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Values of hemodynamic variation in response to passive leg raising in predicting exercise capacity of heart failure with preserved ejection fraction

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Abstract

In heart failure patients with preserved ejection fraction, their hemodynamic parameters usually change when they are from recumbent to passive leg raising. The authors designed this study to investigate the relationship between hemodynamic parameters measured by impedance cardiography (ICG) and 6-minute walk distance (6MWD) of heart failure with preserved ejection fraction (HFPEF). We recruited 49 subjects with HFPEF in the study, and all the subjects were separated into 2 groups: the patients whose hemodynamic parameters rose after passive leg raising were in group 1 (n=26) and the patients whose hemodynamic parameters did not rise after passive leg raising were in group 2 (n=23). Our study then compared the 6MWD, left ventricular ejection fraction, and plasma NT-pro-brain natriuretic peptide between the 2 groups. Group 1 had significantly longer 6MWD than group 2 (515.38 ± 24.97 vs 306.39 ± 20.20 m; $P=0.043$). Hemodynamic parameters measured by ICG significantly correlated with 6MWD in both groups. Patients whose hemodynamic parameters rose in response to passive leg raising were more likely to have better exercise capacity. Hemodynamic variation in response to passive leg raising measured by ICG may be more sensitive in predicting exercise capacity of patients with HFPEF.

Abbreviations: 6MWD = 6-minute walk distance, 6MWT = 6-minute walk test, A = mitral filling late diastolic velocity, A′ = mitral annular late diastolic velocity, ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, BMI = body mass index, CAD = coronary artery disease, CCU = cardiac color ultrasound, CI = cardiac index, CO = cardiac output, COPD = chronic obstructive pulmonary disease, CRD = chronic renal disease, DBP = diastolic blood pressure, E = mitral filling early diastolic velocity, E/A ratio = early-to-late mitral filling velocity ratio, E/E′ ratio = average mitral-to-peak early diastolic annular ratio, E′ = mitral annular early diastolic velocity, HFPEF = heart failure with preserved ejection fraction, ICG = impedance cardiography, IVST = interventricular septal thickness, LAD = left atrial diameter, LSW = left stroke work, LSWI = left stroke work index, LV = left ventricular, LVD = left ventricular diameter, LVEF = left ventricular ejection fraction, LVPWT = left ventricular posterior wall thickness, MAP = mean arterial pressure, NT-proBNP = plasma NT-pro-brain natriuretic peptide, PLR = passive leg raising, S = mitral annular systolic velocity, SBP = systolic blood pressure, SSVR = stroke systemic vascular resistance, SSVRI = stroke systemic vascular resistance index, SV = stroke volume, SVI = stroke volume index, T2DM = type 2 diabetes mellitus.

Keywords: 6-minute walk distance, exercise capacity, heart failure with preserved ejection fraction, impedance cardiography, passive leg raising

1. Introduction

Heart failure with preserved ejection fraction (HFPEF) has been regarded as a clinical entity distinct from other forms of heart failure and defined predominantly by symptoms of dyspnea and fluid retention in the absence of a significant reduction in left ventricular (LV) systolic function.[1,2] The prevalence of HFPEF has been increasing, and the morbidity, mortality, and healthcare costs has been equal to heart failure with reduced ejection fraction.[3] Knowledge of a patient's actual cardiac function is important for the treatment of HFPEF.[4] Predicting exercise capacity and severity of cardiac dysfunction of patients with HFPEF may contribute to better management of HFPEF.

Passive leg raising (PLR) may identify patients with impairment of diastolic functional reserve during exercise.[5] PLR is a reversible fluid-loading maneuver,[6] which may potentially increase intrathoracic blood volume, cardiac preload, and then cardiac output (CO), through circulating venous blood from the legs[7] towards the thorax.[8] CO increased in healthy persons in response to PLR.[9] For patients with impaired cardiac function, 1 of compensatory mechanisms to maintain normal CO is the Frank–Starling mechanism. The Frank–Starling mechanism states that an increase in diastolic filling causes an increase in peak systolic atrial pressure,[10] representing the intrinsic capability of the heart to respond to enhance preload with an increase in force development.[11] Cardiovascular responses to PLR is useful in assessing preload reserve, but it has seldom been

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studied longitudinally in predicting severity of cardiac dysfunction in HFPEF.

Impedance cardiography (ICG), a reliable and noninvasive technique, can be used to measure hemodynamic parameters continually.[12,13] The fundamental of ICG is Ohm law, which states that a constant current travels through a conductor as a result of voltage change directly proportional to variations in impedance.[12,14]A considerable proportion of previous data have confirmed the role of hemodynamic parameters measured by ICG in estimating cardiac function.[15–17] The hemodynamic parameters CO, cardiac index (CI), stroke volume (SV), stroke volume index (SVI), left stroke work (LSW), and left stroke work index (LSWI) correlated positively with cardiac function.[18] Stroke systemic vascular resistance (SSVR) represents the resistance of blood flow in the vascular system. Stroke systemic vascular resistance index (SSVRI) is the systemic vascular resistance normalized for body surface area. Both variables reflect the afterload of the heart and the degree of arteriosclerosis in the systemic artery.[19]

The present study will research the correlation among 6-minute walk distance (6MWD), left ventricular ejection fraction (LVEF), plasma NT-pro-brain natriuretic peptide (NT-proBNP), and hemodynamic parameters in patients with HFPEF. Our study will further explore the values of hemodynamic variation in response to PLR in predicting exercise capacity of patients with HFPEF.

2. Methods

2.1. Patients and controls

This observational study was approved by the Ethics Committee of Tongji Hospital, Wuhan, China. All the subjects had received informed consent and signed in informed consent before enrollment. The study was performed from January 2014 to June 2016. Our study recruited patients with HFPEF, and the inclusion criteria in our study were based on the following: typical symptoms of heart failure; representative signs of heart failure; the LVEF ≥50% (by echocardiography); evidence of diastolic dysfunction on echocardiography (mitral inflow E/A ratio, E' measured at the mitral annulus, and E/E' ratio).[20,21] Subjects with impaired cognition, atrial fibrillation, chronic obstructive pulmonary disease (COPD), asthma, severe hepatic disease, severe renal impairment, hyperthyroidism, arthritis, ankle, knee or hip injuries, and muscle wasting were excluded.[22,23] We even did not recruit patients with systolic blood pressure (SBP) of more than 180 mm Hg, or diastolic blood pressure (DBP) of more than 100 mm Hg or resting heart rate of more than 120, drugs and/or alcohol abuse, or any life-threatening disease.[22,23]Additionally, we excluded patients with recent myocardial infarction, unstable angina, pacemaker implantation, enlarged LV dimension, candidacy for revascularization, cardiomyopathy, left atrial enlargement, and valvular heart disease.

"Responds to PLR" in our study meant that CO calculated by ICG was changed in participants when they were from supine position to PLR. All the subjects were separated into 2 groups according to CO variation in response to PLR: the patients whose CO increased in response to PLR were in group 1 ($n=26$), and the patients whose CO did not increase in response to PLR were in group 2 ($n=23$). The 2 groups were matched for age, sex, height, weight, body mass index (BMI), underlying disease (chronic renal disease, coronary artery disease, diabetes mellitus, hypertension), and basic medicine [β-receptor blocker, digoxin, angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB)].

2.2. Clinical evaluation

The machine to perform ICG was the Cheer Sails Medical (CSM3000 system). The basic principle of ICG was that specific waveform that can be used to calculate SV appeared as a result of the impedance changing with high-frequency (75 kHz) and low magnitude (1.8 mA) current across the thorax during cardiac ejection.[17,23] After 5 minutes' rest, the technician put electrodes on the neck and hypochondriac regions of patients and performed ICG for 3 minutes when the subjects were in the supine position (Fig. 1A). After 30 minutes of rest, the technician performed ICG

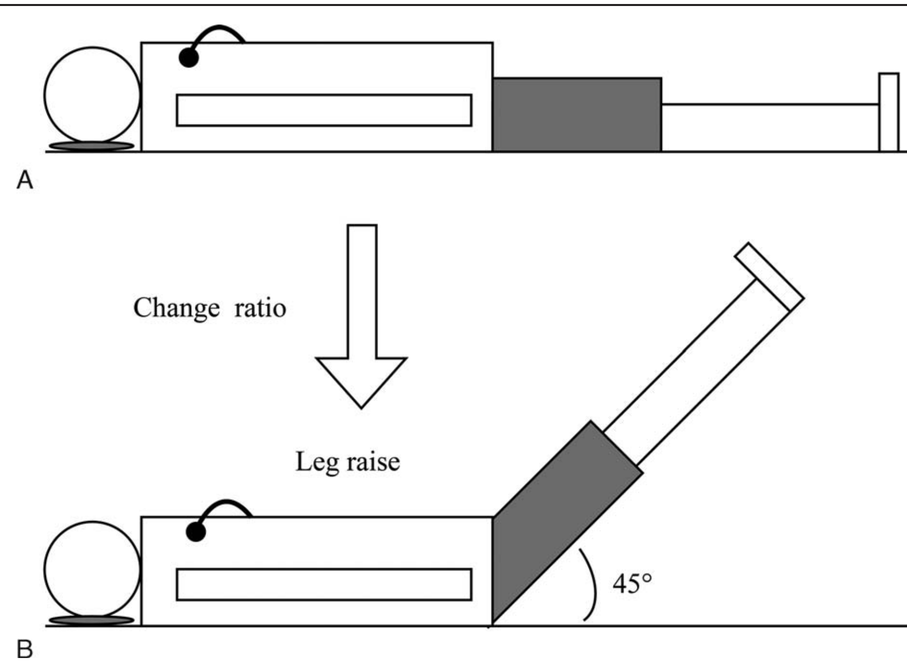

Figure 1. A, The subject was put electrodes on the neck and hypochondriac region and performed ICG when he was in the supine position. B, The subject was put electrodes on the neck and hypochondriac region and performed ICG when he was raising legs at 45°. ICG = impedance cardiography.