Sleep-Disordered Breathing and Cardiovascular Risk

An Analysis
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1. Synopsis

Patients with Sleep-Disordered Breathing (SDB) have a higher risk of developing cardiovascular diseases. Approximately 4% of all men and 2% of all women are affected by Obstructive Sleep Apnea (OSA).

Sleep-disordered breathing occurs with far greater prevalence in cases of cardiovascular disease.

In 35% of all cases, co-prevalent obstructive sleep apnea is found in heart failure with systolic dysfunction and in coronary heart disease. Half of all patients with atrial fibrillation and cardioversion and up to 33% of patients with Lone Atrial Fibrillation (idiopathic atrial fibrillation without structural heart disease) suffer from OSA. In one of two patients affected by acute stroke, obstructive sleep apnea is also present. Up to 23% of patients with Type 2 diabetes are affected by OSA.

Patients with heart failure in New York Heart Association (NYHA) Classes II to III and an ejection fraction of < 40% have SDB rates of up to 71% (Apnea/Hypopnea Index AHI/hr > 10), split into obstructive sleep apnea (43%) and Cheyne-Stokes Respiration (28%).

The data show that patients with sleep-disordered breathing and patients with cardiovascular diseases have many common risk factors such as overweight, dysfunctional sugar and lipid metabolism, hypertension (one of every two persons with high blood pressure is also affected by OSA). There is also a great overlap in the underlying pathophysiological mechanisms, such as hyperactive sympathetic nervous system, the triggering of systemic infection markers like CRP and IL-6, changes in blood coagulation and endothelial dysfunction. All these problems lead to a vicious circle involving the cardiovascular system.

Sleep-disordered breathing and its co-prevalence with existing general cardiovascular diseases represent an additional risk for the cardiovascular system. The disorders therefore urgently require diagnostic clarification and effective therapeutic measures.
Heart Failure
2% of population

NYHA II-III

OSA
2 to 4% of population

SDB 71%

CSR 28%

OSA 43%

< 1% treated

5 to 20% are treated

Therapy
- CPAP
- auto-CPAP
- Bilevel
- ACMV (CS)

Waiting list x Months

Prevalence of Heart Failure and OSA

Cardiovascular Risk ↑

Not treated

Not treated
2. Sleep-Disordered Breathing

Sleep-Disordered Breathing (SDB) such as Cheyne-Stokes Respiration (CSR) was identified as early as the beginning of the 19th century. (1). The public first became acquainted with the problem through the humorous novel “The Pickwick Papers” by Charles Dickens (2). One of the novel’s characters, Joe (The Fat Boy), suffers from obesity and sleepiness and falls asleep whenever he’s not eating. Based on Dickens’ description of Joe’s problems, the name “Pickwick Syndrome” was given to this clinical disease, which includes cardiopulmonary syndrome of the obese, a special type of sleep apnea syndrome.

Today SDB is defined in the “International Classification of Sleep Disorders” (ICSD – 2, 3). Among them are the previously mentioned OSA, Central Sleep Apnea (CSA), for example, of the Cheyne-Stokes Respiration type accompanied by severe cardiac disease.

The best-known sleep-disordered breathing is OSA. It is characterized by recurring episodes of obstructions in the upper airways associated with increased respiratory effort, intermittent deoxygenation, pulmonary-arterial blood pressure increases and accompanying sleep disorders. The major symptoms

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**Fig. 1**
OSA: Collapse of upper airways during sleep
associated with OSA are nighttime apnea interrupted by loud and intermittent snoring and excessive daytime sleepiness.

According to the International Classification of Sleep Disorders (3), obstructive sleep apnea is diagnosed when the following criteria are fulfilled (A, B and D or C and D):

**A** At least one of the following criteria is satisfied:

1. The patient complains of unwanted dozing during the day, daytime sleepiness, non-recuperative sleep, fatigue or insomnia.
2. The patient wakes during the night, experiences apnea, gasps for breath, has feelings of suffocation.
3. The partner reports loud snoring and/or apnea while patient is sleeping.

**B** The following are documented by polysomnography:

1. \( 5 \) / hr or more respiratory events such as apnea, hypopnea or RERAs (Respiratory Effort-Related Arousals) while patient is sleeping.
2. Evidence of respiratory effort during all or some occurrences of respiratory events.

or

**C** Polysomnography shows:

1. \( \geq 15 \) respiratory events / hr of sleep (apnea, hypopnea or RERAs).
2. Evidence of respiratory effort during all or some occurrences of respiratory events.

**D** The illness cannot be better explained by other sleep disorders, neurological disease or medication use.

It is estimated that about 2% of women and 4% of men are affected by obstructive sleep apnea (4, 5, 6). Prevalence is higher in ages 35 to 60.
Fig. 2
Patient with Obstructive Sleep Apnea, clearly recognizable in respiratory effort in the thorax and abdomen channels; polysomnographic recording made with SOMNOlab

Fig. 3
Patient with Cheyne-Stokes Respiration. The central characteristic of this respiratory disorder is apparent in that cessation of breathing correlates to the lack of respiratory effort (thorax and abdomen channels). Cheyne-Stokes Respiration is evident in breathing marked by a crescendo and decrescendo breathing pattern. The diagram is from a polysomnographic recording made by SOMNOlab.
A central respiratory regulation disorder with underlying heart failure is not a rare disease. Approximately 1 to 1.5% of the general population suffers from chronic heart failure (8). In later life (> 50 years) prevalence increases significantly. More than 50% of patients with heart failure in NYHA Classes II-IV are also affected by sleep-disordered breathing. About 30 to 40% of affected patients indicate a central Cheyne-Stokes type (9, 10, 11). A recent study involving patients in NYHA Classes II and III with an ejection fraction of < 40% showed that 71% of the patients had an AHI/hr of > 10, with 43% affected by obstructive sleep apnea and 28% by CSR.

The ICSD-2 differentiates obstructive from central sleep apnea. A variety of central breathing disorders are described as central sleep apnea. In this context the central sleep apnea syndrome of the Cheyne-Stokes type is relevant.

Cheyne-Stokes Respiration was described as a central disorder of respiratory regulation in 1818 by Dr. John Cheyne (1) and in 1854 by Dr. William Stokes (7). Even at that time the connection with etiological heart disease was known and the prognosis was poor.

The definition of central sleep apnea with a Cheyne-Stokes breathing pattern (3) states:

A Polysomnography records ≥ 10 central apnea / hr or hypopnea/hr during sleep; hypopnea shows crescendo-decrescendo pattern in tidal volume, accompanied by arousals and altered sleep structure.

B Association can be confirmed between CSR and severe internal/neurological disease (heart failure, kidney insufficiency, stroke).

C The disease cannot be more effectively explained by another sleep disorder, medication use or intolerance of certain substances.

A central respiratory regulation disorder with underlying heart failure is not a rare disease. Approximately 1 to 1.5% of the general population suffers from chronic heart failure (8). In later life (> 50 years) prevalence increases significantly. More than 50% of patients with heart failure in NYHA Classes II-IV are also affected by sleep-disordered breathing. About 30 to 40% of affected patients indicate a central Cheyne-Stokes type (9, 10, 11). A recent study involving patients in NYHA Classes II and III with an ejection fraction of < 40% showed that 71% of the patients had an AHI/hr of > 10, with 43% affected by obstructive sleep apnea and 28% by CSR.
3. Cardiovascular Diseases

Cardiovascular diseases top the lists of causes for mortality and morbidity in Western industrialized countries.

Nearly 40% of all deaths in industrialized countries are attributed to cardiovascular diseases (13, 14). In the course of industrialization and urbanization, accompanied by lifestyle changes and increasing prosperity, the frequency of cardiovascular disease has risen around the world, regardless of the countries’ race and culture. From an epidemiological viewpoint, researchers speak of “The Age of Inactivity and Obesity” (13).

The following table shows the prevalence and mortality of cardiovascular diseases (cf. 13):

<table>
<thead>
<tr>
<th>Type</th>
<th>Prevalence(^1)</th>
<th>Mortality(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular disease</td>
<td>71,300,000</td>
<td>902,400</td>
</tr>
<tr>
<td>Hypertension</td>
<td>65,000,000</td>
<td>53,400</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>13,200,000</td>
<td>480,000</td>
</tr>
<tr>
<td>Stroke</td>
<td>5,500,000</td>
<td>157,700</td>
</tr>
<tr>
<td>Heart failure</td>
<td>5,000,000</td>
<td>57,400</td>
</tr>
</tbody>
</table>

Fig. 4
Cardiovascular Diseases in the USA, 2003

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Because a number of cardiovascular diseases can lead to heart failure and the interrelation or co-prevalence with sleep-disordered breathing can best be examined in those cases, the subject of heart failure will be treated in the following paragraphs.

Many cardiovascular diseases are etiologically linked to heart failure:

- coronary heart disease (36 – 75 %, depending on the study), often in combination with arterial hypertension
- atherogenic risk factors such as smoking, diabetes mellitus
- arterial hypertension (10 – 50 % as cause or joint cause)
- hypertrophy of the heart
- cardiomyopathy: dilatative, infectious myocarditis, alcohol, metabolic (endocrine, vitamin deficiency), neuromuscular, collagenosis, idiopathic, pregnancy
- heart valve disorders and genetic heart defects (mitral valve insufficiency, aortic stenosis, aortic insufficiency)
- arrhythmia (atrial fibrillation or flutter, ventricular arrhythmia, bradycardia)
- drugs (anthracycline)
- high-output heart failure (pericarditis, anemia, fever/infection, hyperthyrosis)
- primary right heart failure (pulmonary hypertension, tricuspid valve insufficiency)

The prevalence of heart failure in the general population is 1 to 2%. Among the older population the prevalence rises to 15%.

According to the Framingham Heart Study, annual incidence is 0.2 to 0.3% in ages 50 to 59, with a tenfold increase in ages 80 to 89.

Clinical symptoms of heart failure include:

- dyspnea
- tiredness
- peripheral edema

The prevalence of OSA is significantly higher in patients with heart failure than in the general population. OSA can also hasten the progression of coexistent heart failure.

Patients with the above-mentioned cardiovascular diseases very frequently show OSA comorbidity. Up to 50% of all patients with hypertension, for example, are also affected by OSA. The figures in parentheses refer to the following sources:


**Chronic Heart Failure, Prognosis**

Unfavorable prognostic factors of chronic heart failure include:

- diabetes mellitus
- advanced age
- low ejection fraction
- ventricular arrhythmia
- high pressure in pulmonary circulation
- elevated neuroendocrine factors (noradrenaline, renin, aldosterone, angiotensin II, ANP, BNP, endothelin, TNF)
- hyponatremia
- sleep-disordered breathing

Sleep-disordered breathing occurs in 70% of patients with symptomatic heart failure (NYHA II + III); 40% of an obstructive type and 30% central (12).
4. Cardiovascular Morbidity and Mortality, Therapeutic Effects in cases of OSA

In a study of OSA at the start of the 1990s, the Stanford Group was able to document a high prevalence of cardiovascular diseases and a correlation with the severity of sleep apnea syndrome (14). Today many studies published in scientific journals contain impressive evidence of the cardiovascular risk of sleep-disordered breathing.

An increased number of non-fatal cardiovascular incidents are reported in uncontrolled studies involving untreated patients with cases of mild OSA as well as severe OSA (14, 15).

Longitudinal studies confirm the high cardiovascular morbidity of OSA patients (16, 17, 18).

During a seven-year study, regular examinations of patients who rejected CPAP treatment for suspected OSA and who showed no evidence of cardiovascular disease verified a higher incidence of cardiovascular events than in healthy subjects and in CPAP-compliant patients (17).

Two current studies observed the cardiovascular prognosis of OSA patients over a period of 10 years after diagnosis (18, 19). Patients were permitted to accept or reject CPAP treatment. For ethical reasons a randomized study was not conducted. In the study made by Marin et al. (18), higher cardiovascular morbidity and mortality were seen only in those patients with severe OSA who rejected CPAP therapy. However, in a comparison with the general population, no cardiovascular morbidity and mortality could be proven in patients with simple snoring, mild OSA or good CPAP compliance. Doherty et al. (19) verified that untreated OSA patients had an increased cardiovascular mortality.

A recent study (20) also shows a higher cardiovascular risk for patients with untreated cases of mild OSA.

The cardiovascular effect of OSA appears to be particularly pronounced in young patients (21). These results were recently confirmed in a long-term follow-up involving close to 15,000 patients (22). CPAP compliance appeared to have a greater effect than the severity of OSA on the long-term outcome (23).

Sudden deaths at night have been associated with OSA (24, 25). Gami et al. (25) observed that the risk of sudden cardiac death during the night (between midnight and 6 a.m.) rises with the
severity of OSA, while cardiovascular events in patients without OSA or in victims in the general population generally occur between the hours of 6 a.m. and noon.

5. Cardiovascular Pathogenetic Mechanisms and Diseases in cases of OSA

Pathophysiological changes related to cardiovascular diseases occur over the course of OSA:

Among them are:
- increased sympathetic activity
- activation of systemic infection processes
- oxidative stress induced by intermittent deoxygenation
- endothelial dysfunction
- altered coagulation function

Accompanying metabolic dysregulations are:
- increased glucose intolerance
- altered leptin metabolism

**Sympathetic nerve activity**
The autonomous nervous system becomes overactive as the result of its frequent triggering by recurring obstructions of the upper airways during sleep and accompanying hypoxia as well as by the oscillation of intrathoracic pressure (26, 27, 28). CPAP therapy brings about a significant reduction in the elevated levels of catecholamin in plasma and urine (29, 30, 31).

**Infection parameters**
Systematic infection plays a central role in the emergence of arteriosclerosis. The C-reactive protein (CRP) is a decisive marker. CRP levels are regulated by cytokine, particular interleukin IL-6.

It is generally accepted that OSA is associated with elevated levels of CRP and IL-6. The level correlates to the severity
of OSA and confirms the significance of sleep apnea in the pathogenesis of cardiovascular disease (32, 33). It is postulated that intermittent hypoxia activates the inflammatory process.

**Endothelial dysfunction**

Endothelial dysfunction develops as a consequence of cardiovascular risk factors and contributes to the genesis of arteriosclerosis (34). The Sleep Heart Health Study detected increased vascular dysfunction in older patients with OSA (35). Intermittent hypoxemia in OSA seems to be involved in the emergence of endothelial dysfunction (36).

Fig. 6
Possible pathogenetic mechanism of endothelial dysfunction; courtesy of Prof. Dr. med. Hans-Werner Duchna/Bochum
Coagulation function
Altered coagulation and elevated thrombocyte aggregation are detected in OSA patients. Some studies have verified that excessive thrombocyte activation in OSA could be reduced by CPAP therapy (37, 38).

Metabolic dysregulation
Type 2 Diabetes – glucose intolerance – insulin resistance and OSA
Epidemiological studies show that type 2 diabetes is often associated with OSA (39, 40, 41, 42, 43, 44, 45). Nearly one in four diabetics is affected by OSA (46). Evidence is provided of correspondingly high glucose intolerance (44, 42) and insulin resistance (42, 39) in OSA patients. Insulin sensitivity can be increased in OSA patients treated with CPAP (47).

Lipid metabolism and fatty liver
OSA patients have altered lipid metabolism and are prone to developing fatty liver disease. Half the patients are affected by non-alcoholic fatty liver disease (48). Elevated cholesterol levels can be reduced slightly by CPAP therapy (49). The average HDL readings increase after CPAP treatment. This change correlates to the decline in the AHI/hr (50).

Cardiovascular Interrelations
Hypertension
Systemic hypertension
As apnea progresses in OSA patients, a gradual rise in systemic hypertension is detected. The maximum level is reached in the hyperventilation phase after apnea (51). The phenomenon of non-dipping is observed in OSA patients. The disrupted circadian blood pressure profile can be considered an additional cardiovascular risk factor. The proportion of non-dippers in the OSA patient population correlates with the severity of the disease (52).
There is considerable evidence that OSA is an independent risk factor for systemic hypertension (53, 54, 55). In controlled studies confounding factors such as obesity were excluded (56). Data from random sampling, from the general population and from patients support claims made about the role of OSA in the pathogenesis of hypertension (57, 58, 59).
Special attention should be paid to patients with high blood pressure who cannot be effectively treated with drugs (59). In such cases the cause may lie in untreated OSA. Prospective randomized studies have shown that treatment of OSA (CPAP therapy) significantly reduces
blood pressure (60, 61), especially when hypertension is present (62, 63, 64). A blood pressure reduction of about 3.3 to 10 mmHg reduces the risk of cardiac infarction by 15 to 37% and the risk of stroke by 20 to 56% (65). One-half to two-thirds of untreated OSA patients suffer from hypertension (66). On the basis of current data, the professional associations ESH (European Society of Hypertension) and the German Hypertension League (Deutsche Hochdruckliga) have declared obstructive sleep apnea to be the most frequently treatable cause of secondary hypertension.

**Pulmonary Hypertension**

Pulmonary artery blood pressure changes during obstructive apneic events. Intravascular pulmonary artery blood pressure normally drops during apnea and rises when breathing resumes. Transmural pulmonary artery pressure (corrected for intrathoracic pressure swings) rises during the course of apnea, reaching a maximum level during final occluded efforts and remains there during the early phase of hyperventilation (65). This phenomenon is associated with the degree of hypoxemia (as a consequence of apnea) and with the height of intrathoracic pressure swings (66). Mild pulmonary hypertension is a known phenomenon in OSA, with a prevalence of 20% (67). CPAP improves pulmonary hypertension in OSA patients (68).

The data on pulmonary hypertension, however, should be viewed as preliminary findings. Currently there is no agreement on the significance of sleep apnea in cases of pulmonary hypertension.

**Arrhythmia**

Arrhythmia can be caused by OSA (69, 70, 71, 72). New studies show that it occurs in more than 40% of patients (73). It is generally known that bradyarrhythmia occurs in connection with apnea (71). Follow-up studies confirm the incidence of arrhythmia, particularly during REM sleep, and its elimination through CPAP treatment (74, 75). A case report tells of a shift of the sinus rhythm to atrial fibrillation during the sleep of untreated OSA patients (76, 77). A fourfold prevalence in atrial fibrillation in patients with an AHI/hr ≥ 30 was documented in the Sleep Heart Health Study (78). Atrial fibrillation appears to be a risk factor for central apnea too (79, 80, 81).
**Pathophysiology of OSA and Association with Cardiovascular Diseases**

**OSA**
- Intermittent hypoxemia
- Intrathoracic pressure fluctuations
- Arousals

**Possible Link**
- Activation of sympathetic nervous system: Vasoconstriction, acute tachycardia, acute increase in blood pressure, cardiovascular variability LV Wall stress, afterload, acute diastolic dysfunction, left atrial stretch, left atrial enlargement, insulin resistance, hyperleptinemia, hypercoagability, systemic infection, oxidative stress, endothelial dysfunction

**Association with Cardiovascular Diseases and Risks**
- Hypertension, diastolic dysfunction, systolic dysfunction, sinus pause or arrest, atrioventricular block, atrial fibrillation, ventricular ectopy, nocturnal angina, coronary heart disease, cerebrovascular disease, sudden cardiac death

Fig. 7
Pathophysiology of OSA and association with cardiovascular diseases
Coronary Heart Disease (CHD)
The association of coronary heart disease and obstructive sleep apnea is well documented in selected patients (82, 83, 84) and in the cohort data of the Sleep Heart Health Study (85). The relationship between OSA and ischemic heart diseases has been described many times (86, 87, 88). Epidemiological and clinical data allow the conclusion to be made that OSA and CHD are frequently associated and can influence patient prognosis.

Heart failure
Data from the Sleep Heart Health Study show a strong association between sleep-disordered breathing and heart failure. An examination made by the Circulation and Sleep team of the German Sleep Society (DGSM) found sleep-disordered breathing (AHI/hr > 10) in 71% of 203 patients (NYHA II+III, stable, LVEF < 40%) (AHI/hr > 10), 43% of whom were affected by obstructive sleep apnea and 28% by central sleep apnea (12). Similar results were reported by a different team that examined 700 patients with heart failure of NYHA Class ≥ II and an LVEF of ≤ 40% for SDB (sleep-disordered breathing). SDB was registered in 76% of the heart failure patients (40% CSA, 36% OSA, 89).

In a 2008 study of heart failure patients treated with beta blockers, the prevalence of SDB was 61%, split fairly evenly between central and obstructive sleep apnea. It was also found that SDB is associated with atrial fibrillation (increased risk 11.56, p = 0.02) and poor left ventricular ejection fraction (risk 2.77, p = 0.02) (90).

Stroke
The coincidence of sleep-disordered breathing and acute stroke lies between 44 – 72% and after the acute phase remains higher than in the general population (91, 92). The prevalence of central but not obstructive sleep apnea, however, decreases significantly in the post-acute phase of stroke or of transient ischemic attacks (93).

The Wisconsin Sleep Cohort Study clearly demonstrated that an AHI/hr ≥ 20 is associated with a fourfold increase in the risk of stroke. The data came from a prospective study with a four-year follow-up. The results verify that sleep-disordered breathing precedes stroke (94). SDB can either precede stroke or occur as a consequence thereof (95).

The underlying pathophysiological mechanism was assumed to be in the more direct connection between the severity of nocturnal desaturation and the intimia media thickness and/or the appearance of atherosclerotic plaque in the carotid artery of OSA.
patients – regardless of the presence of high blood pressure (96, 97). The high prevalence of hypertension was also blamed in part for the increased prevalence of stroke in patients with SDB. It should be noted that the presence of OSA can worsen the prognosis for patients with stroke. Evidence has been provided that stroke patients with sleep apnea who reject CPAP therapy have a fivefold higher risk of suffering recurring vascular events (99).

**Heart Failure and OSA – A Vicious Circle**

- **OSA**
  - Reduced contractility
  - Systolic and diastolic heart failure
  - Decompensation
  - Death
  - Neurohumoral activation:
    - SNS
    - RAAS
    - Endothelin
    - Vasopressin
    - Natriuretic peptide
    - Cytokine
  - Hemodynamics:
    - Cardiac minute volume ↓
    - Organ perfusion ↓

Compensation:
- Vasoconstriction
- Hypertension
- Remodeling
- Apoptosis

Fig. 8
Heart Failure and OSA
6. Pathogenetic Mechanisms in Obstructive and Central Respiratory Events

**OSA**
When the pharynx closes during an apneic event, the body increases inspiratory effort in order to re-open the airways and counteract desaturation of the blood. As a result of the changed pressure conditions in the thorax, the left ventricular transmural pressure rises and afterload increases with it. Furthermore, the high negative intrathoracic pressure effects a rise in venous blood return. The right ventricle relaxes, triggering a septal shift in the diastolic pressure-volume relation and with it impaired filling of the left ventricle.

The intermittent hypoxemia resulting from apneic/hypopneic phases weakens the contractility of the heart, which receives inadequate supplies of oxygen. The arousals, hypoxia and hypercapnia trigger the sympathetic nervous system, leading to activation of the sympathetic system and a decrease in parasympathetic modulation of the heart rate. This results in increased cardiac pressure load during the day as well as at night.

**CSR – with periodic breathing (Cheyne-Stokes Respiration)**
The incidence of CSR is associated with severe forms of heart failure. The prevalence of CSR in these patients is 30 to 40% (89).

It is assumed that CSR with chronic hypocapnia arises in response to elevated LVEDP (left ventricular end-diastolic pressure) and pulmonary congestion. Hyperventilation pushes the CO$_2$ level below the apnea threshold. When this mechanism becomes chronic, a higher chemosensitivity to CO$_2$ develops. The apneic phases lead to a fall in pO$_2$ and a rise in pCO$_2$. This in turn effects an increase in ventilation (overshooting), a renewed fall in pCO$_2$ and thus the cyclical alternation between apneic phases and hyperventilation that makes up the Cheyne-Stokes pattern. Other effects include intermittent rise in arterial blood pressure, increased activation of the sympathetic nervous system and elevation of the catecholamine level (100).
In cases of CSR, arousals typically occur at the peak of hyperventilation. The disease is associated with sleep fragmentation, cyclical hypoxemia, hyperactivity of the sympathetic nervous system and periodic increases in cardiac rate and blood pressure.

Central sleep apnea has important clinical ramifications for heart failure. The sleepiness already evident in these patients is aggravated by disrupted sleep, but is not as prominent as in patients with obstructive sleep apnea. The nighttime periodic desaturations also worsens the underlying disease by impairing the oxygen supply to the heart muscle and negatively affecting ventricular performance and the stability of the heart rate.

It is known that patients with heart failure and Cheyne-Stokes Respiration have a poorer prognosis than comparable patients without CSR.

Increased activity of the sympathetic nervous system can lead to lower life expectancy in patients with heart failure and CSR and can play a critical role in the progression of the syndrome.

An interesting phenomenon is the overnight shift from obstructive to central apnea in patients with heart failure (101). Among the varied theses being discussed, one says that cardiac output falls and ventricular filling pressure rises during the night in lying heart failure patients (102). This mechanism could be intensified by

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**SDB with Heart Failure**

<table>
<thead>
<tr>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSA</td>
<td></td>
<td></td>
<td>CSR</td>
</tr>
</tbody>
</table>

Fig. 9
Sleep-Disordered Breathing does not occur in isolation in cases of heart failure. Current observations reveal that obstructive sleep apnea is in evidence mainly in an early stage and central sleep apnea in a later stage. These findings reflect practical experience, but conclusive evidence has not yet been provided.
OSA, which can raise pulmonary capillary pressure and reduce cardiac output (103, 104).

A current hypothesis assumes (TD Bradley, Heart Failure lecture, 2008, Milan) that general edema in those patients dissipates over the course of the night, unmasking central events.

Moreover, observations have been made of the phenomenon of central sleep apnea with CSR based on underlying heart failure and co-prevalent obstructive sleep apnea. This comorbidity is frequently encountered in actual cases. Prevalence has not yet been determined by epidemiological studies. A possible explanation (as shown in Illustration 9 on page 22) states that patients lose weight in the course of heart failure and consequently reduce the risk associated with OSA.
7. Diagnostic and Therapeutic Measures

Available data underscore the importance of early detection and effective therapy of sleep-disordered breathing.

The high prevalence of sleep-disordered breathing in cases of heart failure justify the recommendation of SDR screening of all patients with heart failure, arterial hypertension and absolute arrhythmia with atrial fibrillation.

Diagnostics
Devices that are particularly suitable for early diagnostics have modern one to two-channel systems with intelligent analytical algorithms, like SOMNOcheck micro. Nasal cannula and pulsoximeter ascertain respiratory flow, pulse and oxygen saturation along with other parameters such as sleep quality and obstructive or central breathing disorders.

Polygraphy has become established as a screening tool. Checks are made of respiratory flow, effort, snoring, heart rate, oxygen saturation and body position. After treatment has been initiated, information about therapeutic effectiveness (CPAP, Bilevel) can also be obtained.

Findings on sleep quality are acquired through data compiled by electroencephalogram (EEG), electro-oculography (EOG) and electromyogram (EMG). Among other things, these non-invasive methods measure brain waves which register the depth of sleep during the night. The screening devices can be used in a sleep lab or at home.
Fig. 12
Polysomnography with SOMNOcheck 2 R&K

Therapeutic Options

CPAP (Continuous Positive Airway Pressure) devices are the gold standard in the treatment of OSA. With the help of a blower, the CPAP device generates positive pressure that is delivered to the patient via a hose and nasal or full face mask. The air pressure works as a splint to keep the patient’s upper airways open and prevent their collapse. This approach is considered less effective in the treatment of central sleep apnea with a Cheyne-Stokes breathing pattern. In such cases the preferred method is ACMV (AntiCyclical Modulated Ventilation), which is also known as ASV (Adaptive Servo-Ventilation) (cf. SOMNOvent CR).

An auto-CPAP device may be indicated for position or REM-dependent obstructive sleep apnea or for patients with compliance problems since it can continuously and automatically adjust to the needs of the patient.

Options for patients who suffer from Cheyne-Stokes Respiration include oxygen therapy, CPAP or Bilevel devices.

Devices that function on the basis of anticyclical modulated ventilation or adaptive servo-ventilation have proven to be effective in eliminating central respiratory events (105, 106, 107).

Fig. 14
SOMNOvent CR – a new method takes hold

The Anti-Cyclic Modulated Ventilation (ACMV) – supplemented by automatic EEPAP therapy (corresponds to CPAP) – has clear advantages over the classic CPAP method in treatment of Sleep-Disordered Breathing with a specific focus (e.g., Cheyne-Stokes Respiration) or simultaneously occurring obstructive sleep apnea. It balances out respiratory fluctuations with an anticyclical response and thereby modulates pathophysiological respiration in a physiological direction. With SOMNOvent CR central and obstructive events are registered and effectively treated. The intelligent algorithm continuously adjusts to the needs of the patient throughout the night and regulates the patient’s breathing gently so that restful sleep is guaranteed.

Fig. 13
The autoCPAP device SOMNObalance
8. Outlook

Scientific findings in sleep medicine have led to the conclusion that sleep should be made the fourth pillar of prevention. Questions about sleep quality should be integrated in cardiovascular risk scores like PROCAM.

Fig. 15
Sleep – the fourth pillar of prevention
Scientific data clearly show that sleep disordered breathing such as OSA and CSR are systemic diseases which should be carefully diagnosed and treated. Although the field of sleep medicine has become firmly established, it is estimated that more than 90% of patients have not yet been diagnosed. Most of them are in cardiac or neurological clinics for the treatment of cardiovascular diseases such as heart failure and stroke or are in special diabetic clinics or in the care of other specialists. Efficient and effective therapy can be guaranteed only when all cardiovascular risks have been identified and treated. That includes the treatment of sleep disordered breathing.

Who’s Who?

Fig. 16
Who’s Who? Who faces cardiovascular risk? Who is also burdened by comorbidity?
9. Sources

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10. Glossary

AF = atrial fibrillation, temporary or chronic abnormal heart rate resulting from lack of coordination between atria and ventricles, atria are stimulated at a rate of 350 – 600/minute.

ANP = atrial natriuretic peptide

BNP = B-type natriuretic peptide

Cardioversion = Reestablishment of normal heart rate (Sinus rhythm) in event of arrhythmia, usually atrial fibrillation.

CRP = C-reactive peptide

NYHA = New York Health Association

SDB = Sleep-Disordered Breathing

TNF = Tumor necrosis factor
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