. These results confirm the close relationship between sleep alterations and obesity, since excess weight can reduce the duration and quality of sleep, through hormonal, physiological, and behavioral mechanisms (22).

Notably, we did not observe any sex-related differences in sleep characteristics. Some evidence suggests that women tend to sleep longer but generally have poorer sleep quality than men. Our results are consistent with those of a recent meta-analysis, which examined the relationship between short sleep duration and obesity, and did not observe any influence of sex (23).

In our study population, sleep scores were worse in subjects with higher degrees of visceral obesity. These findings are consistent with other studies indicating that individuals with a habitually short sleep have higher BMI than those with a normal sleep duration (24).

In addition, diabetes or IFG/IGT were prevalent, since subjects referred to our clinic have severe obesity or obesity with chronic complications, including metabolic alterations. However, we did not observe any differences in sleep quality and duration, between subjects with and without dysglycemia; similarly, no significant differences occurred for other metabolic parameters, such as fasting blood glucose, lipid profile and fasting insulin levels.

In recent years, several alternative indices of IR, calculated from simple biochemical and anthropometric parameters, have been proposed to identify subjects at greater cardiometabolic risk in daily medical practice; some of these, such as TyG index and Tg/HDL ratio have proven to be easy to use, inexpensive and accurate (14-16).

Although overall high values of TyG index and Tg/HDL ratio were observed in our study population, no differences emerged when subjects were divided according to sleep quality.

Our data suggests a complex and heterogeneous relationship between sleep quality and metabolism, more evident for anthropometric parameters (including WHtR, BMI and waist circumference) than for IR-related variables.

In conclusion, our results, although requiring confirmation in larger populations, suggest an inverse relationship of sleep quality and duration with visceral obesity, in adult men and women, without a clear relationship with recently introduced markers of insulin resistance. The effect of diet, physical activity and weight loss on these variables remains to be clarified.

Conflicts of Interest: There is no potential conflict of interest, and the Authors have nothing to disclose.
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