Evaluation of Resting Cardiac Power Output as a Prognostic Factor in Patients with Advanced Heart Failure

Omer Yildiz, MD[a,*], Gamze Aslan, MD[a], Zumrut T. Demirozu, MD[b], Cemal Deniz Yenigun[c], and Nuran Yazicioglu, MD[a]

If the heart is represented by a hydraulic pump, cardiac power represents the hydraulic function of the heart. Cardiac pump function is frequently determined through left ventricular ejection fraction using imaging. This study aims to validate resting cardiac power output (CPO) as a predictive biomarker in patients with advanced heart failure (HF). One hundred and seventy-two patients with HF severe enough to warrant cardiac transplantation were retrospectively reviewed at a single tertiary care institution between September 2010 and July 2013. Patients were initially evaluated with simultaneous right-sided and left-sided cardiac catheter-based hemodynamic measurements, followed by longitudinal follow-up (median of 52 months) for adverse events (cardiac mortality, cardiac transplantation, or ventricular assist device placement). Median resting CPO was 0.54 W (long rank chi-square = 33.6; $p < 0.0001$). Decreased resting CPO (<0.54 W) predicted increased risk for adverse outcomes. Fifty cardiac deaths, 10 cardiac transplants, and 12 ventricular assist device placements were documented. The prognostic relevance of resting CPO remained significant after adjustment for age, gender, left ventricular ejection fraction, mean arterial pressure, pulmonary vascular resistance, right atrial pressure, and estimated glomerular filtration rate (HR, 3.53; 95% confidence interval, 1.66 to 6.77; $p = 0.0007$). In conclusion, lower resting CPO supplies independent prediction of adverse outcomes. Thus, it could be effectively used for risk stratification in patients with advanced HF. **(Am J Cardiol 2017;120:973–979)**

From the hemodynamic point of view, the heart is a muscular hydraulic pump that can create pressure as well as flow. Cardiac output (CO) is cardiovascular flow through a closed circuit of blood vessels. CO is influenced by cardiac contractility and a complex interaction between vascular resistance, compliance to flow, cardiac filling pressures, and intravascular volume. As a whole, the heart and blood vessels are comparable with a pump and pipes, which can generate hydraulic energy that will be transmitted. Cardiac pumping capability can be defined as the cardiac power output (CPO), which is a product of mean arterial pressure and flow.[1] The heart has a spectrum of CPO composed of maximal CPO, reserve CPO, and resting CPO. During maximal stimulation of the heart, cardiac pumping capacity increases from resting CPO to maximal CPO.[2] Over time, pump dysfunction occurs due to chronic ischemic heart disease, dilated cardiomyopathy, or valvular heart disease. The maximal CPO decrease correlates with the reduction in reserve CPO, and in the case of severe reduction, the resting CPO decreases, leading to cardiogenic shock or severe heart failure (HF).[3] Maximal CPO and reserve CPO can be measured invasively or noninvasively during cardiopulmonary stress testing. They are notable determinants of exercise capacity and a powerful predictor of mortality in patients with chronic HF.[2,4–8] There are fewer data concerning the prognostic value of resting CPO in patients with chronic HF.[8] As worsening resting CPO may be associated with severity of HF,[3] we hypothesize that invasively measured resting CPO is correlated with the long-term transplant- and ventricular assist device–free survival in patients with advanced HF.

Methods

All data were collected retrospectively for consecutive 172 patients ≥ 18 years old with advanced HF, who were referred to be evaluated for heart transplantation to the Florence Nightingale Hospital between September 2010 and July 2013. Informed consent from all patients and institutional review board approval were obtained. The period from the first presentation of the patient to either ventricular assist device placement, heart transplantation or all-cause mortality was defined as the duration of follow-up.

We performed right-sided and left-sided cardiac catheterization for each patient at baseline to assess the hemodynamic measurements used for analysis. Right-sided and left-sided

[a]Department of Cardiology, Sisli Florence Nightingale Hospital, Istanbul, Turkey; [b]Department of Heart Transplantation and Mechanical Circulatory Support, Sisli Florence Nightingale Hospital, Istanbul, Turkey; and [c]Department of Industrial Engineering, Bilgi University, Istanbul, Turkey. Manuscript received March 12, 2017; revised manuscript received and accepted June 7, 2017.

Dr. Yildiz and Dr. Aslan are now at Koc University Hospital, Cardiology Department.

Dr. Demirozu is now at Koc University Hospital, Cardiovascular Surgery Department.

See page 978 for disclosure information.

*Corresponding author: Tel: (90) 850 250 8 250; fax: (90) 212 311 34 10.

E-mail address: oyildiz@kuh.ku.edu.tr (O. Yildiz).

0002-9149/
http://dx.doi.org/10.1016/j.amjcard.2017.06.028

cardiac catheterization was simultaneously performed through cannulation of the femoral vein and artery under fluoroscopic guidance with the patients in the supine position. After placement of a cardiac catheter into the pulmonary artery, a mixed central venous sample was collected from the tip of the catheter. We calculated CO using Fick's equation, and then we divided CO by body surface area to obtain the cardiac index. Pulmonary capillary wedge pressure, pulmonary arterial pressure, and right atrial pressure were measured at a steady state at end-expiration. Mean arterial pressure was measured invasively by placement of a cardiac catheter into the ascending aorta. Resting CPO, in watts, was calculated as mean arterial pressure (mm Hg) multiplied with CO (L/min) and divided by K (conversion factor 2.22×10^{-3}),[9] where mean arterial pressure = [(systolic blood pressure—diastolic blood pressure)/3] + diastolic blood pressure. Resting cardiac power index, in watts per square meters (W/m2), was computed by substituting CO with the cardiac index in the corresponding equation.

Patients with HF were classified based on their functional capacity.[10] According to the New York Heart Association (NYHA), classification patients with advanced HF will be classified as functional capacity class II, III, or IV. In line with American Society of Echocardiography guidelines, the left ventricular ejection fraction was calculated using the biplane modified Simpson's method.[11] Gathered data contain demographic characteristics, medical history, laboratory values, drug, and device therapy.

For each patient, an estimated glomerular filtration rate (eGFR) was calculated from serum creatinine levels by the Chronic Kidney Disease Epidemiology Collaboration equation $(GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] _ 1.159 [if black], where Scr is serum creatinine, κ is 0.7 for women and 0.9 for men, α is –0.329 for women and –0.411 for men, min indicates the minimum of Scr/κor 1, and max indicates the maximum of Scr/κ or 1.), which provides the most accurate GFR estimation compared with a 24-hour creatinine clearance.[12] Patients were categorized into groups according to the cut-off value GFR < 60 ml/min/1.73 m^2 and GFR > 60 ml/min/1.73 m^2 because a value less than 60 ml/min/1.73 m^2 is known to be an indicator of cardiovascular mortality.

We report continuous variable summaries as mean (standard deviation). For comparing continuous variables in 2 strata, we use the unpaired Student's *t* test. We report categorical variables as percentages and compare 2 strata using the Pearson's chi-squared test or Fisher's exact test if required. All p values are reported, and the ones less than 0.10 are boldfaced. Survival curves of the patients are computed by Kaplan–Meier estimates for both low and high resting CPO strata, and the significance of the difference between the strata is tested by the log-rank test. To study the effect of covariates on the survival of the patients, we carried out a stepwise Cox (proportional hazards) regression analysis using the Akaike Information Criterion. All computations are carried out using the statistical computing software R.

Results

Of 172 patients, 161 provided usable lifetime data, and the remaining 11 patients had to be removed from the study as they provided not enough observable lifetime due to death at first contact, having left ventricular assist device (LVAD) implantation at first visit, and so on. For the 161 patients in the study, the observed lifetime is the time from the first contact with the patient to an end point, which may refer to a cardiac death or some form of censoring. A total of 50 cardiac deaths and 111 censoring times are observed. Censoring times are noncardiac deaths (n = 9), heart transplants (n = 10), LVAD implantations (n = 12), and patients who are alive (without heart transplant or LVAD implantation) at the end of the study (n = 80). The baseline characteristics of the patients in the study, stratified by the resting CPO threshold 0.54, are given in Table 1. Baseline hemodynamics stratified by resting CPO threshold are given in Table 2.

Figure 1 provides resting CPO threshold values and the corresponding chi-squared distance between the survival curves

Table 1
Baseline characteristics

Variable	Overall (n = 161)	CPO ≤ 0.54 (n = 33)	CPO > 0.54 (n = 128)	p Value
Age (years)	58.7 (11.2)	57.3 (10.7)	59.1 (11.4)	0.4
Gender (male)	73.9%	66.7%	75.8%	0.4
Estimated glomerular filtration rate				
Dummy	16.98%	27.27%	14.28%	0.13
Chronic obstructive pulmonary disease	13.0%	6.06%	14.84%	0.25
Ischemic cardiomyopathy	55.9%	51.5%	57%	0.71
Ejection fraction	27.4 (4.7) %	24.6 (4.6) %	28.2 (4.5) %	0.0002
Cardiac resynchronization therapy-defibrillator	45.3%	57.6%	42.2%	0.16
New York Heart Association class				
II	29.1%	10.8%	34.1%	<0.0001
III	56.4%	54.1%	57%	<0.0001
IV	14.5%	35.1%	8.9%	<0.0001
Medications				
Beta blocker	83.2%	69.7%	86.7%	0.03
Angiotensin converting enzyme inhibitor/angiotensin II receptor blocker	73.9%	66.7%	75.8%	0.4
Mineralocorticoid receptor antagonist	65%	66.7%	64.6%	0.9
Diuretic	68.3%	69.7%	68%	1