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Clinical Research

Overnight Effects of Obstructive Sleep Apnea and Its Treatment on Stroke Volume in Patients With Heart Failure

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ABSTRACT

Background: We previously showed in heart failure (HF) patients that obstructive respiratory events during sleep and generation of negative intrathoracic pressure during Mueller manoeuvres, mimicking obstructive apneas, acutely reduced stroke volume (SV). We also showed that treating obstructive sleep apnea (OSA) with continuous positive airway pressure (CPAP) increased left ventricular ejection fraction over a 1-month period. We therefore hypothesized that, in HF patients, those with OSA would have greater overnight declines in SV and cardiac output (CO) than in those without sleep apnea, and that therapy of OSA using CPAP would prevent these declines.

Methods: We examined overnight percent change in SV and CO in 32 HF patients with and 28 without OSA using digital photoplethysmography. Among patients with OSA, we also examined changes in SV and CO during a CPAP titration study.

Results: During the baseline polysomnogram SV and CO decreased more overnight in those with OSA than in those without sleep apnea ($-12.6 \pm 7.7\%$ vs $-3.2 \pm 6.8\%$; $P < 0.001$ and $-16.2 \pm 9.9\%$ vs $-3.7 \pm 8.3\%$; $P < 0.001$, respectively). Overnight changes in SV and CO correlated inversely with total apnea-hypopnea index ($r = -0.551$; $P < 0.001$ and $r = -0.522$; $P < 0.001$, respectively). In 21 patients

RÉSUMÉ

Introduction : Nous avons précédemment montré chez les patients atteints d'insuffisance cardiaque (IC) que les événements respiratoires obstructifs survenant durant le sommeil et que la génération de pression intrathoracique négative durant la manœuvre de Mueller, qui imite les apnées obstructives, réduisaient à court terme le volume d'éjection (VE). Nous avons également montré que le traitement de l'apnée obstructive du sommeil (AOS) à l'aide de la ventilation spontanée en pression positive expiratoire continue (CPAP : *continuous positive airway pressure*) augmentait la fraction d'éjection ventriculaire gauche sur une période de 1 mois. Par conséquent, nous avons posé l'hypothèse que les patients atteints d'IC qui ont des AOS pourraient avoir des baisses plus importantes du VE et du débit cardiaque (DC) au cours de la nuit que ceux n'ayant pas d'apnée du sommeil et que le traitement de l'AOS par CPAP pourrait empêcher ces baisses.

Méthodes : Nous avons examiné la variation en pourcentage du VE et du DC au cours de la nuit chez 32 patients souffrant d'IC et 28 patients n'ayant pas d'AOS à l'aide de la photopléthysmographie numérique. Parmi les patients ayant des AOS, nous avons également examiné les changements du VE et du DC au cours d'une étude de titrage de la CPAP.

In patients with heart failure (HF), obstructive sleep apnea (OSA) is common and is associated with increased mortality.[1,2] However, factors contributing to this excess mortality are not well understood. One possibility is that the combined effects of intermittent hypoxia, arousals from sleep, and chronic excessive sympathetically-mediated vasoconstriction arising from OSA, plus negative intrathoracic pressure generation during obstructive apneas could reduce stroke volume (SV) and cardiac output (CO), and impair tissue perfusion.[3] Indeed, in a previous study, we demonstrated that SV and CO decreased acutely during obstructive apneas and recovered during hyperpneas.[4] However, the overnight effects of OSA on SV and CO were not determined.

Nocturnal continuous positive airway pressure (CPAP) therapy alleviates OSA.[3] By doing so, it acutely prevents the generation of exaggerated negative intrathoracic pressure and, thus, reduces left ventricular (LV) transmural pressure. It also

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with OSA, CPAP reduced the total apnea-hypopnea index from 37.7 ± 21.4 to 15.0 ± 16.0 ($P < 0.001$) in association with attenuation of the overnight reduction of SV (from −14.0 ± 7.9% to −3.4 ± 9.8%; $P = 0.002$) and CO (from −17.2 ± 9.0% to −9.7 ± 10.7%; $P = 0.042$).

Conclusions: In patients with HF, coexisting OSA causes overnight declines in SV and CO that are prevented through reversal of OSA by CPAP.

Résultats : Le polysomnogramme initial a montré que le VE et le DC diminuaient plus durant la nuit chez ceux ayant des AOS que chez ceux n'ayant pas d'apnée du sommeil (−12,6 ± 7,7 % *vs* −3,2 ± 6,8 %; $P < 0,001$ et −16,2 ± 9,9 % *vs* −3,7 ± 8,3 %; $P < 0,001$, respectivement). Les variations du VE et du DC au cours de la nuit ont corrélé de manière inverse avec l'index d'apnées-hypopnées totales ($r = -0,551$; $P < 0,001$ et $r = -0,522$; $P < 0,001$, respectivement). Chez 21 patients ayant des AOS, la CPAP a réduit l'index d'apnées-hypopnées totales de 37,7 ± 21,4 à 15,0 ± 16,0 ($P < 0,001$) tout en modérant la réduction du VE (de −14,0 ± 7,9 % à −3,4 ± 9,8 %; $P = 0,002$) et du DC (de −17,2 ± 9,0 % à −9,7 ± 10,7 %; $P = 0,042$) au cours de la nuit.

Conclusions : Chez les patients atteints d'IC, la coexistence d'AOS cause des baisses du VE et du DC au cours de la nuit qui sont évitables en diminuant le nombre d'AOS à l'aide de la CPAP.

prevents recurrent hypoxia and reduces sympathetic nervous system activity in patients with HF.[3,5] However, it has not been determined whether treatment of OSA with CPAP in HF patients has a beneficial overnight effect on SV and CO.

We therefore hypothesized, first, that in patients with HF, those with OSA would experience greater overnight decreases in SV and CO than those without sleep apnea; second, that such decreases will be proportional to OSA severity; and third, that in those with OSA, CPAP will attenuate such overnight reductions in SV and CO.

Methods

For a more detailed description of the methods, please see the *Methods* section of the Supplementary Material.

Subjects

As part of an epidemiological study, we performed polysomnography on consecutive patients with HF, irrespective of symptoms or signs of sleep apnea. Inclusion criteria were: (1) men and women aged ≥ 18 years; (2) HF due to ischemic or nonischemic dilated cardiomyopathy for ≥ 6 months; (3) LV ejection fraction (LVEF) ≤ 45%; and (4) New York Heart Association functional class I-III. Exclusion criteria were: (1) predominantly central apneas and hypopneas (> 50% events central); (2) treated sleep apnea; and (3) unstable angina, myocardial infarction, or cardiac surgery within the previous 3 months. For purposes of this study, subjects were divided into those with < 15 apneas and hypopneas per hour of sleep (apnea-hypopnea index or AHI; no sleep apnea or NSA group) and those with an AHI of ≥ 15 (OSA group).

Demographic characteristics, height, weight, body mass index (BMI), medical history, and medication use were recorded before polysomnography. LVEF, estimated glomerular filtration rate and N-terminal fragment of pro-B-type natriuretic peptide (NT-proBNP) level were assessed within 3 months before polysomnography.

Polysomnography

All subjects underwent overnight polysomnography using standard techniques and scoring criteria for sleep stages and arousals from sleep.[6,7] They all slept on a single pillow with the bed flat. Body position and movements were recorded continuously with video recordings from which technicians scored time spent in particular positions epoch-by-epoch. Thoracoabdominal motion was monitored using respiratory inductance plethysmography, and nasal airflow using nasal pressure cannulae. Oxyhemoglobin saturation (SaO_2) was monitored using oximetry. Apneas and hypopneas were identified and classified as obstructive or central as previously described.[1] The AHI was quantified. Signals were scored by a technician blind to hemodynamic measurements.

Hemodynamic measurements

Noninvasive beat-by-beat measures of arterial blood pressure (BP), heart rate (HR), SV, CO, and total peripheral resistance (TPR) were made using digital photoplethysmography (DPP; Portapres; Finapres Medical Systems BV, Amsterdam, The Netherlands).[4,8] DPP was applied via cuffs wrapped around the third and fourth fingers of the left hand. We have previously validated beat-to-beat changes in DPP-derived SV against echocardiographic Doppler during respiratory manoeuvres mimicking obstructive apneas.[4] The 2 finger cuffs were alternately inflated and deflated every 30 minutes during the night. A splint was applied to the patient's arm to maintain it in an extended position. The DPP has a height correction unit to adjust for differences between finger level and heart level to obtain comparable measurements of BP and SV irrespective of finger level. Continuous indices of SV, CO, and TPR were computed using the Modelflow method.[9]

To obtain baseline and final hemodynamic indices, all hemodynamic indices were quantified as the average during a 5-minute period during the first and last episodes of stage 2 sleep, respectively, from the same finger in the same body position in which similar types and numbers of respiratory events were observed. Hemodynamic analyses were made by a technician blind to scoring of polysomnograms. Overnight percent changes in beat-by-beat SV, systolic and diastolic BP, HR, SV, CO, TPR (%ΔSBP, %ΔDBP, %ΔHR, %ΔSV, %ΔCO, and %ΔTPR, respectively) were calculated.

Effects of CPAP on hemodynamic measurements

Among patients who agreed to a trial of CPAP, all of the aforementioned hemodynamic measurements were repeated during the second polysomnogram in which CPAP was titrated.

This study was performed in accordance with the principles of the revised Declaration of Helsinki. The protocol was