Introduction

Poor sleep is among the most frequently reported symptoms among patients with heart failure (HF) and is experienced by many as 75%. Factors that contribute to poor sleep in this population are multidimensional and may include demographic characteristics (gender, aging), the pathophysiology of HF, comorbid health problems (e.g., pain, depression), symptoms of HF (e.g., dyspnea), medications, and primary sleep disorders. Sleep disordered breathing, including Cheyne Stokes Breathing-Central Sleep Apnea (CSB-CSA) and Obstructive sleep apnea (OSA), are common among patients with heart failure (HF) and contribute in important ways to cardiac dysfunction. However, many HF patients also report chronic insomnia (difficult initiating or maintaining sleep or wakening too early in the morning, accompanied by daytime dysfunction), and periodic limb movements during sleep may also be more common among HF patients.

Sleep disorders may occur individually or in combination and may result in exacerbation of cardiovascular disease, increased mortality, and negative consequences for
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daytime functioning, and quality of life. The purposes of this article are to review the epidemiology, risk factors, pathophysiology, and consequences of sleep disorders among patients with HF and to discuss the assessment and treatment of sleep disorders in these patients.

SLEEP-DISORDERED BREATHING

The two most common forms of sleep disordered breathing common among patients with HF are Cheyne-Stokes breathing/Central Sleep Apnea (CSB-CSA) and Obstructive Sleep Apnea (OSA). It is estimated that more than 50% of HF patients have one or more forms of SDB. The former is thought to be a consequence of HF, while the latter may contribute to the development of HF. Both may contribute to poor cardiac function, morbidity, mortality, and decrements in daytime function and quality of life.

Cheyne-Stokes Breathing/Central Sleep Apnea (CSB-CSA)

Epidemiology & Risk Factors. Cheyne-Stokes breathing (CSB) is characterized by waxing and waning respiration during sleep, with periods of central apnea, or cessation of breathing. Periodic breathing is a term that denotes waxing and waning patterns of tidal volume with hypopneas, rather than apneas. Many patients have both CSB and central sleep apnea (CSB-CSA). Estimates of the prevalence of CSB-CSA among patients with systolic HF range from 27 to 63%.\(^2\)\(^-\)\(^8\) However, lower rates have been found in patients with stable HF (15% and 9% respectively).\(^9\)\(^1\)\(^0\)

Risk factors for CSB-CSA appear to be male gender, hypocapnea, atrial fibrillation,\(^2\) and systolic vs. diastolic HF.\(^1\)\(^0\),\(^1\)\(^1\) Among a demographically and clinically diverse sample
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of stable systolic and diastolic HF patients, patients with central apnea were predominantly male, White, had low ejection fractions, and heart disease of ischemic etiology. Rates of SDB, especially CSB-CSA, also appear to be more common in patients with decompensated HF. For example, 75% of patients admitted to the hospital for decompensated HF had SDB. There has also been speculation that CSA-CSB is an artifact of poorly controlled HF and that rates would decrease with increased use of evidence-based disease management. However, the results of a recent study suggest that current rates of SDB in patients receiving evidence-based disease management (e.g., beta blockers and angiotensin receptor blockers) were not substantially different than in the past when these medications were less frequently prescribed. Variability in reported rates of CSB-CSA may also be due to differences in the risk factor profile of the patient cohort studied, referral bias (study samples including only patients already referred to sleep centers), or differences in methods used to measure and score central vs. obstructive apneas. Nevertheless, the incidence and prevalence are high.

Pathophysiology and Manifestations. CSB-CSA is a respiratory abnormality that results from increased ventricular filling pressure, pulmonary congestion, and hyperventilation due to vagal stimulation of pulmonary irritant receptors. Hyperventilation leads to reductions in PaC02, which, in turn contributes to central apneas due to the loss of the respiratory stimulus of C02. Low cardiac output and prolonged circulation time contribute to the waxing-waning pattern of CSB-CSA. CSB-CSA results in intermittent hypoxia, frequent arousals, sympathetic nervous system activation, and surges in blood pressure and heart rate. Respiratory instability also leads to more frequent obstructive
respiratory events. These cardiovascular alterations may, in turn, exacerbate the pathophysiologic processes associated with HF (e.g., sympathetic activation, inflammatory processes). The cardiorespiratory changes also result in frequent brief arousals during lighter states of sleep that prevent its progression into deeper stages. Although CSB-CSA is linked with these changes, whether it is a sign of worsening HF or contributes to it, is not completely known. Two recent reviews provide detailed information on the pathophysiology of SDB in HF.

**Obstructive Apnea (OSA)**

**Epidemiology & Risk Factors.** OSA is a respiratory disturbance that results from repetitive intermittent partial or complete obstruction of the upper airway during sleep. It is defined as upper airway instability that is associated with snoring, reduction in airflow (hypopnea) or complete cessation of airflow (apnea). Like CSB-CSA, OSA is often associated with excessive daytime somnolence because of frequent brief arousals from sleep. Respiratory events vary in frequency and may include snoring, hypopnea, and complete cessation of breathing (apnea), or a combination of events. Nocturnal oxygen desaturation accompanies the respiratory events. It is usually, but not always, associated with loud snoring. Persons with OSA may report gasping or snorting during sleep and dry mouth and/or headache upon awakening. Bed partners may observe apneic events.

Epidemiological data suggest that OSA occurs in 4% of the American middle-aged adults population. However, it is believed that OSA is under-diagnosed, and estimates of prevalence vary based on measurement and cut-off scores on diagnostic criteria. More
recent reports suggest that as many as 15 million Americans have OSA.\textsuperscript{15} Studies of HF patients suggest that OSA occurs in as many as 11-60\% of systolic and mixed groups of people with class II-IV HF.\textsuperscript{6,10,15} OSA appears to be the most prevalent form of sleep disordered breathing among diastolic HF patients, occurring in approximately half of patients.\textsuperscript{10}

A large body of epidemiological and clinical research evidence links OSA with cardiovascular morbidity and mortality. Two large-scale studies provide the most powerful epidemiological evidence for the linkage between OSA and cardiovascular morbidity and mortality. Researchers for the Wisconsin Sleep Cohort Study\textsuperscript{19} found that there was a linear increase in blood pressure as the apnea-hypopnea index (AHI) (total number of apneas and hypopneas/hour) increased in a sample of 1,060 employed men and women between the ages of 30 and 60 years. Longitudinal follow-up of 760 of these participants demonstrated that there was a dose-response relationship between sleep disordered breathing at baseline and the development of hypertension four years later.\textsuperscript{20}

The Sleep Heart Health Study (SHHS) was a large multi-center community based, prospective study designed to evaluate the linkages between OSA and cardiovascular morbidity and mortality. Data obtained from 6,132 middle-aged men and women revealed that mean systolic and diastolic blood pressure and prevalence of hypertension increased significantly at higher levels of the apnea-hypopnea index. The odds ratio for hypertension, comparing the highest AHI level (>30/hour), with the lowest (< 1.5/hour) was 1.37 (confidence interval = 1.03 – 1.83, p < .005). There was also a statistically significant
relationship between oxygen saturation of less than 90% and hypertension.\textsuperscript{21} SHHS participants with higher AHI levels were 2.38 times more likely to have HF than those with the lowest AHI levels. Although AHI was also associated with coronary disease, the likelihood of having HF was higher at the highest levels of AHI.\textsuperscript{22} Although a causal link between OSA and HF is not proven, it seems likely that HF may be an important consequence through its contributions to hypertension and sympathetic activation.

Risk factors for OSA include obesity and male gender. However, gender differences in the prevalence of OSA diminish during midlife as women lose the protective effects of progesterone, a respiratory stimulant, during menopause. A neck size greater than 16 in men and greater than 15 in women are risk factors. Use of alcohol may also contribute to respiratory depression. Patients with OSA are also more likely to develop Type II diabetes.\textsuperscript{23, 24} Since obesity is a risk factor for the development of OSA, diabetes, and HF, this potential influence must be considered in evaluating the associations among these disorders.

\textit{Pathophysiological Manifestations of OSA.} The primary pathophysiological explanations for the linkages between OSA and hypertension include hypoxemia, increased respiratory effort, and cortical arousal associated with respiratory events. Patients with OSA have higher levels of sympathetic nervous system activation, as measured by elevated circulating catecholamines and skeletal muscle sympathetic nerve activity that may result from obstructive respiratory events and cortical arousals. These changes may lead to higher peripheral vascular tone and subsequent hypertension. Unlike CSB-CSA which is thought to
be a consequence of HF, OSA may be one of the pathways to HF through its contributions to hypertension and neuroendocrine activation. However, this has not been fully proven.\textsuperscript{15} Patients with decompensated HF may be particularly susceptible to the negative effects of LV dysfunction, pulmonary edema, myocardial ischemia, and arrhythmias resulting from the OSA.

CSB-CSA and OSA co-exist among HF patients and the predominance of either condition may change from night to night and over the course of a single night. Tkacova and colleagues\textsuperscript{25} found that obstructive apneic events decreased and central apneic events increased among HF patients with both forms of sleep disordered breathing over the course of a night. These changes appeared to correspond to cardiovascular deterioration associated with increased circulation time and decreasing PC02. The nature of apneic events may also change between nights, alternating between primarily obstructive and central apnea.\textsuperscript{26} In a more recent prospective study, 18% of HF patients with predominant CSA-CSB converted spontaneously to predominantly OSA over 2 years. Conversion was associated with improvements of 3.5% in left ventricular ejection fraction and improvements in dyspnea. There was no change in medications over the 2 year time frame, but those who converted were more likely to be taking spironolactone and were younger and had higher BMI levels. Co-occurrence of OSA and CSB-CSA is referred to as complex sleep disordered breathing. CPAP treatment for OSA may lead to unmasking of CSA-CSB.\textsuperscript{27}

**Consequences of SDB**

*Morbidity & Mortality.* SDB may exacerbate myocardial ischemia and increase the

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risk for arrhythmias, including sinus arrhythmias, atrial fibrillation, ventricular arrhythmias, and sudden cardiac death. Among HF patients both atrial fibrillation and ventricular tachycardia are frequently associated with SDB. A recent study of demonstrated that there was a four-fold increase in the risk of appropriate device firing in patients with implantable defibrillators who had significant SDB, and the discharges were more likely to occur between midnight and 6 AM. HF patients without significant CSA or OSA had significantly longer time to appropriate cardioversions/defibrillations and longer event-free periods. Patients with SDB had earlier device interventions with significant lethal arrhythmias.

Some studies have suggested that SDB is associated with mortality among patients with HF. HF patients who had an apnea hypopnea index greater than 15 (suggestive of moderate-severe SDB) had increased rates of death, after controlling for confounding variables. Others found no difference in mortality or one or 2 year survival or 52-month follow-up. Because CSA-CSB occurs in people with severe or decompensated HF, the increased mortality may be a result of the severity of HF itself.

**Daytime Function and Quality of Life.** Fatigue, excessive daytime sleepiness, mood disturbance, and decrements in daytime function are common among patients with HF and SDB may contribute to these important quality of life dimensions. However, data are inconsistent on the extent to which SDB contributes. For example, SDB was associated with shorter duration of daytime activity, oxygen uptake, and six minute walk distance, but not the shuttle walk test among patients with HF. However, many studies have not
accounted for variables, such as age and gender that may also contribute to these daytime consequences. Data from a recent study, revealed that stable HF patients with severe SDB had a four-fold increase in the odds of being in the lowest quartile of physical function after controlling for age, gender, and body mass index. Central sleep apnea was associated with decreased activity during the day, but SDB was not associated with six minute walk test performance.

Although fatigue, depressive symptoms, and excessive daytime sleepiness are often attributed to SDB, data on the extent to which SDB contributes to these disabling symptoms are not consistent. Rates of excessive daytime sleepiness have been reported to range from 21% of elderly HF patients to 44 percent of systolic HF patients, in comparison with 18% of a comparison group who did not have HF. Although HF patients at any level of SDB had less self-reported daytime sleepiness than a randomly selected community sample, they were more sleepy when evaluated with objective measures. However, in our recent study of 170 stable HF patients, SDB did not independently confer excess risk for excessive daytime sleepiness, fatigue, depressive symptoms, or self-reported poor sleep quality. These findings suggest that self-reports of daytime symptoms and dysfunction may not accurately signal the presence of SDB. Further research is needed on the extent to which SDB may have impact on daytime function. More importantly, there is a need for studies of the effects of treatment.

HF patients are at-risk for poor cognitive function, and sleep deprivation may worsen it, yet CSB-CSA was not associated with cognitive decline or performance on the
psychomotor vigilance test, a measure of reaction time. Given the importance of cognitive dysfunction to self-care and quality of life, further study is needed of the potential role of SDB among HF patients.

**Treatment of sleep disordered breathing**

Obesity is the most important cause of OSA. Weight loss and avoidance of respiratory depressants such as sedative medications and alcohol may play an important role in reducing OSA in patients with HF. However these strategies have not been a focus of research among HF patients.

The best-established treatment for SDB is nocturnal positive airway pressure (PAP), delivered through a mask or other interface with a blower. It splints the airway to prevent collapse during sleep. PAP is thought to be particularly beneficial for HF patients because it increases intrathoracic pressure, reduces cardiac afterload and preload, and reduces venous return to the right atrium. However, in a study with a cross-over design, CPAP had no effect on 6 minute walk distance, plasma catecholamines, or ejection fraction, and the authors concluded that CPAP’s beneficial effects were on alleviation of SDB and not on cardiac function per se. Observational data suggest that mortality was lower in HF patients who underwent CPAP treatment for an apnea hypopnea index of 15 or higher, in comparison with patients who were not treated. However, the HF patients in the untreated group were those who declined treatment. Therefore, the effects might be due to lower rates of overall adherence that might include self-management strategies in addition to CPAP.

A recent study found that Medicare beneficiaries who were newly diagnosed with
HF had better 2 year survival rates when treated for SDB (HR: .33 [95% CI .21-.51], P < .0001). However, only 4% were suspected of having SDB (far less than the prevalence as discussed above) and 2% received treatment. These observational findings suggest the beneficial effects of CPAP but suggest that SDB is under-diagnosed among HF patients. There have been no long term randomized clinical trials of the effects of treatment of CPAP on mortality in HF patients who have OSA.

Adherence to CPAP is a significant concern, particularly since nightly use for the duration of the sleep period is necessary for a positive outcome. Patients may experience discomfort due to the mask and have difficulty tolerating the nightly treatment. Although many find improvements in day time function, some do not perceive that their sleep is improved. Research findings suggest that the most critical time for treatment is in the first few days after CPAP titration and that six hours nightly use is needed for significant improvements in daytime function. These findings suggest the importance of intervention to improve adherence but as reported in a recent Cochrane review, educational interventions alone did not improve adherence, compared with usual care. Although cognitive behavioral strategies were superior to education or usual care, only 46% of patients who received these strategies used CPAP compared with 15% in the control groups. Although there is a need for future studies of the best behavioral methods to promote CPAP adherence, experts agree that there is a need for close follow-up and support, especially during the initial period of acclimatization to the treatment. Patient education and support is generally provided to patients during initial CPAP titration and mask fitting at accredited sleep centers. However,
this is inconsistent and difficulty using this treatment may persist. Therefore, it is important to follow-up with patients when they return for chronic illness management to assure that they are consistently using the treatment and to assist with troubleshooting problems with the mask or equipment. It is also important to note that changes in weight or exacerbation of HF may worsen SDB. Weight loss may improve OSA. Return of excessive daytime sleepiness or snoring may signal the need for re-titration of CPAP. Daytime dysfunction may also signal non-adherence to treatment.

Although CPAP adherence has been the focus of ongoing clinical and research interest in the broader population of patients with OSA, there has been little systematic study of adherence in patients with HF, a group in which it may be particularly challenging due to the many self-management behaviors in which they must engage (e.g., medications, symptom management, fluids & sodium, exercise).

Mandibular repositioning through dental appliances fitted by a dentist and surgical procedures that increase the size of the airway by removing pharyngeal tissue have a role to play on the management of OSA in the general population. They may have beneficial effects in improving OSA among HF patients, but have not been studied in this population. Patients whose OSA is more severe in the supine position may benefit from sleeping in a lateral position. Surgical treatments such as laser-assisted uvulopalatopharyngoplasty (UPP) and reduction of the tongue volume are generally effective in reducing snoring, but are not as effective as CPAP or weight loss in reducing obstructive events. The latter treatments may be used in patients with milder forms of OSA, especially in those who are unable to
tolerate CPAP. However, the effects of these treatments on cardiovascular function have been under-studied.

CPAP acutely reduces apneas and hypopneas and improves left ventricular function, norepinephrine levels, nocturnal oxygen saturation and functional performance in people with CSB-CSA.\textsuperscript{52, 53} However, the findings of a randomized study of HF patients with and without periodic breathing demonstrated improvements in ejection fraction and mortality only in those patients who had periodic breathing\textsuperscript{53} and suggested that the effect of CPAP was through its impact on periodic breathing and not through its direct effect on cardiac function. The Canadian Positive Airway Pressure (CANPAP) study,\textsuperscript{54} a randomized clinical trial of the effects of CPAP only on CSB-CSA demonstrated that there was no improvement in the treatment group at 18-month follow-up, despite early trends. However, these findings generated a great deal of controversy.\textsuperscript{55, 56} In a post-hoc analysis of the CANPAP data, patients (mean follow up period of 23 months) who achieved suppression of CSA had improved left ventricular ejection fraction and transplant-free survival compared with patients who did not achieve suppression of CSA.\textsuperscript{57} Subsequently, Arzt and colleagues\textsuperscript{58} achieved significant reductions in CSB-CSA with CPAP using a gradually adjusted CPAP level over two nights of titration. When patients were evaluated 12 weeks later, additional AHI reductions of 42% were attained, and alleviation of CSA was noted. Nevertheless, the findings of the CANPAP trial have led to the search for more effective treatments that are acceptable to HF patients.

Adaptive servoventilation (ASV) has emerged as a promising treatment for CSA-
CSB. ASV provides inspiratory positive pressure support and expiratory positive airway pressure. Recent studies have compared adaptive servoventilation (ASV) with standard CPAP and/or bilevel positive airway pressure (BPAP) treatments. Due to the ability of ASV to adjust pressure during the inspiratory cycle, it appears to be a more effective treatment of CSB-CSA. Non-controlled trials have shown substantial improvements in AHI and cardiac function and improved AHI, reductions in oxygen desaturation events, and fewer arousals in patients with chronic HF and diastolic HF, respectively.

In a recent study of 31 HF patients with both OSA and CSB-CSA, flow triggered ASV more effectively reduced the apnea hypopnea index, improved left ventricular ejection fraction, increased BNP, and improved quality of life, compared with CPAP. Notably, patients had better compliance with treatment at three month follow-up. Randerath et al (2009) and Oldenburg et al (2008) also found significant reductions in AHI in small studies of patients receiving ASV. Pepperell et al. found significant reductions in serum brain natriuretic peptide and urinary metadrenaline excretion and less daytime sleepiness in patients with moderate to severe HF with CSB-CSA who were randomized to ASV at therapeutic levels for one month compared to a group randomized to receive sub-therapeutic ASV. Despite small sample sizes and predominantly male enrollment in these studies, ASV is emerging as an effective intervention for patients with CSB-CSA, particularly in those for whom standard CPAP treatments paradoxically worsen CSB-CSA. However, the long term effects on morbidity and mortality are not known. Numerous randomized clinical trials are now underway to evaluate the impact of ASV.
Supplemental nocturnal oxygen improves hypoxia, reduces nocturnal epinephrine, and reduces the occurrence of central.\textsuperscript{66-68} It also reduced apneas, periodic breathing,\textsuperscript{69} and frequency of oxygen desaturations during sleep,\textsuperscript{70} but did not improve ventricular function, sleep architecture,\textsuperscript{69} or cardiac function or quality of life over one month.\textsuperscript{68} Although supplemental oxygen is not a first-line treatment for SDB in HF it should be used for patients with CSA-CSB who are not responsive to other treatments.\textsuperscript{71}

Fluid congestion associated with HF itself may contribute to OSA as well as CSA. Therefore, effective treatment with diuretics and other therapies may contribute to improvements. Early reports suggested that beta blocker drugs may reduce central apneas,\textsuperscript{55, 72} but recent evidence is contradictory\textsuperscript{8} and there is also some evidence that their use may contribute to nightmares.\textsuperscript{73} Nevertheless, optimizing, disease management in HF may contribute to improvements in SDB and reduction in its harmful consequences.

Several recent reports suggest the benefits of cardiac resynchronization therapy (CRT) on ejection fraction, apnea hypopnea index, oxygen saturation and sleep quality.\textsuperscript{74-76} These effects are thought to be due to the effects of CRT on circulation time. CRT improves ventricular synchrony and contraction, improving clinical symptoms. A recent study\textsuperscript{77} revealed that CRT had acute effects on the frequency and duration of central respiratory events, and the volume of mitral regurgitation decreased. Although the effects of CRT are promising, there have been no large scale randomized clinical trials to evaluate its long term effects on SDB.
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INSOMNIA

Insomnia is a disorder of initiating or maintaining sleep or awakening too early in the morning that is accompanied by daytime dysfunction. As many as 50% of patients with HF report insomnia symptoms,\textsuperscript{78} including difficulty maintaining sleep (34-47% of patients),\textsuperscript{41, 78-80} falling asleep (23-47%),\textsuperscript{41, 78-80} and waking too early in the morning (24-39%)\textsuperscript{41, 79, 80} in studies of HF patients awaiting transplant HF,\textsuperscript{79} hospitalized HF patients,\textsuperscript{80} and stable outpatients enrolled in a structured HF management program.\textsuperscript{41, 78} HF patients more often reported difficulty initiating and maintaining sleep than a comparison group recruited from the same community,\textsuperscript{41} and rates are higher than those reported by adults responding to the Sleep in America Poll.\textsuperscript{81}

Factors that may contribute to the development of insomnia are multi-dimensional. For HF patients, these may include HF symptoms, the pathophysiology of HF (e.g., increase arousal associated with sympathetic activation), medications, and other sleep disorders, such as SDB and periodic limb movements. Periodic limb movement disorder (PLMD) was more common in a small group of male HF patients compared to a healthy comparison group, and may contribute to sleep fragmentation,\textsuperscript{82} and restless leg syndrome (RLS) is associated with cardiovascular disease.\textsuperscript{83} However, the findings of a recent study suggest that the apnea hypopnea index (AHI), a primary indicator of SDB, was not related to insomnia symptoms.\textsuperscript{78}

The “3-P” model\textsuperscript{84, 85} was developed to guide consideration of the predisposing, precipitating, and perpetuating factors that may contribute to insomnia and may be useful in
guiding assessment and management of insomnia among HF patients.

Predisposing factors may include genetic factors and biological traits (e.g., hyperactivity, hypervigilance, increased metabolic rate), as well as psychological and social factors. For example, psychological traits may include the tendency to worry. Social factors may include the sleep schedule of a bed partner or societal demands (work, family roles).\textsuperscript{84, 85}

Precipitating factors may include medical (e.g., diabetes, pain, asthma, urinary problems) and psychiatric disorders. Stress associated with many types of events, such as death of a family member, changes in health or caregiving, work loss or work stress, illness, marriage, and other events may precipitate insomnia.

Factors that may perpetuate insomnia are cognitive and behavioral in nature. These include dysfunctional beliefs and misperceptions about sleep. Patients with insomnia often believe that insomnia will lead to terrible consequences (e.g., loss of job, auto accident, illness, stress). Dysfunctional behaviors, such as going to bed early and/or staying in bed for extended periods of time engaged in activities (watching TV, reading, playing cards, eating, paying the bills) that are not related to sleep. Individuals use these strategies to compensate for sleep loss.\textsuperscript{86}

Although symptoms associated with illnesses, such as HF, may also contribute to insomnia, behavioral sleep specialists generally agree that treatment of the underlying medical disorder (e.g., HF) is not alone sufficient to address chronic insomnia, once it is associated with dysfunctional beliefs, attitudes and behaviors. In a recent focus group study,
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HF patients who complained of insomnia seldom described typical HF symptoms that may disturb their sleep. Rather, they reported worrying and used strategies such as use of the TV to help them sleep. These findings suggest that behavioral treatments may be useful in improving sleep among HF patients.

Consequences of Insomnia

Insomnia symptoms have been associated with impaired functional performance, including decrements in function, 6 minute walk test distance (6MWT), and self-reported physical function, but others have not found relationships in people with HF. In our recently completed study, we found that insomnia, but not SDB contributed to daytime sleepiness, depressive symptoms, fatigue, and decrements in functional performance, in models that controlled for age, gender, comorbidity, body mass index, and New York Heart Class as well as SDB. Notably, six minute walk distance was 100 feet shorter in the patients with insomnia. The impact of insomnia on self-reported (SF-36 Physical function scale) and six minute walk test performance was mediated by fatigue, sleepiness, and depressive symptoms. These findings, obtained in a cross-sectional study, suggest the potential importance of insomnia to quality of life among HF patients. It is possible that treatment of insomnia may improve daytime symptoms and function in this vulnerable group of patients.

Although insomnia has been under-studied among HF patients, it is associated with the development of clinical depression in the general population and along with short sleep duration, contributed to the development of hypertension and diabetes in population-based
Insomnia and short sleep duration have also been associated with death from cardiovascular disorders. Insomnia is often associated with high levels of arousal that may contribute to cardiovascular dysfunction and aggravate HF.

**Treatment of Insomnia**

The two major forms of insomnia treatment are hypnotic medications and behavioral treatments, including cognitive behavioral therapy for insomnia (CBT-I). They are equally effective in the short term, but the effects of CBT-I are more durable.

Hypnotics are generally indicated in patients with acute or short term insomnia, such as that associated with hospitalization or acute stressors. The major classes of medications used for insomnia are benzodiazepines, barbiturates, nonbarbiturate hypnotics, antihistamines and antidepressants. Choice of the appropriate class of medication is based on nocturnal symptoms of insomnia, daytime consequences, patients’ comorbid condition, and the potential interactions with other medications. Although benzodiazepines were formerly the mainstay of treatment, the non-barbiturate hypnotics zolpidem, zaleplon, eszopiclone, and ramelteon are now frequently used in treating insomnia. For HF patients who are depressed, antidepressants with sedating properties may also be useful. Although a complete description of these drugs and their dosages is beyond the scope of this paper, a guide to assessment and management of insomnia in older adults is available and many resources are available on the internet. (See Table 2). However, caution should be used in prescribing or administering hypnotics to HF patients due to the high prevalence of SDB among HF patients and the potential respiratory depression. It is important to screen patients
for SDB prior to prescribing hypnotic drugs. Once the patient is effectively treated with PAP, hypnotics may be safely used to address insomnia symptoms.

Many patients use over the counter medications, many of which contain diphenhydramine that may contribute to daytime dysfunction, especially among the elderly. Many individuals, including patients with chronic disease such as HF, also use melatonin and herbal remedies to promote sleep. Melatonin shows promise as a treatment for circadian rhythm abnormalities and insomnia and there is evidence that it may have benefits for the cardiovascular system. However, it is important to note that melatonin and herbal products are not regulated by the FDA, preparations may not be consistent, and these drugs may interact with other medications. Therefore, it is important to include assessment for use of these substances into routine health assessment, and advise patients accordingly.

There are multiple behavioral treatments available for insomnia, such as exercise, music, and warm baths, among others. However, the research base for these treatments is inconsistent. Cognitive behavioral therapy for insomnia (CBT-I), a multi-modal group or individual-based treatment, is the most studied and efficacious treatment for primary insomnia (insomnia that is not associated with comorbid disorders) and secondary insomnia (insomnia associated with comorbid medical or psychiatric disorders). CBT-I includes stimulus control (instructions designed to associate the bed with sleep), sleep restriction (limits time in bed to the actual sleep time) relaxation training (reduces somatic and psychological tension), cognitive therapy (alters misconceptions and faulty beliefs about sleep), sleep hygiene (alters health practices, such as caffeine use related to sleep).
CBT-I can be delivered in group and individual formats. CBT-I can be used in combination with hypnotics and has been successful in assisting patients to decrease hypnotic use. Although structured training for CBT-I is desirable for its maximal efficacy, it is now being used in a variety of primary care and chronic care settings. This approach has not been well-studied among patients with HF patients, but our group is currently conducting a clinical trial to address its effects on self-reported and objective sleep characteristics, as well as daytime symptoms and functional performance among HF patients.

CLINICAL EVALUATION OF SLEEP DISORDERS

Given the high prevalence of sleep disorders among patients with HF, assessment of sleep and sleep disorders and their consequences should be an important component of routine clinical assessment in acute, primary care, and chronic care settings. However, recent data suggest that SDB is under-diagnosed among patients with HF. Although similar data are not available for insomnia, our recent focus group work revealed that HF patients were very concerned about their sleep, but perceived that health care providers didn’t care about sleep. The importance of assessment for sleep disorders is underscored by their potential physiological and functional consequences, but worsening sleep may also signal HF exacerbation.

Although a fully detailed guide to sleep assessment is beyond the scope of this chapter, suggestions for sleep assessment in the HF disease management setting are
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provided in Table 1. A wealth of information is available on the internet to clinical sleep assessment, treatment and referral (See Table 2).

It is helpful to begin sleep assessment with a question about overall sleep quality. Specific sleep characteristics that may be indicative of insomnia are the duration of sleep, time taken to fallen asleep (< 20-30 minutes is normal); and waking too early in the morning (a possible sign of depression). Waking frequently at night is less specific and may be associated with insomnia, SDB, or period limb movements during sleep. Snoring, choking or gasping during sleep are specific to OSA and generally do not occur in people who have CSA-CSB alone. People who snore, however, do not necessarily have significant OSA. Conversely, the absence of snoring does not indicate the absence of SDB. Apneas during sleep are common in both CSA-CSB and OSA. It is important to include bed partners in the assessment, as patients may not be aware of apneas or snoring.

Excessive daytime sleepiness, cognitive dysfunction, fatigue, and disturbed mood are common among patients with HF and may be attributable to sleep disorders, but these symptoms may not be reliable indicators of SDB as suggested by studies showing poor correlations. Excessive daytime sleepiness presents safety concerns, as it may have a negative impact on reaction time, decision making, and safe operation of machinery and motor vehicles. Therefore, patients who are suspected of being excessively sleepy should be cautioned about behaviors that may be a safety hazard. Sleepiness should also be assessed in patients who are undergoing treatment for sleep disorders, as lack of improvement may signal ineffective treatment or non-adherence.
Many factors may contribute to disturbed sleep (Table 1). Categories that should be considered during assessment include nocturnal HF symptoms; comorbid medical or mental health disorders; medications; the sleeping environment; primary sleep disorders (e.g., SDB and or periodic limb movement disorder, insomnia) and patient behaviors. Anxiety and depression are common among HF patients and are frequently comorbid with insomnia. Adjustment of medications, treatment of anxiety or depression, or assistance with modifying the sleeping environment may contribute to improvements in sleep.

The gold standard for evaluation of sleep disordered breathing is nocturnal polysomnography (NPSG) conducted in a sleep laboratory. Polysomnography consists of electro-encephalography, chin electromyelography, and electro-oculography to evaluate sleep duration, sleep latency, and sleep stages. Central or obstructive apneas and hypopneas are diagnosed by thorough measurement of effort (chest and abdominal expansion), air flow or pressure (thermistor or nasal cannula), and oxygen saturation (pulse oximetry). Continuous ECG is also obtained, thereby allowing evaluation of the association of dysrhythmias with respiratory events. Other physiological parameters can be measured, such as periodic limb movements, depending on the purposes of the sleep study. Excessive daytime sleepiness can be evaluated by self-report, using such instruments as the Epworth Sleepiness Scale or a Multiple Sleep Latency Test, an objective measure of EDS.

A clinical PSG report includes information on the duration of sleep, sleep stages, sleep latency (time from lights out until sleep onset), and sometimes, an evaluation of the frequency of brief nocturnal arousals. Essential to the diagnosis of sleep disordered
breathing is the Apnea Hypopnea Index (AHI) or Respiratory Index (RDI) (sum of the apneas and hypopneas/hour of sleep) and oxygen saturation. Apneas and hypopneas will also be described as central or obstructive depending on their association with respiratory effort (Central apneas and hypopneas are not associated with effort; obstructive apneas are associated with effort).

Indications for referral of HF patients for specialized sleep evaluations are the subject of ongoing discussion. Epstein et al.\textsuperscript{100} included HF patients in those at high risk for OSA who should be evaluated for symptoms and referred for sleep testing. Patients who snore, are obese and demonstrate excessive daytime sleepiness, or those who have witnessed apneas should be referred for polysomnographic evaluation. Those who complain of frequent nocturnal arousals that are unexplained by environmental factors, disturbed mood, or nocturnal pain are also candidates for evaluation in a sleep laboratory setting. Although polysomnography is not generally indicated for the diagnosis of insomnia, it is often used to rule out SDB. Although there are no specific guidelines for HF, the high prevalence of SDB in these patients suggest the potential importance of a high index of suspicion for this condition. Nocturia that is unexplained by patterns of diuretic use should raise the suspicion of association with SDB and may warrant further testing.

Risk factors for OSA and CSA-CSB were described previously and should be evaluated. Measurement of weight, body mass index, neck size, and central adiposity may indicate increased risk for OSA. HF patients with atrial fibrillation may be at higher risk for CSA-CSB. Patients with fluid overload who are not responsive to standard medication
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management may be at particular risk for SDB. Those HF patients who have received optimal medical management and are symptomatic and/or continue to remodel should also be referred for sleep evaluation.

There has been great interest in the application of home sleep studies for the assessment of sleep disordered breathing, particularly in settings where PSG is not readily available. Such monitors fall into the following classifications: 1) devices that are capable of full portable PSG; 2) devices that permit modified portable sleep apnea testing (at least 2 channels of respiratory movement or respiratory movement and airflow, heart rate or ECG, and oxygen saturation; and 3) devices that obtain continuous recordings of oxygen saturation or airflow. These devices may be used in an attended (laboratory) or unattended (home) setting. Authors of an early evidence-based review recommended that these devices not be used in patients with HF, as the validation studies were conducted primarily in patients without comorbid illness and focused primarily on screening for OSA and not CSB-CSA. While home portable monitoring may be reliable for persons without comorbid conditions under selected circumstances, patients with HF do not fall into this category.

There has been exponential growth in the science and the awareness of HF clinicians about the importance of sleep and sleep disordered breathing over the past several years. A great deal of research is ongoing and may shed important new insight onto the significance and treatment of sleep disorders among HF patients. Clearly evaluation and management of these conditions needs to be a component of ongoing assessment and disease management for this large and vulnerable group of patients.
Table 1. Clinical assessment for sleep disorders

**Self-report**
- 1. Overall sleep quality on a typical night
- 2. Difficulty falling asleep, staying asleep, or waking too early in the morning
- 3. Time to fall asleep (sleep latency) (> 30 mins abnormal)
- 4. Time awake at night (> 30 minutes abnormal)
- 5. Perceived reasons for poor sleep
- 6. Typical Sleep duration
- 7. Sleep scheduling – typical bedtime, wake time on weekdays and weekends
- 8. Daytime napping

**Obtain from bed partner**
- 1. Snoring
- 2. Gasping, choking, morning headaches
- 3. Witnessed apneas

**Physical Exam**
- 1. Signs of fluid overload
- 2. Body mass index
- 3. Central adiposity
- 4. Neck size

**Factors that may contribute to poor sleep**
- 1. Advanced age, gender (men – more likely to have SDB; women – more likely to have insomnia)
- 2. Medications
- 3. Primary sleep disorders (SDB, PLMS)
- 4. Comorbidity (e.g., pain, diabetes)
- 5. Nocturnal symptoms (dyspnea, nocturia)
- 6. Stress and worries
- 7. Social and work-related obligations
- 8. Noisy environment
- 9. Fluid overload
- 10. Nocturia due to fluid overload, prostate enlargement, diuretics

**Consequences of poor sleep**
- 1. Waking up unrefreshed
- 2. Daytime sleepiness
- 3. Fatigue
- 4. Disturbed mood (anxiety, depression)
- 5. Memory impairment
- 6. Accidents or injury
Table 2. Websites containing information for patients, health care providers, and the public regarding sleep and sleep disorders.

**American Family Physician**  
Paper on treatment options for insomnia  

**American Psychological Association**  
Tutorial on why sleep is important and what happens if you don’t get enough  
http://www.apa.org/topics/sleep/why.aspx

**Help Guide**  
Self-help information on insomnia  
http://helpguide.org/life/insomnia_treatment.htm

**United Kingdom National Health Service**  
http://www.nhs.uk/Conditions/Insomnia/Pages/Introduction.aspx

**Healthy Sleep: Harvard University Division of Sleep Medicine**  
Videos and essays on importance of sleep and the science of sleep.  
http://healthysleep.med.harvard.edu/portal/

**BBC Science**  
Interactive website about the science of sleep  
http://www.bbc.co.uk/science/humanbody/sleep/

**American Academy of Sleep Medicine, Sleep Education.com**  
Source for information for the public and patients about sleep and sleep disorders.  
http://www.sleepeducation.com/

**American Academy of Sleep Medicine MedSleep**  
Downloadable case studies, powerpoint slides and other educational materials useful in teaching/learning regarding many sleep-related topics. These materials are free and were prepared through the NIH Sleep Academic Awards Program that was designed to increase knowledge about sleep through medical schools. Includes specific information on the biological and behavioral aspects of sleep.  
http://www.aasmnet.org/MedSleep.aspx

**Mayo Clinic**  
Public education website with detailed information about nature of sleep apnea, signs, symptoms, and treatment  
http://www.mayoclinic.com/health/sleep-apnea/DS00148
National Center for Sleep Disorders Research
Source for information on the importance of sleep, patient and public educational materials, research
http://www.nhlbi.nih.gov/about/ncsdr/index.htm

National Sleep Foundation
Non-profit organization dedicated to improving personal and public sleep health. Conducts annual poll of the U.S. public on the impact of sleep on health and performance (reports available online)
http://www.sleepfoundation.org/

Sleep Research Society
Professional Organization of sleep scientists. Offers materials and guidelines for sale, including updated training material (book and slides) on the Basics of Sleep.
http://www.sleepresearchsociety.org/index.aspx

New Abstracts and Papers in sleep
Email alerting service and searchable index of new abstracts and papers in sleep
http://www.websciences.org/bibliosleep/naps/
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