367. Cardiovascular disease and sleep-disordered breathing

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Prediction of cardiovascular risk from nocturnal pulse wave signal using the autonomic state indicator technology

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Introduction: Analysis of continuous physiological signals measured by pulse oximetry during sleep may provide a novel method to assess cardiovascular (CV) risk. The sleep period appears to be a particularly useful window for assessment.
Methods: Subjects (n=520, 346 males, age 55.0*m*13.4 yrs, BMI 29.9*m*6.1 kg/m^2) were referred to five sleep centers in Germany and Sweden. CV risk factors were assessed and subjects were classified by the ESC/ESH risk matrix into five separate risk classes. The autonomic state indicator (ASI) algorithm extracted patterns of the peripheral pulse wave and SpO_2 signal by amplitude and time/frequency analysis from the overnight digital photoplethysmographic recording and computed a CV risk score (range 0-1, $\geq$0.5 equals to high risk). Nine derived parameters (irregular pulse, RCDC, pulse rate variability, pulse wave variability, pulse propagation time, oxygen desaturations, duration of periodic symmetric desaturations and baseline SpO_2) were used to determine the final score.
Results: In the validation group (n=390), the developed algorithm detected high CV risk (ESC/ESH scores 4 and 5) patients with a sensitivity of 74.5% and specificity of 76.4%. The area under the ROC curve was 0.80. The ASI CV risk score was elevated in patients with an already established CV endpoint (MI and/or stroke, n=50) compared with all other patients (0.73±0.27 vs. 0.42±0.34, p<0.001).
Conclusions: The ASI technique appears to provide a possibility to detect increased CV risk from a recording of physiological signals during sleep. The technique – based on a modified pulse oximeter – may be useful in both sleep and cardiovascular medicine.

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Mortality in heart failure patients with nocturnal Cheyne-Stokes respiration receiving adaptive servoventilation (ASV) therapy

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Sleep-disordered breathing (SDB) with Cheyne-Stokes respiration (CSR) is of major prognostic impact in heart failure (HF) patients. Adaptive Servoventilation (ASV) therapy was recently introduced to especially treat CSR in these patients. First results on mortality (time of death, left-ventricular assist device (LVAD) device implantation and heart transplantation (HTX)) of a prospective registry are presented.
A total of 186 HF patients (NYHA $\geq$ II, EF $\leq$ 45%), treated according to present HF guidelines, with nocturnal CSA (apnoea-hypopnoea-Index, AHI $\geq$ 15/h) received additional ASV treatment (AutoSet CS, ResMed) and were included into a prospective registry. Mean age at inclusion (168 male, 91%) was 67±11 years, BMI 28.8±4.2 kg/qm, NYHA functional class 2.6±0.6, NT-proBNP levels 2722±3420 pg/ml, left ventricular ejection fraction 31±8% and peak VO_2 during cardiopulmonary exercise testing 14.4±4.7 ml/kg/min. AHI before ASV initiation was 38.8±14.8/h, apnoea-index 22.2±15.2/h. After 20.7±16.1 months a total of 35 patients (18.8%) reached a final endpoint: 28 (15.1%) died, 6 (3.2%) received HTX and one (0.5%) LVAD implantation. Within the follow-up period, ASV therapy was discontinued by 26 patients (14.0%) and 15 patients (8.1%) met indication for cardiac resynchronization therapy (CRT).
Mortality in HF patients with nocturnal CSA and ASV treatment remains high. If there is any reduction in mortality and/or hospitalization is currently be investigated by 2 randomized controlled trials, first results are not expected before 2014. With 14% discontinuation, ASV therapy seems to be well tolerated and accepted.

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Sleep disordered breathing in patients undergoing transfemoral aortic valve implantation for severe aortic stenosis

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Purpose: We examined the prevalence of sleep-disordered breathing (SDB) in patients (pts) with severe aortic valve stenosis before and after transfemoral aortic valve implantation (TAVI).
Methods: 79 pts (50% males, average age 83.0±6.3 years) had cardiorespiratory polygraphy (PG) screening before TAVI. 62 of them (48.4% males, mean age 82.5±6.5 years) underwent a second PG screening 21.0±4.7 days after TAVI.
Results: 49 (62.0%) pts had OSA, 25 (31.6%) CSA and only 5 (6.3%) presented without significant SDB (apnoea-hypopnoea-index, AHI <5/h). Of 62 pts evaluated before and after valve implantation 36 (58.1%) had OSA, 21 (33.8%) presented with CSA and no SDB was detected in 5 pts (8.0%). SDB was more severe in CSA compared to OSA (AHI 34.5±18.3/h vs. 18.0±12.6/h, p<0.001). Successful TAVI had a significant impact on CSA, but not on OSA: pts with optimal TAVI results (aortic valve regurgitation, AI $\leq$ grade 1) demonstrated a significant reduction of central respiratory events (39.6±19.6/h to 23.1±16.0/h, p=0.035), while no changes were detected regarding OSA (18.8±13.0/h to 20.25±13.4/h, p=0.376). Pts with primarily suboptimal TAVI results (AI $\geq$ 2) presented with no change in OSA (10.5±7.8/h to 12.5±5.0/h, p=0.5) and an increase in central respiratory events (26.3±13.2/h to 39.2±18.4/h p= 0.036).
Conclusions: There is a high prevalence of OSA and CSA in pts in TAVI candidates. Successful TAVI had no significant impact on OSA, but improved CSA significantly. TAVI resulting in moderate to severe AI is accompanied by a deterioration of CSA. Presence of CSA after TAVI may indicate prognostically relevant haemodynamic alterations like AI and/or heart failure.

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PAI-uPA system in patients with obstructive sleep apnea syndrome (OSAS) in CPAP treatment

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Background: Prothrombotic state in OSAS play a role for cardiovascular risk. Plasminogen activator inhibitor (PAI) is one of the primary regulators of the fibrinolytic system. We evaluated plasma levels of PAI, uPA and uPA/PAI and their correlation with Apnea-Hypopnea Index (AHI), Oxygen Desaturation Index (ODI) and percentage of time with SpO_2 <90% (T<90%) before and after 1 month with CPAP.
Methods: Thirty-nine patients (age 57±1.54; BMI 34.5±1.07) with OSAS (AHI 28.4±3.16; ODI 35.7±3.4; T<90% 23.1±3.3) 20 smokers (S) and 19 no smokers (NS), and 16 age matched healthy control subjects were studied. Before and after 1 month with CPAP, uPA and PAI were measured in serum by ELISA.
Results: At baseline, PAI levels were higher in OSAS compared to controls (95.36±3.99 and 83.96±6.06 ng/ml, respectively). PAI levels were similar in S and NS subjects and were inversely related to AHI, BMI, ODI and T<90% in OSAS. uPA was higher in S compared to NS subjects; moreover, it was slightly higher in the controls compared to the OSAS (S 0.233±0.03, NS 0.221±0.028; S 0.206±0.01, NS 0.182±0.02 ng/ml, respectively). In OSAS uPA levels were inversed related to AHI, BMI, ODI and T<90%. uPA/PAI ratio was higher in controls compared to OSAS. PAI levels after CPAP slightly decreased, while uPA levels slightly increased. We observed an increase in uPA/PAI ratio from 1.90±0.04 and 2.56±0.55 to 2.14±0.32 and 3.1±0.79, in S and NS patients respectively.
Conclusions: Our preliminary data are compatible with an impairment of fibrinolytic activity in OSAS. The increase of uPA/PAI ratio after CPAP suggests a role of the PA system in the reduction of cardiovascular risk through the decrease of the prothrombotic state.

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Treatment of central and obstructive sleep apnea in stable heart failure patients with auto-servo ventilation reduces sleep fragmentation – A randomized controlled trial

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Background: It is of debate, whether treatment of central sleep apnea (SA) reduces sleep fragmentation. Therefore, we tested, whether auto-servo ventilation (ASV, BiPAP-ASV, Philips Respironics) reduces sleep fragmentation in heart failure (HF) patients with severe central or obstructive SA.
Methods: 42 patients with HF (age 66±9y, LVEF <40%) and SDB (apnea-hypopnea index, AHI 48±19/h, 51% central SA) were randomized to either ASV (n=21) or optimal medical treatment alone (control, n=21). Polysomnography (PSG) and 5 days of actigraphy with centralized scoring by blinded raters were obtained at baseline and 12 weeks.
Results: In the ASV-group AHI and central AHI were significantly suppressed compared to the control-group (-40±16 versus -1±13/h, p<0.001 and -24±14 versus +1.7±10/h, p<0.001, respectively). The arousalindex (ArI), sleep stage 1 (S1, PSG) and the fragmentation index (actigraphy) were significantly reduced (-14.7±21.3 versus 2.6±13.3/h, p=0.032 and 36±47 versus -6±41 min, p=0.005, and -11.4±16.0 versus -2.9±9.4/h, p=0.002, respectively) and sleep efficiency (SE) and daytime activity duration (actigraphy) significantly increased in the ASV-group compared to controls (5.5±10 vs. 1.6±6.9/h, p=0.021 and 14±54 vs. -24±41 min, p=0.009, respectively). Effects of ASV on ArI, S1, SE and daytime activity duration were similar in HF patients with obstructive and central SA (p>0.05 for all comparisons).
Conclusions: ASV-treatment significantly improves sleep fragmentation similarly in HF-patients with either central or obstructive SA. These effects were associated with a modest increase of daytime activity duration.

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Tracheal sound intensity relates to daytime high blood pressure in non-apnoeic snorers

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Background: The relationship between snoring and cardiovascular diseases had been assumed to be due to co-existing sleep-disordered breathing (SDB). Recently, we have reported that snoring sound intensity as assessed by ambient sound pressure level during sleep is related to daytime blood pressure independently of SDB in patients with primary snoring or mild SDB. We hypothesized that tracheal sound intensity, which is more immune to environmental noises than ambient sound pressure, during sleep may be related to daytime blood pressure.
Method: Clinical records and polysomnographic records of consecutive 1176 patients with suspected SDB were reviewed. Tracheal sound intensity was assessed as an equal sound pressure level (TS-Leq) during sleep. Daytime high blood pressure (HBP) was defined as taking antihypertensives, or having a systolic blood pressure (SBP)≥140 or a diastolic blood pressure (DBP)≥90 at the patients' first visit to our clinic.
Results: A logistic regression analysis in the entire patients showed that patient' age (p<0.00001), body mass index (BMI; p<0.00001), TS-Leq (p=0.00018), and apnea-hypopnea index (AHI; p=0.012) were independent determinants of HBP. The same analysis in the non-apneic (AHI<5) and normal-weight (BMI<25) patients (n=252) showed only age (p<0.00001) and TS-Leq (p=0.0062) were independent determinants of HBP. The Odds ratio for HBP at 6dB increase of TS-Leq was 1.74 in the non-apneic normal-weight patients.
Conclusion: Tracheal sound intensity during sleep is a determinant of daytime high blood pressure in non-apneic normal-weight patients. It may suggest a pathologic role of non-apneic snoring.

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Acetazolamide improves cardiac dysrhythmias in patients with obstructive sleep apnea at altitude. A randomized controlled trial

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Background: Untreated lowlanders with obstructive sleep apnea syndrome (OSA) benefit from acetazolamide (AC) during an altitude stay in terms of improved nocturnal oxygenation, breathing disturbances and sleep quality (Nussbaumer-Ochsner, Chest 2012). The current study evaluates whether AC reduces the increased rate of cardiac dysrhythmias at altitude.
Methods: 43 OSA patients living at <600m discontinued CPAP 3 days before baseline examination at 490m and during 2 altitude sojourns at 1860-2590m for 3 days each, one on AC 2x250mg/d, the other on placebo, according to a randomized cross-over design. Holter ECG and polysomnography were performed at 490m and at altitude.
Results: At altitude on placebo, heart rate was higher and dysrhythmias were more prevalent than at 490m. AC reduced bradycardia events, apneas/hypopneas and improved oxygen saturation [table].

Dysrhythmias, oxygen saturation and breathing disturbances

	490m	Altitude, placebo	Altitude, AC
Heart rate, 1/min.	67 (60; 76)	75 (68; 83)*	73 (67; 81)*
Bradycardia events, 1/d	0 (0; 14)	3 (0; 178)	0 (0; 17)§
Ventricular extrabeats, 1/d	24 (0; 163)	31 (4; 428)*	26 (4; 291)*
Afib & supraventricular runs, 1/d	0 (0; 0)	0 (0; 1)*	0 (0; 2)
Nocturnal oxygen saturation, %	93 (92; 94)	87 (86; 89)*	89 (87; 91)*§
Apnea/hypopnea index, 1/h	51 (42; 73)	70 (56; 89)*	54 (46; 63)§

Medians (quartiles), n=43. Bradycardia events=heart rate <50/min. for >4 beats. Afib = atrial fibrillation. *P<0.05 vs. 490m, §P<0.05 vs. placebo.

Conclusions: The increased heart rate and the higher prevalence of dysrhythmias at altitude are consistent with increased sympathetic tone associated with hypoxemia. AC reduces bradycardia events at altitude, possibly by improving sleep disordered breathing.
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Impact of CPAP treatment on the changes of maxi-k+ channel beta subunit-1 expression in patients affected by sleep apnea-hypopnea syndrome (SAHS)

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Regulatory function on the vasodilatation of the maxi-K+ channel beta1 subunit has been described in mouse model. CPAP treatment was shown to be related with an increase of the beta1subunit expression.
Objective: To determine the relations between oxymetric and endothelial situation and subunit beta1 expression in the moment of recruitment and after 3 month of CPAP in SAHS patients.
Methods: Prospective study in SAHS patients with CPAP (3 months). SAHS was defined as an apnea-hypopnea index (AHI) ≥15 (cardiorespiratory polygraphy). Endothelial function was evaluated with a test of postocclusive hyperemia by Laser-Doppler flowmetry. Beta1-subunit mRNA expression was made by a blood test in peripheral blood leukocytes.This two determinations were repeated 3 months after CPAP, calculating the parameter beta1b-beta1a.
Results: 33 patients were enrolled with 66,7% males. Polygraphy showed a mean AHI of 61±25.8, desaturation index 60±25, nocturnal saturation 89.45±4.8(%), minimum nocturnal saturation 53.87±20.34(%) and CT90 of 31.3±22.7(%). When investigating the parameter beta1b-beta1a we found a negative correlation with: nocturnal saturation (%) (R= -0.3, p=0.02),minimum nocturnal saturation (%) (R= -0.4, p=0.01) and area under the curve (PU/s), (R= -0,46, p=0.01) and a positive correlation with CT90 (R=0.3, p=0.04) and the slope (PU) (R=0.4, p=0.001).
Conclusions: In our study population individuals showing worst oxymetric parametres or basal vascular endothelial situation initially achieved after 3 month of CPAP the most important improvement of beta1 subunit levels (expressed as higher values in the difference beta1b-beta1a).