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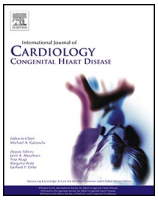

Sleep disordered breathing and adult congenital heart disease

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1. Introduction

During recent decades patients with congenital heart disease (CHD) have benefitted from a substantial improvement in the survival rates at any given age and thus life expectancy [1].

Accordingly for the first time, clinicians responsible for the care of adults with CHD are also challenged with tackling diagnosis and management of acquired comorbid conditions that are associated with reaching an older age. In order to continue improving outcomes for adult congenital heart disease (ACHD) patients, it is key to define the relationship between CHD and such comorbidities. This will enable the identification of modifiable factors and promote the delivery of individualised treatment plans for this patient cohort throughout their lives.

Sleep disordered breathing is one such condition, which is also common amongst those with structurally normal hearts and has an established association with cardiovascular complications as well as impacting quality of life.

1.1. Sleep disordered breathing-an overview

Sleep-disordered breathing (SDB) relates to a wide range of conditions; most commonly it refers to obstructive sleep apnoea (OSA) and central sleep apnoea (CSA), however conditions such as sleep-related hypovolaemia and hypoxemia are also included under this umbrella title [2] (SeeTable 1). These conditions exhibit significant and bidirectional associations with cardiovascular disease [3].

Central sleep apnoea is characterised by recurring episodes of reduced or absent respiratory efforts during sleep [4] with consequent reduced or absent airflow. CSA should be distinguished from conditions which cause obligate hypoventilation, such as neuromuscular diseases for example Motor Neurone Disease. CSA could occasionally be neurological (e.g. in the case of brainstem disorders) but more usually CSA occurs when there is enhanced loop gain in the carbon dioxide (CO_2) homeostasis system in, for example, congestive heart failure [5]. This occurs because the primary stimulus for ventilation during sleep is the partial pressure of carbon dioxide (PaCO2) – detected by central chemoreceptors, which influences the respiratory rate [5]. If PaCO2 levels are above a certain threshold, ventilation is stimulated. In heart failure patients, an exaggerated sympathetic response to hypercapnia [6] is triggered by pulmonary congestion, which activates vagal J-receptors in lung parenchyma [4]. This leads to hyperventilation and a drastic reduction in PaCO2, falling below the threshold necessary for ventilation to be stimulated, resulting in the cessation of breathing [7]. Subsequently, PaCO2 levels rise again, perpetuating a cyclic pattern of hyperventilation and hypoventilation known as Cheyne-Stokes breathing [4]. The delay in detecting hypercapnia by central chemoreceptors is further amplified by the reduced velocity of blood flow in heart failure [8]. A similar mechanism is present in the hypoventilation observed during sudden exposure to high altitude.

On the other hand, obstructive sleep apnoea is a sleep disorder characterised by repetitive partial or complete closure of the upper airway throughout the night, even as respiratory efforts persist against the obstructed airway [9]. A full collapse of the airway leads to an apnoea, while partial collapses result in hypopnea (defined as a flow reduction> 30 %). The pharyngeal airway lacks rigid or bony support [10], making it susceptible to collapse during sleep, primarily due to decreased pharyngeal muscle activity at the onset of sleep [11]. While some degree of airway narrowing is a normal physiological response, certain individuals exhibit a reduced upper airway cross-sectional diameter. This narrowing can result from multiple factors, including anatomical constraints, fat accumulation in obese individuals [12], and, within the context of heart failure, the redistribution of peripheral oedema from the legs to the neck [13]. Airway closure during sleep causes a cessation of ventilation, leading to subsequent hypoxia. The combination of hypoxia and increased respiratory effort against an obstructed airway prompts arousal which if recurrent causes sleep fragmentation and increased sympathetic activation throughout the night [10]; one of the most important cardiac consequences of OSA is loss of the normal nocturnal dip in blood pressure.

Obstructive sleep apnoea exerts numerous pathophysiological responses, which in turn worsen cardiovascular disease, demonstrating the bidirectional relationship between sleep-disordered breathing and

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cardiovascular disease [3].

1.2. Risk factors

In the general population risk factors associated with SDB are age, male gender, and obesity as well as anatomical features such as increased neck circumference and enlarged tonsils or adenoids [3]. The anatomical pattern exhibited by those with far east Asian heritage means that OSA becomes more common at lower body mass indices than those with Caucasian heritage [2].

1.3. Diagnosis

Assessment of sleep disordered breathing includes clinical evaluation of symptom burden and a sleep study. The assessment includes a detailed history on sleep patterns, symptoms of sleepiness, and risk factors. The severity of excessive daytime sleepiness, a common consequence of SDB, is measured using the Epworth Sleepiness Scale [14], although other methods are available where necessary. Physical examination must be conducted to assess the cardiovascular and respiratory systems, BMI, upper airway and neck circumference [15]. Where the ned to screen populations for OSA arises the STOP-BANG questionnaire is useful [16].

A sleep study is conducted to produce the primary diagnostic index used to quantify SDB, the apnoea hypopnea index, expressed as the number of respiratory events per hour of sleep. The classification of SDB severity is stratified as follows [15]:

Mild: AHI 5–15 events/hour Moderate: AHI 15–30 events/hour Severe: AHI >30 events/hour.

Polysomnography (PSG) is the gold standard for the diagnosis of SDB [15], and may yield more precise estimates of AHI since the total sleep time (TST) is measured electroencephalographically. Sleep stage is defined algorithmically using electroencephalogram (EEG), chin electromyogram (EMG) and electrooculogram (EOG) although other parameters notably SpO_2 and electrocardiogram (ECG) are measured. Apnoea/hyponea is measured using nasal airflow and abdominal and thoracic efforts are used to assess whether events are central or obstructive [15].

PSG is used more commonly in clinical research and complex cases; in clinical practice at-home respiratory-polygraphy is more often performed to diagnose SDB. Respiratory-polygraphy reports the SaO_2, pulse rate, nasal air flow and abdominal and/or thoracic efforts [17], but it cannot be used to determine when sleep has started or the stages of sleep directly since there is no EEG signal although some systems attempt to predict this algorithmically using non EEG signals [15]. Pulse oximetry alone can be used to assess hypoxic burden and this may be of value when optimising the care of patients with pulmonary hypertension but in general it has been dropped by most sleep units since it provides a 30 % rate of false negatives.

2. Sleep and cardiovascular disease in structurally normal hearts

It is beyond the scope of this article to describe in detail existing knowledge around sleep and cardiovascular disease in people without CHD, but some general observations may help contextually when thinking about congenital cardiac disease. However, before detailed discussion it is important to note that causality is very difficult to clarify in the clinical environment and some authors use the causality and association somewhat interchangeably. Essentially we see 4 possible inferences from clinical data as shown in Fig. 1, and it can readily be assumed that some clinical questions will never be answered using clinical trial methodology since, for example few patients would consent to enrol in a 20 year trial (which would also be hard to secure funding for) .

OSA is associated with increased risk of a number of cardiovascular comorbidities. The best data come from the sleep heart health study, which was a longitudinal observational study of approximately 5000 north American adults. This study showed an increased risk of both heart failure and coronary artery disease. Demonstration that OSA was a risk factor for heart failure became evident after a median 8.7 years [18], and while a small increased risk of coronary artery disease was apparent at this time point, it became more marked in longer follow up with a mean time to first event of 11.2 years [19]. However, a large randomised trial failed to show a reduction in cardiovascular events when continuous positive airway pressure (CPAP), which is the principal main-stream therapy for OSA, was used of 3 years compared to best usual care (which included lifestyle modification and pharmacological management as recommended by the study participants regular doctors) [20].

OSA is also associated with atrial fibrillation with a 2–3 fold incident risk over 5 years [21] while severe or moderate OSA was present in over half of a cohort of patients with paroxysmal or established AF [22]. Again however CPAP failed to reduce AF burden over a 5 month period [23].

OSA is also associated with pulmonary hypertension, and data from the Mosaic study suggests that OSA may possibly improve right ventricular (RV) dysfunction where present.

Furthermore SDB is also associated with ischaemic stroke as well as poorer neurological recovery after stroke [24,25]. The strongest evidence for the association is related to OSA while the association of CSA and stroke is less well established. The pathophysiological mechanisms

Table 1
Summary of conditions under the umbrella of Sleep Disordered Breathing.

	OSA	CSA	Sleep-related hypoventilation	Sleep-related hypoxemia
Definition	Partial or complete upper airway blockage during sleep.	Lack of respiratory effort during sleep.	A reduced respiratory rate during sleep.	The level of oxygen in the blood is abnormally low during sleep, not due to another sleep-related breathing disorder.
Pathophysiology	Physical obstruction of upper airway	Impaired central respiratory drive or signalling (usually enhanced loop gain)	Reduced respiratory drive, neuromuscular weakness, or increased load; e.g. obesity or lung disease	Impaired gas exchange, often due to respiratory disturbances
Symptoms	Excessive daytime sleepiness, fatigue, insomnia, loud snoring	Cheyne-Stokes pattern, difficulty initiating or maintaining sleep, daytime sleepiness, shortness of breath at night	Excessive daytime sleepiness, fatigue, orhopnea	Excessive daytime sleepiness, fatigue
Risk factors	Obesity, age, male gender, smoking, anatomical features	Congestive heart failure, brainstem pathology, age, male gender	Obesity, age, hypoventilation syndromes, certain medications	Chronic respiratory conditions, obesity, smoking, older age
Polysomnography features	Apneas, hypopneas, increased respiratory effort against an obstructed airway	Absence or reduction of respiratory effort, periodic central apneas	Hypercapnia in a time course corresponding to REM sleep, prolonged periods of low ventilation	Desaturation events - without features of OSA/CSA

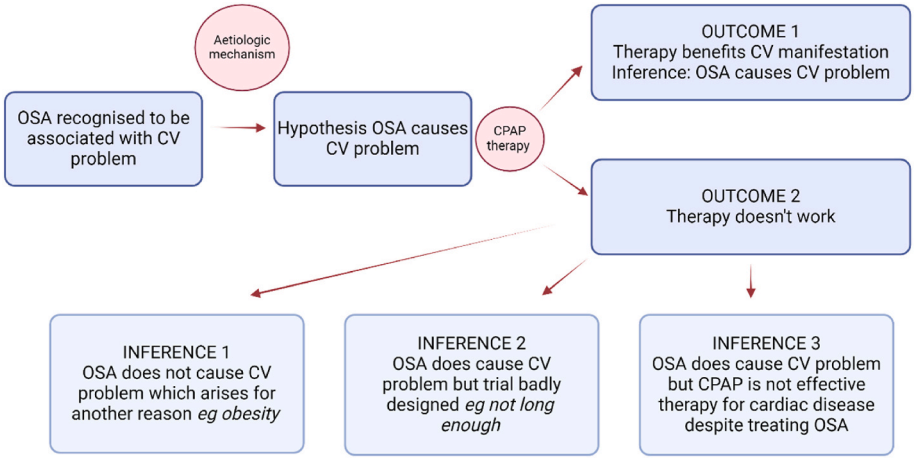

Fig. 1. Inferences made from clinical data showing association between OSA and CV disease.

underpinning this are multifactorial and include vascular impairment secondary to endothelial dysfunction and oxidative stress as well as well as poor cerebrovascular health resulting from reduced oxygenation.

The association between SDB and systemic hypertension is interesting to consider since it is a recognised risk factor for many cardiovascular conditions. Humans, as with other land-based mammals, have a lower blood pressure at night than during the day and OSA is associated with a 'non-dipping' 24-h blood pressure pattern due, it is assumed, to the sympathetic drive associated with arousal. Trials of CPAP have shown that CPAP can reduce blood pressure within one month [26] in patients who are sleepy. Interestingly in patients who are not sleepy, this seems not to be the case, suggesting that arousal may cause both sleepiness and increased sympathetic drive. However, clinicians should be aware that this apparently simple distinction is hard to crystallise in clinical practice; while the Epworth score is commonly used to assess sleepiness (with sleepiness being defined as 10 or more) this is a crude instrument.

3. Sleep and cardiovascular disease in patients with congenital heart disease

The relationship between congenital heart disease and SDB is not as well described as it is in the general population. While the cardiovascular sequelae that affect non ACHD patients are also likely to affect those with CHD, there are concerns that ACHD patients may have specific vulnerabilities in relation to the condition.

The term ACHD is used to characterise a patient cohort with a broad spectrum of structural heart defects of varying complexity. Simple defects may be asymptomatic while complex ones can be life threatening from birth. Each type of lesion has a different effect on the cardiac haemodynamics while any intervention patients receive will itself alter the existing physiology. This results in a very heterogeneous population with unique susceptibilities when it comes to the effects of SDB.

Though describing the intricacies of each type of CHD is beyond the scope of this article there are some subcategories which are important to highlight in the context of SDB due to their specific haemodynamics.

3.1. Cyanotic heart disease

Cyanotic heart disease occurs in a range of complex lesions and is largely due to either obstructive lesions to the pulmonary flow such as pulmonary atresia and/or tetralogy of Fallot or systemic flow such as hypoplastic left heart syndrome, mixing lesions such as truncus arteriosus and lastly in patients with pulmonary arterial hypertension (PAH) and reversal of shunts, such as Eisenmenger Syndrome [27]. Due to the advances in diagnosis and management of cyanotic conditions many children benefit now from reparative surgery and become acyanotic adult survivors [28]. There are, however, patients with unrepaired lesions or those not amenable to repair who receive palliative surgery and still survive into adulthood, albeit cyanotic [29].

Regardless of the underlying lesion, adult patients with cyanotic disease have an increased risk of thromboembolic events. This is due to the effects of chronic hypoxia leading to secondary eythrocytosis and endothelial dysfunction and/or hyperviscosity syndrome [30].

3.2. Univentricular hearts

This category comprises of patients with lesions that result in a functionally univentricular heart and includes hypoplastic ventricles, atretic atrioventricular valves and or pulmonary atresia with intact septum or aortic atresia [31]. They will usually undergo staged palliation surgery resulting in a Fontan circulation. This results in a circulation where systemic venous return is directly connected to the pulmonary artery, in the absence of a subpulmonary ventricle. In order for a Fontan circulation to work it depends on adequate systemic venous return and appropriately low pulmonary vascular resistance to allow for passive flow from the systemic to the pulmonary circulation. In this type of circulation the key determinant to the cardiac output is the preload to the systemic ventricle, with ventricular function playing a secondary role [32].

The Fontan circulation may last for decades but does eventually fail as the chronic effects of non-pulsatile flow to the pulmonary circulation result in remodelling and altered cardiovascular haemodynamics. Patients with Fontan palliation are also at an increased risk of atrial arrhythmias, which increases as they age and contribute to a significant morbidity burden [33].

It is an important group of patients to consider in relation to SDB, as the transpulmonary blood flow is dependent on inspiration, thus even small changes in respiration may have a profound effect on ventricular filling and cardiac output.

4. Overall associations between sleep disordered breathing and ACHD

Several studies have shown that overall there is an increased prevalence of SDB in ACHD, albeit the exact extent is yet unclear. Results show the prevalence of SDB to be between 31 and 77 % in ACHD vs 5–25 % in general [34–36]. The large range in the estimated prevalence in the ACHD population can be attributed to variation in the methodology and patient population in each type of study as diagnostic tools, CHD lesion, and setting i.e. the proportion of outpatient vs inpatients varied between them. However, all studies showed a statistically

significantly increased prevalence.

A study by Cg et al. [35] specifically looking at a patient cohort with the Fontan circulation showed the highest prevalence with 77 % positive for SDB and 36 % with OSA specifically. The study by Miles et al. [36] showed a 59 % prevalence in SDB in patients with pulmonary valve dysfunction suggesting prevalence may differ by lesion, however the study by Momcilovic et al. [34] did stratify the prevalence by ACHD lesion category but did not find any significant difference. Further research to replicate this data is therefore required in order to more accurately calculate the overall risk of SDB and determine whether specific subtypes of CHD have an inherently increase risk.

There is also evidence that there is a younger age of onset of OSA in the ACHD population. The study by Drake et al. [37] had a mean age of 34 years old in the ACHD SDB population which is over a decade younger than the average population at 50 years old [38]. The study by Cg et al. showed that Fontan patients had an even younger average age at 27 years old [35]. This may leave the ACHD population more vulnerable as their life expectancy continues to improve as many of the cardiovascular sequelae worsen in a "dose dependent" relationship as exposure to the altered dynamics of SDB increases over time.

4.1. Risk factors

The studies by Momcilovic et al. and Drake et al. [34,37] also confirmed that established risk factors for the general population are also associated with SDB in the ACHD population. Obesity in particular was showed a positive association in both studies. An overall concerning finding given the levels of obesity in the CHD population have been increasing in recent years in line with the general population in both children and adults [39], although a key factor may also be the reduction in exercise capacity associated with ACHD. It is key to note as it is the only modifiable risk factor for SDB in the ACHD population.

Furthermore, the presence of a genetic syndrome was positively associated with a positive SDB screen. This is important as a significant population of ACHD patients have lesions as part of a syndrome. The reason for this is likely to be the association with craniofacial abnormalities which are common in patients with genetic disorders. Studies have shown patients with a range of genetic syndromes associated with ACHD having a higher risk of OSA. Patient's with Down syndrome have significantly increased prevalence of obstructive sleep apnoea with over 50 % of children screened testing positive [40]. Patients with Marfan syndrome which is associated with aortic arch and aortic valve abnormalities and skeletal deformity also have an increased prevalence of sleep disordered breathing compared to the general population [41,42]. Other genetic syndromes with craniofacial abnormalities associated with ACHD include Turner and Noonan Syndrome [43,44]. There are rare case reports of young onset OSA in both syndromes however larger scale studies to establish an association are lacking.

Having previously detailed the general cardiovascular consequences of sleep disordered breathing above, we can examine how these affect patients with ACHD taking into account the differences between this group and the general population. A summary of the interplay between SDB and ACHD leading to cardiovascular disease can be seen in Fig. 2.

5. Cardiovascular consequences

5.1. Heart failure

Heart failure is the leading cause of mortality in the ACHD population [45,46]. The population is at an increased risk of developing heart failure, and this risk increases with the complexity of the lesion. Heart Failure in ACHD has a more complex mechanism than acquired failure in the general population, and involves an interplay of all or some of the following: volume and pressure overload, cyanosis, myocardial ischaemia, pulmonary and systemic hypertension and rhythm abnormalities [47].

The relationship with SDB is bidirectional. Heart failure is a key risk factor for the development of central sleep apnoea via the mechanism of nocturnal fluid shift affecting chemoreceptors on the respiratory centre of the central nervous system [5], while SDB itself has been shown to increase the risk of heart failure in the general population.

Due to the complexity of ACHD circulations this relationship is less

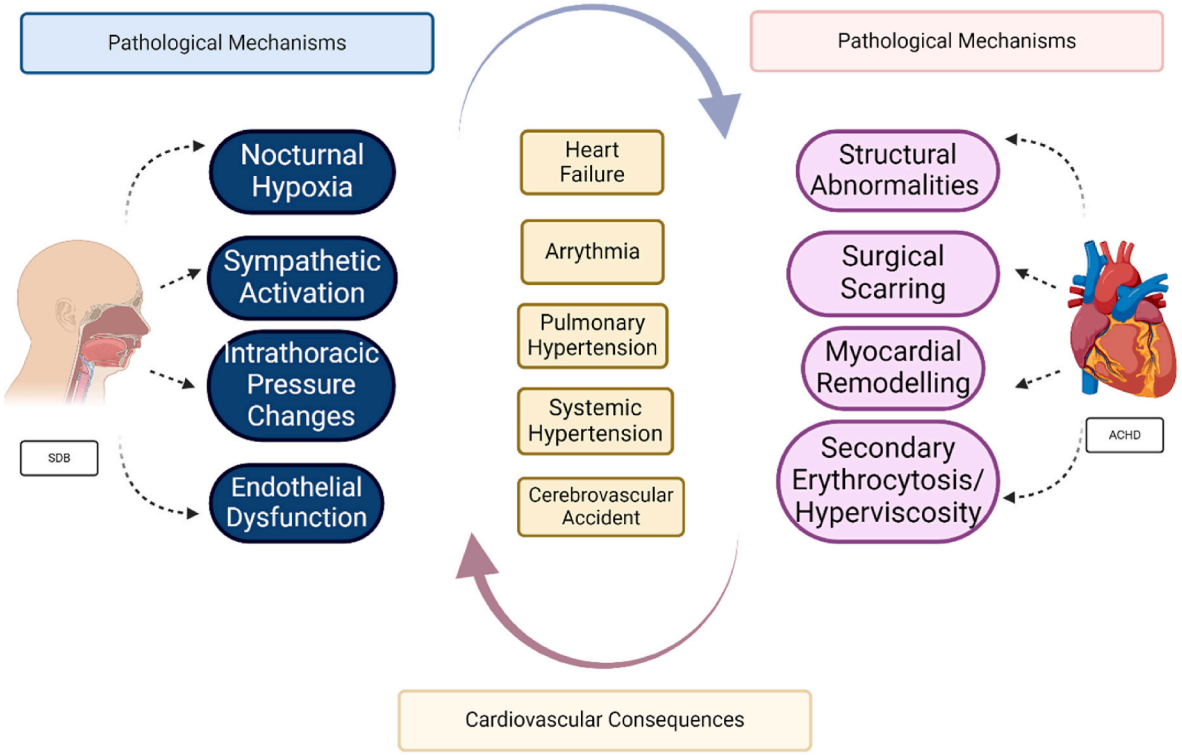

Fig. 2. Interplay between sleep disordered breathing and ACHD leading to cardiovascular disease.

well defined compared to that of acquired left sided heart failure in normal circulations. However, heart failure in both groups results in pulmonary congestion which is has been shown to increase the risk and severity of sleep apnoea. Harada et al. found a positive association between severity of heart failure symptoms and sleep apnoea diagnosis in adults with CHD which lends credence to this theory [48].

SDB is also associated with other cardiovascular conditions as mentioned above, which form part of the mechanism of heart failure in ACHD and may exacerbate the degree of failure in that way.

5.2. Arrhythmia

Cardiac arrhythmias of all types are prevalent in ACHD patients and are a key cause of morbidity and mortality in this population [49]. Though at a cellular level ACHD patients do not differ from the general population the anatomic malformations, the effect of chronically altered haemodynamics and/or postoperative scarring all result in a pro arrhythmogenic substrate.

Both the type of CHD lesion and surgery are associated with different types of arrhythmia. Conduction disturbances are common in patients with CHD leading to atrioventricular node (AVN) displacement or surgical procedures resulting in injury to the area. Sinus arrhythmias are also seen at an increased rate in CHD patients, with the sinoatrial node (SAN) being affected by surgical procedures requiring instrumentation to the superior vena cava such as Glenn and Fontan or more rarely, congenitally absent [50]. Moreover, as patients with CHD grow older the chronic effect of altered circulation and in particular heart failure leads to myocardial remodelling which lead to hypertrophy, fibrosis and dilatation. These patients have an increased risk of both ventricular and atrial arrhythmias. In CHD patients older than 50 the most prevalent arrhythmia is atrial fibrillation [51].

Atrial fibrillation is also the arrhythmia most commonly associated with OSA [22].The studies focusing on the effect on arrhythmias in patients with CHD and OSA are extremely limited, however the study by Drake et al. did examine this. They found a positive association between CHD patients with an implantable cardiac defibrillator (ICD) and a positive OSA screen but did not demonstrate an increased association with atrial arrhythmias [37].

5.3. Pulmonary hypertension

Both CHD and SDB are independently associated with an increased risk of developing pulmonary hypertension [52,53].

Due to the heterogeneity of CHD, the subcategory, onset and severity of PH varies largely. Once again the improved survival of patients with CHD means that the proportion of them who go on to develop PH is also increasing due to the effect of altered haemodynamics on the pulmonary vasculature over time. They now form a growing subgroup of the overall cohort of PH patients with a prevalence of 15.6 per million but are still relatively underrepresented in research.

In the latest iteration of the WHO PH classification we see CHD appearing under multiple groups in an acknowledgement of the complexity of these patients making it difficult to neatly assign them to a single causal category. Furthermore, it is important to consider that as CHD patients age or have surgical interventions they may fit into more than one subcategory of PH and therefore individualised management in CHD patients with PH is crucial [53].

The interface between PH, SDB and CHD is a complex one to unravel. Studies looking into OSA have shown that in isolation it may only result in mild PH. However, the impact of OSA becomes much greater in patients with pre-existing PH. While there is a paucity of data looking at the CHD specific subgroups of PH, studies have looked at the association between OSA and WHO PH category. A study found that while OSA was commonly seen in all PH subcategories it noted that OSA severity was higher in Group 2 PH, the subcategory arising in patients with left ventricular heart failure [54].

While not specific to CHD patients the development of PH in patients with OSA is a poor prognostic factor and negatively impacts both mortality and quality of life.

Patients with univentricular circulations are particularly vulnerable to this. Those who have undergone palliative surgery such as Fontan or bidirectional Glenn's rely on passive, non-pulsatile flow to the pulmonary circulation. Even minimal increase in pulmonary vascular resistance can lead to a failing circulation [55].

5.4. Systemic hypertension

Systemic hypertension is a condition most prevalent in older age and as such has becoming a more prevalent comorbidity the ACHD population as they have started to reach older ages [56].

We should highlight here that there are specific CHD lesions that carry an inherent risk of developing systemic hypertension and at a much younger age. For example, aortic coarctation is associated with developing hypertension both pre and post repair [57], and the geometry of the aortic arch in patients after arterial switch operations is also thought to predispose to increased risk [58]. Additionally, cardiac surgery, which many CHD patients undergo, has been shown precipitate neurohormonal changes which can last years after the procedure and can predispose to hypertension [56].

OSA is a common cause of secondary hypertension in the general population and one linked to treatment resistant hypertension [59]. Data replicated this finding in CHD patients showing that those with positive screen for OSA more likely to have hypertension [37].

It is an important comorbid condition to suspect and treat promptly in order to avoid secondary complications of hypertension, and appropriate management of sleep apnoea ought to be part of the management plan.

5.5. Thromboembolic disease

OSA is a known risk factor for ischaemic stroke in the general population. Patients with ACHD are at an increased risk of thromboembolic events in general and ischaemic stroke specifically. There are varying mechanisms contributing to this depending on the lesion and other comorbidities [60].

Patients with cyanotic disease are particularly vulnerable due to a generalised hyperviscosity syndrome resulting from secondary erythrocytosis and chronic damage to the vascular endothelium [30]. Patients who have received a Fontan palliation are also at an increased risk due to a combination of abnormal blood flow, thrombogenic conduits and low cardiac output with recent studies showing the rate of stroke may be even higher than previously thought due to the high incidence of subclinical infarcts noted on MRI scan [61].

Furthermore, as noted above SDB can contribute to the risk of developing atrial fibrillation, which is common in the ACHD population and is a common cause of ischaemic stroke with embolic aetiology.

The decision to commence anticoagulation in this subgroup of patients with both atrial arrhythmias and CHD with increased prothrombotic risk is done on a case by case basis. Often anticoagulation is commenced even with a low CHA2DS2-VASc score as there is increased risk of embolic stroke due to the nature of their lesion.

While we could not identify any studies looking specifically at the effect on stroke incidence in ACHD patients with sleep disordered breathing, it is nonetheless a concern that OSA will be a further risk factor in an already vulnerable population.

5.6. Lung disease

While the focus of this article is on cardiovascular consequences it is important mention lung disease in the context of congenital heart disease and sleep apnoea. ACHD patients also have an increased prevalence of impaired lung function and in particular reduced Forced Vital

Capacity (FVC). The pathophysiology of this is multifactorial and includes postoperative complications such a phrenic nerve injury leading to diaphragmatic paralysis, and respiratory muscle weakness and pulmonary congestion from congestive cardiac failure. Moreover, such patients may have a stiffer chest wall as a result of surgery especially if there have been pleural complications [62]. While the relationship between restrictive lung disease and SDB is less well described than that with obstructive disease in the so called "overlap syndrome", there is evidence that patients with diaphragmatic dysfunction are at an increased risk of SDB whether this be uni or bilateral [63].

5.7. Management of CHD patients with sleep apnoea

The treatment of Sleep apnoea revolves around lifestyle modification and CPAP. While lifestyle advice alone may suffice in case of mild OSA, it is unlikely to be sufficient in those with moderate to severe disease, and so combination with CPAP is recommended as first line in these patients. Patients with CSA benefit from addressing underlying medical drivers, the key one in this cohort being heart failure. Mandibular advancements splints can be used as a second line option for those with OSA who decline or are unsuitable for CPAP.

It is important to note that while CPAP is an effective way of treating OSA and reducing symptoms, data from the non CHD population shows that not all cardiovascular sequelae improve with CPAP treatment. While hypertension has been shown to improve with CPAP treatment, atrial fibrillation and major cardiovascular events did not [20,23].

Furthermore, when considering CPAP therapy in patients with ACHD and OSA, it is important to consider the effects of positive airway pressure on cardiac haemodynamics. Patients with single ventricle circulations following the Fontan palliation are of particular concern here. As they do not have a sub pulmonary ventricle, transpulmonary flow depends on central venous pressure, normal respiration and the diastolic properties of the single ventricle. There is concern, therefore that by applying CPAP and therefore increasing the intrathoracic and pulmonary arterial pressure, one may ultimately reduce pulmonary flow and thus, cardiac output.

Two teams looked into safe titration of CPAP protocols in Fontan patients. Watson et al. achieved this with careful monitoring of cardiac metrics in a catheter laboratory setting while Boutsikou et al. opted for monitoring with echocardiography [64,65]. Both showed that CPAP can be used safely and effectively in Fontan patients, though careful monitoring is required in order to set up safe protocols in these patients.

5.8. Discussion and recommendations

It is clear that the potential consequences of SDB are far reaching in the ACHD patient cohort as they are at risk of developing cardiac and systemic complications at a relatively young age. Furthermore, ACHD appears to be a patient group at risk of developing SDB at a younger age, thus any additional risk factors such as obesity must be eliminated.

ACHD physicians and patient alike must be aware that SDB is a comorbid condition that may develop as they grow older. Diagnosis may be challenging in this population, particularly in those with more complex disease as the symptoms of fatigue and daytime somnolence are not uncommon amongst them. Therefore, suspecting and investigating for SDB when patients report early symptoms is recommended.

Screening with tools such as the STOP BANG questionnaire or Epworth Scale is advisable but it is important to note they have not been reviewed for sensitivity in ACHD to date. For patients with additional risk factors such as craniofacial differences or obesity, referral for sleep disordered breathing assessment may be prudent regardless of score.

While many risk factors were linked to SDB in this group, there was one key modifiable one: obesity. This adds further support to the current preventive strategy in the CHD population which revolves around encouraging patients to remain slim and physically active. Overweight CHD patients with SDB should be referred to the appropriate teams including dieticians and weight loss services in order to receive the best support and optimise their chances of successful and sustained weight loss. The recent licencing of GLP-1 receptor agonists for weight management in patients with a BMI of over 27 kg/m2 is a novel treatment option to consider in conjunction to lifestyle management. In patients with known cardiovascular disease the use of GLP-1 agonism for weight loss also showed a significant reduction in major cardiovascular events, adding a further benefit to consider in this patient cohort [66].

Education for patients and relatives to be aware of symptoms of sleep apnoea and reporting these to their ACHD team is key for early screening and diagnosis in order to minimise the risk of developing the above complications associated with SDB.

When an ACHD patient is diagnosed with SDB it is paramount to take into account the underlying lesion and address any specific consequences they may be particularly vulnerable to. For example increased risk of thromboembolic disease in those with cyanosis or increased risk of early heart failure in those with univentricular hearts.

It is also important to note that adequate heart failure management may reduce the risk and severity of central sleep apnoea, though as the mechanism of failure in complex CHD patients differs from acquired failure, specific studies investigating the association are required.

When it comes to treatment with CPAP a joint approach between the Sleep and Ventilation and ACHD teams should be sought, particularly in those patients whose circulations may destabilise with the application of positive airway pressure who may require titration of settings in a monitored environment.

Disclaimer

"M. Gatzoulis is an Editorial Board Member of the International Journal of Cardiology Congenital Heart Disease and played no role in the Journal's evaluation of the manuscript".

CRediT authorship contribution statement

M. Vakali: Writing – review & editing, Writing – original draft, Conceptualization. **M. Memon:** Writing – review & editing, Writing – original draft. **M. Gatzoulis:** Writing – review & editing, Supervision, Conceptualization. **M. Polkey:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Michael I. Polkey reports a relationship with Philips Respironics Ltd that includes: consulting or advisory. Co-Author Michael A. Gatzoulis - Editor in Chief of International Journal of Cardiology Congenital Heart Disease If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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