

Editorial

Sleep Apnea Diagnostic in Cardiac Rehabilitation – Needless? Necessary? State of the Art?

Erik Skobel*

Clinic for Cardiac and Pulmonary Rehabilitation, Germany

*Corresponding author: Clinic for Cardiac and Pulmonary Rehabilitation, Germany

Received: October 19, 2014; Accepted: October 20, 2014; Published: October 21, 2014

Editorial

Sleep related breathing disorders (SRBD) are common in cardiovascular disease, obesity and diabetes with massive effect on social-economic burden. Whereas prevention often aims control of blood pressure, weight and glucose level, sleep apnea is not included in general diagnostics. This editorial gives a general view of studies regarding prevalence of sleep apnea in cardiovascular disease and raises question if screening for sleep apnea should be done generally in cardiac rehabilitation.

The number of patients worldwide with diabetes is more than 280 million [1]. The mortality on cardiovascular disease is 17 million patients [2], while the prevalence of SRBD is 3-9 % in women and 10-17 % of men [3]. The rising incidence of obesity will lead to a raising incidence of SRBD in the future.

The prevalence of SRBD in cardiovascular disease is high and has effect on mortality and reoccurrence of cardiac events. But a routinely performed screening for SRBD in cardiovascular disease is rarely used and still under discussion [4].

Obstructive sleep apnea (OSA) is the most prevalent type of SRBD. It is defined as repetitive episodes of partial or complete cessation of airflow in the upper airways during sleep.

Patients with OSA typically present with symptoms such as disruptive snoring, witnessed apnea or gasping, excessive daytime sleepiness, morning headache, sleep disturbance and cognitive dysfunction [5, 6]. OSA has been associated with increases in cardiovascular morbidity and mortality.⁷⁻⁹ The most important mechanisms to cause myocardial damage are increased sympathetic activity, heart rate variability, endothelial dysfunction, systemic inflammation, oxidative stress, platelet activation and metabolic abnormalities [5, 10-18] and are associated with hypertension, cardiac hypertrophy, heart failure, stroke, arrhythmias, myocardial infarction (MI), pulmonary arterial hypertension (PAH), and end-stage renal disease. [4, 5, 19, 20]

The simultaneous absence of inspiratory airflow and respiratory movement indicate the presence of central sleep apnea episodes. Cheyne-Stokes respiration (CSR) is a form of periodic breathing in which apneas and hypopneas with ventilatory periods having a

crescendo-decrescendo pattern of tidal volume [21]. Cheyne-Stokes-respiration (CSR), a frequent breathing disorder in heart failure (HF) patients, is known to have negative impact on mortality, quality of life and increases the incidence of depression [22, 23]. Increased peripheral and central chemo sensitivity, prolonged circulation time, activation of lung vagal irritant receptors by increased LV-filling pressure, and reduced blood gas buffering capacity have been discussed as pathophysiological mechanisms [21, 24].

Diagnosis of SRBD can be made using polysomnography (PSG) or at-home polygraphy. Although the American Academy of Sleep Medicine (AASM) recommends PSG for the evaluation and diagnosis of SDB [21], many centres do not have this type of facility and polygraph is a feasible and validated alternative [25-33]. According to AASM Task Force definitions [21] an AHI of $\geq 5/h$ defines the presence of SRBD, although the AHI cut-off for diagnosing SRBD varies between studies, whereas a cut-off $\geq 15/h$ is clinical significant with profit from nCPAP-therapy if OSA is present [34, 35].

In the last few years different registries evaluated the prevalence of SRBD in cardiovascular disease and add important information about risk evaluation for SRBD.

a) Prevalence of SRBD in diabetes and metabolic syndrome

OSA in diabetes and metabolic syndrome was found between 73% and 86 % and was associated with CAD and worse HbA1c [36, 37, 38, 39, 40]. Severe OSA (AHI > 30/h) was present in 30 % [40]. The International Diabetes Federation recommends a general screening for OSA [1].

b) Prevalence in hypertension

There is a known association between OSA and hypertension with a prevalence of 40-60 %, in refractory hypertension up to 71% [41, 42].

c) Prevalence in CAD and myocardial infarction

In patients with CAD there is a prevalence of 73 % documented. In acute MI 69 % of the patients exhibit medium to severe SRBD [43]. OSA is associated with re-infarction and thrombosis of stent grafts [7].

d) Prevalence of SRBD in HF with reduced (HFREF) and preserved (HFPEF) left ventricular function

In patients with HFREF there is a high prevalence of SRBD (49 % - 72%) with high amount of CSR [23, 44, 45]. Also in hypertrophic cardio myopathy (83 %) [46] and HFPEF (69 %) a high prevalence is reported [47-51]. SRBD in HF are associated with high mortality. Sleepiness is not very common mostly in CSR, but SRBD is associated with lower quality of life and occurrence of depression [23].

e) Prevalence of SRBD in patients with arrhythmia and cardiac pacing

In patients with atrial fibrillation the reported prevalence is between 30-75 % in all types of atrial fibrillation [52-55]. OSA is associated with enlargement of the atrium with higher recurrence rate of atrial fibrillation. Also there is high prevalence in atrial flutter (82 %) [56], Brugada syndrome (45 %) [57] and in patients with cardiac pacers (59 %) with severe SRBD in 21 % [58].

f) Prevalence in heart valve disease

In patients with valvular aortic stenosis SRBD were found in 72 % with OSA and CSR present [59]. The effect on mortality has not been evaluated yet.

g) Prevalence in pulmonary hypertension

SRBD are one reason for pulmonary hypertension owing to lung disease and hypoxia (WHO group III) or can be associated with PAH (WHO group I). Chronic nocturnal hypoxias are patho physiological reason for elevated pulmonary pressure at night with effect on right ventricle and influence on endothelial-related vasoconstriction and dilatation with hypertrophy of media and intima obstruction (based on Endothelin-1). The prevalence of PH in OSA is prescribed between 20 and 73 % [60, 61]. Also in idiopathic pulmonary hypertension and chronic-thromboembolic pulmonary hypertension (CTPH) there is a high prevalence of SRBD (up to 89 %) with nocturnal hypoxemia and sleep apnea [62, 63].

h) Prevalence of SRBD in cardiac rehabilitation (CR)

Cardiac rehabilitation focuses on risk factors for CAD and is an ideal stage for diagnostic of SRBD. So diagnostic and treatment of SRBD are more and more evaluated in cardiac rehabilitation [64]. Sharma et al. for example evaluated a possible prevalence of OSA in CAD patients during cardiac rehabilitation of 50 %. They used the Berlin questionnaire for evaluation. A polygraphy was not used for further evaluation [65]. In our own evaluation we were able to show a prevalence of SRBD of more than 50 % in patients with HFREF during rehabilitation in our facility [66]. In a multi center trial of the German Society of Prevention and Rehabilitation in 9 cardiac rehabilitation facilities in Germany, 1152 patients were screened for sleep-disordered breathing with 2-channel polygraphy. Parameters recorded included the Apnea-hyperpnoea index (AHI), number of de saturations per hour of recording (ODI), mean and minimum nocturnal oxygen saturation, and number of snoring episodes. Patients rated subjective sleep quality on a scale from 1 (poor) to 10 (best) and completed the Epworth Sleepiness Scale (ESS). Clinical significant sleep apnea (AHI \geq 15/h) was documented in 33 % of patients. ESS score and subjective sleep quality differ only slightly significantly between patients with and without apnea. Logistic regression model analysis identified age, body mass index, male gender, diabetes and hemoglobin levels as risk factors for sleep apnea in CR patients [67].

So is a general screening necessary for SRBD in cardiovascular disease and rehabilitation?

A screening for SRBD is recommended in the Guidelines of the International Diabetes Federation [1] and the Guidelines of the European Society for Cardiology for therapy-refractory hypertension (ESH/ESC Guidelines) [6, 68]. As treatment for OSA with nCPAP has high evidence for reducing cardiovascular events, also screening in CAD and after MI is recommended [35, 69]. In HFREF and HFPEF

the presence of OSA is also associated with high mortality and effect on outcome. nCPAP- therapy can reduce the mortality in HF if OSA is present [45]. In central sleep apnea optimal heart failure treatment with beta blockers [70] or cardiac resynchronization therapy (CRT) [71] has positive effect and should be discussed if CSR in HF is present. The use of adaptive servo ventilation (ASV) for central sleep apnea is still under investigation [72]. OSA is associated with atrial fibrillation and the treatment with nCPAP [20] can reduce the risk of recurrence.

As in cardiac rehabilitation screening for SRBD is easy to perform, a screening in patients with diabetes, CAD, MI, HF and atrial fibrillation is recommended. Initiation of treatment with nCPAP is easy to perform and has effect on recurrence and outcome in these patients. Furthermore training for the use of the nCPAP-device is also possible during the rehabilitation process to improve compliance. As a first step in cardiac rehabilitation the use of questionnaires (Berlin, Epworth sleepiness score) should be performed. Secondly 24h-ecg also gives the possibility today to evaluate the risk for sleep apnea. If there is high risk present, 2-channel polygraphy as a screening tool are easy to use and if SRBD is present, six-channel-polygraph or polysomnography are needed. These diagnostic features are not available in all cardiac rehabilitation facilities, as reimbursement by health care providers for diagnostic and treatment of SRBD in cardiac rehabilitation is still refused (in Germany for example).

Here more data is needed to show the benefit of diagnostic and treatment during cardiac rehabilitation to improve outcome in patients with cardiovascular disease. So we need more discussion of these diagnostic features of well known but still under diagnosed SRBD.

General screening for SRBD in cardiac rehabilitation is necessary, but actually not state of the art. Here further work has to be done.

References

- Shaw JE, Sicree RA, Zimmet PZ . Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Res Clin Pract.* 2010; 87: 4-14.
- Bovet P. Cardiovascular disease and the changing face of global public health: a focus on low and middle income countries. . *Public Health Review* 2012:397-415.
- Kendzierska T, Gershon AS2, Hawker G3, Leung RS4, Tomlinson G5 . Obstructive sleep apnea and risk of cardiovascular events and all-cause mortality: a decade-long historical cohort study. *PLoS Med.* 2014; 11: e1001599.
- Lopez-Jimenez F, Sert Kuniyoshi FH, Gami A, Somers VK . Obstructive sleep apnea: implications for cardiac and vascular disease. *Chest.* 2008; 133: 793-804.
- Somers VK, White DP, Amin R, et al. Sleep apnea and cardiovascular disease: an American Heart Association/american College Of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council On Cardiovascular Nursing. In collaboration with the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health). *Circulation* 2008;118: 1080-1111.
- Parati G, Lombardi C, Hedner J, et al. Position paper on the management of patients with obstructive sleep apnea and hypertension: joint recommendations by the European Society of Hypertension, by the European Respiratory Society and by the members of European COST (COoperation in Scientific and Technological research) ACTION B26 on obstructive sleep apnea. *Journal of hypertension* 2012; 30: 633-646.

7. Correia LC, Souza AC, Garcia G, Sabino M, Brito M, Maraux M, Rabelo MM . Obstructive sleep apnea affects hospital outcomes of patients with non-ST-elevation acute coronary syndromes. *Sleep*. 2012; 35: 1241-1245A.
8. Mooe T, Franklin KA, Holmström K, Rabben T, Wiklund U . Sleep-disordered breathing and coronary artery disease: long-term prognosis. *Am J Respir Crit Care Med*. 2001; 164: 1910-1913.
9. Jilek C, Krenn M, Sebah D, Obermeier R, Braune A, Kehl V, Schroll S . Prognostic impact of sleep disordered breathing and its treatment in heart failure: an observational study. *Eur J Heart Fail*. 2011; 13: 68-75.
10. Galletti F, Barbato A, Versiero M, Iacone R, Russo O, Barba G, Siani A . Circulating leptin levels predict the development of metabolic syndrome in middle-aged men: an 8-year follow-up study. *J Hypertens*. 2007; 25: 1671-1677.
11. Minoguchi K, Yokoe T, Tazaki T, Minoguchi H, Tanaka A, Oda N, Okada S . Increased carotid intima-media thickness and serum inflammatory markers in obstructive sleep apnea. *Am J Respir Crit Care Med*. 2005; 172: 625-630.
12. Kourembanas S, Marsden PA, McQuillan LP, Faller DV . Hypoxia induces endothelin gene expression and secretion in cultured human endothelium. *J Clin Invest*. 1991; 88: 1054-1057.
13. Meier-Ewert HK, Ridker PM, Rifai N, Regan MM, Price NJ, Dinges DF, Mullington JM . Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. *J Am Coll Cardiol*. 2004; 43: 678-683.
14. Vgontzas AN, Papanicolaou DA, Bixler EO, Kales A, Tyson K, Chrousos GP . Elevation of plasma cytokines in disorders of excessive daytime sleepiness: role of sleep disturbance and obesity. *J Clin Endocrinol Metab*. 1997; 82: 1313-1316.
15. Prabhakar NR . Sleep apneas: an oxidative stress? *Am J Respir Crit Care Med*. 2002; 165: 859-860.
16. Schulz R, Mahmoudi S, Hattar K, Sibelius U, Olschewski H, Mayer K, Seeger W . Enhanced release of superoxide from polymorphonuclear neutrophils in obstructive sleep apnea. Impact of continuous positive airway pressure therapy. *Am J Respir Crit Care Med*. 2000; 162: 566-570.
17. Suzuki YJ, Jain V, Park AM, Day RM . Oxidative stress and oxidant signaling in obstructive sleep apnea and associated cardiovascular diseases. *Free Radic Biol Med*. 2006; 40: 1683-1692.
18. von Känel R, Loredó JS, Ancoli-Israel S, Mills PJ, Natarajan L, Dimsdale JE . Association between polysomnographic measures of disrupted sleep and prothrombotic factors. *Chest*. 2007; 131: 733-739.
19. Baguet JP, Barone-Rochette G, Tamisier R, Levy P, Pépin JL . Mechanisms of cardiac dysfunction in obstructive sleep apnea. *Nat Rev Cardiol*. 2012; 9: 679-688.
20. Latina JM, Estes NA 3rd, Garlitski AC . The Relationship between Obstructive Sleep Apnea and Atrial Fibrillation: A Complex Interplay. *Pulm Med*. 2013; 2013: 621736.
21. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 2012; 8: 597-619.
22. Arzt M, Floras JS, Logan AG, Kimoff RJ, Series F, Morrison D, Ferguson K . Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: a post hoc analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP). *Circulation*. 2007; 115: 3173-3180.
23. Skobel E, Norra C, Sinha A, Breuer C, Hanrath P, Stellbrink C . Impact of sleep-related breathing disorders on health-related quality of life in patients with chronic heart failure. *Eur J Heart Fail*. 2005; 7: 505-511.
24. Arzt M, Young T, Finn L, Skatrud JB, Ryan CM, Newton GE, Mak S. Sleepiness and sleep in patients with both systolic heart failure and obstructive sleep apnea. *Arch Intern Med*. 2006; 166: 1716-1722.
25. Wang Y, Teschler T, Weinreich G, Hess S, Wessendorf TE, Teschler H . [Validation of microMESAM as screening device for sleep disordered breathing]. *Pneumologie*. 2003; 57: 734-740.
26. Baisch A, Afshar S, Hörmann K, Maurer JT . [Use of a screening device for sleep apnea in clinical practice]. *HNO*. 2007; 55: 90-92.
27. Erman MK, Stewart D, Einhorn D, Gordon N, Casal E. Validation of the ApneaLink for the screening of sleep apnea: a novel and simple single-channel recording device. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 2007; 3: 387-392.
28. Ng SS, Chan TO, To KW, et al. Validation of a portable recording device (ApneaLink) for identifying patients with suspected obstructive sleep apnoea syndrome. *Internal medicine journal* 2009; 39: 757-762.
29. Chen H, Lowe AA, Bai Y, Hamilton P, Fleetham JA, Almeida FR . Evaluation of a portable recording device (ApneaLink) for case selection of obstructive sleep apnea. *Sleep Breath*. 2009; 13: 213-219.
30. Clark AL, Crabbe S, Aziz A, Reddy P, Greenstone M . Use of a screening tool for detection of sleep-disordered breathing. *J Laryngol Otol*. 2009; 123: 746-749.
31. Weinreich G, Armitstead J, Töpfer V, Wang YM, Wang Y, Teschler H . Validation of ApneaLink as screening device for Cheyne-Stokes respiration. *Sleep*. 2009; 32: 553-557.
32. Ragette R, Wang Y, Weinreich G, Teschler H . Diagnostic performance of single airflow channel recording (ApneaLink) in home diagnosis of sleep apnea. *Sleep Breath*. 2010; 14: 109-114.
33. Nigro CA Dibur E, Malnis S, Grandval S, Nogueira F . Validation of ApneaLink Oxá,ç for the diagnosis of obstructive sleep apnea. *Sleep Breath*. 2013; 17: 259-266.
34. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman J Jr, Friedman L . Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep*. 2005; 28: 499-521.
35. Buchner NJ, Sanner BM, Borgel J, Rump LC . Continuous positive airway pressure treatment of mild to moderate obstructive sleep apnea reduces cardiovascular risk. *Am J Respir Crit Care Med*. 2007; 176: 1274-1280.
36. Aronsohn RS, Whitmore H, Van Cauter E, Tasali E . Impact of untreated obstructive sleep apnea on glucose control in type 2 diabetes. *Am J Respir Crit Care Med*. 2010; 181: 507-513.
37. Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R, Ewy GA . Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. *Diabetes Care*. 2003; 26: 702-709.
38. Surani S . Are diabetic patients being screened for sleep related breathing disorder? *World J Diabetes*. 2013; 4: 162-164.
39. Pamidi S, Aronsohn RS, Tasali E . Obstructive sleep apnea: role in the risk and severity of diabetes. *Best Pract Res Clin Endocrinol Metab*. 2010; 24: 703-715.
40. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, Wadden TA . Obstructive sleep apnea among obese patients with type 2 diabetes. *Diabetes Care*. 2009; 32: 1017-1019.
41. Rao M, Rajda G, Uppuluri S, Beck GR, Liu L, Bisognano JD. The role of continuous positive airway pressure in the treatment of hypertension in patients with obstructive sleep apnea-hypopnea syndrome: a review of randomized trials. *Reviews on recent clinical trials* 2010; 5: 35-42.
42. Lavie P, Ben-Yosef R, Rubin AE . Prevalence of sleep apnea syndrome among patients with essential hypertension. *Am Heart J*. 1984; 108: 373-376.
43. Prinz C, Bitter T, Piper C, Horstkotte D, Faber L, Oldenburg O . Sleep apnea is common in patients with coronary artery disease. *Wien Med Wochenschr*. 2010; 160: 349-355.
44. Bitter T, Westerheide N, Hossain SM, Prinz C, Horstkotte D, Oldenburg O . Symptoms of sleep apnoea in chronic heart failure--results from a prospective cohort study in 1,500 patients. *Sleep Breath*. 2012; 16: 781-791.

45. Kourouklis SP, Vagiakis E, Paraskevaidis IA, Farmakis D, Kostikas K, Parissis JT, Katsivas A . Effective sleep apnoea treatment improves cardiac function in patients with chronic heart failure. *Int J Cardiol.* 2013; 168: 157-162.
46. Prinz C, Bitter T, Oldenburg O, Horstkotte D, Faber L . Incidence of sleep-disordered breathing in patients with hypertrophic cardiomyopathy. *Congest Heart Fail.* 2011; 17: 19-24.
47. Oldenburg O, Lamp B, Freudenberg G, Horstkotte D . Screening for sleep-disordered breathing is recommended in patients with chronic heart failure. *Eur Respir J.* 2007; 30: 1023.
48. Schulz R, Blau A, Börgel J, Duchna HW, Fietze I, Koper I, Prenzel R . Sleep apnoea in heart failure. *Eur Respir J.* 2007; 29: 1201-1205.
49. Javaheri S . Sleep disorders in systolic heart failure: a prospective study of 100 male patients. The final report. *Int J Cardiol.* 2006; 106: 21-28.
50. Bitter T, Faber L, Hering D, Langer C, Horstkotte D, Oldenburg O . Sleep-disordered breathing in heart failure with normal left ventricular ejection fraction. *Eur J Heart Fail.* 2009; 11: 602-608.
51. Pedrosa RP, Drager LF, Genta PR, Amaro AC, Antunes MO, Matsumoto AY, Arteaga E . Obstructive sleep apnea is common and independently associated with atrial fibrillation in patients with hypertrophic cardiomyopathy. *Chest.* 2010; 137: 1078-1084.
52. Mansukhani MP, Calvin AD, Kolla BP, Brown RD Jr, Lipford MC, Somers VK, Caples SM . The association between atrial fibrillation and stroke in patients with obstructive sleep apnea: a population-based case-control study. *Sleep Med.* 2013; 14: 243-246.
53. Bitter T, Gutleben KJ, Nölker G, Westerheide N, Prinz C, Dimitriadis Z, Horstkotte D . Treatment of Cheyne-Stokes respiration reduces arrhythmic events in chronic heart failure. *J Cardiovasc Electrophysiol.* 2013; 24: 1132-1140.
54. Gami AS, Pressman G, Caples SM, Kanagala R, Gard JJ, Davison DE, Malouf JF . Association of atrial fibrillation and obstructive sleep apnea. *Circulation.* 2004; 110: 364-367.
55. Stevenson IH, Teichtahl H, Cunningham D, Ciavarella S, Gordon I, Kalman JM. Prevalence of sleep disordered breathing in paroxysmal and persistent atrial fibrillation patients with normal left ventricular function. *Eur Heart J* 2008; 29: 1662-1669.
56. Bazan V, Grau N, Valles E, Felez M, Sanjuas C, Cainzos-Achirica M, Benito B . Obstructive sleep apnea in patients with typical atrial flutter: prevalence and impact on arrhythmia control outcome. *Chest.* 2013; 143: 1277-1283.
57. Macedo PG, Brugada J, Leinveber P, Benito B, Molina I, Sert-Kuniyoshi F, Adachi T . Sleep-disordered breathing in patients with the Brugada syndrome. *Am J Cardiol.* 2011; 107: 709-713.
58. Garrigue S, Pépin JL, Defaye P, Murgatroyd F, Poezevara Y, Clémenty J, Lévy P . High prevalence of sleep apnea syndrome in patients with long-term pacing: the European Multicenter Polysomnographic Study. *Circulation.* 2007; 115: 1703-1709.
59. Prinz C, Bitter T, Oldenburg O, Faber L, Horstkotte D, Piper C . Sleep apnoea in severe aortic stenosis. *Postgrad Med J.* 2011; 87: 458-462.
60. Dumitrascu R, Tiede H, Eckermann J, Mayer K, Reichenberger F, Ghofrani HA, Seeger W . Sleep apnea in precapillary pulmonary hypertension. *Sleep Med.* 2013; 14: 247-251.
61. Ulrich S, Fischler M, Speich R, Bloch KE . Sleep-related breathing disorders in patients with pulmonary hypertension. *Chest.* 2008; 133: 1375-1380.
62. Jilwan FN, Escourrou P, Garcia G, Jaïs X, Humbert M, Roisman G . High occurrence of hypoxemic sleep respiratory disorders in precapillary pulmonary hypertension and mechanisms. *Chest.* 2013; 143: 47-55.
63. Hildenbrand FF, Bloch KE, Speich R, Ulrich S . Daytime measurements underestimate nocturnal oxygen desaturations in pulmonary arterial and chronic thromboembolic pulmonary hypertension. *Respiration.* 2012; 84: 477-484.
64. Penzel T, Fietze I, Schöbel C, Baumann G . [Sleep apnoea syndrome in the rehabilitation setting]. *Herz.* 2012; 37: 44-47.
65. Sharma S, Parker AT. Prevalence of obstructive sleep apnea in a patient population undergoing cardiac rehabilitation. *Journal of cardiopulmonary rehabilitation and prevention* 2011; 31:188-192.
66. Skobel E RP, Schenck S, Henssen O, Jendralski A . Screening for sleep related breathing disorders in patients with chronic heart failure during cardiac rehabilitation. *World Heart Failure Hamburg* 2007: 62.
67. Skobel E AB, Kamke W, Bönner G, Purucker HC, Alt B, Schwaab B, et al. Risk factors for, and prevalence of, sleep apnoea in cardiac rehabilitation facilities in Germany: The Reha-Sleep registry. *European journal of preventive cardiology.* 2014. doi:10.1177/2047487314537916.
68. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *European heart journal* 2013; 34: 2159-2219.
69. Jean-Louis G, Brown CD, Zizi F, Ogedegbe G, Boutin-Foster C, Gorga J, McFarlane SI . Cardiovascular disease risk reduction with sleep apnea treatment. *Expert Rev Cardiovasc Ther.* 2010; 8: 995-1005.
70. Tamura A, Kawano Y, Kadota J . Carvedilol reduces the severity of central sleep apnea in chronic heart failure. *Circ J.* 2009; 73: 295-298.
71. Sinha AM, Skobel EC, Breithardt OA, Norra C, Markus KU, Breuer C, Hanrath P . Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure. *J Am Coll Cardiol.* 2004; 44: 68-71.
72. Cowie MR, Woehrle H, Wegscheider K, et al. Rationale and design of the SERVE-HF study: treatment of sleep-disordered breathing with predominant central sleep apnoea with adaptive servo-ventilation in patients with chronic heart failure. *European journal of heart failure* 2013; 15: 937-943.