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Contrasting Effects of Lower Body Positive Pressure on Upper Airways Resistance and Partial Pressure of Carbon Dioxide in Men With Heart Failure and Obstructive or Central Sleep Apnea

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Objectives This study sought to test the effects of rostral fluid displacement from the legs on transpharyngeal resistance (R_{ph}), minute volume of ventilation (V_{min}), and partial pressure of carbon dioxide (PCO_2) in men with heart failure (HF) and either obstructive (OSA) or central sleep apnea (CSA).

Background Overnight rostral fluid shift relates to severity of OSA and CSA in men with HF. Rostral fluid displacement may facilitate OSA if it shifts into the neck and increases R_{ph}, because pharyngeal obstruction causes OSA. Rostral fluid displacement may also facilitate CSA if it shifts into the lungs and induces reflex augmentation of ventilation and reduces PCO_2, because a decrease in PCO_2 below the apnea threshold causes CSA.

Methods Men with HF were divided into those with mainly OSA (obstructive-dominant, n = 18) and those with mainly CSA (central-dominant, n = 10). While patients were supine, antishock trousers were deflated (control) or inflated for 15 min (lower body positive pressure [LBPP]) in random order.

Results LBPP reduced leg fluid volume and increased neck circumference in both obstructive- and central-dominant groups. However, in contrast to the obstructive-dominant group in whom LBPP induced an increase in R_{ph}, a decrease in V_{min}, and an increase in PCO_2, in the central-dominant group, LBPP induced a reduction in R_{ph}, an increase in V_{min}, and a reduction in PCO_2.

Conclusions These findings suggest mechanisms by which rostral fluid shift contributes to the pathogenesis of OSA and CSA in men with HF. Rostral fluid shift could facilitate OSA if it induces pharyngeal obstruction, but could also facilitate CSA if it augments ventilation and lowers PCO_2. (J Am Coll Cardiol 2013;61:1157–66) © 2013 by the American College of Cardiology Foundation

Sleep apnea occurs in approximately 50% of patients with heart failure (HF), where it is associated with increased mortality (1–3). There are 2 types of sleep apnea: obstructive (OSA) and central (CSA).

OSA is due to repetitive pharyngeal collapse during sleep that occurs when sleep-related loss in pharyngeal dilator muscle tone is superimposed upon a narrow pharynx (4).

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Pharyngeal narrowing can be due to fatty deposition in the neck or fluid retention in the pharyngeal mucosa. Increases

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Abbreviations and Acronyms

AHI = apnea-hypopnea index
BP = blood pressure
CSA = central sleep apnea
eGFR = estimated glomerular filtration rate
HF = heart failure
HR = heart rate
LBPP = lower body positive pressure
LVEF = left ventricular ejection fraction
LFV = leg fluid volume
NC = neck circumference
NT-proBNP = N-terminal of pro–B-type natriuretic peptide
NYHA = New York Heart Association
OSA = obstructive sleep apnea
PCO_2 = partial pressure of carbon dioxide
$PtcCO_2$ = transcutaneous PCO_2
R_{ph} = transpharyngeal resistance
SaO_2 = oxyhemoglobin saturation
V_{min} = minute volume of ventilation

in mucosal fluid volume around the pharynx may reduce pharyngeal cross-sectional area and increase transpharyngeal resistance (R_{ph}) (5). This may explain why OSA is more prevalent in patients with fluid retention, such as HF, than in the general population, despite lower body weight (1,6). It has also been shown that a reduction in overnight rostral fluid redistribution from the legs into the neck due to compression stockings during the daytime can attenuate OSA (7).

CSA is more prevalent in those with HF than in the general population (8), and is found predominantly in men for reasons yet to be elucidated (1). CSA during sleep occurs when partial pressure of carbon dioxide (PCO_2) falls below the apnea threshold due to hyperventilation (9). Several factors can contribute to hyperventilation and hypocapnia in HF patients with CSA, including respiratory control system instability due to increased chemosensitivity (10), pulmonary congestion (11), and arousals from sleep (9). Low cardiac output and prolonged circulation time might also play a role in the pathophysiology of CSA in HF, but these appear to contribute more to causing prolongation of the periodic breathing cycle than to precipitating central respiratory events (12,13). Unlike obstructive apneas and hypopneas, central apneas and hypopneas can sometimes be observed in HF patients with CSA while awake as part of Cheyne-Stokes respiration (14,15). Fluid retention may also play an important role in the pathogenesis of CSA by provoking hyperventilation and hypocapnia partly as a result of pulmonary irritant receptor stimulation by pulmonary congestion (11). In HF patients, PCO_2 is inversely proportional to pulmonary capillary wedge pressure (16), which is higher in patients with CSA than in those without CSA (12). In HF patients, nocturnal PCO_2 is also related inversely, and the frequency of central events, directly, to the amount of fluid displaced rostrally from the legs overnight (17). Under such conditions, increases in ventilation can decrease PCO_2 below the apnea threshold and trigger central apnea (9,18). Because augmented central respiratory drive stimulates both respiratory pump and pharyngeal dilator muscles (19), it is expected that the fluid shift into the lungs of HF patients may cause both an increase in ventilation and a lowering of R_{ph}, both of which will facilitate a drop in PCO_2. These observations suggest that fluid retention also plays a role in the pathogenesis of CSA. Fluid retention may explain, in part, why both types of sleep apnea are more common in HF patients than in the general population, why both types of sleep apnea can coexist in the same HF patient, and why the predominant type can change over time (20–22).

Our group previously showed in healthy, nonobese subjects that applying lower body positive pressure (LBPP) via medical antishock trousers causes rostral fluid displacement from the legs, which results in increases neck circumference (NC) and R_{ph}, decreases in pharyngeal caliber, and increases in pharyngeal collapsibility (5,23,24). The effects of rostral fluid shift from the legs by LBPP on NC, ventilation, PCO_2, and R_{ph} in patients with HF have yet to be determined. We, therefore, undertook the present study to test the hypotheses that the predominant effect of rostral fluid displacement from the legs by LBPP will be to induce pharyngeal obstruction in HF patients with OSA, as manifested by an increase R_{ph}, a reduction in minute volume of ventilation (V_{min}), and an increase in PCO_2, whereas in those with CSA, its predominant effect will be to augment respiratory drive as manifested by an increase in V_{min}, accompanied by reductions in R_{ph} and PCO_2.

Methods

Subjects. Inclusion criteria were men 18 to 85 years of age with HF due to ischemic or nonischemic dilated cardiomyopathy for ≥6 months, left ventricular ejection fraction (LVEF) ≤45%, in New York Heart Association (NYHA) classes I to III, and who were clinically stable without medication changes for ≥3 months. Exclusion criteria were acute decompensated HF, treated sleep apnea, tonsillar hypertrophy, and unstable angina, myocardial infarction, or cardiac surgery within the previous 3 months. Subjects' characteristics and medications were recorded before experiments. Echocardiography, including assessment of mitral regurgitation grades from 0 (none) to 4 (severe), estimated glomerular filtration rate (eGFR), and N-terminal of pro–B-type natriuretic peptide (NT-proBNP) levels were assessed within 3 months before the experiments. The Mallampati Score was assessed at the time of experiments (25). The protocol was approved by the Research Ethics Boards of University Health Network and Mount Sinai Hospital, and all subjects provided written consent before participation.

Polysomnography. All subjects underwent overnight polysomnography using standard techniques and scoring criteria for sleep stages and arousals (26,27). Thoracoabdominal motion was monitored by respiratory inductance plethysmography, and nasal airflow by nasal pressure cannulas. Oxyhemoglobin saturation (SaO_2) was monitored by oximetry. Apneas and hypopneas were defined as >90% and 50% to 90% reduction in tidal volume from baseline, respectively, lasting ≥10 s, and were classified as obstructive or central as