Sleep Disordered Breathing and Heart Failure and the Role of Pacing and Cardiac Resynchronization Therapy

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MIU ET AL.: ***Sleep Disordered Breathing and Heart Failure and the Role of Pacing and Cardiac Resynchronization Therapy.*** *At least 20% of hospital admissions among persons older than 65 are due to heart failure (HF).[1] In 1993, there were 875,000 hospitalizations in the United States with the first listed discharge diagnosis as HF, and about 2.5 million had it listed as an associated condition.[2] Approximately 60 percent of health care expenditures for HF were for hospital care. There were three million office visits annually for HF at a cost of 3 billion dollars per year. Despite the advances of pharmacological therapies, revascularization procedures, device therapies and meticulous cardiac surgical techniques in the last decade, the short and long term mortality of this condition remains high. In the population based sample from the Framingham Heart Study, the one year mortality among men and women was 28 percent and 24 percent and five year mortality was 59 percent in men and 45 percent in women respectively.[3] Unfortunately, much of our understanding and management of heart failure have been focused on while the patient is awake. Relatively little attention is paid to the pathophysiological sequelae of heart failure that occur nocturnally. "Nocturnal" management of heart failure may have an important impact. The purpose of this article is to review the pathogenesis and management of heart failure through management of sleep related breathing disorder. (J HK Coll Cardiol 2006;14:6-15)*

Central sleep apnoea, heart failure, obstructive sleep apnoea

摘要

在年齡大於65歲的住院病人中有至少20%是由於心力衰竭所導致的[1]。1993年在美國有875,000病人出院的第一診斷是心力衰竭，還有2,500,000病人被認爲有相關病症[2]。大約60%的心力衰竭的健康照料支出是花費在醫院中的。每年大約有3,000,000的病患需要醫治，而醫療費用大約在30億美金。儘管在過去的十年間藥物治療、血管再通療法、導管治療和心臟外科技術有很大的進步，但是心力衰竭的近期和遠期死亡率依然很高。基於Framingham心臟中心的病例樣本調查，男性病人和女性病人的一年死亡率爲28%和24%，五年死亡率爲59%和45%[3]。不幸的是，很多我們對於心力衰竭的理解和治療集中病人清醒的時候。相對而言，很少將注意力放在心力衰竭易發生於夜晚這一病理生理結局。而對心力衰竭的“夜間”治療有著重要影響。本文的目的在於回顧心力衰竭的發病機制，以及通過治療睡眠相關呼吸困難的處理方法。

關鍵詞：中央睡眠窒息　心力衰竭　梗阻性睡眠窒息

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Clinical Features and Diagnosis of Sleep Disordered Breathing

Though sleep disordered breathing (SDB) has been described for almost two hundred years ago, it was not until 1965 when Gastaut and co-workers provided a more comprehensive and scientific description of this disease entity.[4] They simultaneously recorded sleep electrophysiologically and breathing in a patient with the "Pickwickian syndrome" and characterized different types of apnoea. They also postulated that the sleepiness was due to the repetitive arousals associated with the resumption of breathing that terminated apnoeic events.

Two forms of sleep disordered breathing (SDB) are now recognized: obstructive sleep apnoea (OSA) and central sleep apnoea (CSA). In the former, episodes of apnoea or hypopnoea occur during sleep as a result of airway obstruction at the level of the pharynx. During the period of airflow obstruction, the inspiratory effort of breathing increases substantially which leads to dysynchrony of thoracoabdominal movement. OSA is usually associated with symptoms like loud snoring, restless sleep, nocturnal dyspnoea, headaches in the morning, and excessive daytime sleepiness. On the contrary, the breathing disorder of CSA is characterized by complete or partial withdrawal of central respiratory drive to the muscles of respiration during sleep. Thoracoabdominal respiratory movement however remains in phase.

Polysomnography is the "gold standard" diagnostic tool for assessing SDB. Measurement of several sleep parameters allows diagnosis of the type of SDB and its severity. The apnoea-hypopnoea index (AHI) – the number of obstructive events per hour – is the most commonly used measurement to quantify OSA: mild OSA - 5 to 15 events/h; moderate - 15 to 30 events/h; and severe - 30 events/h.[5] A "negative" polysomnographic study does not exclude mild OSA, however, because there is night-to-night variability in the occurrence of obstructive events.

There is no consensus on the cut-off AHI value in the diagnosis of sleep apnoea in the scientific community. From most of the medical literature, the diagnosis of sleep apnoea is generally based on the demonstration of an AHI of 10-15/hr.[6,7] If the apnoeic episode occurs together with one or more symptoms of snoring, restless sleep, morning headaches, and excessive daytime sleepiness, it constitutes a sleep apnoea syndrome (SAS). To differentiate whether the apnoeic or hypopnoeic events are obstructive or central in nature, current standards for PSG require the simultaneous monitoring of sleep structure, cardiac rhythm, oxyhaemoglobin saturation, and respiration using noninvasive means such as respiratory inductance plethysmography.[5]

Epidemiology of Sleep Disordered Breathing in the Normal Population

OSA is the most common form of SDB, affecting thousands of patients each year alone in the U.S.[1] Initial descriptions of OSA were of severe apnoea in obese, middle-age male patients.[8,9] It now becomes apparent that clinicians are recognizing OSA in their patients with increasing frequency. In the US, there was a 12-fold increase in the annual number of patients diagnosed with sleep apnoea between 1990 and 1998, from 108,000 to over 1.3 million.[10]

All studies have shown that OSA is a common disorder that represents a huge public health problem.[11] A large prevalence study in state employees found that undiagnosed sleep disordered breathing "is prevalent and has a wide range of severity in middle aged women and men".[12] In this study, 9.1 percent of men and 4.0 percent of women had apnoea/hypopnea indices of 15 or more events per hour.

The reported prevalence of OSA is variable depending on the methodology used. However, three large-scale studies using polysomnography have reported similar prevalence estimates for OSA.[13-15] The Wisconsin Sleep Cohort Study showed that 25% of middle age men and 10% of middle-age women had SDB (AHI 5/hr), with 4% of men and 2% of women also having hypersomnolence, fulfilling the current diagnostic criteria for the sleep apnoea syndrome. In Hong Kong, a community-based study of sleep apnoea among 784 middle-aged (age 30-60) men in Hong Kong using full PSG estimated the prevalence of OSA

syndrome (AHI >5/hr and excessive daytime sleepiness) to be 4.1%.[16] On the other hand, using the similar methodology and diagnostic criteria, the same group of researchers showed a lower prevalence of OSA syndrome (2.2%) among the female cohort.[17] In both men and women, body mass index (BMI) and age are two independent risk factors of SDB among both gender.

Epidemiology of Sleep Disordered Breathing in Patients with Heart Failure

Obstructive Sleep Apnoea (OSA)

In the Sleep Heart Health Study, comprising 6424 men and women, the presence of OSA (defined as AHI >=11/hr) conferred a 2.38 relative increase in the likelihood of having HF, independent of other known risk factors.[18] In the 2 largest case series of patients with HF undergoing polysomnography, OSA was diagnosed in 37% of 450[19] and 11% of 81[20] subjects studied. The prevalence of OSA was greater in men (38%) than in women (31%).[19] Risk factors for OSA differ between men and women; the main risk factor in men is obesity, whereas in women it is older age.

Central Sleep Apnoea (CSA)

Data regarding the prevalence of CSA in heart failure is sparse. In the largest studies involving 450 and 81 patients respectively, the reported prevalences of CSA were 33% and 40%.[19,20] The principal risk factors for CSA are male sex, hypocapnia, atrial fibrillation, and increasing age, but not obesity. For reasons that remain to be elucidated, CSA is rarely seen in women with HF.

Effect of Sleep on Cardiovascular Physiology

The stage of non-rapid eye movement (NREM) sleep, which constitutes approximately 85% of total sleep time is a quiescent period for the cardiovascular system. Metabolic rate, sympathetic nervous system activity, heart rate, cardiac output, and peripheral vascular resistance decrease,[21,22] whereas the vagal tone rises.[23] On the contrary, episodic surges in sympathetic discharge, heart rate, and blood pressure occur in rapid eye movement (REM) sleep. However, since an average human being spends about 85% of sleep in NREM stage, the average blood pressure and heart rate during sleep remain below waking levels.[21]

Pathophysiology and Impact of OSA in Heart Failure

OSA exerts its effect in the progression and perpetuation of heart failure in four major aspects: Mechanical, haemodynamic, humoral and vascular endothelial effects.

Mechanical

During sleep, there is reduced tonic input to upper airway muscles, diminished reflexes that protect the pharynx from collapse and reduced load compensation. In subjects with normal pharyngeal anatomy, the partial withdrawal of pharyngeal dilator muscle tone that accompanies the onset of sleep is insufficient to cause pharyngeal collapse. The preponderance of evidence indicates that the pharynx is abnormal in size and/or collapsibility in patients with OSA. This together with the potential mechanism of increase in soft tissue oedema during supine position in patients with heart failure puts their airway at high risk of occlusion at the onset of sleep.[24]

Hemodynamic

As a result of the mechanical airway obstruction, the ineffective inspiratory effort to open up the collapsed airway dramatically reduces the intrathoracic pressure. This causes an increase in left ventricular transmural pressure which leads to an increase in afterload[25] as well as impairing the relaxation of the ventricle.[26] Moreover, the augmented venous return to the right ventricular tends to exert its pressure effect to the left ventricle via the interventricular septum, potentially jeopardizing left ventricular filling and stroke volume.[27]

Neurohumoral

Activation of the sympathetic nervous system, by both hypoxia and arousal, may induce tachycardia and peripheral vasoconstriction, further increasing

ventricular afterload. During apnoea, the reflex arising from pulmonary stretch receptors that suppresses central sympathetic discharge during normal breathing ceases, disinhibiting central sympathetic outflow. The ensuing hypoxia and hypercapnia further enhance sympathetic activity by stimulating peripheral and central chemoreceptors.[28,29] The resulting vasoconstriction raises peripheral resistance, whereas increased cardiac sympathetic stimulation causes tachycardia and reduces heart rate variability.[30] Even though sleep arousal at the end of obstructive apnoea encourages the resumption of airflow by increasing pharyngeal dilator muscle tone,[27,31] the ensuing excitatory input from cortical centers will cause a further release of sympathetic discharge together with a loss of vagal tone.[21,32] In severe OSA, these cycles of apnoea and arousal can repeat several hundred times each night, exposing the heart and circulation to great fluctuations in central sympathetic activity, blood pressure, and heart rate. Worse yet, the adverse effects of obstructive apnoea on the cardiovascular system can be carried over to daytime. As shown by two investigators, daytime sympathetic nervous activity and systemic blood pressure are increased in patients with OSA.[32,33] Though the mechanism for this is not entirely clear, the episodic apnoea-related hypoxia may be contributory, as hypoxia causes sympathetic activation and blood pressure elevations that persists after removal of the hypoxic stimulus.[33-35]

Vascular Endothelium

Suppression of nitrous oxide (NO) in subjects with OSA was first demonstrated by Ip et al.[36] Moreover, they also showed that the phenomenon can be reversed with the use of nocturnal continuous positive airway pressure (CPAP). Their findings offer support for NO being one of the mediators involved in the acute hemodynamic regulation and long-term vascular remodeling in OSA. Reactive hyperemic blood flow and vascular conductance after forearm arterial occlusion were attenuated in patients with OSA compared with control subjects.[37] After treatment of OSA by CPAP, reactive hyperemic blood flow and vascular conductance increased in association with a reduction in sympathetic nervous system activity. Compromised endothelially mediated vasodilatation in the setting of increased sympathetic vasoconstrictor discharge would predispose patients with OSA to the development of hypertension.[38]

Progression into Heart Failure – The Final Common Pathway

In summary, the aforementioned potential mechanisms in OSA probably interact with one another in the pathophysiology of heart failure, putting extra burden on the already failing heart. OSA increases left ventricular (LV) transmural pressure (i.e., afterload) through the generation of negative intrathoracic pressure and elevations in systemic blood pressure secondary to hypoxia, arousals from sleep, and increased sympathetic nervous system activity (SNA).[39] Apnoea also suppresses the sympathetic inhibitory effects of lung stretch receptors, further enhancing SNA. The combination of increased LV afterload and tachycardia secondary to increased SNA increases myocardial oxygen demand in the face of a reduced myocardial oxygen supply. These conditions predispose a patient acutely to cardiac ischaemia and arrhythmias, and chronically could contribute to LV hypertrophy and, ultimately, failure. The resultant fall in stroke volume will further increase SNA.

Pathophysiology and Impact of CSA in Heart Failure

Cheyne-Stokes respiration (CSR) with central sleep apnoea (CSA) [CSR-CSA] is a breathing disorder seen in patients with advanced congestive heart failure. It is characterized by the presence of central apnoeas and hypopnoeas, alternating with periods of crescendo-decrescendo pattern of ventilation with each swing of ventilation terminating in apnoea.[40,41] Although controversial, most authorities believe CSA-CSR is a consequence of HF as it can be partially reversible after optimal treatment of heart failure.[42] Whether CSA is simply a reflection of a failing heart with elevated left ventricular filling pressures, or whether, for the same degree of cardiac dysfunction, CSA exerts unique and independent pathological effects on the diseased myocardium is debatable.[39,43]

While many mechanisms may be contributory to the pathogenesis of CSA-CSR in heart failure, three

parameters have been shown to correlate with the presence of CSA-CSR and associated central sleep apnoea (CSR-CSA): hyperventilation/hypocapnoea, upper airway irritability and proongation of the circulation time.

Hyperventilation

Hyperventilation with hypocapnia (respiratory alkalosis) is a characteristic feature of some patients with moderate to advanced HF. It is thought to result from pulmonary congestion and the subsequent irritation of pulmonary vagal stretch receptors leading to hyperventilation. Central apnoea is usually initiated during sleep by a further acute increase in ventilation and reduction in $PaCO_2$ that is triggered by a spontaneous arousal.[44] When arterial CO_2 ($PaCO_2$) falls below the threshold level required to stimulate breathing, the central drive to respiratory muscles and airflow cease, and central apnoea ensues.[44-46] Several groups tested the hypothesis that hypocapnia was an important determinant of CSR-CSA in patients with HF. Two observations are consistent with this hypothesis. In two studies, patients with HF and CSR-CSA were compared to those without CSR-CSA.[44,45] There were no differences in ejection fraction, PaO_2, mean nocturnal oxygen saturation (SaO_2), or lung to ear circulation time between the groups. In addition, neither group had significant awake nor sleep-related hypoxemia. However, $PaCO_2$ (33 versus 38 mmHg) and mean sleep transcutaneous PCO_2 (33 versus 43 mmHg) were below normal and were significantly lower in the patients with CSR-CSA. Raising the nocturnal PCO_2 markedly attenuated or abolished the clinical expression of CSR-CSA. In one report, for example, constant inhalation of three percent CO_2 in six patients with severe HF increased the $PaCO_2$ by four to five mmHg and virtually eradicated CSA-CSR duration as a percentage of total sleep time was reduced from 62 percent to 2.2 percent).[47] A similar benefit can be achieved by raising the nocturnal PCO_2 with continuous positive airway pressure[48] or the administration of oxygen.[49]

Upper Airway Irritability

As discussed previously in the section of the pathophysiology of OSA towards HF, OSA could be present in up to 37% of HF subjects.[19] The presence of OSA in the setting of CSA-CSR can exert additional adverse hemodynamic burden to a patient with a failing heart, further compromising cardiac output and enhancing the occurrence of arrhythmic events.

Prolongation of Circulation Time

Patients with CSR-CSA do not respond normally to changes in PaO_2. This is probably due to prolongation of the circulatory time which is characteristic of HF and which correlates strongly to the length of the CSA-CSR cycle; the period of time of hyperventilation and apnoea increases as the circulation time increases.[44,50] And that probably reflects delayed transmission of changes in arterial blood gas tensions from the lungs to the chemoreceptor which leads to a marked increase in the oscillation around the set point. Hence, the prolonged circulation time in HF is contributory to the development of the Cheyne-Stokes respiratory pattern.

Clinical Importance CSA-CSR and its Potential Role in the Progression of HF

CSR-CSA is important clinically because its presence in HF patients has been associated, in a severity-dependent manner, with elevations of sympathetic nervous activity which is an important predictor of HF progression, arrhythmias, and mortality.[51-53] Most importantly, CSR-CSA was shown to be an independent prognostic marker in heart failure.[40] Using AHI as an indicator of the underlying severity of CSR-CSA, Lanfranchi et al showed that patients with AHI >= 30/hr had high cardiac mortality at 30 months. In the same study, the left atrial (LA) area was another independent prognostic marker of adverse cardiovascular outcome.[40] Those patients with the highest risk is identified by a combination of AHI >30/hr and LA >25 cm^2. Successful treatment of CSR by CPAP leads to a significant reduction in sympathetic nervous activity[51] and may reduce mortality rates by up to 40% in patients with CHF and CSR-CSA.[54] Since CPAP has beneficial effects on cardiac function (independent of its effect on CSR), it remains unclear whether CSR-CSA is a result of a failing heart or a major contributor of poor outcomes of patients with HF.

Impact of a Hyperadrenergic State in CSA-CSR in HF

Unlike OSA, no negative intrathoracic pressure is generated during central apnoeas.[43,44] Intuitively, the effect on afterload is less than in OSA. Hence research focus has been directed towards the hyperadrenergic effects of CSA as the mechanism for disease progression. Compared with HF patients matched for ejection fraction and other clinical characteristics but without sleep-related breathing disorders, those with CSA have higher urinary and circulating norepinephrine concentrations during both sleep and wakefulness.[51] The magnitude of these increases is proportional to the frequency of arousals from sleep and the degree of apnoea related hypoxia. Most importantly, the degree of sympathetic activity can be modified upon initiating appropriate heart failure treatment.[42]

Miscellaneous Mechanisms Implicated in the Progression of HF in the Presence of CSA-CSR

CSA-CSR leads to cyclical oscillations in heart rate and blood pressure through mechanisms similar to those described for OSA: hypoxia, arousals from sleep, and adrenergic activation.[55] Similar adverse effect on the cardiovascular system can be exerted by direct cyclic activation of cardiovascular sympathetic neurons by respiratory neurons in the brain stem.[56,57] The presence of cyclical oscillations in heart rate was shown to link with a higher mortality rate in heart failure subjects.[58,59]

Treatment of Obstructive Sleep Apnoea in Heart Failure

Weight loss is a cornerstone of therapy for obese subjects, not only by reducing AHI, but also modifies other traditional cardiovascular risk factors such as hypertension, abnormal lipid metabolism, and insulin resistance. For patients with a normal BMI, severe OSA at diagnosis, or those having difficulty in losing weight, specific treatment of OSA, such as nasal CPAP or an oral appliance will be needed. On the other hand, pharmacological agents is largely ineffective in reducing the severity of OSA.[59]

Abolition of OSA by CPAP in patients with HF prevents recurrent hypoxia, reduces nocturnal blood pressure and heart rate,[60] and increases arterial baroreflex sensitivity.[61] In addition, two recent randomized controlled studies had shown favourable hemodynamic effect as well as significant improvement in left ventricular systolic function in patients with heart failure and OSA.[62,63] The study by Kaneko et al which involved 24 subjects on optimal anti-heart failure regime with left ventricular ejection fraction (LVEF) of 45% or less, treatment of coexisting obstructive sleep apnoea by continuous positive airway pressure reduces systolic blood pressure and improves left ventricular systolic function (LVEF 25.0±2.8 increase to 33.8±2.4% ($P<0.001$) after one month of treatment.[62] Though the results were encouraging, their follow-up period was short and whether there is any carry over effect of the CPAP after withdrawal of treatment was not performed. In a similar study which had a longer period of follow-up (3 months), Mansfield et al. showed that treatment of OSA among patients with HF leads not only to improvement in cardiac function but changes in sympathetic activity. The favourable cardiovascular outcome after CPAP is probably achieved by a combination of increase in heart rate variability, reducing oxygen demand, increasing oxygen supply, blunting of the sympathetic outflow and its vagal modulation which[64] is analogous to the chronic effects of beta-blockade in HF.[65] Although these short-term results are encouraging, there remains a need for randomized trials to determine whether the specific treatment of OSA in HF will improve long-term morbidity and mortality.

Treatment of Central Sleep Apnoea in Heart Failure

Pharmacological Measures

The principal reason for treating CSA is the potential to improve cardiovascular function, quality of life, and longevity.[51,52] Currently, there is no consensus as to whether CSA should be treated, and if so, what optimum therapy of CSA in HF might be. As discussed previously, CSA-CSR is to some extent a manifestation of advanced HF, the first consideration is to optimize drug therapy. Aggressive diuresis to lower cardiac filling

pressure along with angiotensin-converting enzyme inhibitors and beta-blockers may reduce the severity of CSA-CSR.[66] Excessive diuresis , however, can lead to metabolic alkalosis which may predispose to CSA-CSR by narrowing the difference between ambient $PaCO_2$ and the $PaCO_2$ threshold for apnoea.[67-69] Beta-blockers may also reduce the adverse effects of excessive sympathetic activation that is associated with CSR-CSA. Should CSR-CSA persist despite aggressive medical therapy for HF, other interventions may be considered like nocturnal oxygen supplement and CPAP.

Continuous Positive Airway Pressure (CPAP)

Via similar mechanism, HF patients with CSA-CSR and elevated LV end-diastolic pressure, CPAP decreases LV afterload by increasing intrathoracic pressure, augments stroke volume,[43] and reduces cardiac sympathetic activity.[44] It also decreases preload by impeding venous return and reducing right and left ventricular end-diastolic volume.[45] In patients with CSA-CSR, short-term application of CPAP also reduces the frequency of ventricular ectopic beats.[46] which may reduce the chance of occurrence of lethal arrhythmias. A randomized trials of 3-months' duration have demonstrated that nightly application of CPAP increases LV ejection fraction, reduces mitral regurgitation and nocturnal and daytime sympathetic nervous system activity, and improves quality of life.[48,70,71]

There is also randomized data showing the beneficial effect of CPAP on cardiovascular mortality in HF subjects with CSR-CSA. Sin et al[54] have shown that of 29 patients with HF and CSA who received CPAP, those who were complaint to CPAP experienced a significant reduction in the combined rate of mortality and cardiac transplantation over a 5-year period. A larger, long-term, multicenter trial to test the effects of CPAP on the combined rate of mortality and cardiac transplantation in HF patients with CSA-CSR (the CANadian Positive Airway Pressure trial for patients with congestive heart failure and central sleep apnoea [CANPAP]) is recently reported. Two hundred and fifty-eight patients with HF and ejection fraction of 24.5± 7.7% and significant AHI of 40±16/hour were randomized for 2 years with CPAP or no CPAP. At 3 months, CPAP significantly improved apnoea and hypopnoea, nocturnal oxygenation, norepinephine level, ejection fraction and distance walked over the control group. However, there is no overall difference in quality of life, number of hospitalization and survival and need of transplantation.[72] It is therefore likely that CSA is a manifestation of poor heart function. While correction of CSA may improve cardiac and general function, there is no impact on the prognosis of HF itself.

Effect of Pacemaker and Device Therapy on Heart Failure Patients with OSA and CSA

First reported in 2002, the study by Garrigue et al[73] has generated much discussion about the role of pacemaker in the management of OSA and CSA in HF. In his randomized trial, the effect of atrial overdrive pacing on sleep apnoea in subjects without a history of HF but had cardiac pacemakers implanted because of symptomatic bradyarrhythmias was tested. Sleep studies were performed, and among those found to have sleep apnoea, the pacing rate was increased to 15 bpm above the intrinsic heart rate. This overdrive pacing led to a reduction in the frequency of both central and obstructive apnoeas by approximately 50%. The study period was short. Moreover, the mechanism responsible for this effect was not determined. One possibility is that some of these patients may have had pulmonary congestion while in the recumbent position owing to their bradyarrhythmias, or possibly diastolic dysfunction. This may have stimulated hyperventilation and predisposed to CSA. Overdrive pacing could have augmented cardiac output and relieved pulmonary congestion, thereby dampening respiratory controller gain, reducing ventilation, increasing $PaCO_2$, and reducing central apnoeas and hypopnoeas. This mechanism would explain a reduction in central but not obstructive events. If upper airway oedema accumulated while the patient was in the recumbent position,[39,74] augmentation of cardiac output by overdrive pacing could have alleviated this oedema and increased pharyngeal luminal dimensions.

The beneficial effects of overdrive pacing on sleep apnoea have been re-tested in a recent study.[75] In 16

patients with severe OSA and normal ejection fraction, atrial overdrive pacing at 15 bpm over the baseline heart rate had no significant effect on OSA, both acutely and when re-examined at one month, whereas CPAP had a significant effect. It follows that pacing in patient with SDB and normal LV function cannot improve OSA.

Cardiac resynchronization therapy using biventricular pacing is now an established therapy for HF.[76,77] There is an improvement in ejection fraction, exercise capacity, functional class and survival. By improving HF, CSA was reported to be reduced.[78] In this study, 14/24 patients with significant CSA (AHI >5/h) after cardiac resynchronization therapy had reduced AHI from 19.2±10.3 to 4.6±4.4/h, P<0.001) and improved Pittsburg sleep Quality Index. However, in those without CSA, resynchronization therapy has no impact on sleep apnoea and quality of sleep. Thus resynchronization therapy has a distinct role in heart failure patients in which CSA is a significant problem.

Conclusion

SDB is common in the general population and in patients with HF. Treatment of OSA significantly improves cardiovascular risk factors, although improvement in clinical endpoints have yet to be proven. In patients with HF, the role of treatment of CSA using CPAP does not affect survival, but overall well being is improved. Simple pacing therapy is probably not useful for sleep apnoea. Cardiac resynchronization therapy has a distinct role in improving SDB resulting from, or associated, with HF.

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