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Research Article

Carotid-radial pulse wave velocity responses following hyperemia in patients with congestive heart failure

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Abstract

Carotid-radial pulse wave velocity (PWV) normally decreases following hyperemia and is an indicator of vasodilator reserve. This response is impaired in patients with congestive heart failure (CHF). To identify specific factors related to an impaired response, we studied 50 patients (60 ± 14 years, 67% male) with chronic CHF. Baseline PWV was measured using applanation tonometry and repeated 1 minute after release of upper arm occlusion for 5 minutes. Percentage changes (Δ) of PWV were normally distributed and mean ΔPWV was −2.2 ± 15.3%. On univariate analyses, ΔPWV correlated with New York Heart Association class, mean arterial pressure, log brain natriuretic peptide (BNP) levels, and baseline PWV, but not with left ventricular ejection fraction. Multivariate linear regression analysis demonstrated log BNP levels, mean arterial pressure, and baseline PWV (all $P < .05$) as independent predictors of ΔPWV. Hyperemia increased PWV in 42% of patients. On logistic regression, higher BNP levels and lower baseline PWV were independent predictors of a PWV increase. Higher BNP levels and lower baseline PWV are independent predictors of an abnormal hyperemic PWV response in patients with CHF. Higher BNP levels may reflect abnormal vasodilator reserve. Forty-two percent of heart failure patients showed an increase in PWV following hyperemia, which may reflect more severe arterial vasodilator impairment. J Am Soc Hypertens 2014;8(10):687–692. Published by Elsevier Inc. on behalf of American Society of Hypertension.

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Introduction

Alterations in arterial structure and function contribute to the development and progression of chronic congestive heart failure (CHF). Over the past several decades, a variety of techniques have been used to characterize functional abnormalities of the arterial system in CHF patients. Although hemodynamic studies initially demonstrated elevated systemic vascular resistance and increased impedance to ventricular outflow, ultrasound imaging later demonstrated increased stiffness and reduced compliance of the brachial artery (BA).[1–6] The use of high-resolution ultrasound demonstrated impaired arterial vasodilator reserve in response to various provocations in this setting including subnormal endothelial dependent and independent arterial responses.[7–19] In the setting of CHF, endothelial dysfunction has been found related to the severity of symptoms and predictive of progression of left ventricular (LV) diastolic dysfunction.[12] Endothelial dysfunction of peripheral resistance arteries contributes to the increased peripheral resistance in this disease.[9–12] Accordingly, arterial dysfunction is not only a marker, but is also a contributor to the pathogenesis of CHF.[12]

Increased arterial stiffness is a biophysical property of the arterial system that may adversely affect function of the failing LV by increasing pulsatile load and causing early return of reflected waves from the periphery to the heart.[20] Applanation tonometry is increasingly used for the assessment of arterial wave reflection and arterial stiffness. Pulse wave velocity (PWV) is a measure of arterial

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stiffness, which is based on the premise that the transit time of the pressure waveform between 2 arterial sites is shortened in patients with increased arterial stiffness.[21] Arterial stiffness measured by PWV has been shown to be acutely influenced by vascular tone and constitutively released nitric oxide.[22]

Although measurement of carotid-femoral PWV provides an assessment of aortic stiffness, the measurement of carotid-radial PWV in conjunction with provocations known to induce hyperemia has been suggested as a functional measure of arterial vasodilator reserve and possibly endothelial function. Several groups have demonstrated PWV to decrease in healthy subjects following hyperemia provoked by release of arterial cuff occlusion.[22–26] PWV responses (Δ) have been found inversely related to flow mediated dilation (FMD) of the BA assessed by high resolution ultrasound.[25,26] Moreover, blunted PWV responses have been observed in subjects with hypertension, coronary artery disease (CAD) and CHF.[23,25–29] Although the presence of CHF was the strongest predictor of a blunted PWV decline, specific factors related to the hyperemic PWV response in the setting of CHF remain unknown. Accordingly, the objective of this study was to identify factors associated with PWV responses in the setting of CHF.

Methods

The study was approved by the institutional review board and written consent was obtained. We prospectively measured PWV before and after BA occlusion in a convenience sample of 50 patients diagnosed with CHF using clinical criteria by their referring physicians and sent for diagnostic echocardiography. Cardiovascular (CV) risk factors and disease history including: hypertension, diabetes, hypercholesterolemia, known CAD, CHF, smoking, and current medications, New York Heart Association (NYHA) functional class, left ventricular ejection fraction (LVEF), and brain natriuretic peptide levels (BNP) levels were identified by subject interview and chart review. Subjects were excluded if pulses were not adequate for arterial tonometry measurements, or if a rhythm other than sinus was present. After a 12-hour fast (including caffeine, nicotine, and alcohol), studies were performed in a quiet, temperature-controlled room. CV medications were not withheld. Participants were allowed to rest for 10 minutes in the supine position. Baseline blood pressures (BP), augmentation index (AI), and PWV were obtained by applanation tonometry (Sphygmocor, version 8.2; AtCor Medical, New South Wales, Australia), according to previously published methods.[28] Sequential recordings of arterial pressure waveforms at the carotid and radial arteries were used to measure PWV. Distances from the suprasternal notch to the carotid and radial artery sampling sites were measured. PWV distance was calculated as the difference between the 2 distances. PWV was calculated as the ratio of the distance in meters to the transit time in seconds.[30] After the baseline PWV measurements, a Hokanson cuff was applied around the left upper arm and inflated 50 mm Hg above systolic BP for 5 minutes. After release of cuff occlusion, PWV was measured at 1 minute. ΔPWV was defined as $PWV_{1minute} - PWV_{initial}/PWV_{initial} \times 100\%$. BP including mean arterial pressure (MAP) and heart rate were obtained by an automated BP device (Omron HEM-780). The coefficient of variation of individual PWV measurements in our laboratory is 6.3% and the repeatability of the PWV response expressed as the percentage of the coefficient of variation: (standard deviation of the paired differences/the overall mean)/2 $\times$ 100 is 9.2%. BNP levels were assayed by Triage Test (Biosite, Inc, San Diego) and were log transformed.

Statistics

All values are expressed as mean $\pm$ standard deviation. Continuous variables were compared using Student *t*-test and Fischer exact test was used to compare frequencies of dichotomous variables. Univariate associations between variables were analyzed by using Spearman correlation coefficients. Multiple linear regression analyses were performed to determine independent predictors of ΔPWV. Independent sample t-test was used to compare patients that demonstrated an increase in ΔPWV with those who showed a decrease. Multiple logistic regression analysis was performed to determine independent predictors of an increase in ΔPWV. Statistical analyses were achieved using the Statistical Package for Social Sciences (SPSS) 22.0 software (SPSS Inc, Chicago, IL). $P < .05$ was considered significant.

Results

Patient characteristics are shown in Table 1. There were 21 males and 29 females, age 60 $\pm$ 13 years. The etiology of CHF was felt to be ischemic in 50%, hypertensive in 44%, and idiopathic in 6% determined by clinical history and chart review. Mean ΔPWV was $-2.2 \pm 15.3\%$ and values were normally distributed. On univariate analyses, ΔPWV correlated with NYHA functional class ($r = 0.31$, $P = .027$), MAP ($r = 0.36$, $P = .011$), log BNP ($r = 0.39$, $P = .005$), and baseline PWV ($r = -0.31$; $P = .02$), but not with LVEF ($r = -0.023$, $P = .87$), age ($r = 0.14$, $P = .34$), heart rate ($r = -0.11$, $P = .45$), or AI ($r = 0.03$; $P = .87$). Figure 1 shows the correlations of ΔPWV with log BNP levels and baseline PWV values. ΔPWV was significantly correlated with diuretic ($r = 0.31$, $P = .028$) and aspirin ($r = 0.34$, $P = .017$) use but not with beta-blocker, angiotensin converting inhibitor or statin use (all P = not significant). Given the correlation between ΔPWV and baseline PWV, we also determined the correlation between absolute ΔPWV and baseline PWV ($r = -0.34$, $P = .014$). On multivariate linear regression, ΔPWV was independently related log BNP levels