patients in each study group may have been relatively low, which may have compromised statistical power in detecting a clinically meaningful difference. However, given the results of our study, we estimate ≥80% power to detect a clinically meaningful relative risk reduction of 30% in the primary outcome among groups. Our study is the first direct comparison of ACE inhibitors in terms of heart failure effectiveness. Our results suggest no significant differences among patient ACE inhibitors in clinically meaningful outcomes for treating patients with CHF. Thus, when prescribing ACE inhibitors, consideration should likely be given to dosing convenience and cost.

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Simplified Peak Power Reserve in Patients With an Implantable Cardioverter-Defibrillator and Advanced Heart Failure

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The prognostic ability of simplified peak power (SPP) reserve, a novel measure of left ventricular systolic performance, was prospectively studied in patients with advanced heart failure (HF) and implantable cardioverter-defibrillators. Reduced SPP reserve identified patients who are at high risk for experiencing progressive HF.
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Some patients with left ventricular dysfunction and ventricular arrhythmias derive limited benefit from the placement of implantable cardioverter-defibrillators (ICDs), because they die of progressive heart failure (HF). The accurate identification of this group could guide the selection of patients who may benefit from more directed HF therapy. Unfortunately, the tools that are currently available to stratify this population are imprecise. Patients with the most advanced HF symptoms are more likely to die from progressive pump failure as opposed to arrhythmic death. Contractile reserve determined by invasively measured peak power has been used as a prognostic indicator in patients with HF.[1] Ventricular reserve using noninvasive simplified peak power (SPP) is easily obtained, afterload independent, can be preload adjusted, and may add additional predictive power to traditional prognostic measures. We conducted a prospective study to determine whether noninvasive SPP reserve can identify ICD candidates with rapidly progressive HF. Our hypothesis was that in patients with ICDs in New York Heart Association functional class III HF, those with limited SPP reserve would have a greater number of adverse HF events.

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We prospectively enrolled patients in New York Heart Association class III HF who underwent ICD implantation for an American College of Cardiology–American Heart Association class I indication at Barnes-Jewish Hospital–Washington University School of Medicine. Patients with either ischemic or nonischemic cardiomyopathy were included. Patients were excluded for the inability to complete a dobutamine stress echocardiogram (i.e., the development of chest pain, arrhythmia, or hypotension or hypertension necessitating the early discontinuation of the study). A cohort of age-matched control patients without a history of HF or

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TABLE 1 Characteristics of Patients With HF and ICDs

Characteristic	SPP Reserve <1.5 (n = 8)	SPP Reserve >1.5 (n = 10)	p Value
Age (yrs)	66	58	0.41
African-American	0 (0%)	2 (20%)	0.48
Men	6 (75%)	7 (70%)	0.81
Hypertension	3 (38%)	8 (80%)	0.145
Diabetes mellitus	4 (50%)	6 (60%)	0.67
Coronary artery disease	7 (88%)	7 (70%)	0.59
Left ventricular ejection fraction (%)	27 ± 13	37 ± 8	0.06
Mitral deceleration time (ms)	166 ± 42	221 ± 81	0.11
Sodium (mmol/L)	140 ± 3	139 ± 3	0.53
Creatinine (mg/dl)	2.0 ± 1.4	1.1 ± 0.2	0.08
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	8 (100%)	9 (90%)	1.0
β-adrenergic blocker	5 (63%)	5 (50%)	0.66
Antiarrhythmic	3 (38%)	4 (40%)	1.0
Digoxin	4 (50%)	5 (50%)	1.0
Diuretic	8 (100%)	9 (90%)	1.0
SPP reserve (W/ml²)	0.7 ± 0.4	5.7 ± 2.7	0.0001

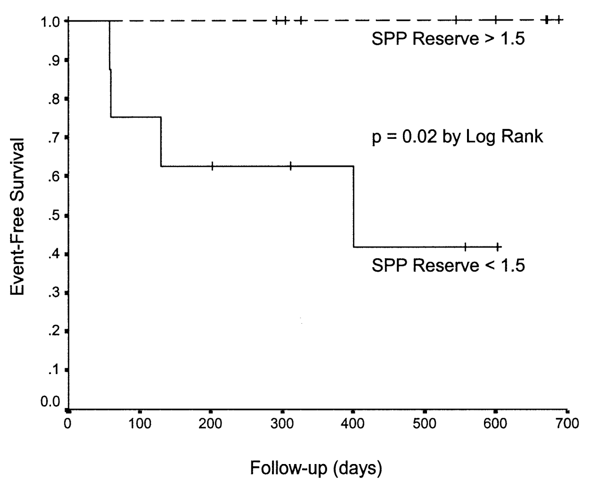

FIGURE 1. Kaplan-Meier curves for the composite end point in patients with ICDs and New York Heart Association class III HF.

arrhythmia was also enrolled and underwent noninvasive SPP reserve measurements only. The Human Studies Committee of Washington University School of Medicine approved all aspects of the study, and written informed consent was obtained from all participants before enrollment.

Dobutamine stress echocardiograms were performed beginning at an initial dose of 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 3 minutes, followed by 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 3 minutes, with subsequent dose increments of 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ every 3 minutes, up to a maximum of 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The infusions were discontinued when the patients achieved 85% of their target heart rate for their age group or if chest pain, ST-segment depression, or new regional wall motion abnormalities developed. Echocardiograms at rest and dobutamine stress echocardiograms were used to determine the left ventricular ejection fraction and SPP reserve.

SPP was calculated according to the methods described by Armstrong and colleagues,[2] where peak power is equal to the product of peak aortic flow and mean arterial pressure. Peak aortic flow was defined as the product of peak aortic velocity and aortic annulus area. Aortic velocity was measured by continuous-wave Doppler in the apical 5-chamber view. The aortic annulus diameter was measured from the parasternal long-axis view at rest. Mean arterial pressure was obtained by a sphygmomanometer at the brachial artery. SPP reserve, as described in the following equations, equals the difference between SPP at maximal dobutamine stress and SPP at rest divided by the square of end-diastolic volume, an estimate of preload: (1) SPP reserve = SPP maximum dobutamine − SPP baseline; (2) SPP = aortic flow × mean arterial pressure; (3) aortic flow = aortic annulus area × peak aortic velocity; and (4) mean arterial pressure = ([2 × systolic pressure] + diastolic pressure)/3.

Patients were followed in the Washington University Medical Center Arrhythmia Clinic every 3 months. At each follow-up visit, clinical information was obtained, including a history of shocks, ICD interrogation, HF hospitalizations, or cardiac transplantation. Mortality data were collected from hospital records and family interviews.

The composite end point of HF hospitalizations, cardiac transplantation, and all-cause mortality was analyzed by the Kaplan-Meier method. Analyses were performed with SPP reserve dichotomized at 1.5 W/ml^2. This value was chosen a priori on the basis of a previous study.[1] Continuous variables were compared using the unpaired Student's *t* test, and categorical variables were compared using Fisher's exact test. Analyses were performed using SPSS version 10.0 for Windows (SPSS, Inc., Chicago, Illinois) statistical software.

Twelve age-matched normal control patients underwent dobutamine stress echocardiography and the determination of SPP reserve. Their mean age was 61 years. Their mean baseline ejection fraction was 73 ± 11%, and their mean SPP reserve was 35.2 ± 19 W/ml^2. Eighteen patients in New York Heart Association class III HF who had ICDs were enrolled. Their mean age was 61 years. Their mean baseline ejection fraction was 32 ± 11%, and their mean SPP reserve was 3.5 ± 3.2 W/ml^2.

SPP reserve discriminated HF patients from controls without overlap (mean 3.5, range 0.05 to 10.34 vs mean 35.2, range 21.8 to 51.3, respectively; $p < 0.0001$). The study population had a mean follow-up of 15.5 months. There were no differences in the baseline characteristics of the 2 groups of patients with HF and ICDs: those with adequate (>1.5 W/ml^2) and poor (<1.5 W/ml^2) SPP reserve (Table 1). There was 1 death, 1 heart transplantation, and 3 HF hospitalizations in the group with poor SPP reserve and no end points in the group with adequate SPP reserve. There were 4 ICD shocks in the group with poor SPP reserve and 1 ICD shock in the group with adequate SPP reserve. Kaplan-Meier analysis of the composite end point of death, heart transplantation, or HF hospitalization showed a significantly ($p = 0.02$) greater event rate in the group with poor SPP reserve (Figure 1). SPP reserve discriminated the 2 groups of patients with HF and ICDs without overlap, whereas the ejection fraction showed considerable overlap. The mean SPP reserve of the group with death or transplantation was 0.63 ± 0.4 W/ml^2, and the mean SPP reserve of the surviving patients was 4.9 ± 2.3 W/ml^2 ($p = 0.02$).

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For ICDs to show a continued survival benefit in patients with advanced HF, the risk for sudden cardiac death from life-threatening ventricular arrhythmias must be sufficiently greater than the risk for dying from other causes.[3] As ICD indications continue to expand, it is increasingly important to discriminate patients who are less likely to die of HF, thus identifying a subpopulation more likely to enjoy a survival benefit from ICD therapy.

The prognostic values of the left ventricular systolic ejection fraction, mitral deceleration time, and serum sodium concentration for mortality have been well established.[4–6] These measurements are insensitive and are relatively poor predictors of survival in patient with advanced HF. Peak oxygen consumption stress testing (VO_2 max) has greater prognostic ability than the left ventricular ejection fraction and has been useful for the risk stratification of ambulatory patients who may benefit from cardiac transplantation.[7] It has not been used to predict survival in patients with ICDs and is not easily measured in patients with more advanced HF and those unable to reach aerobic threshold.

Therefore, an ideal prognostic tool would have the predictive power of VO_2 max, be noninvasive, and be easy to use in patients with advanced HF. One such instrument that has emerged as a novel echocardiographic measure of ventricular function is SPP reserve. It has an advantage over other echocardiographic measures in that it is not significantly affected by afterload, can be adjusted for preload,[8] and correlates well with VO_2 max.[2] The present study demonstrates that SPP reserve identifies patients with advanced HF and ICDs who are more likely to have progressive HF.

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