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Cerebral Hypoperfusion Is Exaggerated With an Upright Posture in Heart Failure

Impact of Depressed Cardiac Output

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ABSTRACT

OBJECTIVES The purpose of this study was to examine cerebral blood flow (CBF) supine and during upright sitting in HF patients and control subjects to test the hypothesis that patients with HF will have a greater reduction in CBF from supine to seated compared with the control group.

BACKGROUND Reduced CBF has been reported in patients with heart failure (HF). However, previous work has only examined CBF while supine, although an upright posture common to daily living may lead to further reductions.

METHODS In 22 HF patients and 22 age- and sex-matched control subjects, continuous heart rate, mean arterial pressure, and end-tidal carbon dioxide readings were collected while supine and seated upright. Cardiac output was estimated from pulse contour analysis and was corrected for body size (cardiac index). The right internal carotid artery was imaged by using ultrasound to estimate CBF.

RESULTS Heart rate increased less in response to the upright posture in HF patients versus control subjects ($p = 0.006$). Mean arterial pressure was unchanged, whereas end-tidal carbon dioxide decreased in response to position ($p = 0.004$) but did not differ between groups. Cardiac index was lower in patients with HF ($p < 0.001$) and decreased in both groups in response to the upright posture ($p = 0.025$), with a trend for a greater decrease in the HF group ($p = 0.065$). CBF decreased more in response to the upright posture in the HF group than in the control group ($p = 0.007$).

CONCLUSIONS The reduction in CBF was exaggerated in the upright posture in HF patients and may increase the risk for subsequent cognitive impairment. (J Am Coll Cardiol HF 2015;3:168–75) © 2015 by the American College of Cardiology Foundation.

Heart failure (HF) is an independent predictor of cognitive decline (1) that affects ~25% to 50% of patients (2). Cerebral hypoperfusion secondary to impaired cardiac function is believed to contribute to the burden of cognitive impairment. Indeed, when heart function is improved with cardiac transplantation or cardiac resynchronization therapy, improvements in cognition and cerebral blood flow (CBF) have been noted (3–6). Although several studies have reported reduced CBF in patients with HF (7–9), these reports measured CBF only while supine.

Upright positions, a part of normal daily living, are associated with gravity-driven hydrostatic gradients in the body and the translocation of blood to the lower extremities. In generally healthy adults, upright posture is associated with small reductions in CBF. This is a consequence of complex interactions among reductions in local perfusion pressure, cardiac output, and/or arterial partial pressure of carbon

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dioxide, even though mean arterial pressure (MAP) is not reduced in the upright position (10,11). In HF, in which supine cardiac output is already limited, upright posture may increase the vulnerability to cerebral hypoperfusion, thus furthering the risk of chronic ischemia and cognitive impairment.

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The purpose of the present study was to evaluate the cardiovascular and cerebrovascular response to an upright, seated position in HF patients compared with control subjects. We hypothesized a greater CBF decrease in response to the upright position in the HF group compared with the control group and that the decrease would be greatest in those with a lower supine resting cardiac output.

PATIENTS AND METHODS

Twenty-two community-dwelling patients with HF and 22 age- and sex-matched control subjects in generally good health and with no history of HF participated in the study. The HF patients had a clinical diagnosis of HF and exhibited clinical and therapeutic stability for 1 month. Exclusion criteria included cardiac transplant recipients, New York Heart Association functional class IV, stroke within the past 10 years, arterial blood pressure ≥160/90 mm Hg, and documented diagnosis of dementia. The experimental procedures for this study were approved by the Office of Research Ethics at the University of Waterloo (ORE 18543 and 15731) and the Hamilton Integrated Research Ethics Board (HIREB 13-338) in accordance with the Declaration of Helsinki. All participants volunteered freely after reading and signing an informed consent form and were aware of their rights to withdraw from the study at any time.

STUDY DESIGN. This study used a cross-sectional design. Left ventricular ejection fraction and New York Heart Association class were obtained from the medical records of the HF patients. All participants provided a list of recent medications and continued to take these medications according to their normal schedule.

STUDY PROCEDURE. Participants completed the Montreal Cognitive Assessment (MoCA), 2 timed 8-m usual walking speed tests and anthropometric measures (i.e., height, weight, waist/hip ratio). Participants then lay supine on a bed and were instrumented to continuously monitor heart rate, arterial blood pressure, cardiac output, and end-tidal carbon dioxide ($ETCO_2$). An estimate of CBF was obtained with an ultrasound after 10 min (for stabilization). Participants were assisted to a seated position, and the procedure was repeated.

INSTRUMENTATION AND MEASUREMENTS. Montreal Cognitive Assessment. The MoCA is a screening tool for mild cognitive impairment and has been used previously in a population with HF (12,13). Initial testing of the MoCA in a sample of older adults demonstrated a cutoff score of <26/30 for mild cognitive impairment and yielded a sensitivity of 90% and a specificity of 78% (14).

Cardiovascular and Cerebrovascular Assessments. Heart rate (electrocardiogram; ECG Module, Finapres Medical Systems, Amsterdam, the Netherlands) and arterial blood pressure (finger-cuff plethysmography; Finometer Pro, Finapres Medical Systems) were collected beat-to-beat throughout the test. Cardiac output was estimated from the Modelflow algorithm (15) and corrected for body surface area to yield a cardiac index (CI). Total peripheral resistance was calculated as MAP divided by cardiac output. Breath-by-breath exhaled carbon dioxide was sampled through a nasal cannula and analyzed by using infrared spectroscopy (Ohmeda 5200 CO_2 Monitor, Ohmeda, Madison, Wisconsin) to estimate $ETCO_2$ in millimeters of mercury. Measures of heart rate, arterial blood pressure, cardiac output, and $ETCO_2$ were collected at 1 kHz (PowerLab, Chart version 5.5.6, ADInstruments, Colorado Springs, Colorado). Steady state beat-by-beat data were averaged for 1 min after at least 5 min in each posture.

CEREBRAL BLOOD FLOW. CBF was quantified by using extracranial ultrasound measured bilaterally supine (right internal carotid artery [RICA] and left internal carotid artery [LICA]) and unilaterally seated (RICA). An 8- to 12-Hz linear array transducer (L14-6s with M5 system, Mindray, Shenzhen, China) was used to image the internal carotid artery (ICA) 1 to 2 cm distal to the carotid bifurcation to minimize turbulent flow from the carotid bulb. ICA diameter was measured during the diastolic phase by electronic calipers in triplicate and averaged. The Doppler function of the same probe permitted measurement and time-averaging of the mean flow velocity from the ICA. CBF through the ICA was calculated as follows: $CBF = \text{mean flow velocity} \times \pi(\text{diameter}/2)^2$.

STATISTICAL ANALYSIS. Participant and medical characteristics between HF patients and control subjects were compared by using Student *t* tests for continuous variables and *z* tests for categorical variables. Cardiovascular and cerebrovascular baseline

ABBREVIATIONS AND ACRONYMS

CBF = cerebral blood flow

CI = cardiac index

$ETCO_2$ = end-tidal carbon dioxide

HF = heart failure

ICA = internal carotid artery

LICA = left internal carotid artery

MAP = mean arterial pressure

MoCA = Montreal Cognitive Assessment

RICA = right internal carotid artery