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Clinical Investigation

Gender Difference in the Association between Aortic Pulse Pressure and Left Ventricular Filling Pressure in the Elderly: An Invasive Hemodynamic Study

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ABSTRACT

Background: This study was conducted to determine the association between aortic pulse pressure (APP) and left ventricular (LV) filling pressure in the elderly of both genders.
Methods: A total of 211 stable elderly subjects (age ≥65 years, mean age 72.1 ± 5.2 years, 53.6% women) who underwent invasive coronary angiography (ICA) for the evaluation of coronary artery disease (CAD) were prospectively investigated. APP was measured in the ascending aorta using a pigtail catheter immediately before ICA. E/e′, reflecting LV filling pressure, was assessed by transthoracic echocardiography.
Results: There were positive linear correlations between APP and E/e′ in both genders, but the correlation power was stronger in women than in men ($r = 0.402$, $P < .001$ vs $r = 0.208$, $P = .040$). The significance of this association between APP and E/e′ remained after controlling for potential confounders in multiple linear regression analysis in women ($\beta = 0.359$, $P < .001$), but not in men ($r = 0.139$, $P = .108$).
Conclusions: Invasively measured APP is independently associated with E/e′ in elderly women, but not in elderly men undergoing ICA. Aortic stiffness may be a potential mechanism for more prevalent LV diastolic dysfunction and heart failure with preserved ejection fraction in elderly women. (*J Cardiac Fail 2017;23:224–230*)
Key Words: Aortic pulse pressure, diastolic function, gender difference, heart failure with preserved ejection fraction.

Heart failure (HF) is the leading cause of hospitalization and death in industrialized countries.[1] Recently, clinical HF syndrome caused by predominant abnormalities in diastolic function without impaired systolic function—HF with preserved ejection fraction (HFpEF)—has been recognized.[2–4] HFpEF is clinically important because it is common and associated with poor morbidity and mortality, similar to HF with reduced ejection fraction.[4] Prior studies have demonstrated that patients with HFpEF are more likely to be older and female.[2,3] However, despite extensive studies, underlying pathophysiology explaining the higher incidence of HFpEF in elderly women is still poorly understood.

Aortic stiffness is a marker of arteriosclerosis and correlates with the risk of cardiovascular morbidity and mortality.[5,6] Increased aortic stiffness has been suggested as a significant contributor to the development of left ventricular (LV) diastolic dysfunction.[7] A recent study has demonstrated that the impact of aortic stiffness on LV diastolic function is stronger in women than in men, which may contribute to the greater risk of LV diastolic dysfunction and HFpEF in women.[8]

Central aortic pulse pressure (APP) is a reliable indicator of aortic stiffness. Cardiac catheterization is the gold standard for assessing central aortic hemodynamics [7]; however, invasive approaches are limited in the clinical setting because

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of its risk and cost. For this reason, most previous studies have used noninvasive methods for the evaluation of aorta-ventricular interaction.[8–11] Therefore, data on this issue obtained using invasive measurement have been scarce. Invasive hemodynamic studies may provide further insight into the higher susceptibility of older women to LV diastolic dysfunction and HFpEF.

In this context, this study was conducted to determine the association between aortic stiffness and LV diastolic function in the elderly of both genders using an invasive hemodynamic method.

Materials and Methods

Study Population

This prospective, single-center study was performed at Boramae Medical Center (Seoul, Korea). Between March 2013 and July 2014, consecutive elderly subjects (≥65 years of age) who were referred for elective invasive coronary angiography (ICA) were asked to participate in this study. All study candidates underwent transthoracic echocardiography during hospitalization for ICA (within 24 hours of ICA). A total of 323 subjects were recruited, and 112 subjects with the following conditions were excluded: (1) acute myocardial infarction, (2) unstable vital signs, (3) ongoing chest pain, (4) overt HF or history of HF requiring hospitalization, (5) LV systolic dysfunction (LV ejection fraction <50%), (6) regional wall motion abnormalities, (7) nonsinus rhythm, (8) valvular dysfunction more than mild degree, (9) significant calcification of mitral annulus, and (10) pericardial effusion. After such exclusions, 211 elderly subjects were analyzed in this study.

We obtained demographic characteristics, including age, weight, height, and traditional risk factors (histories of hypertension, diabetes mellitus, dyslipidemia, and smoking). Body mass index (BMI) was calculated as body weight (kilograms) divided by the square of body height (meters). Hypertension was defined as either repeated measurements of blood pressure >140/90 mmHg or currently using antihypertensive medications. Diabetes mellitus was defined as a fasting serum glucose level of 126 mg/dL or greater at least twice, hemoglobin A1c >6.5%, or currently using antihyperglycemic medications. Dyslipidemia was defined as either a history of dyslipidemia or currently using antidyslipidemic medications. Smoking was defined as a history of cigarette smoking during the past 12 months. Brachial systolic and diastolic blood pressures were measured by a trained nurse. Blood samples for laboratory tests were collected after overnight fasting of 8 hours; total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglyceride, hemoglobin A1c, serum creatinine, and high-sensitivity C-reactive protein were measured. Estimated glomerular filtration rate (eGFR) was calculated using the following formula: $175 \times \text{serum creatinine}^{-1.154} \times \text{age}^{-0.203}$ (× 0.742 if a woman). Information on the use of concomitant medications, including calcium channel blockers, beta-blockers, renin-angiotensin system blockers, and statin, were obtained. The study protocol was approved by the Institutional Review Board of Boramae Medical Center (Seoul, Korea), and informed consent was obtained from each study patient. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Cardiac Catheterization

Immediately before ICA, APP was measured in the ascending aorta using a 5F fluid-filled pigtail catheter in the supine position, as previously described.[7] Briefly, using a hemodynamic monitoring system (Horizon XVu-hemodynamic monitoring system; Mennen Medical, Haifa, Israel), pressure tracing was recorded at a speed of 100 mm/s. The amplitude and duration of the waveform was measured with the printed-out waves. The difference between the peak systolic pressure and the pressure of end-diastole was defined as APP. In some patients (n = 131), the pigtail catheter moved across the aortic valve into LV cavity, and LV end-diastolic pressure (LVEDP) was also measured. In each case, 3 consecutive beats were averaged. ICA was performed using the standardized technique. A diseased coronary artery was defined as ≥50% stenosis among major epicardial coronary arteries or its branches sized at >2 mm in luminal diameter.

Echocardiography

All echocardiographic assessments were made using transthoracic 2-dimensional echocardiography (Sequoia, Siemens Medical Solutions, Mountain View, CA; or Vivid 9, GE Medical system, Milwaukee, WI). All conventional 2-dimensional measurements, including LV diastolic/systolic dimension and ventricular wall thickness, were made according to current guideline recommendations.[12] The LV ejection fraction was calculated using Simpson's biplane method. The LV mass (LVM) was calculated with the following validated formula: LVM (g) = 0.8 × [1.04 ((LV end-diastolic dimension + diastolic posterior wall thickness + diastolic septal wall thickness)^3 − (LV end-diastolic dimension)^3)] + 0.6 g, and was indexed to the body surface area (LVM index [LVMI]).[12] The parameters of LV diastolic function were measured according to current guideline recommendations.[13] Pulsed-wave Doppler imaging was used to obtain the value of peak velocity of mitral inflow during early diastole (E), late diastole (A), and deceleration time, which were measured at the tip of the mitral leaflets from an apical-4 chamber view. On the same view, the early peak velocity of septal annulus (e′) was measured using color-coded tissue Doppler imaging. LV filling pressure was estimated by E/e′.[14] Left atrial volume was measured using the biplane method and was indexed to body surface area (left atrial volume index [LAVI]).[12]

Statistical Analysis

Continuous variables are presented as mean ± standard deviation and were compared between the 2 groups using the Student *t* test. Categorical variables are expressed as frequency (percentage) and were compared between the 2