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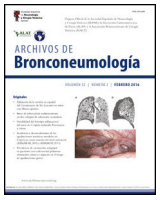

Editorial

New European Guidelines 2023 for Hypertension: When and Why Should We Think About Sleep Apnea?

The 2023 European Society of Hypertension (ESH) Guidelines for the diagnosis and treatment of hypertension have been released during the 32nd annual meeting of the Society, in June 2023 in Milan (Italy), and published in the Journal of Hypertension, the official Journal of the Society.[1] Major novelties of the European Guidelines include among others (1) the assessment of cardiovascular risk, with recognition of novel risk factors such as low birth weight, frailty, migration and environmental exposure to air pollution, (2) the definition via ambulatory blood pressure monitoring of the different clinical phenotypes of the hypertensive state (white coat and masked controlled or uncontrolled hypertension, nighttime hypertension and dipping, orthostatic hypertension, etc.), (3) the thresholds and targets of antihypertensive drug treatment, (4) the key importance of combination drug treatment as initial step of the therapeutic intervention, (5) the need for reinforcing patient's compliance to treatment, (6) the re-evaluation of the therapeutic importance of beta-adrenergic blocking drugs, (7) the need for a well structured clinical follow-up, (8) the diagnosis and management of hypertensive urgencies and emergencies, (9) the resistant hypertensive state and (10) the renewed role of renal denervation in the difficult-to-treat clinical hypertensive phenotypes.

Obstructive sleep apnea syndrome (OSAS) has been referred to about 50 times in different parts of the Guidelines document and received special attention in a specific paragraph under the heading "hypertension and other selected comorbidities".[1] This editorial will briefly review the scientific and clinical relevance as cardiovascular risk factor of OSAS as documented in the European Guidelines, by addressing two main questions, i.e. when and why in current daily practice clinicians should consider the presence of sleep apnea.

As far as the first question is concerned, namely which clinical conditions should arise the suspicion of the presence of OSAS (Fig. 1), Guidelines emphasize the importance of the obese state and of the metabolic syndrome as the main partially reversible risk factors for sleep apnea.[1] The interplay between OSAS and obesity, however, represents a vicious circle considering that while the obese state may increase the risk of developing OSAS, sleep apnea may predispose subjects to worsening obesity, by modifying the neuroendocrine mechanisms favoring food intake and increased hedonic stimulus in the brain.[2] Part of these interactions has been thought to be responsible for the recently described association between OSAS and cancer.[3] As shown in Fig. 1, Guidelines recognize that several factors (some of them potentially reversible by specific therapeutic interventions) may favor the development as well as the progression of OSAS, including anatomic factors and fat deposition on airway walls favoring pharyngeal narrowing and decreased airway size, as well as the presence of an inflammatory state of the adipose tissue, alterations in sleep duration and quality interfering with eating behavior and favoring day-time sleepiness. A further pathogenetic process is represented by the oxidative stress and the enhanced sympathetic cardiovascular overdrive, the latter being of very common detection in the obese state particularly when complicated by OSAS.[4]

Guidelines, however, emphasize that conditions which may encourage suspicion about the presence of OSAS are represented by a reduced (less than 6 h) sleep time, nocturnal hypertension or an extreme dipping, a non dipping or a reverse dipping profile.[1] Common link to all the above mentioned conditions is the presence of a sympathetic overdrive.[5] In a recent study by our group we found that greater levels of sympathetic activation, as documented by abnormally elevated muscle sympathetic nerve traffic values recorded in the peroneal nerve via the microneurographic technique, characterize hypertensive patients with short sleep time duration.[6] Of particular interest was the observation that the adrenergic overdrive seen in these patients was accompanied by (and probably dependent on) an impaired modulation of the sympathetic neural function by the arterial baroreflex, i.e. the homeostatic mechanism which physiologically exerts a tonic restraint on neuroadrenergic cardiovascular drive.[6]

The Guidelines document highlights two additional conditions characterized by elevated blood pressure values, in which OSAS detection is quite common. These include resistant hypertension and difficult-to-control hypertension.[1] Resistant hypertension, defined as the clinical fenotype in which three or more antihypertensive drugs, employed at full daily dosage and including a diuretic, are unable to obtain a blood pressure control, can be detected in about 3–5% of all hypertensive states. In the ESH Guidelines emphasis is given to OSAS as a condition frequently involved in the developing mechanisms of the resistant hypertensive state, which is characterized by a large number of pathophysiologic alterations, all detectable in OSAS, such as elevated circulating aldosterone and endothelin plasma levels, sympathetic overactivity, blood volume and sodium overload.[7] It is thus mandatory in this clinical hypertensive phenotype, and also in all clinical conditions characterized by an essential hypertensive state difficult to be controlled by combination drug treatment, to perform a detailed diagnostic work-up which includes throughout polysomnographic examination an evaluation of the apnea/hypopnea index, taken as index when greater that 5 units of OSAS presence and clinical severity.

The therapeutic interventions adopted for OSAS have been accurately reviewed in the Guidelines document.[1] Particular emphasis

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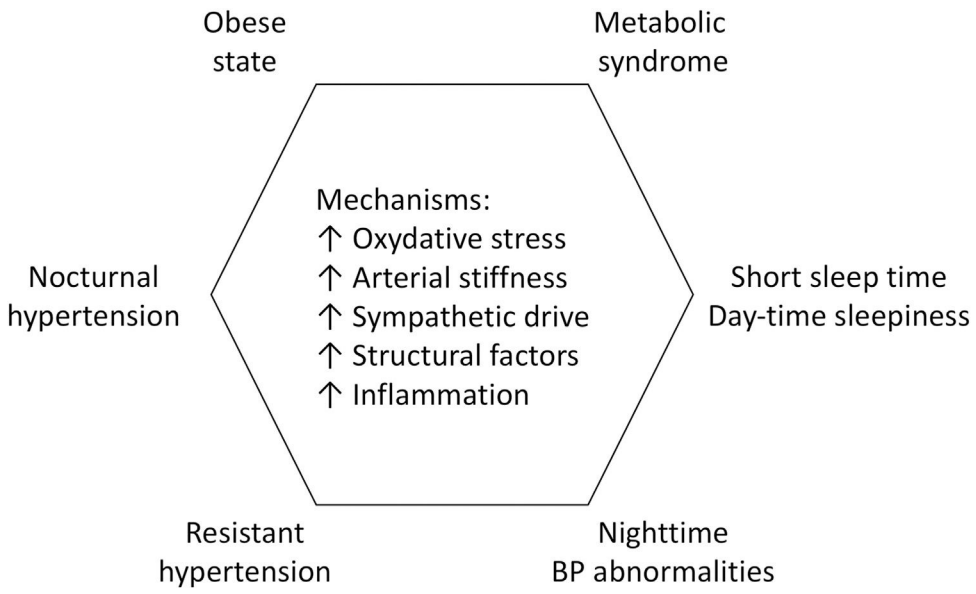

Fig. 1. Clinical conditions favoring the occurrence of obstructive sleep apnea and related pathophysiological mechanisms. BP: blood pressure.

has been given to dietary-induced body weight reduction, exercise training programs and in the severe obese state to gastric bypass surgery. Continuous positive airway pressure (CPAP) may allow to improve the hypoxic state and to obtain small blood pressure reductions, amounting on average to about 3.0 mmHg.[1,8] Finally, bilateral renal nerves ablation may allow to achieve, together with a significant 24 h ambulatory blood pressure reduction (of average magnitude amounting to 8 mmHg), a decrease in sympathetic nerve traffic and an amelioration of the apnea/hypopnea index, as marker of OSAS presence and severity.[9,10] Despite treatment, however, normalization of the polysomnographic derived apnea/hypopnea index, and thus full recovery from sleep apnea syndrome, cannot be achieved in current clinical practice. It appears therefore that the abnormality is irreversible, being thus regarded as one of the mechanisms responsible for the so-called "residual cardiovascular risk".[11] According to the definition mentioned in the ESH Guidelines document this term refers to the evidence that antihypertensive treatment in unable to bring back the cardiovascular risk of the treated hypertensive patients to the level of the one displayed by healthy normotensive subjects.[1] Lack of apnea/hypopnea index normalization may also occur in another cardiovascular disease in which the presence of "residual risk" has been documented, namely chronic heart failure.[12] Of pathophysiological interest is the observation that at the development of the residual risk may concur the sympathetic overdrive characterizing both hypertension and chronic heart failure, particularly when complicated by OSAS, which may be reduced but not fully normalized by treatment.[13] Future investigations are thus needed to try to achieve a complete regression of OSAS.

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Conflict of interests

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