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Review article

Obstructive sleep apnea syndrome (OSAS) in women: A forgotten cardiovascular risk factor

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ABSTRACT

Sleep-disordered breathing is a highly prevalent disorder with negative impact on healthcare systems worldwide. This condition has detrimental effects on cardiovascular health and quality of life, and is frequently associated with a variety of comorbidities, including cardiovascular disease, heart failure, diabetes and atrial fibrillation. Nevertheless, it remains frequently undiagnosed and undertreated, especially in specific populations. Studies on sleep-disordered breathing have been conducted mainly on male patients, and the prevalence and severity of this disorder in women are underestimated. Recently, some clinical and laboratory evidence has highlighted the epidemiological and pathophysiological differences between men and women with sleep-disordered breathing. In this review, we discuss sex-related mechanisms of sleep-disordered breathing in frequently associated disorders, to improve clinical understanding of this condition and to simplify the practical application of targeted interventions. The aim is to improve prognosis among female patients and guarantee a better quality of life and a reduction in healthcare costs.

1. Introduction

Sleep-disordered breathing (SDB) is a common condition, associated with multiple comorbidities including cardiovascular (CV) and metabolic diseases [1]. According to the latest classification of the American Academy of Sleep Medicine, SDB comprises a wide range of sleep-related breathing disorders, including obstructive sleep apnea syndrome (OSAS), central sleep apnea, and sleep-related hypoventilation [2]. SDB prevalence differs according to sex categories, as it is more prevalent in men than women. For example, OSAS has a 3 to 1

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prevalence ratio for men compared to women. This epidemiological consideration shifted the researchers' attention away from the female population [3–6]. Nevertheless, under-diagnosis and the related under-treatment has penalized SDB female patients, because in the last decade, women have represented up to 40–50 % of presentations at sleep clinics [7,8] (Table 1).

The sex-specific cardiovascular (CV) risk profile differs between men and women, particularly when all the peculiar CV risk factors are properly considered [9]. Alongside traditional CV risk factors, sex/gender-specific ones have been included in recent years, which are important in the cardiovascular risk stratification of men and women [10,11]. The sex-specific CV risk factors which clinicians should take into account are, for men, hypogonadism, while for women, hypertension during pregnancy and gestational diabetes, preterm delivery, fetus' excess or deficit of weight at birth, polycystic ovary syndrome, history of breast cancer treated with cardiotoxic chemotherapic agents (e.g. anthracyclines or trastuzumab) or chest radiotherapy, systemic autoimmune diseases (more frequent among women), depression, together with other known risk factors related to the female gender, which impact on behavior, lifestyle, and access to healthcare assistance [10–16].

Among the too often little considered CV risk factors, OSAS must certainly be included, undoubtedly widespread among men and women in different proportions according to age groups, but rarely considered as a risk factor in female patients [17] (Table 1).

The prevalence of SDB and comorbidities was increased in post-menopausal women [18] and in women with polycystic ovary syndrome [19,20], suggesting estrogen may play an important, possibly beneficial role.

As known, overweight and obesity are among the most predisposing factors of SDB [21]. Women after menopause often show a body weight increase, due to hormonal changes (namely, sarcopenic obesity). This specific risk factor, together with the loss of estrogens' protection, leads to an increased CV risk. For this reason, it is necessary to examine this condition with a sex/gender perspective, to better characterize female patient CV risk, especially in the post-menopausal age. This narrative review assesses the "state of the art" about OSAS among women, evaluating if this should be included among the sex/gender specific risk factors.

2. Methods

This narrative review is based on a literature search conducted in October 2024. No restrictions in terms of publication date, language or sample size were applied. Electronic databases (Pubmed, MEDLINE, EMBASE, Clinicaltrials.gov) were searched for OSAS topic. Specifically, the authors included in the review all the most recent studies, reviews and meta-analyses that investigated the relationship between OSA and cardiovascular disease in the female population. Older studies were included in the review when considered milestones on the topic discussed.

2.1. OSAS as a cardiovascular risk factor in men and women

The OSAS is a chronic sleep-related breathing disorder characterized by recurrent episodes of a partial or complete collapse of the upper airway, resulting in reduced or absent airflow lasting for at least 10 s [22]. These phenomena leads both to acute adaptations, with sleep fragmentation, fall in blood oxygen saturation, significant variations of intrathoracic pressure and increased sympathetic activity, and long-term negative effects, such as reduced quality of life and social functioning, cognitive impairment, excessive day time sleepiness, and increased incidence of cardiovascular disease (CVD), metabolic diseases, and cerebrovascular events [21]. Moreover, a strong association between OSAS and premature death exists [23].

.Chronic obstructive pulmonary disease (COPD) and OSAS are two

Table 1
Main studies elucidate the OSAS role in cardiometabolic risk profile among women.

Articles	Article type	Main evidences	Conclusions
Bublitz, M et al. Life 2022 [8]	Narrative review	Rates of SDB are higher among men, likely driven by differences in symptom presentation between men and women, with women presenting with more "atypical" symptoms, and lack of sensitivity in SDB screening tools to detect SDB in women.	More research is needed. An increased awareness among health care providers and the lay public of the SDB-specific sex and gender differences will serve to minimize disparities.
Moghtaderi I et al. Sleep Breath 2022 [17]	Original article 319, one center study among veterans women		Findings support the need for increased attention to identification and management of SDB in women veterans, especially those with conditions associated with elevated SDB risk.
Wimms A, et al. Biomed Res Int. 2016 [29]	Review	Prevalence data do show that more men than women are affected by OSA; however, these differences are not reflected in clinical populations. This indicates that females are being diagnosed and treated for OSA less frequently than males.	Better knowledge of gender differences in OSA will help to improve the awareness and diagnosis of OSA in women, and the development and availability of therapeutic options.
Geer JH, et al. Yale J Biol Med. 2021 [30]	Review	Obstructive sleep apnea is associated with significant symptoms and health consequences in women yet remains underdiagnosed in women in part due to differences in presenting symptoms, differences in polysomnographic findings, and/or sociocultural factors.	Future guidelines and screening tools should incorporate emerging data on sex and gender-related differences in OSA presentation since the literature is biased toward male subjects, which limits the generalizability of conclusions. Additionally, there is a need for investigators to focus on gender-related phenotypes, biomarkers, diagnostic criteria, and treatment decision-making and outcomes.
Hegner P, et al. Front Physiol. 2021 [32]	Review	Recent clinical and basic science evidence increasingly points to different mechanisms in men and women with sleep-disordered breathing. SDB is associated with a variety of comorbidities, including cardiovascular disease, heart failure, diabetes, and atrial fibrillation.	Women with SDB rather are more likely to develop HFpEF and men HFrEF..
Fabozzi A, et al. Sleep Breath. 2024 [39]	Original article	Females presented a significantly higher frequency of hypopneas than men, as well as a lower number of	These differences in the nocturnal home sleep cardiorespiratory monitoring could reflect different pathophysiological

(*continued on next page*)

Table 1 (*continued*)

Articles	Article type	Main evidences	Conclusions
		desaturation events per hour.	mechanisms of OSAS onset between the two sexes, which should be investigated in future scientific studies.
Snyder B, et al. 2018 [71]	Review	Sleep apnea is diagnosed more frequently in men than women, suggesting a role of sex hormones in the pathology of the disease. Furthermore, there are sex differences in the development and progression of comorbid diseases associated with sleep apnea.	While the impact sleep apnea has on cardiovascular events has been the subject of many research studies, the role of sleep apnea in neurodegeneration is less established. Risk factors for sleep apnea and the implications of the observed sex differences in this disease.
Lebek S. al Front. Med. 2021 [72]	Review	Women are often underrepresented in current HF guidelines, and recent trials with HFpEF patients were negative but suggest a potential sex difference. Thus, a better understanding of gender-dependent mechanisms of diastolic dysfunction is urgently warranted.	We suggest that there may be a gender difference with respect to myocardial ACE2 expression in response to SDB-dependent hypoxia, favoring hypertrophy and subsequent HFpEF development in women.
Lavalle S et al. Life 2024 [123]	Review	OSAS-related complications include cardiovascular disorders, neurological impairments, metabolic dysfunction, and a potential link to cancer.	The comprehensive analysis of biomarkers provides insights into the complex interplay between OSAS and systemic complications, offering avenues for future research and therapeutic advancements in this multifaceted sleep disorder.

common chronic diseases with increasing incidence worldwide, frequently with a simultaneous presentation, imposing great costs to the healthcare systems [24]. Moreover, both COPD and OSAS represent a remarkable risk factor for CVD [25] for men and women, as stated in recent guidelines on CVD prevention endorsed by the European Society of Cardiology (ESC) [26].

.The actual prevalence of OSAS is a matter of debate, as methodological differences exist between the epidemiological studies carried out to date. According to the Wisconsin Sleep Cohort study, the prevalence of moderate to severe OSAS (i.e., apnea-hypoxia index, AHI, $\geq$15 events per hour) among 30–70 years old participants is about 10 % (13.0 % in the male subgroup and 5.6 % in the female subgroup) with a 30 % increase between 1990 and 2010, and an absolute increase respectively of 7.5 % in men and 4.2 % in women [27]. The same study showed a significant increase in prevalence of OSAS with age, from 26.6 % in men and 8.7 % in women aged 30 to 49 years to 43.2 % and 27.8 % in the same groups aged 50 to 70 years.

Apart from age, there is a relevant association between OSAS and overweight, with an increase of OSAS prevalence from 7.0 % in a male population aged 30 to 49 years with a body mass index (BMI) <25, to 44.6 % in a same aged male population but with a BMI of 30–39.9, and an increase from 1.4 % to 13.5 % in female populations with the same characteristics [25,28]. Sex-specific anatomical differences in adipose tissue deposition and airway size may account for some of the discrepancies in sleep apnea prevalence and severity.

Further reports using contemporary scoring and sleep study recording systems reported a much greater prevalence of moderate to severe OSAS up to 50 % in men and 23 % in women [5].

.The difference in prevalence of OSAS between sex groups has not been confirmed in clinical populations, and it could be the result of frequent misdiagnosis or under-diagnosis in female population due to different reported symptoms and inability of physicians to respond to OSAS symptoms in women [29] (Table 1). In particular, women are more likely to experience unspecific symptoms of OSA, such as insomnia, mood disorders, overtiredness, and morning headache. Thus, they may be easily and frequently treated for other conditions, such as depression, thyropathy, and sleep disorders. Moreover, as the abovementioned symptoms are usually attributed to menopausal manifestations in older women, this may further delay the diagnosis of OSA [30] (Tables 1 and 2).

Historically, the so called “big three” risk factors for OSAS are male sex, greater body mass index, and greater age [31]. Nevertheless, OSAS has been now identified as a not-at-all-rare condition in women, and OSAS prevalence in older women becomes closer to that of men [5,32] (Table 1).

A recent study by Fietze et al. [33] on 1208 participants (median age 54 years, 54 % men) confirmed a continuous increase of OSAS with age both for men and women, but with a later onset for women, and identified several clinical and demographic factors associated with OSAS, including sex, age, BMI, waist-to-hip ratio, snoring, and self-reported CVD. Alcohol consumption was associated with OSAS only in the female subgroup. The abovementioned associations were stronger in the female group, confirming that gender plays a significant role into both OSAS pathophysiological mechanisms and therapy responsiveness. OSAS acts not only as a CVD risk factor, but also as a worsening factor in outcomes related to CVD. However, as OSAS and CVD share several comorbidities and risk factors, the demonstration of a causative link between these two conditions has been extremely hard [34]. A recent meta-analysis confirmed a positive and continuous association between OSAS severity and relative CVD risk, independently from the characteristics of the specific populations but more relevant if a longer follow-up was considered [35].

.However, the current standard-of-care treatment of OSAS with positive airway pressure (PAP) did not improve hard CV outcomes in patients with CVD, suggesting that a differential pathophysiological link probably exists between OSAS and specific CVD. In this regard, recent ESC guidelines suggest interventions associated with significant behavior to PAP [26,36,37].

Similarly, the effect of gender on the development of CV complications in OSAS is still unclear. As the prevalence of OSAS is at least twice in men than in women, it is not possible to adequately stratify clinical data by sex [38]. Recent studies specifically analyzed the consequences of OSAS in a female population, and demonstrated that women with OSAS generally have more comorbidities (i.e., CVD, hyperlipidemia, diabetes) and are more prone to develop cognitive issues and brain matter injury [39] (Tables 1 and 2). Additionally, female OSAS patients generally complain about poorer life quality, which is in turn related to clinical depression, the latter being greatly associated with increased CV risk [40].

.Hormone replacement therapy seems to not clearly modify the hypertensive pattern evolution during menopause transition, as recently described [41]. Therefore, the risk factors and cardiometabolic profile related to OSAS and hypertension in women should be fully understood.

Moreover, women show weaker autonomic responses, possibly associated with worse blood pressure regulation and brain perfusion [29].

.The anatomical peculiarities of women and the changes outlined in the airways’ anatomy and physiology during specific conditions (e.g. pregnancy and after menopause), that increase the risk of snoring and SDB, have not been adequately approached from a therapeutic point of

TABLE 2
Main differences in female and male patients with SDB.

Age	CVD prevalence increases with age, both in men and in women. In the female population, the first CV event related to coronary artery disease generally develops 10 years later that in the male population, due to diminished estrogen levels [30].
Family HTx of CVD	The effects of genetic risk in CVD are more significant in women with a strong family history as compared to men. Premature death due to CV complications is more frequent in patients who have a strong paternal history as compared to a maternal history [30].
Smoking	A recent meta-analysis reported that in women >45 years old, smoking determines a 25 % increased risk for CVD compared to men. In pregnant women, it is associated to increased risk of preterm birth and low weight at birth. Moreover, smoking increases the risk of premature menopause, and the combination of smoking with the use of oral contraceptives has a complementary effect on the CV risk [44].
Sedentarism and physical inactivity	According to the World Health Organization data, physical inactivity (PI) is more frequent and severe in the female population for all age groups, with a global average of 31.7 % for inactive women vs. 23.4 % for inactive men. In childhood, PI is associated to the accumulation of numerous harmful habits in adulthood, with the strongest association documented in females. In fertile women, PI correlates with many cardio-metabolic risk factors, that are strongly associated with adverse pregnancy outcomes, which predicts the risk of subsequent CVD. In older adults, PI and sedentary behavior influence CV health status and this correlation is more significant in older female as compared to older male [104,105].
Obesity	Obesity is an independent risk factor for CVD. Globally, it is more prevalent in women than in men. Data from the Framingham Heart Study shows that obesity increases the risk of coronary artery disease by 64 % in women when compared with 46 % in men [100–103].
Dyslipidemia	Under the age of 35, total cholesterol levels are similar for both sexes, while after the age of 50 women have higher levels of total cholesterol, LDL-C and lipoprotein a [Lp(a)] compared to men, the latter accounting for increasing CV risk in postmenopausal women. Furthermore, it seems that hypertriglyceridemia acts as a more potent CV risk factor in women than in men, as every increase of 1 mmol/L in triglyceride levels lead to an increase of 32 % and 76 % of CV risk, respectively, in men and women. Finally, conditions such as polycystic ovarian syndrome and familiar hypercholesterolemia determine higher cardiovascular risk for young women. Dyslipidemia in pregnancy also leads to worse outcomes for patients and creates increased cardiovascular risk at an older age. Dyslipidemia remains under-screened and undertreated compared to men [39].
Hypertension	Hypertension affects more men than women until 45 years of age, as for the protective effects of estrogen, while after the age of 55 the prevalence of hypertension higher in women than in men. The association between hypertension and poor CVD outcomes is stronger in women than in men. Moreover, women experience sex-specific risk factors for hypertension, such as gynecological disorders and adverse pregnancy outcomes [51–63].
Diabetes mellitus and insulin resistance	Insulin resistance is associated to obesity, dyslipidemia, hypertension and impaired glucose tolerance, the latter potentially evolving into type 2 diabetes mellitus (T2DM). T2DM determines a 2-fold higher hazard ratio for CVD, with women experiencing a relative risk for CVD 44 % greater than men and a higher adjusted hazard ratio of fatal events [32,39].
Sex-specific CV risk factors	Sex-specific risk factors unique to women include: breast cancer treatment; Adverse Pregnancy Outcomes (APO, such as hypertensive disorders of pregnancy, gestational diabetes mellitus, preterm delivery, and newborn size for gestational age); gynecological conditions (such as premature menarche, menopause, polycystic ovarian syndrome, and infertility). Moreover, autoimmune diseases, thrombophylic conditions, stress and depression are more prevalent in women and enhance women's CV risk factors across the lifespan [80,82,88].

CVD: cardiovascular disease, SDB: sleep disorders of breathing.

view with specific intervention programs for women.

In summary, there are many gender-related differences in clinical presentation and manifestations of OSAS that could substantially impact on short and long-term outcomes, and much scientific evidence demonstrating that female OSAS patients may experience more adverse CV outcomes, as they suffer from a greater burden of CV risk factors and systemic inflammatory status. Moreover, women with OSAS more frequently experience depressive symptoms and complain of reduced life quality. Finally, female gender was identified as an independent significant predictor of CVD in younger and nonobese patients with OSAS (Fig. 1).

2.2. Endothelial dysfunction and oxidative stress

Endothelial dysfunction is considered the "primum movens" for CV disease development, especially among women who suffer from micro vessels damage more often than from large arterial vessels disease [42,43]. In a study by Faulx and colleagues, an increase in the AHI and a reduction in flow-mediated dilatation and peak blood flow were observed following transient occlusion of the brachial artery cuff. Because this interaction was sex-specific for women, the authors concluded that women with SDB may be more susceptible to SDB-related early CVD than men [44] (Table 2).

Endothelial dysfunction is also associated with thrombosis [30,45]. According to data from Arzt et al., an increased risk of deep vein thrombosis and pulmonary embolism exist in SDB patients, regardless of the established risk factors for thromboembolic events [46].

As is well known, menopause is a turning point not only for a woman's reproductive life [47]. Indeed, the progressive reduction of the ovarian estrogens production begins years before actual menopause. The physiological reduction of estrogens causes numerous effects on the endothelium and cardiomyocytes (which host estrogens receptors). In particular, the beta-receptor for estrogens modulates, in the endothelial cells, the production of nitric oxide, which in turn determines arteriolar vasodilation; moreover, it regulates the diapedesis of polymorphonuclear cells, reducing, when present, inflammation of the vascular wall. Furthermore, it demonstrated apoptotic and oxidative stress regulation activity mediated by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase. Therefore, after menopause, the regulation of these systems in the vascular system is considerably reduced. In cardiomyocytes estrogens modulate hypertrophy and ameliorate contraction throughout sarcoplasmic reticulum activity (using phosphokinase A regulation) [48]. Estrogens reduction negatively impacts on sleep respiratory profile even during menopause transition [49], while moderate and severe OSAS rates were significantly greater in the menopausal group.

2.3. Arterial hypertension

Among CV conditions, the causal link between arterial hypertension (AH) and OSAS is the most widely studied. In particular, OSAS severity at baseline and the relative risk of developing AH during follow-up share a linear, dose-dependent relationship, especially for resistant AH cases [50,51]. Two prospective community-based studies, the Sleep Heart Health Study (SHHS) and the Vitoria Sleep Cohort Study (VSCS) did not confirm this association, probably reflecting methodological differences, despite that all data were adjusted for all the possible confounders such

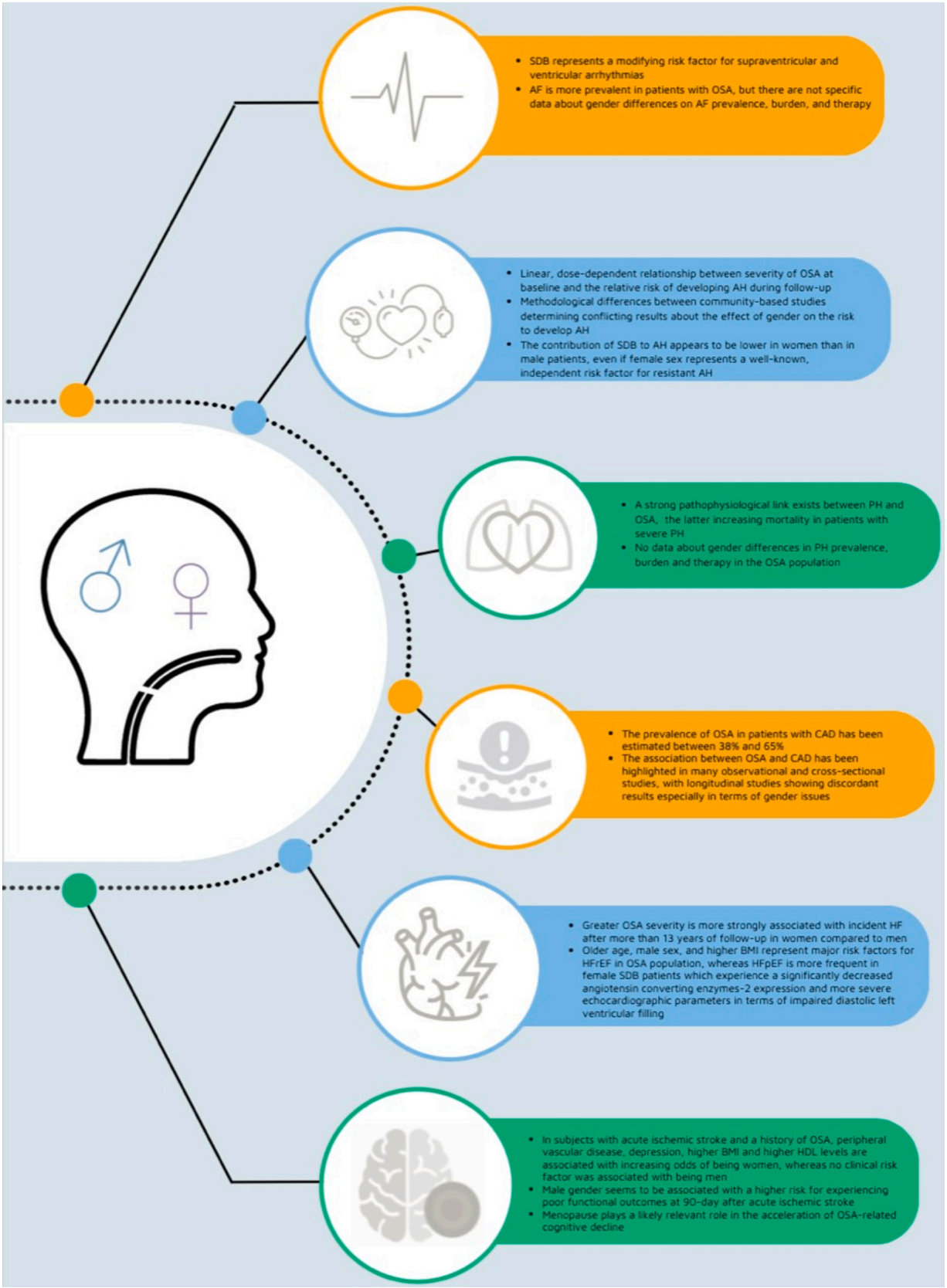

Fig. 1. Main links between SDB and CVD.
SDB, sleep-disordered breathing; AF, atrial fibrillation; OSA, obstructive sleep apnea; AH, arterial hypertension; PH, pulmonary hypertension; CAD, coronary artery disease; HFrEF, heart failure with reduced ejection fraction; BMI, body mass index; HFpEF, heart failure with preserved ejection fraction; HDL, high-density lipoproteins.

as age, BMI, and sex [52,53]. There are conflicting results about the effect of gender on the risk of developing AH, with markedly obese men showing nearly 2-fold greater AH risk than women [54]. However, a post-hoc analysis of VSCS, using a more rigorous end point for incident AH, confirmed the association between moderate and severe OSAS and more severe AH forms, but only in the male subgroup [55]. A potential explanation is that 81 % of the female sample in the VSCS were young and had normal weight, and 67 % were premenopausal at the baseline [56]. Conversely, as in the real-world clinical scenario most women referred for OSAS evaluation are more obese and older than referred men, they could have a greater prevalence of AH than the male subgroup, as subsequently confirmed by Mokhlesi et al. [57].

Thus, long-term exposure to chronic intermittent hypoxia is a cardinal feature of sleep apnea syndrome and is sufficient to cause sympathetic-excitation and elevated blood pressure in human subjects and various animal models [58].

In contrast, the contribution of SDB to hypertension is lesser in women than in male patients [46]. While an increased OR for hypertension of 3.7 was reported for men with an AHI in the greatest third of the population, no significant risk increase was observed in similar female patients [59].

Furthermore, much evidence confirmed that OSAS is associated with a 5-fold greater risk of developing resistant AH, regardless of other related risk factors, with 83 % of OSAS patients referring to a resistant AH clinic and a prevalence between 63 % and 80 % of OSAS in patients admitted to a resistant AH clinic [60,61]. Female sex represents a well-known, independent risk factor for resistant AH, which is in turn associated with a remarkable increased long-term risk of major adverse events, according to data from the WISE study [62].

This suggests that CVD risk is mediated differently in female SDB patients than in men, and a sex/gender specific approach in further studies is needed.

2.4. Cardiac rhythm abnormalities

Epidemiological data have demonstrated that some of the most significant association of SDB and cardiac outcomes are with cardiac arrhythmias, which are linked with both OSAS and CSA, with a strong causal association. SDB contributes to cardiac arrhythmogenesis with acute, subacute, and long-term mechanisms. SDB acute effects comprise autonomic nervous system fluctuations, recurrent hypoxia, alterations in carbon dioxide/acid-base status, and disrupted sleep architecture; moreover, the intrathoracic pressure alterations directly affect cardiac function. Subacute effects include direct cardiac mechanical damage leading to atrial distension and increase in left ventricular pressure and transmural gradient, as well as electrophysiological alterations and inflammatory status. Chronic effects determine cardiac structural and electrophysiologic substrate alterations and remodeling, including increased fibrosis and metabolic dysregulation [63,64].

In this regard, SDB treatment is associated with improved arrhythmias-related outcomes.

These data support the need to consider SDB as a modifying risk factor for cardiac arrhythmias, as highlighted by the latest scientific statement from the American Heart Association [65]. However, there are also clear bidirectional interactions between SDB and cardiac arrhythmias, as CVD can itself worsen SDB, and most of the available data are observational, highlighting the need for rigorous, adequately powered, randomized interventional trials in this clinical scenario.

Going further into details, both bradyarrhythmias and ventricular arrhythmias are more prevalent in patients with OSA, with a prevalence of 18 % and 14–74 %, respectively [3].

Furthermore, OSAS acts as a consistent and well-recognized risk factor for the onset, progression, and persistence of atrial fibrillation (AF), as it negatively affects the maintenance of sinus rhythm after cardioversion or catheter ablation. OSAS prevalence varies from 21 % to 74 % in patients with AF and both conditions share common risk factors (i.e. obesity, male gender, age, smoking, alcohol intake, heart failure) and independent association with unfavorable CV outcomes [66]. The incidence of significant AF detected in an unselected pacemaker population is greater in patients with severe SA than in patients with non-severe SA (25.0 % vs 13.9 %, $p = 0.002$) [67].

The potential effects of continuous positive airway pressure ventilation (CPAP) on AF management are still under study. So far, there are not specific data about gender differences on AF prevalence, burden, and therapy.

2.4.1. Atrial fibrillation

As Monahan and colleagues have previously highlighted [68], life-threatening arrhythmias' risk was increased in SDB patients. Specifically, AF and its recurrence are greater in patients with OSAS than in those without diagnosed OSAS, even after interventional therapy with pulmonary vein isolation [69]. In particular, SDB is associated with increased diastolic sarcoplasmic reticulum (SR) calcium (Ca++) leak, increased late I-Na + current, and reduced connexin-43 expression [70,71] (Table 1). Estrogens have recently been implicated in Na + current regulation and Ca++ store handling [72] (Table 1). SR Ca++ leak and increased Na + influx are important in the development of AF and arrhythmias in SDB patients [24,73]. Estrogen has recently been implicated in Na current regulation and Ca store handling, in humans and animal models [56]. Notably, SR Ca leak and late Ina, increased in ovariectomized animals, inverted to physiologic behavior after estradiol replacement therapy [56].

2.4.2. Repolarization abnormalities and ventricular arrhythmias

Differences in some repolarization markers among men and women were investigated [74,75]. Increase in diastolic pressure due to greater intrathoracic pressures during SDB could promote and induce mechanical and bio humoral alterations leading to myocardial hypertrophy [76]. In addition to its role in heart failure, Calcium/calmodulin-dependent protein kinase II (CaMKII) is associated with the development of arrhythmias, and there are already several CaMKII inhibitors preclinically tested as antiarrhythmic drugs [77–79].

CaMKII expression appears strictly related to sex-hormone concentrations, allowing for some of the sex-specific variation in SR Ca++ leak and late INa regulation [80] (Table 2). Increased late INa and SR Ca leak can trigger arrhythmias by enhancing the frequency of early-after-depolarizations (EAD) and delayed-after-depolarizations (DAD) in the cardiac action potential [81]. These conditions share the pathophysiological basis with chronic heart failure and its bio humoral alterations.

2.5. Pulmonary hypertension

Pulmonary hypertension (PH) coexists in about 10–20 % of patients with moderate-to-severe OSAS and, in contrast, OSAS prevalence in patients with PH ranges from 70 to 80 %.

A strong pathophysiological link between these two conditions exists: even though PH secondary to OSAS is usually mild, OSAS in turn leads to subsequent worsening of pulmonary vascular resistance and is associated with increased mortality, especially in patients with severe PH. Moreover, the effect of CPAP is quite limited in this population [18]. Chronic thromboembolic pulmonary hypertension (CTEPH) could be related to SDB among women. The SpO_2 mean was shown as an independent predictor for pulmonary vascular resistance and cardiac output in women ($p = 0.001$, $p < 0.001$, $p = 0.001$, respectively) [82] (Table 2). The authors combined T90%, SaO_2, and minimal SpO_2 to develop a new composite parameter, called the hypoxemia scoring index (HSI), which showed in female patients great capacity for predicting CTEPH risk.

2.6. Coronary artery disease

OSAS prevalence in patients with coronary artery disease (CAD) is estimated between 38 % and 65 %, and the association between these

two conditions has been highlighted in many observational and cross-sectional studies. However, longitudinal studies showed discordant results, with the association between OSAS and incident CAD being weakened after correction for common risk factors and being confirmed only in some groups, i.e. in a younger male subgroup as shown in the SHHS [83].

However, in patients with pre-existent CAD, OSAS presence increases CV mortality, even if OSAS treatment is not associated with a relevant reduction of hard CV outcomes [84].

.Recently it was underlined that a sex/gender-specific approach to ischemic heart disease in women is necessary [85]. The specific symptoms and peculiar clinical presentation reduce the recognition of ischemic heart disease (IHD) in women by clinicians. CV risk stratification must include sex/gender specific risk factors. SDB must also be considered as a risk factor among women who suffer from IHD.

2.7. Heart failure

SDB prevalence in patients with heart failure (HF) is greater than in the general population, and ranges from 50 to 70 %, with OSAS accounting for a minor portion of cases.

While the epidemiology of SDB in patients with HF with reduced ejection fraction (HFrEF) has been widely analyzed and estimated between 12 and 53 %, with older age, male sex, and greater BMI being major risk factors, poor data are available about patients with HF with preserved ejection fraction (HFpEF) [86].

However, the causal relationship between OSAS and HF is still a matter of debate, as traditional scores for SDB analysis, i.e. AHI, showed inadequacy in the prediction of incident HF. The sleep apnea-specific hypoxic burden (SASHB) has been recently proposed as an alternative, more comprehensive score, best reflecting the disease burden associated both with OSAS and HF, especially in male subgroups [87].

So far, little is known about gender differences in HF and OSAS. Roca et al. showed that greater OSAS severity was more strongly associated both with greater high-sensitive-cardiac troponin T (hs-TnT) levels and with incident HF after >13 years of follow-up in women compared to men. These results suggest that greater attention to screening of women for OSAS may help to reduce their risk of developing CVD [88] (Table 2).

Lebek et al. [89] preoperatively evaluated 377 patients for SDB, approximately 84 % were men undergoing elective coronary artery bypass graft surgery. HFpEF was significantly more common among SDB patients compared to those without SDB (28 vs. 17 %). The HFpEF was more frequent in female SDB patients (48 % vs. only 25 % in male). Intriguingly, significantly decreased angiotensin converting enzymes-2 expression was preferentially observed in women with SDB (2.66 $\pm$ 0.42 vs. 4.01 $\pm$ 2.47 in men with SDB, p value = 0.005). Echocardiographic characteristics of HFpEF were also significantly correlated with SDB severity, as female patients with SDB were significantly more likely to exhibit impaired diastolic left ventricular filling (echocardiographic E/e') compared with men, and minimum oxygen saturation and time of oxygen saturation < 90 % were significantly correlated with E/e'.

2.8. Stroke and neurodegenerative diseases

As highlighted in a recent study [90] SDB is strictly related to hypercoagulation, increased platelet count, clotting factors, and to inflammation and oxidative stress, as abovementioned. This condition could be connected to blood brain barrier alteration and to neurodegeneration, which is highly frequent among old patients, especially among old women [91]. Moreover, SDB severity is mainly reflected by a greater AHI, with reduced gray matter volume in the entorhinal cortex and hippocampus in amyloid-positive individuals. This aspect demonstrates that SDB is strictly linked to a greater risk of cognitive decline [92]. A recent retrospective study by Edrissi et al. explored the clinical characteristics associated with gender differences in a subject population with acute ischemic stroke and OSAS history. The authors highlighted those patients with peripheral vascular disease, depression [93], greater body mass index, and greater high-density lipoprotein levels were associated with increasing odds of being women, whereas no clinical risk factor was associated with being men [94]. Conversely, it seems that male gender is associated with a higher risk for experiencing poor functional outcomes at 90-days after acute ischemic stroke [95]. Furthermore, there is a growing body of evidence supporting the role of OSAS in the risk, manifestation and possibly progression of dementia, particularly Alzheimer's disease, potentially mediated by oxidative stress and chronic neuroinflammation, with menopause playing a likely relevant role in the acceleration of OSAS-related cognitive decline [96–98]. To date, the treatment of OSAS on dementia seems to positively mitigate cognitive decline [99]. However, further data are needed, especially regarding gender differences in the relationship between SDB and dementia in terms of primary and secondary prevention.

2.9. Primary and secondary prevention of OSAS: the paramount role of diet and physical activity

Among the well-known risk factors for OSAS, obesity is probably the most important and modifiable one. This condition, defined as a "chronic, progressive, relapsing and treatable multi-factorial, neurobehavioural disease" according to the Obesity Medicine Association 2021, is globally and rapidly increasing [100] (Table 2). The so-called "globesity" represents a major issue for healthcare worldwide, with 38 % of the global population being currently overweight or obese and the 53 % of the adult European population having a body mass index (BMI) $\geq$ 25. Female gender is linked to a doubled risk of being overweight or obese, which starts early during reproductive decades and increases proportionally with age [100]. Moreover, obese women experience a doubled mortality risk as compared with obese men and are more commonly exposed to obesity-related comorbidities, especially in terms of noncommunicable diseases and mental health [101]. In this regard, the Women's Preventive Services Initiative developed an executive summary for counseling midlife women to prevent obesity [102]. Similarly, the International Federation of Gynecology and Obstetrics (FIGO) recently published an updated best practice advice about obesity management across women's life courses, underscoring the need for a prompt and effective global call for action in terms of obesity prevention and management, from the pre-conception decades until menopause, especially for the lifelong health implications associated with obesity. The most relevant tools in this scenario are nutrition and exercise [103]. On this point, we must face the dramatic statistics regarding the global epidemiology of physical inactivity, which is more frequent and severe in the female population for all age groups, with a worldwide average of 31.7 % for inactive women vs. 23.4 % for inactive men [104]. This gender gap in physical activity begins early in life and determines significant short-term and long-term adverse effects on female health outcomes [105] (Table 2).

In OSAS patients, obesity increases mechanical respiratory loads, worsening airflow narrowing and obstruction, and determines an increase in leptin resistance, inflammatory status, and oxidative stress, further deteriorating ventilatory response and upper airway neuromuscular control [105] (Table 2). As a condition significant OSAS is present in about 40 % of obese subjects, and about 70 % of patients with OSAS are obese. The American Academy of Sleep Medicine strongly recommends lifestyle improvement for OSAS, including dietary-induced weight loss and physical exercise [106]. In this regard, much more attention should be paid to promoting targeted intervention for weight control and against sedentary lifestyle in the female population since women are more frequently overweight or obese and more sedentary than men, as discussed.

Furthermore, gender strongly influences the body's adaptations to exercise and different nutrients. In particular, the specific hormonal changes in women significantly impact their interaction with food, and this relationship is strongly affected by mental health status and stress,

as recently demonstrated by the COVID-19 pandemic. Thus, promoting a gender-medicine based approach to any dietary program, focused on the specific women's life stage, is mandatory [107], especially after menopause [108,109].

The benefits of different dietary patterns (e.g., lower-carbohydrate diet, Mediterranean diet) were evaluated in the OSAS population, and the positive effects of these approaches may exceed the well-known benefits of weight reduction, contributing to a remarkable improvement of cardiometabolic risk profile, which may in turn positively impact CV risk. Melaku et al. demonstrated that in a population of >14,000 subjects from the National Health and Nutrition Examination Survey, the participants with the healthiest diet quality had 28 % reduced odds of being at high risk of sleep apnea compared with those with the most inferior diet quality. In contrast, those with the greatest Dietary Inflammatory Index had 55 % greater odds of being at increased risk for sleep apnea [110] (Table 2). Similarly, Zuraikat et al. highlighted, in a prospective cohort study of 432 US women from the American Heart Association Go Red for Women, that greater adherence to a Mediterranean diet is associated with fewer sleep disturbances [111]. Physical exercise, likewise, seems to play a similar role, both in terms of OSAS prevention and improvement. First, scientific evidence demonstrated that physically active subjects have a reduced risk of OSAS compared to sedentary subjects [112,113]. Moreover, the Wisconsin Sleep Cohort Study showed, in a population of 1521 randomly selected adults, an association between exercise hours and reduced incidence of mild and moderate OSAS, with a decrease in exercise adherence being associated with worsening OSAS [114]. These positive effects may be mediated by fluid redistribution and central adiposity reduction. Furthermore, exercise can reduce oxidative stress, inflammation, and sympathetic activation that occur in OSAS patients [115]. A recent meta-analysis by Peng et al. demonstrated that exercise reduces OSAS severity, especially when aerobic training is combined with resistance training, and ameliorates cardiopulmonary fitness and sleep quality [116]. However, there is still a lack of data regarding the role of gender differences in this clinical scenario, in terms of tailored dietary strategies and physical exercise protocols. The abovementioned findings support the part of a gender-focused, personalized approach to improve high-quality and anti-inflammatory dietary strategies and promote healthy behavior, with strong adherence to physical exercise (apart from calorie restriction and simple weight loss), to reduce sleep apnea risk and ameliorate CV and OSAS-related outcomes [117], among patients of all ages [118] (Table 2).

2.10. Future perspectives and new trends

More research is needed to better define the unique pathophysiology and clinical presentation of SDB in women. Also, an increased awareness among health care providers and the lay public of the SDB-specific sex and gender differences will serve to minimize disparities in identification and treatment of SDB in women.

More population-based [119–121] and case-control [122,123] (Table 1) studies are needed for a correct clinical-therapeutic approach to OSAS in both sexes. A significant help in understanding the basic pathophysiological mechanisms (oxidative stress and inflammation markers) [124] that regulate the pathology in men and women could come from animal models, as already highlighted in some studies [125,126]. Moreover, the use of machine learning and artificial intelligence tools could be promising for a correct risk stratification of SBD in adult patients, ensuring a correct global therapeutic approach [127].

.The correct stratification of primary and secondary cardiovascular risk could allow targeted intervention planning, aimed at improving the prognosis among male and female patients, guaranteeing better life quality and reducing healthcare costs.

3. Discussion

In women, OSAS are less frequent than in man, but prevalence increases after menopause and in specific comorbid conditions (e.g. obesity). OSAS among post-menopausal women should be evaluated alongside other cardiovascular risk factors to enable a more accurate stratification of individual risk. This comprehensive approach acknowledges that OSAS does not occur in isolation but often coexists with other conditions, such as hypertension, diabetes, and metabolic syndrome, which collectively contribute to cardiovascular risk.

As abovementioned, men and women affected by OSAS often have similar comorbidities, but with different nuances. OSAS are the clinical expression of a complex cardiometabolic decompensation. In the presence of hypertension disorders resistant to therapy, metabolic syndrome and visceral obesity, OSAS should always be suspected and investigated, especially in post-menopausal women. Undoubtedly, reducing body weight and the adoption of a healthier lifestyle have been demonstrated efficacious in CV risk reduction. Moreover, the use of specific drugs aimed to improve the cardiometabolic risk (e.g. GLP1 receptor agonists) can significantly improve not only CV general outcomes, but also SDB [128,129].

By integrating OSAS into a broader cardiovascular risk profile, clinicians can better identify high-risk individuals, as recognizing OSAS as part of a constellation of cardiovascular risk factors can help pinpoint women who may be at higher risk for adverse cardiovascular outcomes. The development of tailored interventions is mandatory, combining the effect of OSAS and other risk factors enables more targeted, individualized intervention strategies that address the cumulative risk burden, rather than treating OSAS in isolation. This integrated approach can lead to more effective prevention and treatment strategies, reducing both cardiovascular morbidity and mortality among women with OSAS.

Contributors

Federica Moscucci contributed to conceptualization, data collection, drafting and editing the paper.

Valentina Bucciarelli contributed to data collection, drafting and editing the paper.

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References

[1] M.R. Bonsignore, T. Saaresranta, R.L. Riha, Sex differences in obstructive sleep apnoea, European Respiratory Review: an official journal of the European Respiratory Society 28 (154) (2019) 190030.

[2] M.J. Sateia, International classification of sleep disorders-third edition: highlights and modifications, Chest 146 (5) (Nov 2014) 1387–1394, https://doi.org/10.1378/chest.14-0970 (PMID: 25367475).

[3] Y. Yeghiazarians, H. Jneid, J.R. Tietjens, S. Redline, D.L. Brown, N. El-Sherif, R. Mehra, B. Bozkurt, C.E. Ndumele, V.K. Somers, Obstructive sleep apnea and cardiovascular disease: a scientific statement from the American Heart Association, Circulation 144 (3) (Jul 20 2021) e56–e67, https://doi.org/10.1161/CIR.0000000000000988 (Epub 2021 Jun 21. Erratum in: Circulation. 2022 Mar 22;145(12):e775. PMID: 34148375).

[4] R. Heinzer, H. Marti-Soler, P. Marques-Vidal, N. Tobback, D. Andries, G. Waeber, et al., Impact of sex and menopausal status on the prevalence, clinical presentation, and comorbidities of sleep-disordered breathing, Sleep Med. 51 (2018) 29–36, https://doi.org/10.1016/j.sleep.2018.04.016.

[5] R. Heinzer, S. Vat, P. Marques-Vidal, H. Marti-Soler, D. Andries, N. Tobback, et al., Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study, Lancet Respir. Med. 3 (2015) 310–318, https://doi.org/10.1016/S2213-2600(15)00043-0.

[6] V. Jain, M. Al Rifai, R. Turpin, H.N. Eken, A. Agrawal, D. Mahtta, Z. Samad, S. Coulter, F. Rodriguez, L.A. Petersen, S.S. Virani, Evaluation of factors underlying sex-based disparities in cardiovascular care in adults with self-reported premature atherosclerotic cardiovascular disease, JAMA Cardiol. 7 (3) (Mar 1 2022) 341–345, https://doi.org/10.1001/jamacardio.2021.5430, e215430, PMID: 34985497; PMCID: PMC8733863.

[7] K.A. Franklin, C. Sahlin, H. Stenlund, et al., Sleep apnoea is a common occurrence in females, Eur. Respir. J. 41 (2013) 610–615.

[8] M. Bublitz, N. Adra, L. Hijazi, F. Shaib, H. Attarian, G. Bourjeily, A narrative review of sex and gender differences in sleep disordered breathing: gaps and opportunities, Life (Basel, Switzerland) 12 (12) (2022) 2003, https://doi.org/10.3390/life12122003.

[9] E. Davis, M.K. Higgins, K.A. Wood, J. Cimiotti, R.A. Gary, S.B. Dunbar, Sex differences in cardiac risk factors in young adults: a secondary analysis and surveillance study, J Cardiovasc Nurs 38 (2) (Mar-Apr 01 2023) 168–178, https://doi.org/10.1097/JCN.0000000000000888 (Epub 2022 Feb 14. PMID: 35170485; PMCID: PMC9375778).

[10] M. Garcia, S.L. Mulvagh, C.N. Merz, J.E. Buring, J.E. Manson, Cardiovascular disease in women: clinical perspectives, Circ. Res. 118 (8) (Apr 15 2016) 1273–1293.

[11] S. Sciomer, F. Moscucci, S. Maffei, S. Gallina, A.V. Mattioli, Prevention of cardiovascular risk factors in women: the lifestyle paradox and stereotypes we need to defeat, Eur. J. Prev. Cardiol. 26 (6) (Apr 2019) 609–610, https://doi.org/10.1177/2047487318810560 (Epub 2018 Oct 29. PMID: 30373379).

[12] B. Vogel, M. Acevedo, Y. Appelman, C.N. Bairey Merz, A. Chieffo, G.A. Figtree, M. Guerrero, V. Kunadian, C.S.P. Lam, A.H.E.M. Maas, A.S. Mihailidou, A. Olszanecka, J.E. Poole, C. Saldarriaga, J. Saw, L. Zühlke, R. Mehran, The Lancet women and cardiovascular disease commission: reducing the global burden by 2030, Lancet 397 (10292) (Jun 19 2021) 2385–2438.

[13] V. Bucciarelli, A.V. Mattioli, S. Sciomer, F. Moscucci, G. Renda, S. Gallina, The impact of physical activity and inactivity on cardiovascular risk across women's lifespan: an updated review, J. Clin. Med. 12 (13) (Jun 28 2023) 4347, https://doi.org/10.3390/jcm12134347 (PMID: 37445383; PMCID: PMC10342501).

[14] A.V. Mattioli, F. Moscucci, S. Sciomer, S. Maffei, M. Nasi, M. Pinti, V. Bucciarelli, A. Dei Cas, G. Parati, M.M. Ciccone, P. Palmiero, M. Maiello, R. Pedrinelli, C. Pizzi, F. Barillà, S. Gallina, Cardiovascular prevention in women: an update by the Italian Society of Cardiology working group on 'Prevention, hypertension and peripheral disease', J. Cardiovasc. Med. (Hagerstown) 24 (Suppl. 2) (May 1 2023) e147–e155, https://doi.org/10.2459/JCM.0000000000001423 (PMID: 37186565).

[15] V. Bucciarelli, A.L. Caterino, F. Bianco, C.G. Caputi, S. Salerni, S. Sciomer, S. Maffei, S. Gallina, Depression and cardiovascular disease: the deep blue sea of women's heart, Trends Cardiovasc. Med. 30 (3) (Apr 2020) 170–176, https://doi.org/10.1016/j.tcm.2019.05.001 (Epub 2019 May 11. PMID: 31109802).

[16] A.V. Mattioli, F. Coppi, V. Bucciarelli, S. Gallina, Cardiovascular risk stratification in young women: the pivotal role of pregnancy, J. Cardiovasc. Med. (Hagerstown) 24 (11) (Nov 1 2023) 793–797, https://doi.org/10.2459/JCM.0000000000001557 (Epub 2023 Sep 29. PMID: 37773880).

[17] I. Moghtaderi, M.R. Kelly, G.C. Carlson, C.H. Fung, K.R. Josephson, Y. Song, D. Swistun, R. Zhu, M. Mitchell, D. Lee, M.S. Badr, D.L. Washington, E.M. Yano, C.A. Alessi, M.R. Zeidler, J.L. Martin, Identifying gaps in clinical evaluation and treatment of sleep-disordered breathing in women veterans, Sleep Breath. (Dec 16 2022), https://doi.org/10.1007/s11325-022-02765-1 (Epub ahead of print. PMID: 36525174; PMCID: PMC10272283).

[18] D.R. Dancey, P.J. Hanly, C. Soong, B. Lee, V. Hoffstein, Impact of menopause on the prevalence and severity of sleep apnea, Chest 120 (2001) 151–155.

[19] A.N. Vgontzas, R.S. Legro, E.O. Bixler, A. Grayev, A. Kales, G.P. Chrousos, Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance1, J. Clin. Endocrinol. Metab. 86 (2001) 517–520.

[20] N. Helvaci, Polycystic ovary syndrome and the risk of obstructive sleep apnea: a meta-analysis and review of the literature 6 (7) (2017) 437–445.

[21] D.J. Gottlieb, N.M. Punjabi, Diagnosis and management of obstructive sleep apnea: a review, JAMA 323 (14) (2020) 1389–1400.

[22] R.L. Riha, Defining obstructive sleep apnoea syndrome: a failure of semantic rules, Breathe (Sheff.) 17 (3) (Sep 2021) 210082, https://doi.org/10.1183/20734735.0082-2021 (PMID: 35035552; PMCID: PMC8753646).

[23] D.E. Jonas, H.R. Amick, C. Feltner, R.P. Weber, M. Arvanitis, A. Stine, et al., Screening for obstructive sleep apnea in adults: evidence report and systematic review for the US preventive services task force, JAMA 317 (4) (2017) 415–433.

[24] K.F. Rabe, H. Watz, Chronic obstructive pulmonary disease, Lancet 389 (10082) (2017) 1931–1940.

[25] M. Tang, Y. Long, S. Liu, X. Yue, T. Shi, Prevalence of cardiovascular events and their risk factors in patients with chronic obstructive pulmonary disease and obstructive sleep apnea overlap syndrome, Front. Cardiovasc. Med. 8 (2021) 694806, https://doi.org/10.3389/fcvm.2021.694806.

[26] Visseren FLJ, F. Mach, Y.M. Smulders, D. Carballo, K.C. Koskinas, M. Bäck, A. Benetos, A. Biffi, J.M. Boavida, D. Capodanno, B. Cosyns, C. Crawford, C. H. Davos, I. Desormais, E.D. Angelantonio, O.H. Franco, S. Halvorsen, F. D. Richard Hobbs, M. Hollander, E.A. Jankowska, M. Michal, S. Sacco, N. Sattar, L. Tokgozoglu, S. Tonstad, K.P. Tsioufis, I. van Dis, I.C. van Gelder, C. Wanner, B. Williams, ESC Scientific Document Group, 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice: developed by the Task Force for Cardiovascular Disease Prevention in Clinical Practice with representatives of the European Society of Cardiology and 12 medical societies with the special contribution of the European Association of Preventive Cardiology (EAPC), Rev Esp Cardiol (Engl Ed) 75 (5) (May 2022) 429, https://doi.org/10.1016/j.rec.2022.04.003 (English, Spanish, PMID: 35525570).

[27] P.E. Peppard, T. Young, J.H. Barnet, M. Palta, E.W. Hagen, K.M. Hla, Increased prevalence of sleep-disordered breathing in adults, Am. J. Epidemiol. 177 (9) (2013) 1006–1014.

[28] C. Antonaglia, G. Passuti, Obstructive sleep apnea syndrome in non-obese patients, Sleep & breathing = Schlaf & Atmung 26 (2) (2022) 513–518, https://doi.org/10.1007/s11325-021-02412-1.

[29] A. Wimms, H. Woehrle, S. Ketheeswaran, D. Ramanan, J. Armitstead, Obstructive sleep apnea in women: specific issues and interventions, Biomed. Res. Int. 2016 (2016) 1764837.

[30] J.H. Geer, J. Hilbert, Gender issues in obstructive sleep apnea, Yale J. Biol. Med. 94 (3) (Sep 30 2021) 487–496 (PMID: 34602886; PMCID: PMC8461585).

[31] C.V. Senaratna, J.L. Perret, C.J. Lodge, A.J. Lowe, B.E. Campbell, M.C. Matheson, et al., Prevalence of obstructive sleep apnea in the general population: a systematic review, Sleep Med. Rev. 34 (2017) 70–81.

[32] Philipp Hegner, Simon Lebek, Lars Siegfried Maier, Michael Arzt, Stefan Wagner, The effect of gender and sex hormones on cardiovascular disease, heart failure, diabetes, and atrial fibrillation in sleep apnea, Front. Physiol. (12) (Oct 20 2021) 741896.

[33] I. Fietze, N. Laharnar, A. Obst, R. Ewert, S.B. Felix, C. Garcia, et al., Prevalence and association analysis of obstructive sleep apnea with gender and age differences - results of SHIP-Trend, J. Sleep Res. 28 (5) (2019) e12770.

[34] B. Lechat, S. Appleton, Y.A. Melaku, K. Hansen, R.D. McEvoy, R. Adams, P. Catcheside, L. Lack, D.J. Eckert, A. Sweetman, The association of co-morbid insomnia and sleep apnea with prevalent cardiovascular disease and incident cardiovascular events, J. Sleep Res. 31 (5) (2022 Oct) e13563, https://doi.org/10.1111/jsr.13563. Epub 2022 Feb 15. PMID: 35166401.

[35] X. Zhang, J. Fan, Y. Guo, J. Zhou, F. Chen, Z. Jin, et al., Association between obstructive sleep apnoea syndrome and the risk of cardiovascular diseases: an updated systematic review and dose–response meta-analysis, Sleep Med. 71 (2020) 39–46.

[36] J.R. Tietjens, D. Claman, E.J. Kezirian, T. De Marco, A. Mirzayan, B. Sadroonri, et al., Obstructive sleep apnea in cardiovascular disease: a review of the literature and proposed multidisciplinary clinical management strategy, J. Am. Heart Assoc. 8 (1) (2019) e010440.

[37] A.K. Mitra, A.R. Bhuiyan, E.A. Jones, Association and risk factors for obstructive sleep apnea and cardiovascular diseases: a systematic review, Diseases 9 (4) (Dec 2 2021) 88, https://doi.org/10.3390/diseases9040088.

[38] L.S. Freitas, L.F. Drager, Gender and cardiovascular impact of obstructive sleep apnea: work in progress!, J. Thorac. Dis. 9 (10) (2017) 3579–35788.

[39] A. Fabozzi, F. Pasqualotto, M. Laguardia, P.F. Natuzzi, R. Capone, A. Steffanina, D. Pellegrino, F. Olmati, C. Antonaglia, P. Palange, Gender differences in obstructive sleep apnea syndrome: a pilot study, Sleep Breath. 28 (4) (Aug 2024) 1645–1650.

[40] S.E. Schiza, I. Bouloukaki, Does gender matter: sex-specific aspects of symptoms, outcome, and therapy of obstructive sleep apnea, Curr. Opin. Pulm. Med. 26 (6) (Nov 2020) 642–649, https://doi.org/10.1097/MCP.0000000000000728 (PMID: 32890020).

[41] V. Rimpilä, L. Lampio, N. Kalleinen, T. Vahlberg, A. Virkki, T. Saaresranta, O. Polo, Evolution of sleep-disordered breathing and blood pressure during menopausal transition, J. Sleep Res. 32 (4) (Aug 2023) e13829, https://doi.org/10.1111/jsr.13829 (Epub 2023 Feb 3. PMID: 36737407).

[42] L.R. Smith, M.O. Salifu, I.M. McFarlane, Non-obstructive coronary artery disease in women: current evidence and future directions, Int J Clin Res Trials. 5 (2) (2020) 152.

[43] D. Ioannidou, G. Kalamaras, S.C. Kotoulas, A. Pataka, Smoking and obstructive sleep apnea: is there an association between these cardiometabolic risk factors?-gender analysis, Medicina (Kaunas) 57 (11) (Oct 20 2021) 1137.
[44] Michael D. Faulx, Emma K. Larkin, Brian D. Hoit, Joan E. Aylor, Andrew T. Wright, Susan Redline, Sex influences endothelial function in sleep-disordered breathing 27 (6) (Sep 15 2004) 1113–1120.
[45] P. Poredos, M.K. Jezovnik, Endothelial dysfunction and venous thrombosis, Angiology 69 (7) (Aug 2018) 564–567.
[46] M. Arzt, R. Luigart, C. Schum, L. Lüthje, A. Stein, I. Koper, C. Hecker, R. Dumitrascu, R. Schulz, "Circulation and Sleep" Working Group of the German Society of Sleep Research and Sleep Medicine (DGSM), Sleep-disordered breathing in deep vein thrombosis and acute pulmonary embolism, Eur. Respir. J. 40 (4) (Oct 2012) 919–924.
[47] S. Sciomer, C. De Carlo, F. Moscucci, S. Maffei, Age at menopause: a fundamental data of interest to acquire in female patients' anamnesis, Int. J. Cardiol. (215) (Jul 15 2016) 358–359, https://doi.org/10.1016/j.ijcard.2016.04.107 (Epub 2016 Apr 26. PMID: 27128561).
[48] Salerni S, Di Francescomarino S, Cadeddu C, Acquistapace F, Maffei S, Gallina S. The different role of sex hormones on female cardiovascular physiology and function: not only oestrogens. Eur. J. Clin. Investig. 2015 Jun;45(6):634–45. doi: https://doi.org/10.1111/eci.12447. Epub 2015 May 10. PMID: 25845675.
[49] E. Dugral, G. Ordu, Differences in polysomnography parameters of women in the post and transitional phases of menopause, Cureus 13 (12) (Dec 21 2021) e20570, https://doi.org/10.7759/cureus.20570 (PMID: 35103149; PMCID: PMC8773356).
[50] P.E. Peppard, T. Young, M. Palta, J. Skatrud, Prospective study of the association between sleep-disordered breathing and hypertension, N. Engl. J. Med. 342 (19) (2000) 1378–1384.
[51] S.C. Goncalves, D. Martinez, M. Gus, E.O. de Abreu-Silva, C. Bertoluci, I. Dutra, et al., Obstructive sleep apnea and resistant hypertension: a case-control study, Chest 132 (6) (2007) 1858–1862.
[52] I. Cano-Pumarega, J. Duran-Cantolla, F. Aizpuru, E. Miranda-Serrano, R. Rubio, C. Martinez-Null, et al., Obstructive sleep apnea and systemic hypertension: longitudinal study in the general population: the Vitoria Sleep Cohort, Am. J. Respir. Crit. Care Med. 184 (11) (2011) 1299–1304.
[53] G.T. O'Connor, B. Caffo, A.B. Newman, S.F. Quan, D.M. Rapoport, S. Redline, et al., Prospective study of sleep-disordered breathing and hypertension: the Sleep Heart Health Study, Am. J. Respir. Crit. Care Med. 179 (12) (2009) 1159–1164.
[54] V. Mohsenin, H.K. Yaggi, N. Shah, J. Dziura, The effect of gender on the prevalence of hypertension in obstructive sleep apnea, Sleep Med. 10 (7) (2009) 759–762.
[55] I. Cano-Pumarega, F. Barbe, A. Esteban, M. Martinez-Alonso, C. Egea, J. Duran-Cantolla, et al., Sleep apnea and hypertension: are there sex differences? The Vitoria Sleep Cohort. Chest. 152 (4) (2017) 742–750.
[56] J.R. Carter, B. Mokhlesi, Sex differences in the risk of incident hypertension with sleep apnea: does postmenopausal status matter? Chest 152 (4) (2017) 695–697.
[57] B. Mokhlesi, S.A. Ham, D. Gozal, The effect of sex and age on the comorbidity burden of OSA: an observational analysis from a large nationwide US health claims database, Eur. Respir. J. 47 (4) (2016) 1162–1169.
[58] K.D. O'Halloran, Cardiovascular sequelae of the sleep apnoea syndrome: sex, stress and therapeutic strategies, Acta Physiol (Oxford) 225 (2) (2019 Feb) e13170, https://doi.org/10.1111/apha.13170 (Epub 2018 Aug 29, PMID: 30102847).
[59] J. Hedner, K. Bengtsson-Boström, Y. Peker, L. Grote, L. Råstam, U. Lindblad, Hypertension prevalence in obstructive sleep apnoea and sex: a population-based case-control study, Eur. Respir. J. 27 (3) (Mar 2006) 564–570, https://doi.org/10.1183/09031936.06.00042105 (PMID: 16507857).
[60] A.M. Ahmed, S.M. Nur, Y. Xiaochen, Association between obstructive sleep apnea and resistant hypertension: systematic review and meta-analysis, Front Med (Lausanne). (10) (Jun 2 2023) 1200952, https://doi.org/10.3389/fmed.2023.1200952 (PMID: 37332747; PMCID: PMC10272746).
[61] E.S. Muxfeldt, V. Margallo, L.M. Costa, G. Guimarães, A.H. Cavalcante, J. C. Azevedo, F. de Souza, C.R. Cardoso, G.F. Salles, Effects of continuous positive airway pressure treatment on clinic and ambulatory blood pressures in patients with obstructive sleep apnea and resistant hypertension: a randomized controlled trial, Hypertension 65 (4) (Apr 2015) 736–742, https://doi.org/10.1161/HYPERTENSIONAHA.114.04852 (Epub 2015 Jan 19. PMID: 25601933).
[62] S.M. Smith, T. Huo, B. Delia Johnson, V. Bittner, S.F. Kelsey, D. Vido Thompson, C. Noel Bairey Merz, C.J. Pepine, R.M. Cooper-Dehoff, Cardiovascular and mortality risk of apparent resistant hypertension in women with suspected myocardial ischemia: a report from the NHLBI-sponsored WISE Study, J. Am. Heart Assoc. 3 (1) (Feb 28 2014) e000660, https://doi.org/10.1161/JAHA.113.000660 (PMID: 24584740; PMCID: PMC3959684).
[63] X. Li, T. Zhou, H. Ma, T. Huang, X. Gao, J.E. Manson, L. Qi, Healthy sleep patterns and risk of incident arrhythmias, J. Am. Coll. Cardiol. 78 (12) (Sep 21 2021) 1197–1207, https://doi.org/10.1016/j.jacc.2021.07.023 (PMID: 34531019; PMCID: PMC8454031).
[64] Di Fusco SA, Pignalberi C, Santini L, Colivicchi F, Santini M. Arrhythmias and sleep apnea: physiopathologic link and clinical implications. J. Interv. Card. Electrophysiol. 2020 Apr;57(3):387–397. doi: https://doi.org/10.1007/s10840-020-00707-z. Epub 2020 Mar 28. PMID: 32221782.
[65] R. Mehra, M.K. Chung, B. Olshansky, D. Dobrev, C.L. Jackson, V. Kundel, D. Linz, N.S. Redeker, S. Redline, P. Sanders, V.K. Somers, American Heart Association Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology; and Stroke Council. Sleep-disordered breathing and cardiac arrhythmias in adults: mechanistic insights and clinical implications: a scientific statement from the American Heart Association, Circulation 146 (9) (Aug 30 2022) e119–e136, https://doi.org/10.1161/CIR.0000000000001082 (Epub 2022 Aug 1. PMID: 35912643; PMCID: PMC10227720).
[66] B. Huang, H. Liu, B.J. Scherlag, L. Sun, S. Xing, J. Xu, et al., Atrial fibrillation in obstructive sleep apnea: neural mechanisms and emerging therapies, Trends Cardiovasc. Med. 31 (2) (2021 Feb) 127–132, https://doi.org/10.1016/j.tcm.2020.01.006. Epub 2020 Jan 22. PMID: 32008837.
[67] J. Marti-Almor, P. Marques, L. Jesel, R. Garcia, E. Di Girolamo, F. Locati, et al., Incidence of sleep apnea and association with atrial fibrillation in an unselected pacemaker population: results of the observational RESPIRE study, Heart Rhythm. 17 (2) (2020) 195–202.
[68] K. Monahan, A. Storfer-Isser, R. Mehra, E. Shahar, M. Mittleman, J. Rottman, et al., Triggering of nocturnal arrhythmias by sleep-disordered breathing events, J. Am. Coll. Cardiol. 54 (2009) 1797–1804.
[69] D. Linz, R.D. Mcevoy, M.R. Cowie, V.K. Somers, S. Nattel, P. Levy, et al., Associations of obstructive sleep apnea with atrial fibrillation and continuous positive airway pressure treatment: a review, JAMA Cardiol. 3 (2018) 532–540.
[70] Hegner P, Snyder B, Tafelmeier M, Camboni D, Schopka S, Schmid C, Maier LS, Arzt M, Wagner S. Sleep-disordered breathing is independently associated with reduced atrial connexin-43 expression. Heart Rhythm. 2021 Dec;18(12):2187–2194. doi: https://doi.org/10.1016/j.hrthm.2021.09.009. Epub 2021 Sep 10. PMID: 34517118.
[71] Snyder B, Cunningham RL. Sex differences in sleep apnea and comorbid neurodegenerative diseases. Steroids. 2018 May;133:28–33. doi: https://doi.org/10.1016/j.steroids.2017.12.006. Epub 2017 Dec 16. PMID: 29258810; PMCID: PMC5864541.
[72] J.M. Firth, H.Y. Yang, A.J. Francis, N. Islam, K.T. Macleod, The effect of estrogen on intracellular Ca(2+) and Na(+) regulation in heart failure, JACC Basic Transl. Sci. 5 (2020) 901–912.
[73] Lebek S, Pichler K, Reuthner K, Trum M, Tafelmeier M, Mustroph J, Camboni D, Rupprecht L, Schmid C, Maier LS, Arzt M, Wagner S. Enhanced CaMKII-Dependent late INa induces atrial proarrhythmic activity in patients with sleep-disordered breathing. Circ Res. 2020 Feb 28;126(5):603–615. doi: https://doi.org/10.1161/CIRCRESAHA.119.315755. Epub 2020 Jan 6. Erratum in: Circ Res. 2020 Apr 10;126(8):e60. PMID: 31902278.
[74] G. Piccirillo, F. Moscucci, M. Fabietti, C. Di Iorio, F. Mastropietri, T. Sabatino, D. Crapanzano, G. Bertani, G. Zaccagnini, I. Lospinuso, D. Magrì, Age, gender and drug therapy influences on Tpeak-tend interval and on electrical risk score, J. Electrocardiol. 59 (Mar-Apr 2020) 88–92, https://doi.org/10.1016/j.jelectrocard.2020.01.009 (Epub 2020 Jan 24. PMID: 32023499).
[75] F. Moscucci, S. Sciomer, S. Maffei, A. Meloni, I. Lospinuso, M. Carnovale, A. Corrao, I. Di Diego, C. Caltabiano, M. Mezzadri, A.V. Mattioli, S. Gallina, P. Rossi, D. Magrì, G. Piccirillo, Sex differences in repolarization markers: telemonitoring for chronic heart failure patients, J. Clin. Med. 12 (14) (Jul 16 2023) 4714, https://doi.org/10.3390/jcm12144714 (PMID: 37510828; PMCID: PMC10381165).
[76] T. Li, Q. Ou, X. Zhou, X. Wei, A. Cai, X. Li, G. Ren, Z. Du, Z. Hong, Y. Cheng, H. Liu, Left ventricular remodeling and systolic function changes in patients with obstructive sleep apnea: a comprehensive contrast-enhanced cardiac magnetic resonance study, Cardiovasc Diagn Ther. 12 (4) (Aug 2022) 436–452, https://doi.org/10.21037/cdt-22-38 (PMID: 36033230; PMCID: PMC9412210).
[77] K. Huynh, Ruxolitinib is a CaMKII inhibitor that can be repurposed to prevent arrhythmias, Nat. Rev. Cardiol. 20 (9) (Sep 2023) 580, https://doi.org/10.1038/s41569-023-00910-1 (PMID: 37400626).
[78] M. Ji, L. Su, L. Liu, M. Zhuang, J. Xiao, Y. Guan, S. Zhu, L. Ma, H. Pu, CaMKII regulates the proteins TPM1 and MYOM2 and promotes diacetylmorphine-induced abnormal cardiac rhythms, Sci. Rep. 13 (1) (Apr 10 2023) 5827, https://doi.org/10.1038/s41598-023-32941-6 (PMID: 37037889; PMCID: PMC10085977).
[79] M. Arzt, M.A. Drzymalski, S. Ripfel, S. Meindl, A. Biedermann, M. Durczok, K. Keller, J. Mustroph, S. Katz, M. Tafelmeier, S. Lebek, B. Flörchinger, D. Camboni, S. Wittmann, J. Backs, C. Schmid, L.S. Maier, S. Wagner, Enhanced cardiac CaMKII oxidation and CaMKII-Dependent SR Ca leak in patients with sleep-disordered breathing, Antioxidants (Basel). 11 (2) (Feb 8 2022) 331, https://doi.org/10.3390/antiox11020331 (PMID: 35204213; PMCID: PMC8868143).
[80] A. Pardutz, Z. Hoyk, H. Varga, L. Vecsei, J. Schoenen, Oestrogen-modulated increase of calmodulin-dependent protein kinase II (CamKII) in rat spinal trigeminal nucleus after systemic nitroglycerin, Cephalalgia 27 (1) (Jan 2007) 46–53, https://doi.org/10.1111/j.1468-2982.2006.01244.x (PMID: 17212683).
[81] G. Piccirillo, F. Moscucci, G. D'Alessandro, M. Pascucci, P. Rossi, S. Han, L. S. Chen, S.F. Lin, P.S. Chen, D. Magrì, Myocardial repolarization dispersion and autonomic nerve activity in a canine experimental acute myocardial infarction model, Heart Rhythm. 11 (1) (Jan 2014) 110–118, https://doi.org/10.1016/j.hrthm.2013.10.022 (Epub 2013 Oct 9. PMID: 24120873; PMCID: PMC4078249).
[82] H.T. Li, P. Yuan, Q.H. Zhao, S.G. Gong, R. Jiang, J.L. Li, H.T. Liu, H.L. Qiu, W. H. Wu, C.J. Luo, J. He, L. Wang, J.M. Liu, Sex-specific differences in sleep-disordered breathing and nocturnal hypoxemia in chronic thromboembolic pulmonary hypertension and chronic thromboembolic pulmonary disease, Front Cardiovasc Med. (9) (Oct 17 2022) 966973, https://doi.org/10.3389/fcvm.2022.966973 (PMID: 36324750; PMCID: PMC9618641).
[83] E. Shahar, C.W. Whitney, S. Redline, E.T. Lee, A.B. Newman, F.J. Nieto, et al., Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study, Am. J. Respir. Crit. Care Med. 163 (1) (2001) 19–25.

[84] S. Mandal, B.D. Kent, Obstructive sleep apnoea and coronary artery disease, J. Thorac. Dis. 10 (Suppl. 34) (2018) S4212–S4220.

[85] F. Moscucci, F. Lavalle, C. Politi, A. Campanale, G. Baggio, S. Sciomer, Acute coronary syndrome in women: a new and specific approach is needed, Eur. J. Prev. Cardiol. 29 (11) (Aug 22 2022) e305–e308, https://doi.org/10.1093/eurjpc/zwac143 (PMID: 35881512).

[86] H.K. Khattak, F. Hayat, S.V. Pamboukian, H.S. Hahn, B.P. Schwartz, P.K. Stein, Obstructive sleep apnea in heart failure: review of prevalence, treatment with continuous positive airway pressure, and prognosis, Tex. Heart Inst. J. 45 (3) (2018) 151–161.

[87] A. Azarbarzin, S.A. Sands, L. Taranto-Montemurro, D. Vena, T. Sofer, S.W. Kim, et al., The sleep apnea-specific hypoxic burden predicts incident heart failure, Chest 158 (2) (2020 Aug) 739–750, https://doi.org/10.1016/j.chest.2020.03.053. Epub 2020 Apr 13. PMID: 32298733; PMCID: PMC7417383.

[88] G.Q. Roca, S. Redline, B. Claggett, N. Bello, C.M. Ballantyne, S.D. Solomon, et al., Sex-specific association of sleep apnea severity with subclinical myocardial injury, ventricular hypertrophy, and heart failure risk in a community-dwelling cohort: the atherosclerosis risk in communities-sleep heart health study, Circulation 132 (14) (2015) 1329–1337.

[89] P. Hegner, M. Tafelmeier, L. Rupprecht, C. Schmid, L.S. Maier, et al., Female patients with sleep-disordered breathing display more frequently heart failure with preserved ejection fraction, Front. Med. 8 (2021) 675987, https://doi.org/10.3389/fmed.2021.675987.

[90] C. Zolotoff, L. Bertoletti, D. Gozal, V. Mismetti, P. Flandrin, F. Roche, N. Perek, Obstructive sleep apnea, hypercoagulability, and the blood-brain barrier, J. Clin. Med. 10 (14) (2021) 3099, https://doi.org/10.3390/jcm10143099.

[91] C. André, E. Kuhn, S. Rehel, V. Ourry, S. Demeilliez-Servouin, C. Palix, F. Felisatti, P. Champetier, S. Dautricourt, P. Yushkevich, D. Vivien, V. de La Sayette, G. Chételat, R. de Flores, G. Rauchs, Medit-Ageing Research Group, Association of sleep-disordered breathing and medial temporal lobe atrophy in cognitively unimpaired amyloid-positive older adults, Neurology 101 (4) (2023) e370–e385, https://doi.org/10.1212/WNL.0000000000207421.

[92] C.B. Appiah, J.J. Gardner, G.E. Farmer, R.L. Cunningham, J.T. Cunningham, Chronic intermittent hypoxia-induced hypertension: the impact of sex hormones, Am. J. Physiol. Regul. Integr. Comp. Physiol. 326 (5) (2024 May 1) R333–R345, https://doi.org/10.1152/ajpregu.00258.2023. Epub 2024 Feb 26. PMID: 38406843; PMCID: PMC11381015.

[93] Edwards C, Almeida OP, Ford AH. Obstructive sleep apnea and depression: a systematic review and meta-analysis. Maturitas 2020 Dec;142:45–54. doi: https://doi.org/10.1016/j.maturitas.2020.06.002. Epub 2020 Jun 8. PMID: 33158487.

[94] C. Edrissi, C. Rathfoot, K. Knisely, C.B. Sanders, N. Poupore, T. Nathaniel, Gender disparity in a cohort of stroke patients with incidence of obstructive sleep apnea, J. Vasc. Nurs. 40 (1) (2022) 17–27, https://doi.org/10.1016/j.jvn.2021.10.002.

[95] Devenish AN, Nisar T, Criswell A, et al. Sex differences in 90-day functional outcomes for acute ischemic stroke patients with obstructive sleep apnea. Cureus. 2023;15(5):e39652. Published 2023 May 29. doi:https://doi.org/10.7759/cureus.39652.

[96] C. Lal, I. Ayappa, N. Ayas, et al., The link between obstructive sleep apnea and neurocognitive impairment: an official American thoracic society workshop report, Ann. Am. Thorac. Soc. 19 (8) (2022) 1245–1256, https://doi.org/10.1513/AnnalsATS.202205-380ST.

[97] X. Liu, Y. Ma, R. Ouyang, et al., The relationship between inflammation and neurocognitive dysfunction in obstructive sleep apnea syndrome, J. Neuroinflammation 17 (1) (2020) 229, https://doi.org/10.1186/s12974-020-01905-2 (Published 2020 Aug 1).

[98] N.J. Gervais, J.A. Mong, A. Lacreuse, Ovarian hormones, sleep and cognition across the adult female lifespan: an integrated perspective, Front. Neuroendocrinol. 47 (2017) 134–153, https://doi.org/10.1016/j.yfrne.2017.08.002.

[99] M. Kujovic, T. Lipka, M. Zalman, L. Baumann, M. Jänner, B. Baumann, Treatment of hypertension and obstructive sleep apnea counteracts cognitive decline in common neurocognitive disorders in diagnosis-related patterns, Sci. Rep. 13 (1) (2023) 7556, https://doi.org/10.1038/s41598-023-33701-2 (Published 2023 May 9).

[100] https://obesitymedicine.org/wp-content/uploads/2021/08/2021-Obesity-Algorithm-PowerPoint.pdf.

[101] N. Kapoor, S. Arora, S. Kalra, Gender disparities in people living with obesity - an unchartered territory, J Midlife Health. 12 (2) (2021) 103–107, https://doi.org/10.4103/jmh.jmh_48_21.

[102] D. Chelmow, K.D. Gregory, C. Witkop, et al., Preventing obesity in midlife women: a recommendation from the Women's Preventive Services Initiative, Ann. Intern. Med. 175 (9) (2022) 1305–1309, https://doi.org/10.7326/M22-0252.

[103] C.V. Maxwell, R. Shirley, A.C. O'Higgins, et al., Management of obesity across women's life course: FIGO best practice advice, Int. J. Gynaecol. Obstet. 160 (Suppl. 1) (2023) 35–49, https://doi.org/10.1002/ijgo.14549.

[104] World Health Organization, World Health Organization Global Action Plan on Physical Activity 2018–2030: More Active People for a Healthier World, World Health Organization, Geneva, Switzerland, 2018.

[105] R. Lv, X. Liu, Y. Zhang, N. Dong, X. Wang, Y. He, H. Yue, Q. Yin, Pathophysiological mechanisms and therapeutic approaches in obstructive sleep apnea syndrome, Signal Transduct Target Ther. 8 (1) (2023 May 25) 218, https://doi.org/10.1038/s41392-023-01496-3. PMID: 37230968; PMCID: PMC10211313.

[106] L.J. Epstein, D. Kristo, P.J. Strollo Jr., et al., Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults, J. Clin. Sleep Med. 5 (3) (2009) 263–276.

[107] V. Bucciarelli, F. Moscucci, C. Cocchi, S. Nodari, S. Sciomer, S. Gallina, A. V. Mattioli, Climate change versus Mediterranean diet: a hazardous struggle for the women's heart, Am Heart J Plus. (45) (Jul 29 2024) 100431, https://doi.org/10.1016/j.ahjo.2024.100431.

[108] Bonanni E, Schirru A, Di Perri MC, Bonuccelli U, Maestri M. Insomnia and hot flashes. Maturitas 2019 Aug;126:51–54. doi: https://doi.org/10.1016/j.maturitas.2019.05.001. Epub 2019 May 14. PMID: 31239118.

[109] Caretto M, Giannini A, Simoncini T. An integrated approach to diagnosing and managing sleep disorders in menopausal women. Maturitas 2019 Oct;128:1–3. doi: https://doi.org/10.1016/j.maturitas.2019.06.008. Epub 2019 Jun 28. PMID: 31561815.

[110] Y.A. Melaku, A.C. Reynolds, S. Appleton, A. Sweetman, Z. Shi, A. Vakulin, P. Catcheside, D.J. Eckert, R. Adams, High-quality and anti-inflammatory diets and a healthy lifestyle are associated with lower sleep apnea risk, J. Clin. Sleep Med. 18 (6) (Jun 1 2022) 1667–1679, https://doi.org/10.5664/jcsm.9950 (PMID: 35232539; PMCID: PMC9163619).

[111] F.M. Zuraikat, N. Makarem, M.P. St-Onge, H. Xi, A. Akkapeddi, B. Aggarwal, A Mediterranean dietary pattern predicts better sleep quality in US women from the American Heart Association Go Red for Women Strategically Focused Research Network, Nutrients 12 (9) (Sep 16 2020) 2830, https://doi.org/10.3390/nu12092830 (PMID: 32947817; PMCID: PMC7551612).

[112] P.E. Peppard, T. Young, Exercise and sleep-disordered breathing: an association independent of body habitus, Sleep 27 (3) (May 1 2004) 480–484, https://doi.org/10.1093/sleep/27.3.480 (PMID: 15164902).

[113] S.F. Quan, G.T. O'Connor, J.S. Quan, S. Redline, H.E. Resnick, E. Shahar, D. Siscovick, D.L. Sherrill, Association of physical activity with sleep-disordered breathing, Sleep Breath. 11 (3) (Sep 2007) 149–157, https://doi.org/10.1007/s11325-006-0095-5 (PMID: 17221274).

[114] K.M. Awad, A. Malhotra, J.H. Barnet, S.F. Quan, P.E. Peppard, Exercise is associated with a reduced incidence of sleep-disordered breathing, Am. J. Med. 125 (5) (May 2012) 485–490, https://doi.org/10.1016/j.amjmed.2011.11.025 (PMID: 22482846; PMCID: PMC3339801).

[115] D.A. Dobrosielski, C. Papandreou, S.P. Patil, J. Salas-Salvadó, Diet and exercise in the management of obstructive sleep apnoea and cardiovascular disease risk, Eur. Respir. Rev. 26 (144) (Jun 28 2017) 160110, https://doi.org/10.1183/16000617.0110-2016 (PMID: 28659501; PMCID: PMC5559698).

[116] J. Peng, Y. Yuan, Y. Zhao, H. Ren, Effects of exercise on patients with obstructive sleep apnea: a systematic review and meta-analysis, Int. J. Environ. Res. Public Health 19 (17) (2022) 10845, https://doi.org/10.3390/ijerph191710845.

[117] M.P. St-Onge, S. Jelic, Diet as adjunctive therapy for sleep apnea risk: not only how much but also what to eat, J. Clin. Sleep Med. 18 (6) (Jun 1 2022) 1487–1489, https://doi.org/10.5664/jcsm.10042 (PMID: 35393938; PMCID: PMC9163613).

[118] Bucciarelli V, Moscucci F, Dei Cas A, Coppi F, Angeli F, Pizzi C, Renda G, Nodari S, Maffei S, Montisci R, Pedrinelli R, Sciomer S, Perrone Filardi P, Mattioli AV, Gallina S. Maternal-fetal dyad beyond the phenomenology of pregnancy: from primordial cardiovascular prevention on out, do not miss this boat! Curr Probl Cardiol. 2024 Jun 7;49(9):102695. doi: https://doi.org/10.1016/j.cpcardiol.2024.102695. Epub ahead of print. PMID: 38852910.

[119] D.D. Sin, I. Mayers, G.C. Man, L. Pawluk, Long-term compliance rates to continuous positive airway pressure in obstructive sleep apnea: a population-based study, Chest 121 (2) (2002) 430–435, https://doi.org/10.1378/chest.121.2.430.

[120] Bin YS, Cistulli PA, Ford JB. Population-based study of sleep apnea in pregnancy and maternal and infant outcomes [published correction appears in J Clin Sleep Med. 2017 Jan 15;13(1):147–150. doi: https://doi.org/10.5664/jcsm.6426]. J Clin Sleep Med. 2016;12(6):871–877. Published 2016 Jun 15. doi:https://doi.org/10.5664/jcsm.5890.

[121] I. Malhamé, M.H. Bublitz, D. Wilson, L. Sanapo, E. Rochin, G. Bourjeily, Sleep disordered breathing and the risk of severe maternal morbidity in women with preeclampsia: a population-based study, Pregnancy Hypertens. 30 (2022) 215–220, https://doi.org/10.1016/j.preghy.2022.10.013.

[122] P. Lavie, P. Herer, L. Lavie, Mortality risk factors in sleep apnoea: a matched case-control study, J. Sleep Res. 16 (1) (2007) 128–134, https://doi.org/10.1111/j.1365-2869.2007.00578.x.

[123] G.L. Hundemer, H. Imsirovic, T. Kendzerska, A. Vaidya, A.A. Leung, G.A. Kline, R. Goupil, F. Madore, M. Agharazii, G. Knoll, M.M. Sood, Screening for Primary Aldosteronism Among Hypertensive Adults with Obstructive Sleep Apnea: A Retrospective Population-Based Study, Am. J. Hypertens 36 (7) (2023 Jun 15) 363–371, https://doi.org/10.1093/ajh/hpad022. PMID: 36827468; PMCID: PMC10267649.

[124] S. Lavalle, E. Masiello, G. Iannella, et al., Unraveling the complexities of oxidative stress and inflammation biomarkers in obstructive sleep apnea syndrome: a comprehensive review, Life (Basel). 14 (4) (2024) 425, https://doi.org/10.3390/life14040425 (Published 2024 Mar 22).

[125] Zong S, Du P, Li H, Wang M, Xiao H. Advances in animal models of obstructive sleep apnea. Front Med (Lausanne). 2023;10:988752. Published 2023 Feb 7. doi: https://doi.org/10.3389/fmed.2023.988752.

[126] Koritala BSC, Lee YY, Gaspar LS, et al. Obstructive sleep apnea in a mouse model is associated with tissue-specific transcriptomic changes in circadian rhythmicity and mean 24-hour gene expression. PLoS Biol. 2023;21(5):e3002139. Published 2023 May 30. doi:https://doi.org/10.1371/journal.pbio.3002139.

[127] S. Yook, D. Kim, C. Gupte, E.Y. Joo, H. Kim, Deep learning of sleep apnea-hypopnea events for accurate classification of obstructive sleep apnea and determination of clinical severity, Sleep Med. 114 (2024) 211–219, https://doi.org/10.1016/j.sleep.2024.01.015.

[128] G.S. Papaetis, GLP-1 receptor agonists, SGLT-2 inhibitors, and obstructive sleep apnoea: can new allies face an old enemy? Arch Med Sci Atheroscler Dis. (8) (Feb 28 2023) e19–e34, https://doi.org/10.5114/amsad/161170 (PMID: 37153372; PMCID: PMC10161791).

[129] S. Dragonieri, A. Portacci, V.N. Quaranta, P. Carratu, Z. Lazar, G.E. Carpagnano, A. Bikov, Therapeutic potential of glucagon-like peptide-1 receptor agonists in obstructive sleep apnea syndrome management: a narrative review, Diseases 12 (9) (2024) 224, https://doi.org/10.3390/diseases12090224.