

Effect of Mediterranean Diet vs Prudent Diet Combined with Physical Activity on OSAS: A Randomised Trial

Running Head: Effect of MD vs PD on OSAS

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ABSTRACT

We aimed to evaluate the effect of the Mediterranean diet (MD) compared with that of a prudent diet (PD) combined with physical activity on obese OSAS patients who were treated with CPAP.

Nine hundred patients were evaluated and forty obese patients (body mass index: ≥ 30.0 kg/m²) who met the inclusion criteria, with moderate to severe OSAS (apnoea-hypopnoea index: >15 and daytime sleepiness: >10) based on overnight attended polysomnography, were included in the study. After randomization, 20 followed the MD and 20 a PD for a 6-month period. All patients were counselled to increase their physical activity.

Concerning sleep parameters, only apnoea-hypopnoea index during rapid eye movement sleep (AHI/REM) was reduced to a statistically significant degree, by 18.4 ± 17.6 in the MD group and by 2.6 ± 23.7 in the PD group ($p < 0.05$). The MD group showed also a greater reduction in waist circumference (WC) (-8.7 ± 3.6), WC/height ratio (-0.04 ± 0.02) and WC/hip ratio (-0.04 ± 0.03), compared with the other group (-5.7 ± 3.8 , -0.03 ± 0.02 , 0.02 ± 0.02 and -2.6 ± 1.7 , respectively, $p < 0.05$).

Our results showed that the MD combined with physical activity for 6 months period was effective in reducing the AHI/REM without any statistical significant effect in the other sleep parameters, compared to a PD in obese adults with moderate to severe OSAS.

Keywords: obstructive sleep apnoea syndrome; Mediterranean diet; physical activity; apnoea-hypopnoea index during rapid eye movement sleep; abdominal obesity

The trial is registered at ClinicalTrials.gov, number NCT01312558.

INTRODUCTION

Obstructive sleep apnoea syndrome (OSAS) is considered to be one of the most prevalent sleep-related breathing disorders, with an enormous effect on public health. Approximately 2-4% of the general adult population experiences some degree of this syndrome [1]. This percentage increases even more with obesity, up to 20-40%, especially in individuals with an excessive body mass index (BMI) ≥ 30 kg/m² [2]. OSAS is associated with significant systemic consequences, including cardiovascular morbidity and mortality, and the risk increases with the severity of the syndrome [3]. The pathophysiology underlying the link between OSAS and the cardiovascular system is attributed largely to systemic inflammation and oxidative stress, which are both contributors to endothelial dysfunction [4]. The treatment modalities of OSAS include continuous positive airway pressure (CPAP), weight loss, upper airway surgery, and oral devices [5]. CPAP is the first line therapy, as a means of maintaining upper airway patency [6], and it is well known that this intervention reduces morbidity and mortality [7]. In severe cases of OSAS the weight loss strategy is essential and must accompany CPAP treatment [8]. A growing body of evidence in OSAS supports the beneficial role of weight reduction, induced by diet alone [9-12] or in combination with exercise [13], leading to a reduction in apnoeas and hypopnoeas. However, randomised controlled trials examining this issue are rare, while available observational studies suffer from several biases and confounders and their data are limited [14]. To the best of our knowledge, only two randomised studies inducing weight loss have been reported so far. Both observed a clinically meaningful improvement in patients with mild [12] and moderate to severe [11] OSAS. Most of the weight reduction and sleep apnoea studies did not include exercise in their intervention program. Exercise combined with a change in dietary behaviour has been

shown to result in greater weight loss [15]. Moreover, these studies evaluated the effects of low and very low calorie diets on obese patients with OSAS. It was suggested recently that the Mediterranean diet is beneficial for weight loss [16], but its role in obese OSAS patients has never been explored. The Mediterranean diet promotes satiation and encourages consumption of a variety of palatable foods, optimizing adherence to a caloric restricted diet [17]. This dietary pattern would result in greater weight loss and hence greater improvement in OSAHS compared to a general weight reduction diet.

Therefore, we aimed to evaluate the effect of the Mediterranean diet compared with that of a prudent diet on obese OSAS patients who were treated with CPAP while receiving counselling to increase their physical activity.

METHODS

Participants

A series of consecutive patients, who were diagnosed with OSAS by overnight attended polysomnography (PSG) in the Sleep Disorders Unit, Department of Thoracic Medicine, Medical School, University of Crete, during a one-year period (November 2008-October 2009) were evaluated and the study population was selected based on the following criteria. Inclusion criteria were as follows: a) age 18-65 years; b) body mass index (BMI) ≥ 30 kg/m²; c) apnoea-hypopnoea index (AHI) >15 events/h. Exclusion criteria were: a) diseases such as cardiac ischaemic disease, diabetes mellitus, thyroid disorders, psychotic disease and malignancies, alcoholism; b) upper airway surgery; c) gestation; d) diet for weight reduction the last 6 months or other medications affecting weight; e) eating habits close to the Mediterranean diet at the entry phase; f) therapy with sleeping pills. The study flowchart is shown in figure

1. After the visit to the study physicians and confirmation that the patients fulfilled the inclusion/exclusion criteria, the subjects were allocated randomly to two study groups using a computer-generated random number sequence. No stratification was used in the allocation of the participants into the two groups. The groups were matched by gender. In view of the use of both diets, blinding of staff or patients was not considered feasible. The primary outcome measure was the change of OSAS severity as reflected mainly by AHI and saturation indexes. In addition to these measurements we recorded the AHI during rapid eye movement sleep. This study was approved by the ethical committee of the University of Crete and all the participants provided signed consent.

Intervention

Two groups of patients with moderate to severe OSAS were formed. In both groups, the patients received CPAP therapy and lifestyle intervention including a programme of increasing physical activity, mainly involving walking for at least 30 minutes daily. At the same time the two groups were advised to follow a low-calorie diet, one a prudent diet (PD group) and the other a Mediterranean diet (MD group). In all patients a specific motivation programme and education in reducing calorie intake were offered, aiming to restrict the daily energy to 1200-1500 kcal for women and 1500-1800 kcal for men. The general guidelines to the participants in the MD group were consumption of six servings per day of non-refined cereals; five or more servings per week of potatoes; five servings per day of various vegetables (two of them as salad); four servings per day of various fresh fruits; three or more servings per week of legumes; three servings per week of fish (at least one serving of fatty fish); one serving per day of nuts; three servings per week of poultry without skin; three servings per week of red meat and seven glasses each week of red wine. The

recommended intake of fruits, vegetables, legumes, non-refined cereals and fish was three times higher in the MD group than in the PD group, whereas the red meat intake in the former group was one third of that in the latter. The moderate daily consumption of nuts and alcohol (red wine) was only recommended in the MD group. In both groups the moderate consumption of olive oil was recommended, because based on the local conditions almost all the people living in the island of Crete produce and consume this type of oil. Patients in both groups were also advised to eliminate or limit the consumption of cream, butter, margarine, carbonated and/or sugared beverages, commercial bakery products (e.g. sweet desserts, cakes, biscuits/cookies, puddings, and custard), potato fries and processed meats (i.e. burgers and sausages) and to consume two servings per day of low-fat dairy products.

The intervention lasted for 6 months, and consisted of a total of 7 visits, including dietician visit and consultation. The study dietician was responsible for providing dietary and exercise counselling at each visit. Additionally compliance with CPAP therapy was monitored.

Procedures and measurements

Overnight attended polysomnography (PSG) (Alice 5, Respiromics) was performed in the Sleep Disorders Unit of the University of Crete. Patients underwent a full diagnostic PSG study, according to standard techniques, with monitoring of the electroencephalogram (EEG) using frontal, central and occipital leads, electro-oculogram (EOG), electromyogram (EMG), flow (by oronasal thermistor and nasal air pressure transducer), thoracic and abdominal respiratory effort by uncalibrated impedance plethysmography belts, oximetry, and body position. Snoring was recorded by a microphone placed on the anterior neck. A single modified type II EKG lead was used for cardiac monitoring. Polysomnographic recordings were manually interpreted

over 30-second periods, in accordance with the American Academy of Sleep Medicine (AASM) guidelines [18,19]; the scorer was blinded to the PSG findings of the initial and final clinical assessment. The determination of sleep stages and arousals was performed according to the AASM 2007 criteria and by using EEG montages including frontal, central and occipital leads. Two sleep recordings were performed during the study. The first was conducted at baseline and the second at 6 months. Patients with apnoea-hypopnoea index >15 events/h and Epworth Sleepiness Scale >10 were assigned as having moderate to severe OSAS and underwent a CPAP titration study. After CPAP initiation patients were followed up by the Sleep Disorders Unit CPAP clinic. The hours per day and percentage of days that CPAP was used were monitored (IC card, Respironics, Inc., Murrysville, PA, USA) at the monthly clinical assessment. All patients exhibited good compliance, using CPAP >4 hours/day and >5 days per week, which are the criteria of regular use [25]. The end of PSG study was done without CPAP. One day prior the PSG, CPAP was ceased.

Anthropometric measurements (weight, height, waist and neck circumferences) were carried out by an expert at baseline and at each visit and a subject was defined as obese when BMI was ≥ 30.0 kg/m² [20]. Body fat was estimated by the 4-skinfold-thickness method [21] at baseline, and at the 6-month visit. Adherence to the diets was evaluated by a semi-quantitative food frequency questionnaire [22] at baseline, at the 3-month visit, and at the 6-month visit. In addition, overall dietary habits were evaluated through a special diet score (MedDietScore, range 0-55) that assessed adherence to the Mediterranean dietary pattern [23]. Physical activity was assessed using the long version of the self-reported International Physical Activity Questionnaire [24] at baseline, at the 3-month visit, and at the 6-month visit. Participants were also questioned regarding their educational level and smoking

status. Educational level was categorised in four levels (primary school=0, secondary school=1, post-high school education=2, higher education=3).

Statistical analysis

Mean values and standard deviations are used to describe the baseline characteristics of the two treatment groups. The Student *t*-test was used to assess equality between the treatment groups at baseline. Changes in sleep recordings and anthropometric measures during the follow up were calculated by subtracting the baseline measurement from the 6-month follow-up measurement, and the mean difference in changes between the treatment groups was calculated. The statistical significance of between-group differences in changes was assessed with the Student *t*-test. All data were analysed with the Statistical Package for Social Sciences (SPSS) version 18.0. A p-value less than 0.05 was considered significant.

RESULTS

Forty patients were randomized to the PD group (n=20) or MD group (n=20). All of them successfully completed this small underpowered study. No side effects of both treatments were reported.

During the selection of the study population, 837 patients were excluded based on the abovementioned exclusion criteria (109 patients had ischemic heart disease, 78 patients had diabetes mellitus, 126 patients had thyroid disorders, 21 patients suffered from malignancies, 28 had undergone upper airway surgery, 3 were alcoholics, 11 were under therapy with sleeping pills, 43 were receiving antidepressant medication, 203 had a BMI < 30.0 kg/m², 70 were < 18 years old and 145 were > 65). Another 23 patients refused to participate in the intervention program (fig 1).

Table 1 shows the characteristics of the two groups at baseline. Despite the randomisation, BMI was higher in the PD group compared with the MD group

(37.9 ± 4.6 vs. 35.3 ± 3.6 , $p:0.04$). There were no significant differences between the two intervention groups in the other baseline characteristics ($p>0.05$). In general, the patients studied were middle aged (48.9 ± 12.7 years); the majority were men (85.0%), with moderate to severe OSAS (AHI: >15 events/h and daytime sleepiness: ESS >10) and BMI: 36.6 ± 3.7 kg/m².

After 6 months, patients in the MD group showed a greater adherence to the Mediterranean dietary pattern than did those in the PD group (Table 2). More specifically, the change in MedDietScore was 12.7 ± 4.9 in the MD group and 0.95 ± 4.5 in the PD group ($p>0.001$). Apart from MedDietScore, patients in the MD group also improved their level of physical activity (MET-min/week) more than did those in the PD group ($p<0.05$). There was also a statistically significant difference between the two study groups regarding the change in several anthropometric indices. Patients in the MD group showed a greater decrease in waist circumference (WC) (-8.7 ± 3.6), WC/height ratio (-0.04 ± 0.02), and WC/hip ratio (-0.04 ± 0.03) than those in the PD group (-5.7 ± 3.8 , -0.03 ± 0.02 , and -0.02 ± 0.02 , respectively, $p<0.05$), while there was no difference between the two groups regarding the change in neck circumference (NC) and NC/height ratio ($p>0.05$). Body fat also decreased more in the MD group than in the PD group (-4.3 ± 2.5 vs. -2.6 ± 1.7 , $p<0.05$). At the end of the intervention, although patients in the MD group had reduced their weight and BMI more than those in the PD group (9.0 ± 3.9 vs. 7.2 ± 4.2 kg and 3.2 ± 1.5 vs. 2.5 ± 1.4 kg/m², respectively), these changes did not reach statistical significance ($p>0.05$). There were no significant differences in the changes in sleep parameters between the two groups ($p>0.05$), except in the apnoea-hypopnoea index to rapid eye movement ratio (AHI/REM). This ratio, improved significantly more in participants in the MD group than in those in the PD group. Specifically, AHI/REM decreased by 18.4 ± 17.6 in the MD group and by

2.6±23.7 in the PD group ($p<0.05$). The observed difference in AHI/REM between the two groups was independent of the baseline value, as the statistical difference persisted after adjustment for the baseline level of AHI/REM abnormality ($p=0.02$). The change in AHI during REM sleep from the beginning until the end of treatment for each patient separately is shown in figure 2. AHI/REM reduction was fairly and negatively correlated with increased exercise scores and positively with decreased waist diameter between time points ($r=-0.503$, $p=0.001$ and $r=0.488$, $p=0.002$ respectively). We also controlled the time spent in supine position during REM sleep between baseline and 6-month polysomnographies and there was no statistical difference in the PD group (baseline: 5 ± 9.1 min, 6 months: 13 ± 17.1 min, $p=0.09$) and in the MD group respectively (baseline: 5.5 ± 12.6 , 6 months: 7.3 ± 8.7 , $p=0.6$).

DISCUSSION

This study investigated the effect of the Mediterranean diet compared to that of a prudent diet on obese OSAS patients treated with CPAP while receiving counselling to increase their physical activity. Weight loss trials including both diet and exercise in their program have the potential to deliver significant health benefits in terms of treating OSAS in the majority of patients with mild [12] and mild to moderate [26] OSAS. According to the findings of this study, the MD diet combined with physical activity for a 6 months period of time, did not lead to a greater improvement in overall OSAS severity than the PD diet, despite better exercise program compliance. Participants in the MD group demonstrated a greater decrease in waist circumference, waist to height ratio, and waist to hip ratio than did the PD group. This means that individuals succeeded in decreasing their abdominal fat. It has been reported that abdominal fat, BMI and NC and are significant clinical predictors of OSAS [27,28]. Neck circumference has been suggested to be more predictive of OSAS than general obesity and the lack of impact on overall OSAS severity could be related to lack of significant difference in the change in NC [29]. The only sleep parameter with a remarkable

reduction was the AHI during REM sleep in patients in the Mediterranean diet arm compared with those following a prudent diet. The finding of AHI/REM was not a primary endpoint and further studies are needed in order to clarify this point. This was independent of the baseline value of AHI/REM. This is an interesting finding, since REM sleep abnormalities are associated with decreased upper airway muscle activation [30,31], impaired genioglossus reflex responsiveness to negative pressure [32], and reduced chemosensitivity [33]. All these factors are related to the severity of the syndrome [34]. Recent reports have also related an increased AHI/REM with the risk of developing significant systemic consequences. Mahmood et al recently reported that an increased prevalence of diabetes type II was related with this specific phenotype of OSAS [35]. However, its clinical significance remains unclear, although compared to NREM sleep, during REM sleep there is an increase in the duration of apnea episodes, which maybe cause more severe desaturation events [36]. There is no evidence from previous weight loss trials using conventional diet programmes to support this finding. This significant difference in the change in AHI/REM between the treatment groups could be related to the notable difference in the change in relevant body circumference indices. It is possible that the MD along with increased physical activity could promote changes of relevant anthropometric determinants such as waist size and finally better outcome. However, more studies dealing with this specific research question are needed to clarify this point. It has been suggested that abdominal fat is a risk factor for OSAS in obese patients [37]. It is related with a reduction in pharyngeal lumen size due to fatty tissue within the airway or in its lateral walls, and a decrease in upper airway muscle protective force due to fatty deposits in the muscle. It has also been reported that abdominal fat is associated with reduced upper airway size secondary to the mass effect of the large abdomen on the chest wall and tracheal traction [38]. Moreover, an association between increased BMI and the development of hypoventilation is well recognized, as abdominal fat accumulation is known to impair diaphragmatic excursion and rib cage expansion [39]. Since, diaphragm consists the main inspiratory muscle during REM sleep [40] abdominal obesity may mechanically affect the expansion of the diaphragm, probably by encroaching into the chest by the chest wall or diaphragm or by impeding the descent of the diaphragm during forced inspiration [41]. While obesity alone does not account for the development of hypoventilation, it would be possible that by

decreasing abdominal fat, breathing would have improved during REM sleep. Therefore, it is likely that the patients in the MD group reduced AHI/REM more than those in the PD group because of the greater reduction in abdominal fat, via an improvement in the mechanical load associated with OSAS [42]. The greater decrease in body fat in the MD group, as estimated by the skin-fold method, could also be considered to strengthen our results, since body fat measured in this way has been considered as a significant predictor for OSAS [43]. The difference between the two treatment groups in the changes in the above anthropometric indices and in body fat could be attributed to the greater adherence to the prescribed diet and level of physical activity in the patients in the MD group. It has been shown that exercise training alone is not an adequate intervention strategy for most individuals with OSAS but may serve well as an adjunct treatment strategy in the conservative management of OSAS. The results could be attributed to the combination of more adherence to the hypocaloric diet and exercise in the MD group. Additionally, several reports have shown that abdominal obesity is substantially reduced when combining the above lifestyle modifications [44-46].

Potential mechanisms linking MD adherence to better compliance with a weight loss dietary programme compared to the prudent diet used in this study may include its lower energy density [47] and its relatively low glycaemic load [48]. These beneficial factors, along with its higher fibre [47] and water [49] content lead to increased satiation and lower calorie intakes. Moreover, the Mediterranean diet is highly palatable, which can increase both tolerance and compliance among individuals following it [50].

Regarding physical activity, there was a higher adoption of counselling by patients in the MD group. This observation was independent of factors such as age (older age), gender (female gender), educational level (low educational level) [51] and smoking [52], which could interfere with the participants' ability to become physically active. These factors did not differ between the two groups at baseline. Recently, it was suggested that an increment in physical activity in conjunction with a healthy diet

would lead to optimum weight loss [53]. However, in the present study no difference in weight loss was observed between the two groups.

Strength of the present study was that participants in both groups were 100% compliant with CPAP and therefore the differences in weight loss and dietary adherence between the groups would not be attributed to CPAP. As the patients knew that their compliance is being evaluated and represents one of the end points of the study, this may significantly increased their motivation. Moreover, the physician responsible for the patients encouraged and reminded them during the study often for the health risks of not using CPAP. On the other hand, a limitation of the study was the small size of the sample studied. This could be attributed to the characteristics of the population, the rigorous exclusion criteria and the lack of willingness of 23 patients to participate. The duration of the study was also relatively short, given that it has been shown that weight regain is common after weight loss [54], and weight loss programmes should last at least one year. However, it has been proposed that the Mediterranean dietary pattern can protect against weight gain [55]. All these limitations could adversely affect the external validity of our study and the results should be viewed with great caution. Moreover, the clinical application of our data may be valid only for patients with similar characteristics to those in the population studied.

In conclusion, this randomised weight loss trial showed that the Mediterranean diet combined with physical activity for 6 months period was effective in reducing the AHI during REM sleep without any statistical significant effect in the other sleep parameters, compared to a prudent diet in obese adults with moderate to severe OSAS. However in view of the beneficial role of the Mediterranean diet and physical activity further studies with more patients and potentially longer period will be needed

in order to clarify the role of MD in the therapeutic plan of the above mentioned patients and to address the potential mechanisms.

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Table 1 Patient characteristics at baseline*

	Prudent diet group (N=20)	Mediterranean diet group (N=20)	P value**
Sex, male/female (n)	17/3	17/3	1
Age (years)	45.8±14.2	52.2±10.5	0.09
Educational level	2.9±1.1	2.6±1.2	0.41

Current smoking n (%)	6 (30)	6 (30)	1
MedDietScore	28.1±4.1	28.9±4.2	0.5
MET-min/week	1457.3+1391.9	1390.9+1393.9	0.5
Height (m)	1.68±0.09	1.69±0.06	0.7
Weight (kg)	108.9±19.8	101.5±12.5	0.2
BMI (kg/m ²)	37.7±4.6	35.3±3.8	0.04
WC (cm)	119.3±14.4	115.6±9.3	0.3
WC/height ratio (cm/m)	0.7±0.06	0.67±0.05	0.09
WC/hip ratio (cm/cm)	0.98±0.07	1±0.06	0.4
NC (cm)	44.3±4.1	43.4±3.8	0.5
NC/height ratio (cm/m)	26.2±2.02	25.6±2.2	0.4
%BF Skfs	32.7±5.5	34.1±3.7	0.4
Sleep efficiency (%)	70.3±15.01	66.3±15.9	0.4
NREM (%TST)	87.9±19.8	89.9±12.5	0.7
SWS (%TST)	6.7±4.5	6.7±5.8	1
REM (%TST)	7.7±3.4	5.4±3.7	0.06
AHI (events/h)	58.7±34.9	52.4±32.8	0.6
AHI/REM (events/h)	56.4±36.7	67.9±26.2	0.3
AI (events/h)	52.1±20.3	56.5±20.4	0.5
Desat/h	56.9±33.7	49.4±29.9	0.5
MSaO ₂	92.1±2.9	92.1±2.7	1
LSaO ₂	78.2±8.4	77.4±6.9	0.7

MedDietScore, Mediterranean score; MET, metabolic equivalent of task; BMI, body mass index; WC, waist circumference; NC, neck circumference; BF Skfs, body fat skinfolds; NREM, Non-rapid eye movement; SWS, Slow-wave sleep; REM, rapid eye movement; AHI, apnoea-hypopnoea index; AI, arousal index; Desat/h, desaturations per hour; MSaO₂, mean arterial oxygen saturation; LSaO₂, lowest arterial oxygen saturation

* Data are means (± SD).

** Student *t* test was used.

Table 2 Changes in characteristics after 6-month intervention*

	Prudent diet group (N=20)	Mediterranean diet group (N=20)	P value**
MedDietScore	0.95±4.5	12.7±4.9	< 0.001
MET-min/week	47.3±934.9	369.3±672.4	0.014
Weight (kg)	-7.2±4.2	-8.9±3.9	0.162
BMI (kg/m ²)	-2.5±1.4	-3.2±1.5	0.102
WC (cm)	-5.7±3.8	-8.7±3.6	0.013
WC/height ratio (cm/m)	-0.03±0.02	-0.04±0.02	0.044
WC/hip ratio (cm/cm)	-0.02±0.02	-0.04±0.03	0.045
NC (cm)	-0.26±6.05	-2.9±5.4	0.169

NC/Height ratio (cm/m)	-0.26±3	-1.6±2.6	0.152
%BF Skfs	-2.6±1.7	-4.3±2.5	0.032
Sleep efficiency (%)	71.7±13.8	72.7±12.4	0.8
NREM (%TST)	90.6±4.2	92±5.6	0.4
SWS (%TST)	7.8±4.2	6.8±3.6	0.4
REM (%TST)	9.5±4.8	7.3±5.6	0.2
AHI (events/h)	-14±22.6	-15.6±11.4	0.791
AHI/REM (events/h)	-2.6±23.7	-18.4±17.6	0.025
AI (events/h)	-10.2±19.3	-12.1±24.9	0.787
Desat/h	-13.5±22.6	-13.1±9.8	0.933
MSaO ₂	1±1.5	1.5±1.7	0.379
LSaO ₂	3.1±3.9	4.9±3.8	0.163
CPAP use for the six months (hours/day)	6.1±1.1	6.3±1.3	0.66
CPAP use for the six months (days/week)	6.4±0.7	6.4±0.7	0.75

MedDietScore, Mediterranean score; MET, metabolic equivalent of task; BMI, body mass index; WC, waist circumference; NC, neck circumference; BF Skfs, body fat skinfolds; NREM, Non-rapid eye movement; SWS, Slow-wave sleep; REM, rapid eye movement; AHI, apnoea-hypopnoea index; AI, arousal index; Desat/h, desaturations per hour; MSaO₂, mean arterial oxygen saturation; LSaO₂, lowest arterial oxygen saturation

* Data are means (± SD).

** Student *t* test was used.

Figure 1 Study flowchart.

A total of 40 patients were enrolled; 20 were randomly assigned to the Mediterranean diet, and 20 were randomly assigned to a prudent diet.

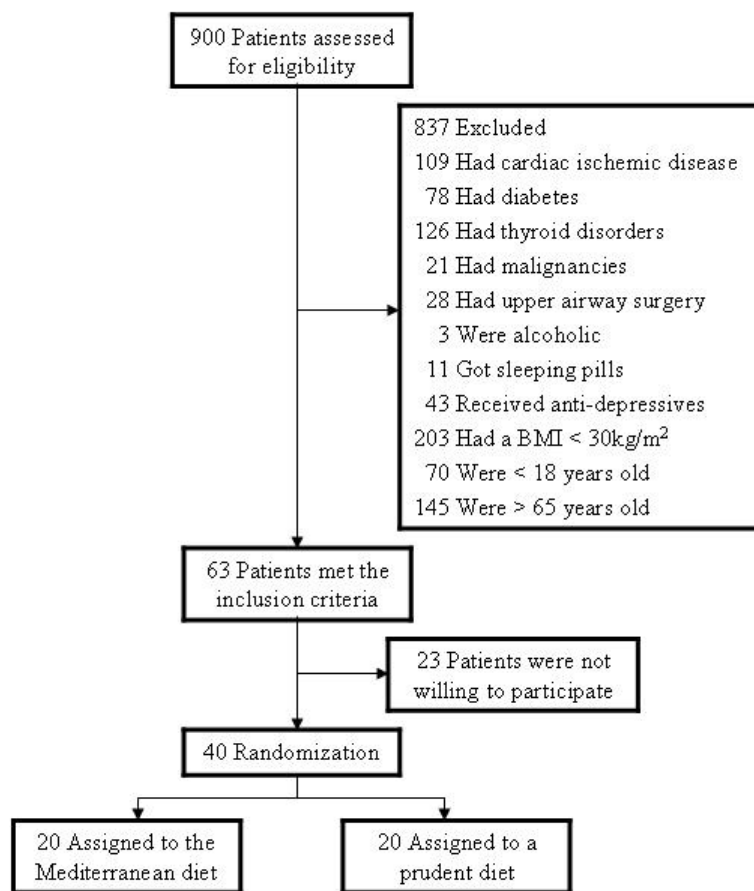


Figure 2 Individual values of apnoea-hypopnoea index per hour (AHI) during rapid eye movement (REM) sleep, before (closed circles) and after (open circles) 6 months, in the prudent diet versus the Mediterranean diet group. Rectangles with solid lines represent mean values.

