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REVIEW

Anthropometric Correlation with Pathophysiology of Obstructive Sleep Apnea (OSA): A Review

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Abstract

Obstructive sleep apnoea syndrome (OSAS) is a type of breathing disorder with upper airway obstruction, leading to oxy-haemoglobin desaturations and sleep disturbance. However awareness regarding various anthropometric parameters used to analyse OSA syndrome pre-clinically is inadequate. In developing nations, like India, resources are not adequate for analysis of sleep disturbances. That is why the prevalence and validity of various anthropometric parameters including neck circumference, Body mass index and waist circumference to be established and verified regularly. We have also seen the data from oral aspect and its anomalies. Various articles from Pubmed, scopus, google scholar were searched for data. These body measurements may provide pre-clinical aspect of OSA, whether it is present or not. Discussion was done on these anthropometric parameters and which parameter is gold standard for the pre-clinical investigations.

Keywords Obstructive sleep apnea · Anthropometric parameters

1 Introduction

Sleep is defined as a state of human mind and body, characterized by physiological reduction in sensory activity, voluntary muscles and consciousness. Sleep plays a major role in many of the body functions and developments such as learning, memory, neural development, emotional regulation, cardiovascular and metabolic functions [1]. Studies have consolidated in last two decades that a good quality of sleep is essential for the healthier life.

Now a day's technology and social modernization in our life have led to increase sleep disorder prevalence. A range of pathological changes in respiratory effort during physiological sleep, leading to increased disordered breathing which may be due to nasal or upper airway obstruction referred as sleep disordered breathing (SDB). Obstructive sleep apnoea syndrome (OSAS) is a type of SDB which is characterized by recurrent events of partial or complete upper airway obstruction due to increase in negative intrathoracic pressure during sleep or atonia of tongue during REM sleep, leading to oxy-haemoglobin desaturations [2]. There are enough evidence suggesting OSAS as a risk factor for future development of cardiovascular diseases (CVD) including hypertension, coronary artery disease (CAD) and, metabolic syndrome, neurologic disorders such as stroke, dementia, multiple sclerosis and social effects such traffic trauma [3, 4].

In this review the literature search began with key words such as "sleep apnea," "obesity," "anthropometric parameter," "upper airway anatomy." and "sleep study," using Google scholar, Medline, Scopus and PubMed. For additional sources, reference list of the identified articles were also searched. We tried to report original findings from publications that contain relevant theoretical information on the areas which are addressed in this review. The purpose of this study is to provide a brief review of the present scientific knowledge on the clinical, anthropometric and polysomnographic characteristics of non-obese and obese patients with OSA and finding out literature gaps in these areas.

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2 Epidemiology

OSA is a chronic disorder of modern society with estimated prevalence of 2.4–4.9% in men and 1–2.1% in women [5]. According to literature based analysis published in 2019, prevalence of OSA using American academy of sleep medicine (AASM) 2012 diagnostic criteria; it was estimated that 936 million (95% CI 903–970) adults aged 30–69 years (male and female) are having mild to severe OSA and around 425 million (399–450) adults of same age group have moderate to severe OSA globally [12]. Highest numbers of affected individuals are from China, later followed by USA, Brazil and India [12]. In other parts of the world like United States have prevalence of sleep disorders around 56%, Western Europe have 31% and 23% in Japan [7]. In rural population of South India, prevalence of OSAS was estimated using Berlin questionnaire was 8.72% in total, with males estimating around 7.4% and 11.7% in female [6]. Patients who are obese, having type II diabetes mellitus, cardiovascular disorders such as stroke, Heart failure, atherosclerosis and myocardial infarction are more prone to OSA [8]. It was reported in study at South Delhi, that OSA found to be 9% and OSAS is 2.8% [9]. A study did in North Indian hospitals, reported prevalence of OSA and OSAS in males to be 4.4% and 2.5%, 2.5% and 1% in females [10]. Obese population are more at risk of OSA, around 33.5%, reported by Singh et al., in North Indian population [11].

3 Pathophysiology

3.1 Normal Sleep physiology

As per AASM, sleep architecture is majorly divided into two stages:

1. Non-rapid eye movement (NREM)
2. Rapid eye movement (REM)

Sleep begins with NREM sleep which consist of three stages; stage 1 (N1) showing alpha waves in electroencephalogram (EEG) constituting 2–5% of sleep cycle, NREM stage 2 (N2) characterize by sleep spindle and K-complexes constitutes 45 to 55% of sleep cycle, NREM stage 3 is also known as slow wave sleep (SWS), is 10–15% of total sleep cycle [13, 14]. REM stage is associated with dreaming, desynchronized brain activity which constitutes 20–25% of sleep cycle [14–17]. Total sleep cycle is of about 90 to 120 min that includes three stages of NREM and REM stage [14].

3.2 Upper Airway Anatomy

The upper airway is a tubular structure, which begins with the nasal cavity (choanae) and ends at the vocal folds. This is a multipurpose structure, performing various functions such as swallowing of food, breathing air in or out and speech. The upper airway consists of numerous muscles making it prone to collapse in patient with OSA. The cross sectional area of the upper airway in the patients with OSA is narrower than the healthy subjects [18]. There are many reasons behind the narrowing of upper cross sectional area like larger tonsils, fat deposition at the base of tongue or along the airway in obesity [19]. Another important factor is position of hyoid, which determine the airway length and the

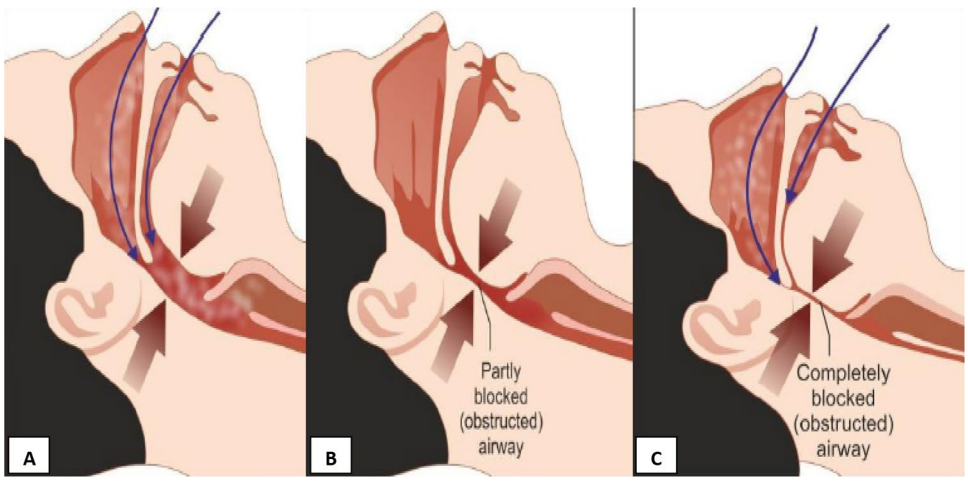

Fig. 1 Figures showing normal sleep and pathophysiological changes during obstructive sleep apnea. **a** Show normal open airway during sleep in supine position. **b** Show partially blocked upper airway due to atonia. **c** Show completely blocked upper airway due to atonia and relapse of tongue

collapsibility of upper airway [20]. Upper airway collapse is shown in Fig. 1.

3.3 Mechanism of obstruction in upper airway

The largest dilating muscle of tongue is genioglossus, due to decreased activity in the patients with OSA compared to normal individuals [21]. On contraction of genioglossus, tongue protude, leading to widening of oropharyngeal airway in the anterior–posterior aspect [21]. The hypoglossal nerve (12th cranial nerve) innervates genioglossus and it provides input from chemoreceptor, respiratory neurons and negative pressure receptors of the airways [22]. Inspiration leads to increase activity of genioglossus, to prevent airway collapse from negative airway pressure [23]. In OSA patients, velopharynx is one of the common sites for obstruction [24]. Other muscles which are maintaining the upper airway patency are tensor veli palatini control stiffness, levator veli palatini for elevation, musculus uvulae for uvular position, palatoglossus for positioning of tongue, together composing soft palate [24]. The muscles of hyoid act bi-directionally, anteriorly and upward via mylohyoid and geniohyoid, and caudally via sternohyoid and thyrohyoid, this together helps in airway dilation [26].

3.4 Breathing during awake and sleep

During awake stage, humans are obligate nose breather. While during sleep, they breathe again via nose and it is not affected by any stages of sleep or changes in position of body [27]. SDB is mainly due to nasal obstruction as nose is the foremost anatomical boundary of upper airway. Nasal pathology in SDB is explained by number of pathophysiology mechanisms like Starling resistor model, the nasal ventilator reflex, an unstable upper airway and the role of nitric oxide (NO) [28]. The Starling resistor model explains the basis for treatment of OSA with nasal continuous positive airway pressure (CPAP) [29]. This model consists of two rigid segments as a part of tube, with a collapsible segment interposed in between, within the box. The nose and trachea representing the rigid tube in humans and muscular pharyngeal regions is considered to be collapsible segment. Hence for the normal patency of pharynx during sleep, the pressure inside the pharynx should be greater in comparison to surrounding tissue outside [16]. When the pressure inside the pharynx falls in comparison to outside leading to collapse is known as pharyngeal critical closing pressure [30].

On observing studies it suggested that Pharyngeal critical closing pressure (P_{CRIT}) plays a major role in the pathogenesis of OSA [31]. P_{CRIT} is both sensitive (majority of people have upper airway collapse) and specific (many normal people do not have upper airway collapse) for ruling out OSA [32]. Elevated levels of P_{CRIT} can be attributed to many structural defects in the upper airway and irregular neuromuscular control [33]. It is seen that OSA severity increased during REM in comparison to NREM sleep due to decrease in neuromuscular tone in some patients, specially children and women [34, 35]. Neuromuscular activity in the pharyngeal region is led by many chemical and mechanical reflexes [32]. In conditions like hypercapnia, stimulated neuromuscular activity in upper airway, causing decrease in P_{CRIT} [36] and in Hypocapnia, there is increase in P_{CRIT} [37]. During phasic activation of pharyngeal muscles, upper airway demonstrated decrease in collapse during expiration in comparison to inspiration [38]. Now once there is a collapse in upper airway, there are many factors that response to obstruction and expresses OSA as shown in Fig. 2.

3.5 Role of polysomnography in OSA

Polysomnography is a sleep study which is performed in the laboratory to analyze the apnea–hypopnea index (AHI), which is required for the diagnosis of OSA. As apnea is complete obstruction of upper airflow anatomy and hypopnea is a partial obstruction of upper airflow anatomy [39, 40]. Hypopnea is also measured by desaturations in the level of oxygen by 3% or more or arousal from the sleep. The AHI is generally calculated by adding all apneas and hypopneas and then they are divided by total sleep time. Together both this should last for 10 s or more to be considered as an event [39, 40]. If both of these occur for 15 or more events per hour, or 5 or more per hour with symptoms of daytime sleepiness, impaired cognition or mood disorder or cardiovascular comorbidities, is considered to be as OSA [39–41]. PSG signals are classified into three groups: for the recognition of sleep related events are electroencephalogram (EEG), electrooculogram (EOG), submental electromyogram (EMG), those which are required for the monitoring of cardiac arrhythmic events are electrocardiogram (ECG) and for the airflow or respiratory related events are oximetry, oronasal thermistor, nasal canula and thoracoabdominal effort. A microphone may be used which is attached to the neck for recording of snoring. EEG is used to measure the sleep stages from the central, frontal and occipital regions of the brain. The EEG activity in the reticular nucleus of the thalamus shows hyperpolarization of neurons, generating EEG spindles and afferent input to the cortex are blocked and maintain sleep [42]. During REM sleep, it is generally designated for mild OSA, with AHI range around 5 to 14. Moderate OSA with AHI between 15 to 30, have fragmented sleep with sleep architecture is preserved. Severe OSA is present in both REM and NREM stage with AHI above 30. Althought it more common in NREM sleep related OSA and in older men [43]. REM OSA is having 5 or more events in REM stage and less than 5 events in NREM stage with total REM sleep duration of 30 min [43]. NREM OSA have AHI

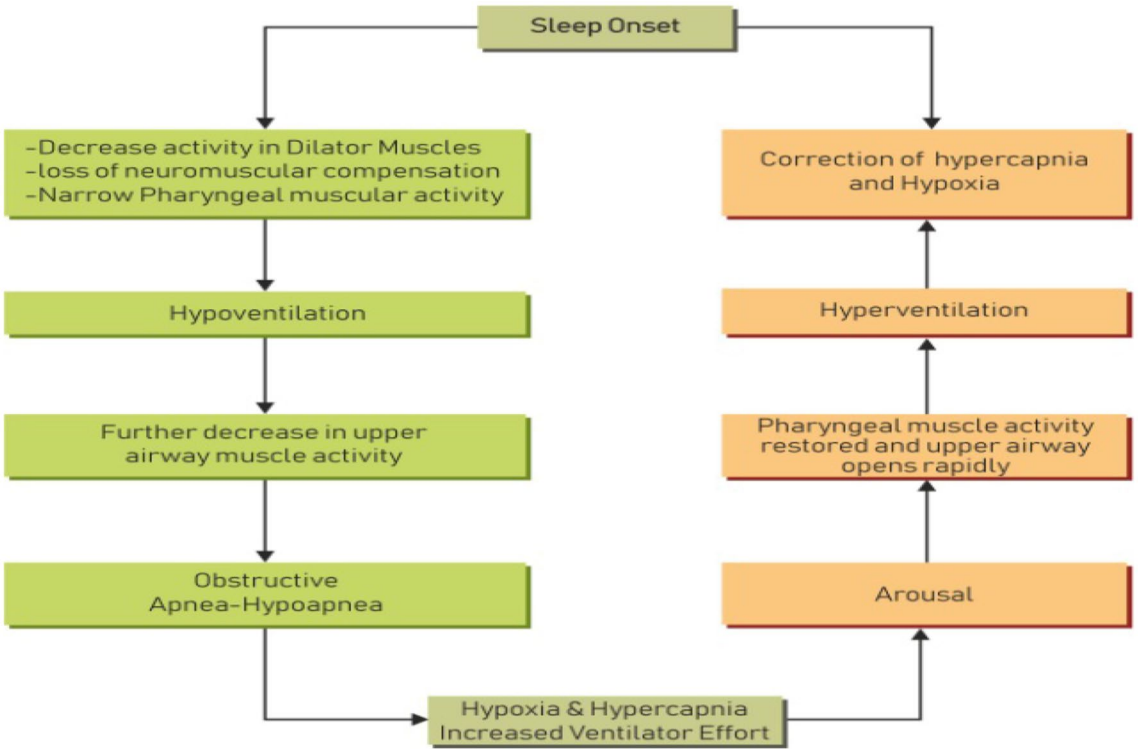

Fig. 2 The diagrammatic representation of pathophysiology of obstructive sleep apnea

in NREM stage more than 5 events [43]. REM OSA shows hypotonia of the muscles involving upper airway leading to obstruction [44]. EOG helps in identification of sleep stage (REM or NREM) by noting activity of electropotential difference between the retina and cornea. EMG is used to measure the muscle tension in chin and jawline region in conditions like bruxism and leg movements in condition like REM behavior disorder. ECG is used to analyze any cardiac abnormalities. In this way PSG helps in diagnosing SBD and its variant.

4 Risk factors for OSA

4.1 Genetic disorders

OSA is genetically transmissible and there are much evidence suggesting genetic contribution towards OSA susceptibility [45]. Genetic factors contribute around 40% of variance in AHI [46]. In relation to snoring, twin studies have shown that monozygotic twins are more prone to habitual snoring than in dizygotic twins [47]. Orofacial birth defects such as Pierre-Robin syndrome and Down syndrome are also cause of OSA. Down syndrome is a chromosomal disorder having enlarged tongue, tonsils and adenoids leading to upper airway obstruction causing OSA [48]. Pierre-Robin syndrome is a genetic mutational disorder in which infant has a retrognathia or micrognathia again leading to OSA [49]. In Marfan syndrome, craniofacial dysmorphisms with lax upper airway muscles leads to OSA [50]. OSA is linked to various loci of the major histocompatibility complex (MHC). The genetic relationship between OSA and obesity is implicated with various genetic markers like HLA-A2, HLA-A33, HLA-B7, B65, B63, B73 [51].

4.2 Anthropometric parameters

4.2.1 Body Mass Index

BMI is convenient to measure but does not identify body composition. Studies have shown BMI with body composition relates more closely with AHI [52]. It is also argued that BMI, age, internal laryngeal circumference and NC are important parameters for OSA [53]. BMI with data on body mass and height, indicates nutritional status in many of the epidemiological studies, until they develop body composition for these surveys [54]. And later on papers on body composition is proven to be superior in OSA prediction in comparison to BMI [52].

Higher BMI values were correlated with lower oxygen saturation, higher apnea–hypopnea index (AHI) and decrease in sleep efficiency. BMI greater than 28 kg/m^2 increases the

risk for OSA in persons around eight to twelve times [57]. Persons with upper body obesity and BMI > 40 kg/m^2 are more at risk of OSA [58]. A study by martin et al. reported that in both genders if BMI is greater than 30 kg/m^2 it is associated with the development of OSA [59]. In Turkish population, soylu et al. showed that BMI over 27.7 kg/m^2 in females and 28.9 kg/m^2 in males is risk factor for developing OSA [60]. Caucasian population is showing BMI for obesity at 30 kg/m^2 but on the other hand Asian populations have obesity at the cut-off value of 25 kg/m^2 [61]. Korean population, shows cut-off values for BMI is around 23.05 kg/m^2 for females and 24.95 kg/m^2 of males [62]. Mostly Asians are having higher percentage of body fat whether it is upper body or middle than the Caucasian of the same of sex, age and BMI [63]. Due to this reason, a percentage of Asian population who are having BMI below the current WHO BMI cut-off value of 25 kg/m^2 are at risk of OSA.

4.2.2 Obesity

Obesity is considered to be one of the major predisposing factors for OSA, so it is relatively important to signify their roles and importance. In around 40% of patients with obesity have severe OSA [64]. A study showed that there is 4–6% more chances of developing OSA with 10% gain in body weight or 6 kg/m^2 rise in Body Mass Index (BMI) [65]. It was seen in patients with OSA, if fat is deposited at specific sites it gets worse. Sites including upper airway, results in decrease in the size of lumen and leading to collapse of upper airway, leading to apnea [66]. In addition, if fat is deposited around the thorax (Abdominal obesity), it reduces chest compliance and lung functional residual capacity and may cause in increase oxygen demand [67]. Obesity in visceral region is common in OSA population [68]. There are many studies based on different population that have documented correlation between apnea–hypopnea index (AHI) and BMI. Obesity is graded on the basis of various anthropometric parameters such as BMI, hip circumference (HC), neck circumference (NC), waist cirumference (WC), waist to hip ratio (W:H), Mallampati score (MS) and thyromental distance (TD) [69–71]. All these factors contribute to OSA and predict its correlation with OSA [69].

4.2.3 Neck Circumference

NC is measured using non-stretchable plastic tape, subject in standing position, measurement is done in the midway of neck, between mid-cervical spine posterior and mid anterior neck. In males there is laryngeal prominence, so it is measured bellow the prominence. NC is more significantly correlated with OSA than any other anthropometric parameters. NC is higher among male than in females [72]. NC is considered to be marker of central obesity, stated by Onat et al. [19]. NC is considered to be gold standard in 1991 for the prediction of OSA in comparison to other factors [55]. Generally NC is the reflection of upper body obesity and is considerably better marker than BMI for OSA [70]. It is stated that neck circumference greater than 43 cm in male and 38 cm in females are at greater risk of OSA [73]. In a study, 11 women out of 13 had NC greater than 38 cm and 7 man out of 12 had NC more than 43 cm [73]. In 2003, NC was considered better marker for AHI measurement [74].

4.2.4 Waist Circumference

Waist circumference (WC) is measured using non-stretchable tape above hip-bones, over the navel region. WC is a type of abdominal obesity defined at 90 cm or more in male and 80 cm or more in female in Asian population whereas in Middle East and Caucasian population it is 94 cm or more in male and 80 cm or more in female [75]. In a study, cut-off value of WC at 94 cm in males and 80 cm in females is considered to be risk factor for OSA [65]. Soylu et al. studied the cut-off value at 105 cm in males and 101 cm for females in Turkish population [66]. Another study reported WC at 88.5 cm for males and 76.5 cm in females is a risk factor for OSA [75]. Although different races have different criteria for abdominal obesity, with western countries have higher WC than Asian countries.

4.3 Hip Circumference And Waist/Hip Ratio

HC is measured with the help of tape at a level parallel to the floor, placing around the widest circumference of the buttocks. HC is directly related with WC, is inversely associated with the levels of blood glucose and blood pressure [76]. HC provide more specific measure for subcutaneous gluteofemoral adipose tissue than WC. It is of greater possibility that larger HC reflects greater muscle mass. A study reported by Manolopolous et al. that there are evidence from in vitro and in vivo studied of adipose tissue, that gluteofemoral fat is protective for our body by collecting excess fatty acids and exposure from high levels of lipids [77]. HC contribution in OSA is more in relation with WC as waist to hip ratio (WHR). The difference between these adverse effects of increased level of WC and the defensive effects of HC on the other may be due to the observation, that most of the pathological influence of adiposity is due to visceral, instead of the superficial fat [78]. There is increase in superficial fat leading to increase in WC and this misleads the real effect of visceral obesity. In this way WHR improves the assessment of adiposity and help in prediction of obesity and its role in OSA [77].

5 Oral anomalies

In population who are non-obese, an orofacial anomaly such as retrognathia and micrognathia lead to OSA [79]. Additional features that may influence to OSA are enlarged palatine tonsils, large uvula, high-arched palate, deviation of nasal septum, increase in anterior facial height, short anterior cranial base, macroglossia, displaced hyoid bone, long soft palate and decrease in posterior upper airway space [80–83]. Airway evaluation to be done by checking condition of tongue size and state, grading of tonsils size to be done by universally accepted standard (Grades 1–4) [84]. Classification predicting severity of airway space for intubation is to be graded 1–4 as the Mallampati score [85]. Nasal conchae hypertrophy was also evaluated as one of the cause for airway obstruction and breathing disorder [86]. A study had demonstrated that increase in BMI with tonsillar hypertrophy and higher mallampati score indicates greater risk for OSAS [86]. Mandibular assessment for the effect of its repositioning, both vertical and horizontal, on the upper airway can be done using a device known as George gauge or wax bite [87]. One more technique termed as acoustic reflexion, which evaluates restriction at airway site and the position of mandible which may be restricting the upper airway [88]. Oral appliance therapy is required for the effective treatment craniofacial anomalies. Many authors have suggested for the mandibular advancement or reposition devices (MRD or MAD), which increases efficacy without giving much problem to patients and any temporomandibular jaw (TMJ) problems [89]. One of the appliances such as Kleerway was very effective in reducing AHI to < 15 per hour in 71% of the patients [90]. Surgical procedures such as uvulopalatopharyngoplasty (UPPP) and uvulopalatopharyngoglossoplasty (UPPGP) are performed to open the upper airway.

6 Conclusion

OSA is highly prevalent in modern day society and often unrecognized by healthcare professionals. The long-term pathophysiologic consequences of OSA results in impaired cardiac functioning, sympathetic nervous system overdrive, proinflammatory effects like increase in Interleukin 6, 8 and endothelial dysfunction. Thus early recognition of abnormal anthropometric parameters in asymptomatic patients or patients with comorbidities such as hypertension, stroke, heart failure, CAD etc. is essential to cut down long term complications of OSA. The anthropometric parameters such as NC, WC and BMI are significantly connected with accumulation of adipose tissue in the upper part of the body, correlated well with severity of OSA syndrome. Physiological and pathological analysis of the upper airway helps in providing insight into this disease and how to prevent. Studies have been carried out in recent past, for the improvement of our understanding in physiological mechanism of OSA. Still more research is required to correlate anthropometric parameters and OSA phenotypes. In this way new groups of patients with different phenotypes will be defined based on anthropometric and pathophysiological traits in order to choose precise management approach (Table 1).

Table 1 BMI criteria as per various health organizations

Body mass indices (BMI)	WHO criteria [55]	Asian Indian criteria [56]
Underweight	< 18.5 kg/m^2	< 18.5 kg/m^2
Normal	18.5–24.9 kg/m^2	18.0–22.9 kg/m^2
Overweight	25–29.9 kg/m^2	23–24.9 kg/m^2
Obese	> 30 kg/m^2	> 25 kg/m^2

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Compliance with ethical standards

Conflict of interest The authors report no conflicts of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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