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Original article

Impact of an interdisciplinary weight loss and lifestyle intervention on testosterone and scores for sexual activity on the FOSQ in men with obesity and obstructive sleep apnea: secondary analyses of data from the INTERAPNEA randomized trial☆

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ABSTRACT

Background: Low circulating testosterone and reduced sexual activity are common in men with obstructive sleep apnea.
Objectives: To evaluate the effect of an interdisciplinary weight loss and lifestyle intervention on circulating testosterone concentrations and, secondarily, on scores on the intimate relationships and sexual activity subdomain of the Functional Outcomes of Sleep Questionnaire (FOSQ).
Methods: Eighty-nine men were assigned to either usual care ($n = 49$) or an 8-week interdisciplinary intervention ($n = 40$). Assessments were conducted at baseline, at the end of the intervention (8 weeks), and 6 months post-intervention. Plasma testosterone was measured by chemiluminescence immunoassay. Sexual activity was assessed using the intimate relationships and sexual activity subdomain of the FOSQ. Sleep parameters and body weight and composition were also evaluated.
Results: Compared with the control group, higher plasma testosterone concentrations were observed in the intervention group at 8 weeks (between-group difference 77.6 [95% CI 4.2 to 150.1] ng/dL; $p = 0.042$) and at 6 months (between-group difference 90.4 [95% CI 11.7 to 169.0] ng/dL; $p = 0.027$). Scores on the FOSQ intimate relationships and sexual activity subdomain increased in the intervention group both at 8 weeks (between-group difference 1.0 [95% CI 0.5 to 1.5]; $p = 0.004$) and 6 months (between-group difference 0.8 [95% CI 0.2 to 1.3]; $p = 0.003$) compared with controls. Changes in testosterone and FOSQ-derived sexual activity scores correlated

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; CONSORT, Consolidated Standards of Reporting Trials; CPAP, continuous positive airway pressure; FOSQ, Functional Outcomes of Sleep Questionnaire; GnRH, gonadotropin-releasing hormone; OSA, obstructive sleep apnea; TMHBC, Transtheoretical Model of Health Behavior Change.

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with favorable changes in sleep quality, body weight and body composition, particularly from baseline to 6 months and from 8 weeks to 6 months (all $p < 0.05$).
Conclusions: In men with overweight or obesity and moderate to severe obstructive sleep apnea, an interdisciplinary weight loss and lifestyle intervention increased circulating testosterone concentrations compared with usual care. Improvements were also observed in scores on the intimate relationships and sexual activity subdomain of the FOSQ; however, these findings should be considered exploratory because this subdomain does not assess erectile function, libido, hypogonadal symptoms, or validated multidimensional domains of male sexual function. Further studies using comprehensive endocrine profiling and validated male sexual function instruments are warranted.
Clinical trial registration: ClinicalTrials.gov NCT03851653.

1. Introduction

Obstructive sleep apnea (OSA) is characterized by repetitive upper airway obstruction during sleep, resulting in recurrent sleep fragmentation and oxygen desaturation [1]. Because sleep duration and quality are essential for maintaining systemic homeostasis, OSA has been increasingly recognized as a key contributor to metabolic, cardiovascular and endocrine dysfunction [2]. In men, OSA is not only a major complication of obesity but also a risk factor for disturbances in the hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary–gonadal (HPG) axes, leading to reduced circulating testosterone concentrations, which correlate with higher apnea–hypopnea index (AHI) values [3].

Testosterone plays a fundamental role in regulating sleep architecture and circadian rhythmicity. Variations in its secretion are more tightly coupled to sleep patterns than to the circadian rhythm itself [4]. Accordingly, men with OSA commonly exhibit lower circulating testosterone levels, largely attributable to obesity and aging, and to a lesser extent, to sleep fragmentation and nocturnal hypoxia [5]. Similar associations have been reported in men without OSA, where nocturnal hypoxemia and excess body weight are linked to reduced testosterone levels [6]. Continuous positive airway pressure (CPAP) therapy has been proposed to ameliorate hypogonadism in patients with OSA. However, recent evidence reports inconsistent results, suggesting that complementary or alternative strategies should be considered [7]. For its part, the presence of obesity impairs HPG function through the alteration of multiple mechanisms (i.e. aromatase-mediated conversion of testosterone to estradiol, hyperleptinemia, secretion of endocrine factors which acts as disruptors of HPG axis, oxidative stress, etc.), creating and sustaining a self-perpetuating cycle [8].

Low testosterone adversely affects male sexual health and overall quality of life. The coexistence of OSA, obesity, hypogonadism, and sexual dysfunction therefore represents a major clinical concern [9]. Although testosterone replacement therapy can improve hypogonadism and sexual dysfunction, it may exacerbate OSA symptoms in some cases [10]. Conversely, growing evidence supports the role of lifestyle interventions, particularly weight-loss and exercise, as effective non-pharmacological strategies to improve testosterone status and sexual function [11]. Ultimately, it must be pointed out the need for personalized approaches supported by behavioral modifications and multidisciplinary care to address obesity-related issues, including male infertility [12].

The interdisciplinary INTERAPNEA trial, which implemented an 8-week weight loss and lifestyle intervention in men with overweight obesity and moderate-to-severe OSA, has previously demonstrated sustained improvements in the AHI, body composition, and cardiovascular disease risk factors [13]. Building upon that evidence, we hypothesized that the clinical benefits observed in the parent INTERAPNEA trial could be accompanied by changes in circulating testosterone concentrations. As a secondary patient-reported outcome, we also explored changes in the intimate relationships and sexual activity subdomain of the Functional Outcomes of Sleep Questionnaire (FOSQ). Therefore, the present secondary analyses aimed to determine the effect of the INTERAPNEA interdisciplinary weight loss and lifestyle intervention on circulating testosterone concentrations and to explore changes in FOSQ-derived sexual activity scores in men with overweight or obesity and CPAP-treated moderate-to-severe OSA. We also examined whether changes in these outcomes were associated with changes in OSA-related sleep variables, body weight, and body composition.

2. Materials & methods

2.1. Study design

This study was ancillary to the parent INTERAPNEA trial, which involved an 8-week interdisciplinary weight loss and lifestyle intervention combined with usual care (CPAP therapy) among men with overweight or obesity diagnosed with moderate-to-severe OSA. The INTERAPNEA trial was designed to investigate the impact of lifestyle modifications –based on the Transtheoretical Model of Health Behavior Change (TMHBC)– on OSA severity (assessed by the AHI) and other comorbidities. Detailed information regarding rationale, protocol and methodology have been published elsewhere [13,14].

All procedures adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines, complied with the ethical standards of the Helsinki Declaration and received approval from the regulatory authorities and the Clinical Research Ethics Committees of the University of Granada (Granada, Spain), Virgen de las Nieves University Hospital (Granada, Spain), and the Regional Government of Andalusia (Spain) (0770-N-19). The clinical trial was registered with the National Institutes of Health database (ClinicalTrials.gov NCT03851653).

2.2. Study participants and intervention protocol

A total of 89 men aged 18 to 65 years with body mass index (BMI) $\geq$ 25 and moderate-to-severe OSA (AHI $\geq$ 15 events/h of sleep, all receiving CPAP therapy) were enrolled to participate in the INTERAPNEA trial. Patients' recruitment was carried out in collaboration with the sleep-disordered breathing unit of Virgen de las Nieves University Hospital (Granada, Spain).

Briefly, participants were randomly assigned to either the control group ($n = 49$) or the intervention group ($n = 40$) and were analyzed according to the intention-to-treat principle. Fourteen participants from the control group were lost to follow-up ($n = 35$), resulting in a total of 75 participants analyzed at the 8-week intervention endpoint (Fig. S1).

The study protocol consisted on an 8-week group-based intervention led and supervised by experts, focusing on five modules: smoking cessation, avoidance of alcohol, nutritional behavior modification, moderate aerobic exercise, and sleep hygiene. Physical exercise program included supervised weekly 60–90 min sessions of aerobic exercise at moderate intensity (i.e. 55–65% of the heart rate reserve), and an individualized goal-setting of daily walking for 60 min at moderate intensity assessed by a heart rate monitor. Participants in both groups continued receiving standard care with CPAP therapy. More detailed information regarding participants, eligibility criteria and the intervention protocol has been published previously [13,14].

2.3. Outcomes

All study variables were evaluated at baseline, at the end of the intervention (8 weeks), and 6 months post-intervention. Adverse events were meticulously documented at each assessment, regardless of their severity or relationship to the intervention or study participation.

2.3.1. Plasma testosterone

Blood samples were drawn after overnight fasting (i.e.12-h) and centrifugated to obtain plasma aliquots, which were stored at −80 °C until analysis. Total testosterone concentrations (ng/dL) were assessed using a Beckman Coulter DxI 800 immunoassay system employing chemiluminescent technology (Beckman Coulter). All samples were analyzed within the same analytical run to eliminate inter-assay variability (intra-assay coefficient of variance <10%).

2.3.2. Sleep variables

Sleep outcomes were assessed by a full-night, in-laboratory polysomnography. Participants were instructed to abstain from CPAP use during the previous week. The frequency of apnea and hypopnea events per hour of sleep were determined by AHI, categorized as follows: normal (<5 events/h), mild (5–14 events/h), moderate (15–30 events/h), and severe (>30 events/h). The oxygen desaturation index – defined as the number of oxygen desaturation events >3% per hour of sleep – was also examined, and sleep efficiency (%) was calculated as the ratio of total sleep time to total time spent in bed.

2.3.3. Anthropometric and body composition parameters

Body weight (kg) and height (m) were measured using a calibrated scale and stadiometer (model 799, Electronic Column Scale, Hamburg, Germany). Body composition parameters, including fat mass (kg) and visceral adipose tissue (g), were evaluated using a whole-body dual-energy-X-ray absorptiometry scanner (Discovery Wi, Hologic, Inc., Bedford, MA, USA).

2.3.4. Sexual activity assessment

Sexual activity was established using the score of the intimate relationships and sexual activity subdomain (items 27–30) of the Functional Outcomes of Sleep Questionnaire (FOSQ). Each item is scored from 1 to 4, with lower values indicating greater difficulty. A score of 0 in any item is considered “not applicable” or missing and is excluded from the calculation. The score of this subscale is computed as the mean of the answered items, also ranging from 1 to 4.

2.4. Statistical analysis

The present work is a sub-study of the INTERAPNEA trial, which was originally powered to detect changes in AHI. The primary analyses included linear mixed-effects models to determine the effects of the intervention on circulating testosterone concentrations and FOSQ-derived sexual activity, with group, time of assessment, and their interaction terms as the fixed effect. Age, marital status, and occupational status were also incorporated as fixed effects. The restricted maximum-likelihood method and an unstructured covariance matrix were used account for within-participant clustering arising from the repeated-measures design. Given the secondary nature of these analyses and the non-specific assessment of sexual activity, the analyses of FOSQ-derived sexual activity scores were interpreted as exploratory and hypothesis-generating.

Missing data were assumed to be missing-at-random; all reported values are model-based estimates. Additionally, a logistic model predicting attrition based on baseline characteristics (participants set, allocation group, OSA severity, age, and BMI) was used to calculate attrition propensity. As expected, only participants set significantly predicted attrition, due to the occurrence of the COVID-19 pandemic at the trial endpoint (third participant set at the 8-week intervention). Therefore, the assumptions of data missing at random was confirmed, consistent with recent recommendations for handling missing data in randomized trials affected by a pandemic. An intention-to-treat approach, including all participants as originally allocated after randomization, was used for all analyses.

The relationship between changes in circulating testosterone levels and FOSQ-derived sexual activity scores over time with changes in sleep, body weight, and body composition variables within the intervention group were examined using repeated-measures correlation analysis. Ninety-five percent of confidence intervals were obtained from the 2.5th and 97.5th percentiles. All analyses were performed using the R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Study participants

The baseline characteristics of the study participants are summarized in Table S1. Both study groups were balanced with respect to baseline characteristics, with no significant differences observed in any of the outcomes at baseline between the control and intervention groups (all $p \geq 0.05$).

3.2. Effect of the intervention on testosterone and sexual activity

Higher plasma testosterone concentrations were observed in the intervention group compared with the control group at intervention endpoint (between-group difference, 77.6 [95% CI, 4.2 to 150.1] ng/dL; $p = 0.042$) and 6 months post-intervention (between-group difference, 90.4 [95% CI, 11.7 to 169.0] ng/dL; $p = 0.027$) (Table 1 and Fig. 1). Similarly, higher FOSQ-derived sexual activity scores were observed in the intervention group compared with the control group at the intervention endpoint (between-group difference, 1.0 [95% CI, 0.5 to 1.5]; $p = 0.004$) and 6 months post-intervention (between-group difference, 0.8 [95% CI, 0.2 to 1.3]; $p = 0.003$) (Table 1). No significant differences were observed when age was included as a fixed effect in the linear mixed models (data not shown).

3.3. Association of changes in plasma testosterone concentrations over time with changes in sleep variables, body weight and composition outcomes within the intervention group

From baseline to 6 months, and from the end of the intervention (8 weeks) to 6 months post-intervention, higher plasma testosterone concentrations were significantly associated with increased sleep efficiency and reduced AHI, oxygen desaturation index, body weight, fat mass, and visceral adipose tissue within the intervention group (all $p \leq 0.029$; Table 2 and Fig. S2A–F). These associations persisted when evaluating changes from baseline to the end of the intervention (8 weeks) for AHI, body weight, and composition variables (all $p \leq 0.028$; Table 2 and Fig. S2A–F). No significant differences were observed when age was included as a fixed effect in the linear mixed models (data not shown).

3.4. Association of changes in FOSQ-derived sexual activity scores over time with changes in sleep variables, body weight and composition outcomes within the intervention group

From baseline to 6 months, and from the end of the intervention (8 weeks) to 6 months post-intervention, higher sexual activity scores derived from FOSQ scale were significantly associated with reduced AHI, oxygen desaturation index, body weight, fat mass, and visceral adipose tissue within the intervention group (all $p \leq 0.017$; Table 3 and Fig. S3A–F).

These associations remained when evaluating changes from baseline to the end of the intervention (8 weeks) for AHI and body weight (all $p \leq$

Table 1
Changes in testosterone concentrations and sexual activity over time.

	Control (n = 49)			Intervention (n = 40)			Difference between groups, mean (95% CI)[a]	*P* value
	Mean (95% CI)	Change from baseline, mean (95% CI)	P value	Mean (95% CI)	Change from baseline, mean (95% CI)	P value		
Testosterone (ng/mL)								
At baseline	397.1 (340.6 to 453.5)	–		405.5 (345.0 to 465.9)	–		–	
At 8 weeks	402.5 (341.9 to 463.1)	5.4 (−59.8 to 70.7)	0.979	488.4 (428.4 to 548.5)	83.0 (21.7 to 144.2)[c]	0.004	77.6 (4.2 to 150.1)[b]	0.042
At 6 months	408.9 (344.2 to 473.6)	11.9 (−58.1 to 81.9)	0.915	507.8 (444.7 to 570.8)	102.3 (36.6 to 168.0)[d]	<0.001	90.4 (11.7 to 169.0)[b]	0.027
From 8 weeks to 6 months	–	6.5 (−64.6 to 77.5)	0.975	–	19.3 (−45.8 to 84.4)	0.761	12.9 (−65.1 to 90.8)	0.753
Sexual activity (n)								
At baseline	3.1 (2.8 to 3.4)	–		3.3 (3.0 to 3.6)	–		–	
At 8 weeks	2.7 (2.4 to 3.1)	−0.4 (−0.9 to 0.1)	0.079	3.9 (3.6 to 4.3)	0.6 (0.2 to 1.1)[c]	0.004	1.0 (0.5 to 1.5)[c]	<0.001
At 6 months	3.0 (2.7 to 3.4)	−0.1 (−0.6 to 0.4)	0.919	4.0 (3.6 to 4.4)	0.7 (0.2 to 1.2)[c]	0.003	0.8 (0.2 to 1.3)[d]	0.010
From 8 weeks to 6 months	–	0.3 (−0.2 to 0.9)	0.286	–	0.1 (−0.4 to 0.5)	0.962	−0.28 (−1.35 to 0.79)	0.607

Abbreviations: CI, confidence interval.
[a] Using the group × visit interaction term from a linear mixed-effects model including study group, time (baseline, 8 weeks and 6 months), and study group × time, age, marital status, and occupational status as fixed effects and participant as random effects.
[b] $p < 0.05$ from the time × study group interactions.
[c] $p < 0.01$ from the time × study group interactions.
[d] $p < 0.001$ from the time × study group interactions.

0.005; Table 3 and Fig. S3A–F).

3.5. Relationship between plasma testosterone levels and FOSQ-derived sexual activity scores within the intervention group

Changes in testosterone concentration within the intervention group (from baseline to the end of the intervention (8 weeks, and from the 8-week to 6 months post-intervention)) were positively associated with changes in FOSQ-derived sexual activity scores (all $r \geq 0.25$; all $p < 0.035$). No significant association was observed from baseline to 6 months post-intervention ($r = 0.25$; $p = 0.158$) (Tables 2, 3, and Fig. S4).

4. Discussion

The present secondary analyses of the INTERAPNEA randomized clinical trial demonstrate the beneficial effects of an 8-week interdisciplinary weight loss and lifestyle intervention on plasma testosterone concentrations among men with overweight or obesity and CPAP-treated moderate-to-severe OSA, with these improvements being sustained 6 months post-intervention. In addition, changes in plasma testosterone levels were significantly associated with improvements in sleep parameters, body weight, and body composition variables over time. Improvements were also observed in the FOSQ intimate relationships and sexual activity subdomain. However, these questionnaire-derived findings should be interpreted cautiously because this subdomain does not constitute a validated multidimensional assessment of male sexual function. Overall, these results support the potential endocrine relevance of lifestyle-based weight loss in this population offering a non-pharmacological alternative that warrants further exploration in both clinical practice and research, while generating exploratory evidence regarding sexual activity.

The main risk factors for OSA include male sex, older age, and obesity, which explains its higher prevalence among men with obesity. Moreover, OSA frequently coexists with multiple clinical and metabolic comorbidities [15]. A consistent finding in men with OSA, even in cases of mild severity, is a reduction in circulating testosterone concentrations, which may lead to hypogonadism and its associated consequences [16]. The diagnosis of male hypogonadism relies on both clinical manifestation and biochemical confirmation, with normal circulating testosterone concentrations generally ranging between 350 and 750 ng/dL, although slight variations exist across studies [17]. Accordingly, we observed mean baseline testosterone concentrations within the normal range, albeit slightly low (≈400 ng/dL), in both study arms. These levels remained relatively stable in the control group over time, whereas a significant increase (≈100 ng/dL) was observed in the intervention group during follow-up. These findings highlight the potential of this lifestyle-based intervention to prevent or ameliorate secondary hypogonadism in men with overweight or obesity and OSA.

Interestingly, the increase in plasma testosterone concentrations was associated with a better sleep and body composition profile. It is well known that men with obesity, who typically exhibit low-normal testosterone concentrations –associated with reduced lean mass and increased fat mass and central adiposity– experience increases in circulating testosterone concentrations proportional to the magnitude of weight loss. This reflects the bidirectional relationship between obesity and testosterone [18]. Furthermore, associations among testosterone, sleep, and body composition variables have been previously described. In this context, circulating testosterone concentrations have been negatively correlated with OSA severity (AHI) and BMI [19]. Additionally, an inverted U-shaped relationship has been reported between testosterone and sleep duration, and between sleep duration and muscle mass [20].

Regarding the FOSQ intimate relationships and sexual activity subdomain, men in the intervention showed higher FOSQ-derived sexual activity scores, whereas those in the control group showed no significant changes over time. These increases in FOSQ-derived sexual activity scores were also associated with a better body composition profile and improved sleep patterns. Moreover, a positive correlation was observed between circulating testosterone concentrations and FOSQ-derived sexual activity scores. Interestingly, previous studies have observed similar trends regarding testosterone levels and domains of male sexual function. For instance, pharmacological interventions using testosterone replacement therapy in older men with low testosterone concentrations, resulted in increased testosterone levels and subsequent improvements in sexual activity, desire, and function, these variables assessed by Derogatis Interview for Sexual Functioning in Men–II [21]. Likewise, increases in circulating testosterone concentrations after weight loss, either through bariatric surgery or dietary interventions, have been

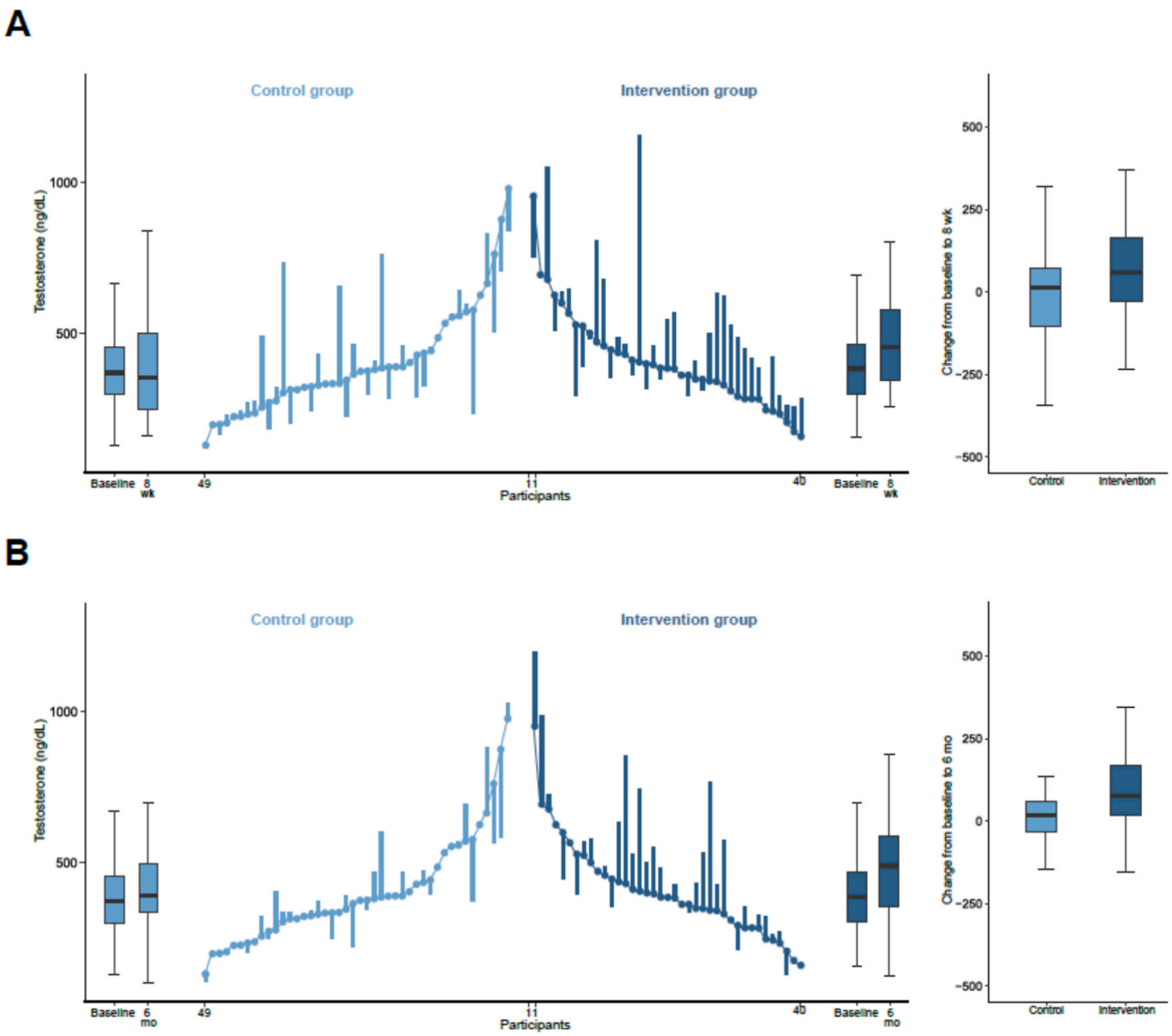

Fig. 1. Effect of intervention on plasma testosterone concentrations over time.
Boxplots display the median (black line) and the first and third quartiles (box edges). Whiskers extend to the most extreme data points within 1.5 interquartile ranges from the first and third quartiles. Vertical lines in the parallel plots represent individual changes in plasma testosterone concentrations from baseline to the end of the intervention (8 weeks) (A) and to 6 months post-intervention (B).

shown to positively impact sexual activity, dimension evaluated by Sexual Desire Inventory, in men with obesity [22]. Nevertheless, evidence supporting beneficial effects of weight loss and lifestyle-based interventions on objectively measured sexual activity remains limited. Our findings should be interpreted within the limits of the instrument used, being these results exploratory and hypothesis-generating. The FOSQ subdomain captures perceived difficulty in intimate relationships and sexual activity in the context of sleep-related functional outcomes. Male sexual function is a multidimensional construct that is commonly assessed using a variety of validated patient-reported outcome measures. Available instruments differ in their scope and may evaluate domains such as erectile function, sexual desire, orgasmic function, ejaculatory function, intercourse satisfaction, and overall sexual satisfaction [23]. Therefore, the present findings should not be interpreted as evidence that the intervention improved male sexual function broadly defined. Rather, they suggest a favorable change in a sleep-related patient-reported sexual activity domain, which should be confirmed in future studies using validated male sexual function instruments.

The associations among OSA, obesity and low testosterone levels in men are complex and remain inconclusive. Several mechanisms have been proposed to explain this intricate relationship: I) the excessive adiposity may have a major impact on the respiratory process by different means including anatomical deposition around the upper airway, the reduction of pharyngeal patency or decreasing end-expiratory lung volume [24]; II) poor tissue oxygenation may result in different metabolic disturbances (e.g. the constitutive activation of hypoxia-inducible factors, which regulate lipid metabolism, may promote diminished lipogenic gene expression, impaired fatty acid β-oxidation, and augmented lipid storage capacity) [25]; III) the disturbances in the HPG axis through hypoxia –with the impairment of Leydig cell function due to a decline in gonadotropin-releasing hormone (GnRH) and luteinizing hormone– would affect testosterone production [26]; IV) obesity causes hypogonadotropic hypogonadism through different mechanisms namely related with endocrine disturbances, such

Table 2
Repeated-measures correlation analyses examining the associations between changes in plasma testosterone concentrations and changes in sleep, body weight, body composition and sexual activity derived from FOSQ scale outcomes over time within the intervention group.

Outcomes	Testosterone, ng/dL		
	r	95% CI	P value
Age, years	0.174	−0.18 to 0.49	0.331
Changes from baseline to 8 weeks			
Apnea-hypopnea index, events/h	−0.38	−0.62 to −0.07	0.017
Oxygen desaturation index ≥ 3%, events/h	−0.30	−0.56 to 0.01	0.059
Sleep efficiency, %	0.27	−0.05 to 0.54	0.092
Body weight, kg	−0.45	−0.67 to −0.16	0.004
Fat mass, kg	−0.35	−0.60 to −0.05	0.026
Visceral adipose tissue, g	−0.35	−0.60 to −0.04	0.028
Sexual activity, points	0.35	0.05 to 0.60	0.026
Changes from baseline to 6 months after intervention			
Apnea-hypopnea index, events/h	−0.43	−0.67 to −0.10	0.013
Oxygen desaturation index ≥3%, events/h	−0.40	−0.65 to −0.06	0.022
Sleep efficiency, %	0.41	0.08 to 0.66	0.017
Body weight, kg	−0.53	−0.74 to −0.23	0.001
Fat mass, kg	−0.53	−0.74 to −0.23	0.002
Visceral adipose tissue, g	−0.64	−0.80 to −0.38	<0.001
Sexual activity, points	0.25	−0.10 to 0.54	0.158
Changes from 8 weeks to 6 months after intervention			
Apnea-hypopnea index, events/h	−0.33	−0.52 to −0.11	0.005
Oxygen desaturation index ≥3%, events/h	−0.26	−0.46 to −0.03	0.029
Sleep efficiency, %	0.30	0.07 to 0.49	0.010
Body weight, kg	−0.36	−0.54 to −0.14	0.002
Fat mass, kg	−0.38	−0.56 to −0.17	<0.001
Visceral adipose tissue, g	−0.42	−0.59 to −0.21	<0.001
Sexual activity, points	0.25	0.02 to 0.45	0.035

Abbreviations: CI, confidence interval; FOSQ, Functional Outcomes of Sleep Questionnaire.

Table 3
Repeated-measures correlation analyses examining the associations between changes in sexual activity derived from FOSQ scale and changes in sleep, body weight, body composition and plasma testosterone concentrations over time within the intervention group.

Outcomes	Sexual activity, points		
	r	95% CI	P value
Age, years	−0.22	−0.51 to 0.13	0.213
Changes from baseline to 8 weeks			
Apnea-hypopnea index, events/h	−0.49	−0.69 to −0.21	0.001
Oxygen desaturation index ≥3%, events/h	−0.43	−0.65 to 0.14	0.005
Sleep efficiency, %	0.15	−0.16 to 0.44	0.337
Body weight, kg	−0.43	−0.65 to −0.14	0.004
Fat mass, kg	−0.30	−0.55 to 0.01	0.060
Visceral adipose tissue, g	−0.15	−0.44 to 0.16	0.329
Testosterone, ng/dL	0.35	0.05 to 0.60	0.026
Changes from baseline to 6 months after intervention			
Apnea-hypopnea index, events/h	−0.48	−0.70 to −0.17	0.003
Oxygen desaturation index ≥3%, events/h	−0.43	−0.66 to −0.11	0.009
Sleep efficiency, %	0.22	−0.12 to 0.52	0.204
Body weight, kg	−0.40	−0.65 to −0.08	0.016
Fat mass, kg	−0.46	−0.69 to −0.14	0.006
Visceral adipose tissue, g	−0.50	−0.71 to −0.19	0.002
Testosterone, ng/dL	0.25	−0.10 to 0.54	0.158
Changes from 8 weeks to 6 months after intervention			
Apnea-hypopnea index, events/h	−0.47	−0.63 to −0.27	<0.001
Oxygen desaturation index ≥3%, events/h	−0.41	−0.58 to −0.19	<0.001
Sleep efficiency, %	0.18	−0.05 to 0.39	0.121
Body weight, kg	−0.40	−0.57 to −0.19	<0.001
Fat mass, kg	−0.35	−0.53 to −0.13	0.002
Visceral adipose tissue, g	−0.27	−0.47 to −0.05	0.017
Testosterone, ng/dL	0.25	0.02 to 0.45	0.035

Abbreviations: CI, confidence interval; FOSQ, Functional Outcomes of Sleep Questionnaire.

as the resistance to leptin, which may affect the stimulation of kisspeptin neurons and GnRH secretion, or the increased aromatase activity, promoting testosterone conversion into estradiol [27].

In this context, our findings may have clinical relevance primarily from an endocrine perspective, rather than as evidence of improved male sexual function. The observed increase in circulating testosterone concentrations suggests that structured lifestyle-based weight loss may contribute to improving testosterone status in men with OSA and overweight or obesity. This is particularly relevant because obesity is a potentially reversible contributor to low testosterone concentrations, and routine testosterone replacement therapy is not generally recommended when functional hypogonadism may be addressed through weight loss and management of underlying comorbidities [28]. However, the findings related to FOSQ-derived sexual activity scores should be interpreted more conservatively. They do not establish an effect on male sexual function, but they indicate an area for further investigation using validated instruments and more comprehensive hormonal assessment. A major strength of this study is its pioneering evidence showing that a structured weight loss and lifestyle intervention can improve circulating testosterone in men with OSA, showing a possible beneficial effect in sexual activity that must be further investigated. The comprehensive and interdisciplinary design supports its feasibility for translation into real-world clinical practice. Another strength is the use of full-night, in-laboratory polysomnography at all time points, baseline, at the end of the intervention (8 weeks), and 6 months post-intervention, providing a gold-standard assessment of sleep and OSA severity. However, several limitations should be acknowledged. The sample included only men with overweight/obesity and moderate-to-severe OSA, limiting generalizability to women, individuals without obesity, or those with mild OSA. Furthermore, the exclusively Spanish cohort restricts the applicability of results to other populations. Moreover, the FOSQ intimate relationships and sexual activity subdomain is not a validated multidimensional instrument for assessing male sexual function. It does not specifically evaluate erectile function, libido, hypogonadal

symptoms, sexual desire, orgasmic function, or sexual satisfaction. Consequently, the FOSQ-derived findings should not be interpreted as definitive evidence of improved male sexual function. Moreover, other hormones and parameters such as SHBG, LH, and FSH were not measured, which may limit the interpretation of the endocrine profile and underlying mechanisms. Finally, as a secondary analysis of a clinical trial, the study is subject to inherent limitations, including lack of dedicated sample size estimation, potential residual confounding, and constraints in variable selection and measurement tools. Future studies involving more diverse samples, longer follow-ups, and comprehensive outcome assessments are warranted to confirm the broader efficacy of lifestyle-based interventions in managing OSA-related complications.

5. Conclusion

This secondary analysis of the INTERAPNEA randomized trial suggests that an interdisciplinary weight loss and lifestyle intervention improves circulating testosterone concentrations in men with overweight or obesity and moderate-to-severe OSA. These changes were associated with improvements in sleep parameters, body weight, and body composition over time. Improvements were also observed in FOSQ-derived sexual activity scores; however, these findings should be considered exploratory because the instrument used does not assess validated multidimensional domains of male sexual function. These results support the potential role of lifestyle modification in improving testosterone status in this population and highlight the need for dedicated studies combining comprehensive hormonal assessment with validated measures of male sexual function.

CRediT authorship contribution statement

Lourdes Herrera-Quintana contributed to conceptualization, formal analysis, and writing the original draft.

Héctor Vázquez-Lorente contributed to conceptualization, formal analysis, and writing the original draft.

Jonatan R Ruiz contributed to conceptualization, formal analysis, methodology, and review and editing of the draft article.

Francisco J. Amaro-Gahete contributed to conceptualization, formal analysis, methodology, and review and editing of the draft article.

Almudena Carneiro-Barrera contributed to conceptualization, formal analysis, methodology, and review and editing of the draft article.

All authors saw and approved the final version and no other person made a substantial contribution to the paper.

Ethical approval

Approval for all human subject/patient-related procedures was obtained from the regulatory authorities and the Clinical Research Ethics Committees of the University of Granada (Granada, Spain), Virgen de las Nieves University Hospital (Granada, Spain), and Junta de Andalucía (Spain) (0770-N-19) in accordance with the last revised ethical guidelines of the Declaration of Helsinki. All participants gave their oral and written informed consent to be included before their enrollment, including consent regarding publishing their data.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors used no generative AI or AI-assisted technologies in the writing process.

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Declaration of competing interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.maturitas.2026.109045.

Data availability

There are no linked research data sets for this paper. This data has not been previously presented anywhere and will be shared upon reasonable request to the corresponding authors. Lourdes Herrera-Quintana & Almudena Carneiro-Barrera (email: lourdesherrera@ugr.es; acarneiro@uloyola.es).

References

[1] N.M. Punjabi, The epidemiology of adult obstructive sleep apnea, Proc. Am. Thorac. Soc. 5 (2008) 136–143, https://doi.org/10.1513/pats.200709-155MG.
[2] T.A. Alvarenga, G.L. Fernandes, L.R. Bittencourt, S. Tufik, M.L. Andersen, The effects of sleep deprivation and obstructive sleep apnea syndrome on male reproductive function: a multi-arm randomised trial, J. Sleep Res. 32 (2023) e13664, https://doi.org/10.1111/jsr.13664.
[3] H. Mohammadi, M. Rezaei, A. Sharafkhaneh, H. Khazaie, M.R. Ghadami, Serum testosterone/cortisol ratio in people with obstructive sleep apnea, J. Clin. Lab. Anal. 34 (2019) e23011, https://doi.org/10.1002/jcla.23011.
[4] G. Wittert, The relationship between sleep disorders and testosterone, Curr. Opin. Endocrinol. Diabetes Obes. 21 (2014) 239, https://doi.org/10.1097/MED.0000000000000069.
[5] R. Luboshitzky, L. Lavie, Z. Shen-Orr, P. Herer, Altered luteinizing hormone and testosterone secretion in middle-aged obese men with obstructive sleep apnea, Obes. Res. 13 (2005) 780–786, https://doi.org/10.1038/oby.2005.88.
[6] A. Viana, A. Daflon, A. Couto, D. Neves, M. de Araujo-Melo, R. Capasso, Nocturnal hypoxemia is associated with low testosterone levels in overweight males and older men with normal weight, J. Clin. Sleep Med. 13 (12) (2017) 1395–1401, https://doi.org/10.5664/jcsm.6832.
[7] A. Cignarelli, M. Castellana, G. Castellana, S. Perrini, F. Brescia, A. Natalicchio, G. Garruti, L. Laviola, O. Resta, F. Giorgino, Effects of CPAP on testosterone levels in patients with obstructive sleep apnea: a meta-analysis study, Front. Endocrinol. 10 (2019) 551, https://doi.org/10.3389/fendo.2019.00551.
[8] V.A. Genchi, E. Rossi, C. Lauriola, R. D'Oria, G. Palma, A. Borrelli, C. Caccioppoli, F. Giorgino, A. Cignarelli, Adipose tissue dysfunction and obesity-related male hypogonadism, Int. J. Mol. Sci. 23 (2022) 8194, https://doi.org/10.3390/ijms23158194.
[9] K.L. Melehan, C.M. Hoyos, B.J. Yee, K.K. Wong, P.R. Buchanan, R.R. Grunstein, P. Y. Liu, Increased sexual desire with exogenous testosterone administration in men with obstructive sleep apnea: a randomized placebo-controlled study, Andrology 4 (2016) 55–61, https://doi.org/10.1111/andr.12132.
[10] S. Kim, K. Cho, Obstructive sleep apnea and testosterone deficiency, World J. Mens Health 37 (2019) 12–18, https://doi.org/10.5534/wjmh.180017.

[11] G. Corona, G. Rastrelli, C. Sparano, L. Vignozzi, A. Sforza, M. Maggi, Advances in the treatment of functional male hypogonadism, Expert. Rev. Endocrinol. Metab. 19 (2024) 163–177, https://doi.org/10.1080/17446651.2023.2296022.
[12] T.A. Pereira, N. Thaker, A.C. Rubez, V.F.N. Lima, H.L. Bernie, S.C. Esteves, Managing obesity-related male infertility: insights from weight loss intervention, Hum. Reprod. 40 (2025) 2027–2037, https://doi.org/10.1093/humrep/deaf180.
[13] A. Carneiro-Barrera, F.J. Amaro-Gahete, A. Guillén-Riquelme, L. Jurado-Fasoli, G. Sáez-Roca, C. Martín-Carrasco, G. Buela-Casal, J.R. Ruiz, Effect of an interdisciplinary weight loss and lifestyle intervention on obstructive sleep apnea severity: the INTERAPNEA randomized clinical trial, JAMA Netw. Open 5 (2022) e228212, https://doi.org/10.1001/jamanetworkopen.2022.8212.
[14] A. Carneiro-Barrera, F.J. Amaro-Gahete, G. Sáez-Roca, C. Martín-Carrasco, A. L. Palmeira, J.R. Ruiz, Interdisciplinary weight loss and lifestyle intervention for daily functioning and psychiatric symptoms in obstructive sleep apnea: the INTERAPNEA randomized clinical trial, J. Clin. Psychiatry 84 (2023) 22m14502, https://doi.org/10.4088/JCP.22m14502.
[15] A. Graziani, G. Grande, A. Ferlin, The complex relation between obstructive sleep apnoea syndrome, hypogonadism and testosterone replacement therapy, Front. Reprod. Health 5 (2023) 1219239, https://doi.org/10.3389/frph.2023.1219239.
[16] L. Su, Y.-H. Meng, S.-Z. Zhang, Y. Cao, J. Zhu, H. Qu, Y.-Z. Jiao, Association between obstructive sleep apnea and male serum testosterone: a systematic review and meta-analysis, Andrology 10 (2022) 223–231, https://doi.org/10.1111/andr.13111.
[17] A.M. Lincoff, S. Bhasin, P. Flevaris, L.M. Mitchell, S. Basaria, W.E. Boden, G. R. Cunningham, C.B. Granger, M. Khera, I.M. Thompson, Q. Wang, K. Wolski, D. Davey, V. Kalahasti, N. Khan, M.G. Miller, M.C. Snabes, A. Chan, E. Dubcenco, X. Li, T. Yi, B. Huang, K.M. Pencina, T.G. Travison, S.E. Nissen, TRAVERSE Study Investigators, Cardiovascular safety of testosterone-replacement therapy, N. Engl. J. Med. 389 (2023) 107–117, https://doi.org/10.1056/NEJMoa2215025.
[18] D.M. Kelly, T.H. Jones, Testosterone and obesity, Obes. Rev. 16 (2015) 581–606, https://doi.org/10.1111/obr.12282.
[19] O. Canguven, B. Salepci, S. Albayrak, A. Selimoglu, M. Balaban, M. Bulbul, Is there a correlation between testosterone levels and the severity of the disease in male patients with obstructive sleep apnea? Arch. Ital. Urol. Androl. Organo Uff. Soc. Ital. Ecogr. Urol. E Nefrol. 82 (2010) 143–147.
[20] T.W. Auyeung, T. Kwok, J. Leung, J.S.W. Lee, C. Ohlsson, L. Vandenput, Y.K. Wing, J. Woo, Sleep duration and disturbances were associated with testosterone level, muscle mass, and muscle strength—a cross-sectional study in 1274 older men, J. Am. Med. Dir. Assoc. 16 (2015) 630.e1–630.e6, https://doi.org/10.1016/j.jamda.2015.04.006.
[21] G.R. Cunningham, A.J. Stephens-Shields, R.C. Rosen, C. Wang, S. Bhasin, A. M. Matsumoto, J.K. Parsons, T.M. Gill, M.E. Molitch, J.T. Farrar, D. Cella, E. Barrett-Connor, J.A. Cauley, D. Cifelli, J.P. Crandall, K.E. Ensrud, L. Gallagher, B. Zeldow, C.E. Lewis, M. Pahor, R.S. Swerdloff, X. Hou, S. Anton, S. Basaria, S. J. Diem, V. Tabatabaie, S.S. Ellenberg, P.J. Snyder, Testosterone treatment and sexual function in older men with low testosterone levels, J. Clin. Endocrinol. Metab. 101 (2016) 3096–3104, https://doi.org/10.1210/jc.2016-1645.
[22] M. Biernikiewicz, A. Rusiecka, D. Kałka, Obesity and sexual desire: a systematic review and meta-analysis, J. Sex. Med. 22 (2025) 677–693, https://doi.org/10.1093/jsxmed/qdaf057.
[23] F.A. Yafi, L.M. Huynh, T. Ahlering, R. Rosen, What is a "validated questionnaire"? A critical review of erectile function assessment, J. Sex. Med. 17 (2020) 849–860, https://doi.org/10.1016/j.jsxm.2020.02.005.
[24] D.A. D'Annibale, M. Mimoto, K.C. McCowen, A. Malhotra, Glucagon-like peptide-1 receptor agonists for the treatment of obstructive sleep apnea, Curr. Opin. Pulm. Med. 31 (2025) 591–596, https://doi.org/10.1097/MCP.0000000000001208.
[25] E.B. Rankin, J. Rha, M.A. Selak, T.L. Unger, B. Keith, Q. Liu, V.H. Haase, Hypoxia-inducible factor 2 regulates hepatic lipid metabolism, Mol. Cell. Biol. 29 (2009) 4527–4538, https://doi.org/10.1128/MCB.00200-09.
[26] L. Fan, W. Sun, B. Chen, S. Zhang, S. Zhang, X. Yang, Y. Li, W. Zheng, Easy blood oxygen accumulation distribution area index (EBOADAI) integrating apneic events and hypoxemic burden: association with testosterone deficiency and sexual health in adult males, Aging Male 28 (2025) 2568139, https://doi.org/10.1080/13685538.2025.2568139.
[27] J. Wydra, A. Wydra, P. Kucharczyk, G. Kapuściński, W. Zgliczyński, M. Rabijewski, Selective estrogen receptor modulators and aromatase inhibitors in the treatment of functional male hypogonadism, Endokrynol. Pol. 76 (2025) 349–358, https://doi.org/10.5603/ep.105142.
[28] C.N. Jayasena, R.A. Anderson, S. Llahana, J.H. Barth, F. MacKenzie, S. Wilkes, N. Smith, P. Sooriakumaran, S. Minhas, F.C.W. Wu, J. Tomlinson, R. Quinton, Society for Endocrinology guidelines for testosterone replacement therapy in male hypogonadism, Clin. Endocrinol. 96 (2022) 200–219, https://doi.org/10.1111/cen.14633.