Left Ventricular Peak Power During Exercise: A Noninvasive Approach for Assessment of Contractile Reserve

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Cardiac peak power, a contractility index based upon instantaneous changes in intracavitary pressure and systolic peak flow, was measured at rest and during supine exercise in 26 patients with coronary artery disease and 8 healthy subjects. The pathophysiological significance of this index was compared with left ventricular ejection fraction (LVEF) during exercise. Cardiac peak power, ejection fraction, end-diastolic volume, stroke volume, cardiac output and systemic vascular resistance were measured at rest, during three stages of supine bicycle ergometry and two stages of recovery. Cardiac peak power increased continuously in healthy subjects, from 5.4 ± 0.8 W/ml at rest to 11.4 ± 3.1 W/ml at peak exercise, $p < 0.001$. In patients, peak power increased initially, reached a plateau in stage 2, and subsequently remained unchanged in stage 3 (5.6 ± 2 versus 5.6 ± 1.6 W/ml, p = ns). Ejection fraction demonstrated a flat response during exercise in patients, contrasting with a 42% increase in cardiac peak power. The lack of increase in ejection fraction was attributed to its dependence on afterload. Peak power showed no correlation with systemic vascular resistance ($r = 0.01$, p = ns). In a subgroup of patients with low resting LVEF (LVEF = 26% ± 7%), peak power increased 70% during exercise, from 2.0 ± 0.7 to 3.5 ± 1.7 W/ml, $p < 0.05$, in contrast to a flat ejection fraction response. Thus, cardiac peak power, a relatively afterload-independent index of left ventricular performance and contractility can be obtained noninvasively during exercise.

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Left ventricular pump function results from a complex interaction between changes in left ventricular pressure, volume and ejection time. Indices based upon isolated changes in pressure or volume alone such as rate of rise of pressure, velocity of circumferential fiber shortening, flow velocity or acceleration do not provide a comprehensive assessment of left ventricular pump function. In clinical practice, left ventricular ejection fraction (LVEF) is the most frequently used index of left ventricular function. Although, easily obtained, this parameter is known to be afterload dependent. It is also known that some patients exhibit very little symptoms, good exercise capacity and maximum oxygen uptake despite a marked impairment in LVEF (*1*). The extent of LVEF impairment at rest or its response to exercise does not adequately reflect left ventricular pump function as well as contractile reserve in these patients. The clinical value of LVEF has been questioned both at rest in patients after thrombolysis (*2*) as well as during exercise (*3*). Aortic peak velocity of flow and acceleration rate, obtained by continuous wave Doppler, have also been used to assess cardiac mechanical performance and contractility at rest and during exercise (*4,5*). Although relatively simple to obtain, a strong inverse correlation has been observed between aortic peak flow velocity and systemic vascular resistance.

Multifactorial performance indices, such as end-systolic pressure-volume relations (*6,7*), stroke work or dp/dt_{max} (maximal rate of pressure rise) – end-diastolic volume relation (*8,9*) or the ejection fraction-afterload stress relation (*10,11*) based on left ventricular pressure-volume relationships, are considered to provide a more comprehensive evaluation of left ventricular pump function. For the most part, such indices have been derived invasively, thereby limiting widespread and repetitive clinical use. Cardiac power, an expression of the rate at which the left ventricle does work, is a contractility index based upon instantaneous changes in intracavitary pressure and systolic flow. This was first measured invasively in 1976 (*12,13*). It was shown to be a good discriminative index for assessing functional status in patients with coronary artery disease. Power has since been proposed as a means of providing a valid measure of contractile capacity and cardiac reserve in the setting of congestive heart failure (*14*). Recent experimental data indicate that cardiac peak power is a relatively afterload independent contractility index (*15–17*). Preliminary studies have shown that central arterial pressure and cardiac power can be obtained noninvasively in man (*18–21*).

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The purpose of the present study was to evaluate noninvasively obtained cardiac peak power, a pressure-volume derived cardiac performance and contractility index, at rest and during exercise and to compare its performance to ejection fraction response in patients with variable degrees of left ventricular dysfunction.

METHODS

Patient Population

Twenty-six patients with angiographically documented coronary artery disease (mean age 63 ± 10 yr) and eight healthy subjects (mean age 49 ± 9 yr) were studied. The patient group consisted of 25 men and 1 woman, and the healthy group of 6 men and 2 women. All patients were free from symptoms of chest pain or shortness of breath for at least 1 yr prior to the study and were capable of performing at least two stages of supine bicycle ergometry. Thirteen patients had previous myocardial infarction (6 inferior, 4 anterior and 3 non-Q wave); 15 patients had undergone coronary artery bypass grafting (CABG) at least 1 yr prior to the study. Five patients had multivessel disease but were asymptomatic with conventional treatment. Eight patients were on no cardiac medication, nine patients received digoxin and/or diuretics. Of the remaining nine patients, seven were on calcium antagonists and two on beta blockers. Radionuclide baseline LVEF was 47% ± 15% (range 25%–67%) in the patient group and 66% ± 7% (range 55%–77%) in the healthy subjects group.

Exercise Protocol

Exercise was performed on a supine bicycle ergometer. Baseline rest equilibrium radionuclide angiocardiography (ERNA), blood pressure, heart rate and resting ECG were recorded in supine position with legs resting on the ergometer pedals. After stabilization, with reproducible central arterial pressure recordings, all patients underwent up to three stages of exercise, each stage of 3 min duration, with a baseline level of 25 W and increments of 25 W/stage followed by 6 min of recovery. Heart rate, blood pressure, ERNA and ECG were recorded during each stage of exercise and recovery. Exercise was stopped after three stages or earlier if severe fatigue or dyspnea occurred. Data were obtained during the last 2 min of each stage of exercise and in two sequential immediate postexercise intervals.

Ventricular Volume Measurements

The patient's red blood cells were labeled with 20 mCi of ^{99m}Tc using the modified in vitro technique. A standard field of view gamma camera, equipped with a low-energy, all-purpose collimator interfaced with a minicomputer (PCS 512, Picker International), was used for ERNA. Sixteen frames per cardiac cycle were acquired in the left anterior position with each acquisition for 2 min. Left ventricular time-activity curves were generated employing fast Fourier curve fitting analysis using four harmonics. LVEF was determined from serial time-activity curves in the standard manner. Absolute left ventricular volume curves were determined from ERNA data using the method proposed by Massardo et al. (*22*). Left ventricular volume is derived from a ratio of total counts in the end-diastolic region of interest to a reference left ventricular pixel (of known dimension) with maximum counts (*22*). This method has been incorporated in our automated software for ERNA analysis. Absolute peak ejection flow was calculated from the first derivative of the first half of the left ventricular volume curve.

Validation of Flow Measurements

Systolic flow measurement from left ventricular volume curve was independently validated against Doppler flow measurements over the ascending aorta using a 5 MHz standard vascular Doppler probe (BV105, Oxford Sonicaid Ltd). The off-line analysis of the digitized Doppler signal is based on calculating the average flow from several cardiac cycles. The area below the velocity envelope measured by Doppler was calibrated using a calibration factor (stroke volume divided by the area under the uncalibrated flow wave). In nine patients, the peak flow rate (mean ± s.d.) by Doppler probe was 431.6 ± 56.0 ml, by ERNA it was 436.1 ± 48.5 ml ($r = 0.92$). The time to peak flow by Doppler probe was 96.4 ± 12.7 msec and by ERNA 106.6 ± 13.6 ($r = 0.86$). The time to peak flow derived from ERNA was slightly longer than with Doppler peak flow. But these differences are trivial.

Noninvasive Central Arterial Pressure Measurement

Central arterial pressure was measured employing a modification of a device reported previously (*18,19*). This device has been substantially upgraded in all its components compared to prior preliminary reports. New features include integration of pressure-volume curves, computation of power, accurate detection of pressure points during exercise and accurate mathematical curve fitting techniques. The device consists of four elements:

1. A standard sphygmomanometric cuff equipped with an internal transducer for measurement of intra-cuff pressure. The cuff is provided with an automatic microprocessor controlled deflating device for gradual deflation.
2. A 5 MHz Doppler flow sensor attached to an elastic band for placement over the brachial artery 1–3 cm below the occlusive cuff.
3. A standard three lead (I, II, III) ECG monitoring system.
4. The above elements are integrated and connected through an analog to digital converter to a central processing unit consisting of an Intel 80286/12 MHz microprocessor. The output is displayed on a color monitor screen.

The theoretical basis of noninvasive measurement of central arterial pressure has been reported previously (*18–20*). Briefly, by applying an occlusive pressure on the brachial artery during systole, a temporary standing fluid column is created in which the rising intra-arterial pressure at the axillary artery level is transmitted to the brachial artery with minimal distortion. The time interval from the beginning of the electrical depolarization (QRS complex) to the breakthrough of the pressure wave detected by the brachial Doppler sensor is measured for each cardiac cycle. By applying successively decreasing occlusive pressures on the brachial artery, from peak systolic pressure to diastolic pressure, and measuring the respective time intervals from the start of QRS complex to brachial breakthrough during 30–40 consecutive cardiac cycles, multiple pressure points are obtained that are subsequently used to generate one composite cardiac pressure cycle (Fig. 1). By plotting the decreasing pressure values versus the respectively measured time intervals, a calibrated average central arterial pressure curve is obtained. The raw pressure points thus obtained are smoothed by applying a high degree polynomial fit. Pressure measured by this technique has been validated previously using a micromanometer tipped Millar catheter (*18,20*). An excellent correlation ($r = 0.99$) has been observed between simultaneously measured noninvasive and invasive pressures in the ascending aorta (*20*).

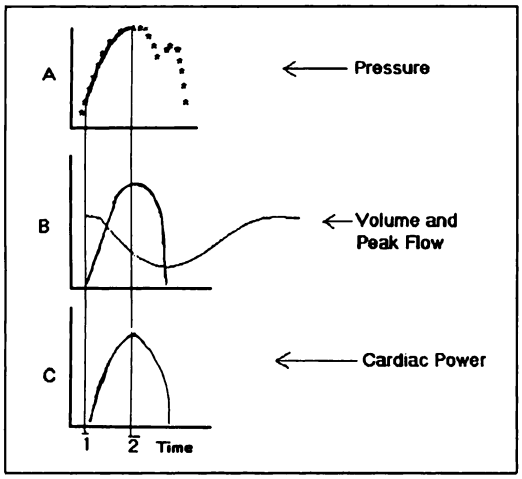

FIGURE 1. Schematic representation of central arterial pressure (A), volume and flow (B) and cardiac power (C) curves. (A) Display of pressure data acquisition. Dotted line = a complete pressure curve and continuous line = pressure measured and fitted by the device. (B) ERNA-derived left ventricular volume and flow curves. (C) Cardiac power curve. Data between vertical lines 1 and 2 represent that used for peak power calculations. Data at line 2 define values of peak flow, pressure at peak flow and the respective peak power.

Measurement of Cardiac Power

Cardiac power is an index of cardiac function representing the amount of work performed per unit time and is derived from the product of instantaneous flow and pressure. Power is calculated from the formula:

$$\text{Power} = P \times dV/dT,$$

in which P = systolic pressure and dV/dT = the change in volume during systole.

dV/dT, is the first derivative of left ventricular volume curve and thereby represents the change in volume during systole or systolic flow. Power measurement was computed for each stage by aligning a pair of pressure and the corresponding volume curve such that the beginning of the ejection phase on ERNA coincided with the beginning of the rise in systolic pressure. These two points indicating the start of the ejection phase are reasonably well defined and correct alignment was achieved in all measurements. Each central arterial pressure point was multiplied by the corresponding dV/dt obtained from the volume curve. In this manner, instantaneous systolic power values were obtained and a power-time curve was generated for the systolic part of the cardiac cycle (Fig. 1). The maximal value of power (peak power) obtained from this curve represented the product of peak flow multiplied by pressure at peak flow. Peak pressure was always reached before or at peak flow. Due to its dependency on preload (*15,16*), peak power was normalized to end-diastolic volume.

Additional Hemodynamic Parameters

Stroke volume (SV) and cardiac output (CO) were derived and double product (heart rate × systolic pressure) and systemic vascular resistance (SVR) were calculated by using the pressure, volume and heart rate data. SVR was calculated according to the traditional formula:

$$SVR = 80 \times (MAP\text{-}5)/CO,$$

where 5 is an approximation of the right atrial pressure and MAP is mean central arterial pressure.

To evaluate dependence of ventricular performance indices on afterload, in the sense of arterial input impedance opposing ventricular ejection, we used SVR as an approximation, because aortic input impedance is difficult to determine in humans. In a recent human study, aortic input impedence was obtained noninvasively at rest, but its validity for studying changes during exercise is not yet known (*21*).

Statistical Methods

For subanalysis, the patients were divided into two groups according to their baseline resting LVEF: Group I—LVEF < 35% (n = 7) and Group II—LVEF ≥ 35% (n = 19).

Patients were also categorized in two groups according to the exercise LVEF response: Group A—increase in LVEF of ≥5% absolute units (n = 8) and Group B—no change or decrease in LVEF (n = 18).

Data are expressed as mean ± s.d. Student's unpaired t-test was used for comparison between the groups. In the 17 patients who completed three stages of exercise and in the 8 healthy subjects, one-way analysis of variance (ANOVA) was used to analyze changes occurring between the stages of exercise. When ANOVA showed statistical significance, paired t-tests were performed between the stages. In addition, a paired t-test was performed when data between rest and peak exercise in all 26 patients were compared. Linear regression analysis was used for correlations. A probability of <0.05 was considered significant.

RESULTS

Exercise Performance

Of the 26 patients in the study, 17 performed three stages of exercise and reached a double product of 21.3 ± 7.1K. The nine remaining patients performed only two stages, reaching a double product of 21.5 ± 5.8K (p = ns). The reasons for stopping exercise short of the three stages were shortness of breath and fatigue. None of the patients developed chest pain during exercise. All patients except one had a normal ECG during exercise. One patient had 1.5 mm ST depression at peak exercise. There was no significant difference in double product between the nine patients receiving cardioactive medication (calcium antagonists and beta-blockers) and the remaining 17 patients (19.7 ± 6.0 versus 22.2 ± 7.1K).

All healthy volunteers completed at least three stages of exercise, two reached Stage 4, and two Stage 5. Although they had better exercise tolerance than patients, they achieved a similar double product at peak exercise, 25.0 ± 4.8K (p = ns).

Changes in Hemodynamic Parameters

The changes from rest to peak exercise in heart rate, MAP, EDV, cardiac output and SVR are shown in Table 1. Whereas the changes in heart rate and blood pressure were comparable between healthy subjects and patients, it is important to note that SVR decreased to 489 ± 113 dyn * sec * cm^5 in healthy subjects compared to 1135 ± 501 dyn * sec * cm^5 in patients ($p < 0.01$). When analyzing the changes between the stages in the 17 patients who completed three stages, SVR dropped gradually from stage

TABLE 1
Hemodynamic Parameters at Rest and Peak Exercise in Patients and Healthy Subjects

	Patients (n = 26)			Healthy subjects (n = 8)		
	Rest	Peak exercise	p	Rest	Peak exercise	p
Heart rate	71 ± 15	116 ± 29	0.001	69 ± 13	136 ± 15	0.001
MAP	108 ± 15	122 ± 17	0.01	96 ± 10	111 ± 11	0.01
EDV	196 ± 74	191 ± 74	ns	170 ± 57	182 ± 48	ns
SV	84 ± 21	84 ± 28	ns	114 ± 46	134 ± 34	ns
ESV	112 ± 74	107 ± 67	ns	56 ± 18	48 ± 17	ns
CO	5.8 ± 1.9	9.5 ± 3.7	0.001	7.6 ± 3.3	18.2 ± 4.3	0.001
LVEF	47 ± 15	48 ± 16	ns	66 ± 7	74 ± 5	ns
PP	3.9 ± 1.4	5.5 ± 1.78	0.001	5.4 ± 0.8	11.4 ± 3.1	0.001
SVR	1545 ± 533	1135 ± 501	0.01	1177 ± 545	489 ± 113	0.001

CO = cardiac output (liter/min); EDV = end-diastolic volume (ml); ESV = end-systolic volume (ml); MAP = mean arterial pressure (mmHg); PP = peak power normalized to EDV (W/ml); SV = stroke volume (ml); SVR = systemic vascular resistance (dyn * sec * cm^5).

to stage, reaching statistical significance in Stages 1 and 3 compared to rest (Fig. 2B). In healthy subjects, SVR dropped markedly in Stage 1 and remained practically unchanged at peak exercise (Fig. 2A).

Cardiac output increased gradually and significantly in both patients and healthy subjects (Fig. 2A, B). End-diastolic volume remained unchanged in patients during all stages of exercise. In healthy subjects, there was a significant augmentation in EDV in Stage 2 compared to baseline (from 170 ± 57 to 196 ± 52 ml, $p < 0.03$) with a slight decrease at peak exercise to 182 ± 48 ml.

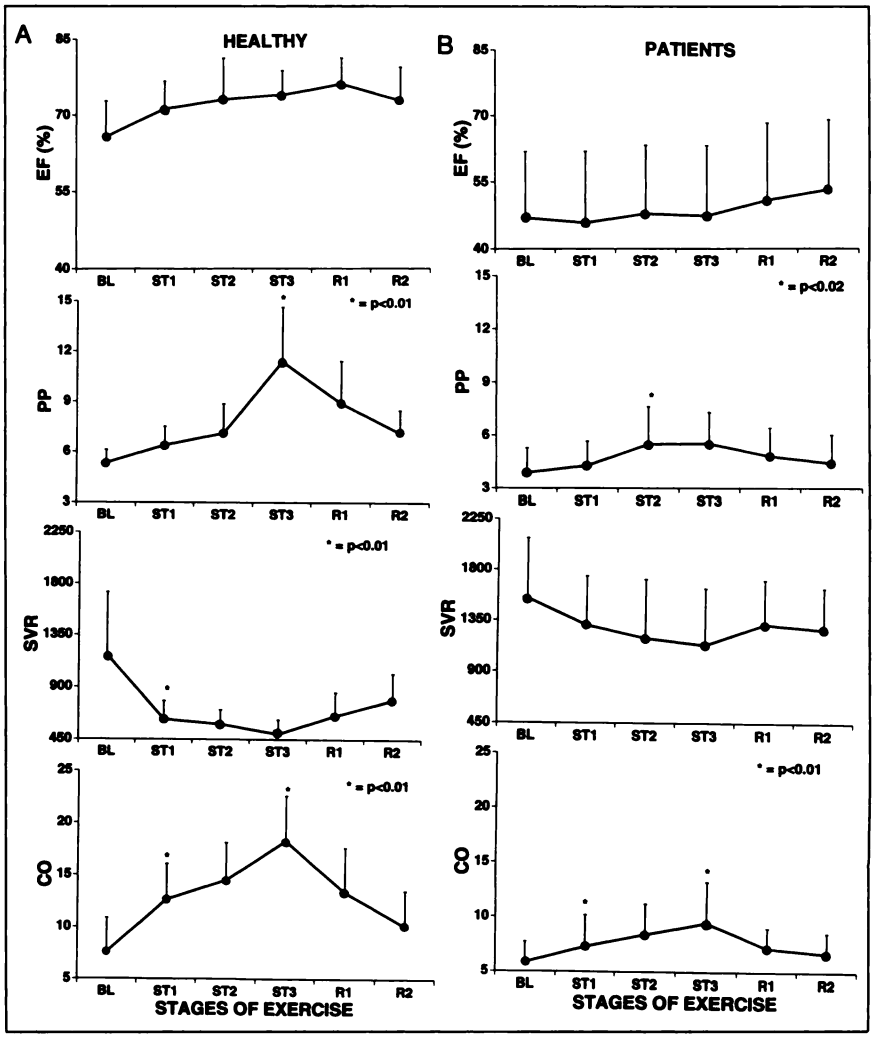

FIGURE 2. (A) Hemodynamic changes during exercise in eight healthy subjects at baseline (BL), three stages of exercise (ST1–3) and two stages of recovery (R1, 2). P value refers to changes between rest and stages of exercise. EF = ejection fraction (%); PP = peak power in W/ml; SVR = systemic vascular resistance; and CO = cardiac output in liter/min. (B) Hemodynamic changes during exercise in 17 patients (at rest, three stages of exercise and two stages of recovery); p value refers to rest versus the respective exercise stage. EF = ejection fraction (%); B = peak power in W/ml; SVR = systemic vascular resistance; CO = cardiac output in liter/min. P value in Stage 1 refers to rest versus Stage 1; p value in Stage 3 refers to Stage 1 versus Stage 3.

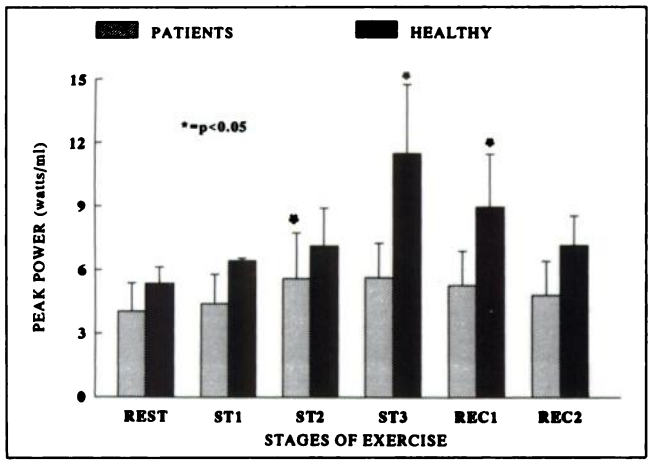

FIGURE 3. Changes in cardiac peak power during various stages of exercise in 17 patients and 8 healthy subjects (p value refers to changes between rest and stages of exercise for each group individually).

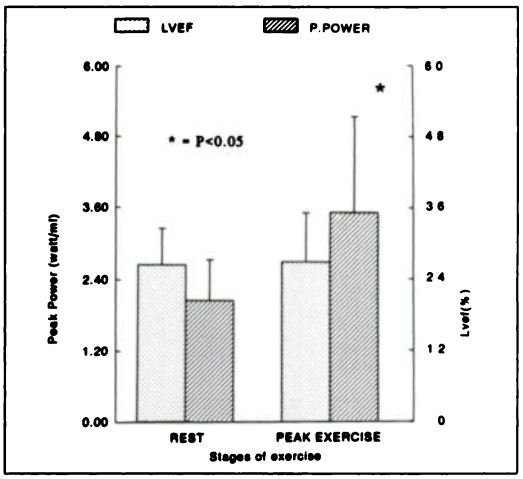

FIGURE 4. Comparison between cardiac peak power and ejection fraction in patients with severely impaired LV function (p value refers to changes in peak power between rest and peak exercise).

Changes in LVEF

In healthy subjects, LVEF increased by 8% from rest to exercise Stage 1, and by 12% from rest to peak exercise. Most of the increment was achieved between rest and Stage 1 of exercise (from 66% ± 7% to 71% ± 6% at Stage 1 to 74% ± 5% at peak exercise, Fig. 2A). Interestingly, the major increment in LVEF corresponded temporally with the largest decrease in SVR. SVR decreased from 1177 ± 545 dyn * sec * cm^5 at rest to 622 ± 155 dyn * sec * cm^5 in Stage 1 (47%) and to 489 ± 113 dyn * sec * cm^5 (58%) at peak exercise. In contrast, LVEF in patients showed a flat response and remained practically unchanged throughout the entire exercise period (from 47% ± 15% to 47% ± 16% at peak exercise, Fig. 2B). In contrast to healthy subjects, there was a relatively modest decrease in SVR in the 17 patients, from 1660 ± 555 to 1135 ± 501 dyn * sec * cm^5 (27%).

Changes in Peak Power

Cardiac peak power increased gradually during exercise in healthy subjects from 5.4 ± 0.8 to 11.4 ± 3.1 W/ml, $p < 0.001$ (Table 1, Figs. 3 and 4). In the 17 patients completing three stages, after an initial increase from 4 ± 1.3 to 5.6 ± 2.17 W/ml, $p < 0.01$, in Stage 2, peak power reached a plateau and subsequently remained unchanged (5.6 ± 1.6 W/ml, p = ns, Fig. 2B). Thus, the difference in ventricular performance between healthy subjects and patients as expressed by peak power became more accentuated as exercise progressed (1.3 W/ml at rest versus 5.8 W/ml at peak exercise, $p < 0.01$), with healthy subjects continuing to increase contractile performance at higher levels of exercise (Fig. 3). These results indicate that healthy subjects possess substantial contractile reserve, with continuing augmentation as exercise progresses. In contrast, patients appear to reach a limit of contractile reserve at a relatively early stage of exercise and are unable to further augment ventricular performance. There was no relationship between the exercise-induced changes in peak power and SVR (Fig. 5).

Comparison of Peak Power and LVEF

When patients were divided into two groups based on LVEF response to exercise, the magnitude of SVR decrease was substantially greater in those who augmented LVEF with exercise (Group A) (−936 ± 582 dyn * sec * cm^5) than in those who did not (Group B) (−188 ± 625 dyn * sec * cm^5, $p < 0.01$). However, peak power increased to the same extent in both groups (2 ± 0.9 versus 1.5 ± 0.9 W/ml, p = ns). This pattern of comparable increase in pumping ability of the two groups was also substantiated by a similar increase in cardiac output and MAP (Table 2). Thus, in spite of a different response in exercise LVEF, left ventricular mechanical performance of the two groups as measured by peak power was similar. There was a modest correlation between LVEF and peak power at rest (r = 0.66) but their correlation at peak exercise was rather weak (r = 0.22).

Peak Power in Patients with Severely Impaired LVEF

Group I patients with poor left ventricular function (<35%) demonstrated a flat LVEF response at peak exercise, with ejection fraction remaining essentially unchanged (26% ± 7% versus 27% ± 8%, p = ns). In contrast, peak power increased by 70% from 2 ± 0.7 to 3.5 ±

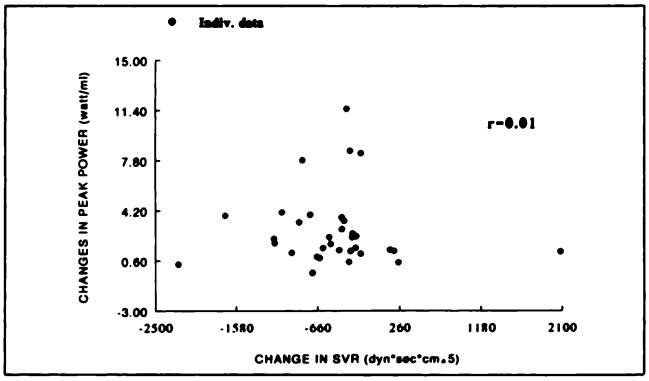

FIGURE 5. Correlation between changes in peak power and SVR in total population; r = −0.01 (y = −352.2 − 58x, p = ns).

TABLE 2
Hemodynamic Parameters at Rest and Peak Exercise in Patients with ≥5% Increase in LVEF on Exercise (Group A) Versus Those Who Do Not (Group B)

	Group A (n = 8)			Group B (n = 18)		
	Rest	Peak exercise	p	Rest	Peak exercise	p
Heart rate	68 ± 15	123 ± 31	0.002	72 ± 15	115 ± 30	0.001
MAP	107 ± 13	122 ± 15	0.05	108 ± 16	121 ± 17	0.02
EDV	213 ± 72	221 ± 76	ns	188 ± 74	178 ± 68	ns
SV	76 ± 20	100 ± 17	0.02	87 ± 21	77 ± 29	ns
ESV	137 ± 80	122 ± 75	ns	102 ± 68	101 ± 62	ns
CO	5.2 ± 1.5	12.1 ± 3.6	0.001	6.1 ± 1.9	8.4 ± 3.2	0.01
LVEF	40 ± 14	50 ± 15	0.001	50 ± 14.4	47 ± 16	ns
PP	3.2 ± 1.2	5.2 ± 1.6	0.01	4.19 ± 1.36	5.7 ± 1.8	0.009
SVR	1777 ± 688	841 ± 245	0.003	1442 ± 207	1265 ± 530	ns

Abbreviations same as in Table 1.

1.7 W/ml, $p < 0.005$ (Table 3, Fig. 4). This increase in peak power was associated with an increase in cardiac output, from 5.4 ± 2 to 8.7 ± 3 liter/min, $p < 0.04$, and very good exercise tolerance. Group 2 patients with a normal baseline ejection fraction (54% ± 9%) behaved similarly to Group I patients, with ejection fraction remaining flat, while peak power increased by 39% (from 4.6 ± 0.9 to 6.3 ± 1 W/ml, $p < 0.001$) at peak exercise.

DISCUSSION

We have combined measurements of central arterial pressure (which is comparable to LV pressure) during ejection and ventricular volumes from ERNA, to obtain cardiac peak power noninvasively during exercise. Peak power response to exercise was distinctly different in asymptomatic patients with coronary artery disease when compared to healthy subjects. In healthy subjects, peak power increased gradually and continuously over three stages; in patients, peak power reached an early plateau in Stage 2 and was maintained at that level at peak exercise. These patterns suggest that patients with coronary artery disease, even in the absence of ischemia, utilize contractile reserve maximally at an early stage of exercise and subsequently may be unable to augment contractility further as exercise progresses. This pattern of ventricular performance could not be inferred from the LVEF response during exercise. In contrast to power, LVEF response was flat throughout exercise in coronary patients.

Since LVEF is afterload-dependent, changes in this parameter may reflect alterations in afterload, changes in cardiac contractility or both. In this study patients with a normal exercise increase (>5%) in LVEF had a significantly greater decrease in SVR than the group with poor ejection fraction reserve. In contrast, peak power increased during exercise to the same extent in both groups. From these data, one could infer that the ejection fraction response was as much a function of afterload stress as contractility in these patients. The change in peak power did not correlate with changes in SVR (Fig. 5), which suggests that this index is at least relatively independent of afterload and that within the physiologic range it may be a more direct measure of contractile performance than LVEF.

Interestingly, in patients with severely depressed baseline ejection fraction (<35%), exercise peak power increased by 74% from baseline. This was comparable to the

TABLE 3
Hemodynamic Parameters at Rest and Peak Exercise in Patients with Low Ejection Fraction (Group I) and in Those with Preserved Ejection Fraction (Group II)

	Group I (n = 7)			Group II (n = 19)		
	Rest	Peak exercise	p	Rest	Peak exercise	p
Heart rate	75 ± 15	128 ± 23	0.001	69 ± 15	112 ± 29	0.001
MAP	103 ± 12	123 ± 8	0.004	109 ± 16	121 ± 18.7	0.04
EDV	281 ± 73	263 ± 70	ns	164 ± 43	165 ± 55	ns
SV	72 ± 21	70 ± 26	ns	87 ± 19	89 ± 26	ns
ESV	209 ± 69	193 ± 55	ns	77 ± 32	76 ± 36	ns
CO	5.4 ± 1.9	8.69 ± 3.3	0.004	5.95 ± 1.9	9.8 ± 3.9	0.001
EF	26 ± 7	27 ± 8	ns	54 ± 9	55 ± 10	ns
PP	2.01 ± 0.67	3.5 ± 1.7	0.005	4.6 ± 0.9	6.3 ± 1.06	0.001
SVR	1708 ± 780	1315 ± 713	0.01	1485 ± 389	1068 ± 113	0.002

Abbreviations same as in Table 1.

augmentation of cardiac peak power during exercise in patients with coronary artery disease but preserved LV function (Table 3). However, the absolute value of peak power at rest was higher in patients with normal baseline LVEF than in patients with low ejection fraction. The exact mechanisms by which the ventricle with severely impaired function at rest is able to augment mechanical performance during exercise comparable to the ventricle with preserved baseline function is not yet clear. Analysis of baseline parameters of these two groups reveal that the only striking hemodynamic difference is baseline EDV. The group with impaired LVEF had a significantly larger EDV (281 ± 73 ml) than patients with normal ejection fraction (164 ± 43 ml, $p < 0.001$). Perhaps some of the patients with altered left ventricular function were able to utilize an enhanced Starling effect due to prior ventricular enlargement and remodeling. In this group, the response of peak power to exercise appears to correlate better with the patient's functional status than did LVEF.

The value of assessing pressure-volume based contractility indices has been shown by several investigators (*6–10,23,24*). Previously, to obtain pressure-volume measurements in man, one had to measure pressure invasively during left ventricular catheterization and volume had to be measured either by radionuclide angiography (*24*), echocardiography (*24*) or invasively using an impedance catheter (*23*). The invasive approach was used by Stein and Sabbah (*12,13*) for the initial assessment of the ejection rate-of-change of power. They showed that this index had good discriminative value in differentiating functional status. In a previous study using an initial prototype of the present device, ejection rate-of-change of power measured immediately postexercise was obtained noninvasively and was shown to differentiate between healthy subjects and patients with small myocardial infarction (*19*). Previous work concerning cardiac power has predominantly been performed by invasive means in man or experimental animals. Furthermore, no data exist concerning cardiac peak power during physical exercise. However, Kelly et al. have shown recently that aortic Doppler flow signal and applanation tonometry can be used to noninvasively determine aortic input impedance and left ventricular output at rest in man (*21*). Our study is an effort to develop a pressure-volume based index of left ventricular contractility at rest as well as during exercise from the realm of experimental cardiology to clinical cardiology, so that the clinical relevance of this index can be tested in larger patient populations.

Peak Power as a Contractility Index

In an experimental canine study, Kass and Beyar (*15*) demonstrated that maximal power is sensitive to changes in contractility induced by infusion of dobutamine. In this study, a comparison was made between maximal power and two established contractility indices: slope of the end-systolic pressure volume relation (E_{es}) and slope of the dP/dT_{max}-end-diastolic volume relationship over a wide range of pharmacologically altered inotropic states. A correlation of $r = 0.86$ and $r = 0.82$ ($p < 0.01$) was found between power and the two indices respectively. It was also shown that maximal power is independent of extreme changes in afterload but is linearly dependent upon preload changes. This preload dependence can be adequately accounted for by normalization to EDV.

In humans it is difficult, if not impossible, to reproduce the controlled circumstances of the experimental hemodynamic laboratory. A complex model of left ventricular mechanics has been used to assess the sensitivity of peak power versus other known indices of contractility (see Appendix). The model, which takes in account complex ventricular geometry and deformation patterns of pressure and flow data, was shown to comply with experimental data. Analysis using this model shows that peak power is superior to other commonly used contractility indices and linearly matches contractility changes over a wide range of preload variations. The response of flow-derived indices (ejection fraction, maximal flow velocity and maximal acceleration) were found to be significantly dependent on preload and afterload (Fig. 6) and much less sensitive to change in contractility than peak power.

Exercise provides a model for assessing catecholamine-mediated increases in contractility in man. These changes, however, are also modulated by alterations in loading. In this study, peak power increased substantially during exercise: by 100% in healthy subjects and by more than 40% in patients (Fig. 2), thus reflecting the increase in contractility inherent to exercise. We also demonstrated that peak power is not influenced by changes in afterload as reflected by its lack of relationship to SVR (Fig. 6B). Preload effects were minimized, although not entirely eliminated, by normalizing peak power to the EDV of each stage.

Clinical Significance of Ventricular Performance Indices

Hemodynamic variables measured at rest and during exercise or catecholamine infusion have been used previously to categorize the pathophysiologic state of patients with heart failure (*25–27*). Although cardiac peak power is a more complex measurement, it has several advantages over previously described indices. Its main advantage stems from being a more direct contractility index which appears independent of afterload. True pump or contractile performance during exercise may have prognostic relevance. To support this view, several recent studies have shown that the pumping ability of the heart at peak exercise, as characterized by stroke work or left ventricular hydraulic power output, has prognostic value (*28,29*).

Limitations of the Study

Limitations of the study can be related primarily from the complexity of the measurements involved. Although we were able to measure arterial pressure during exercise, there is inherent noise in the pressure data acquisition due to body movement, respiration, etc. This was compensated for by using mathematical curve fitting techniques. In ad-

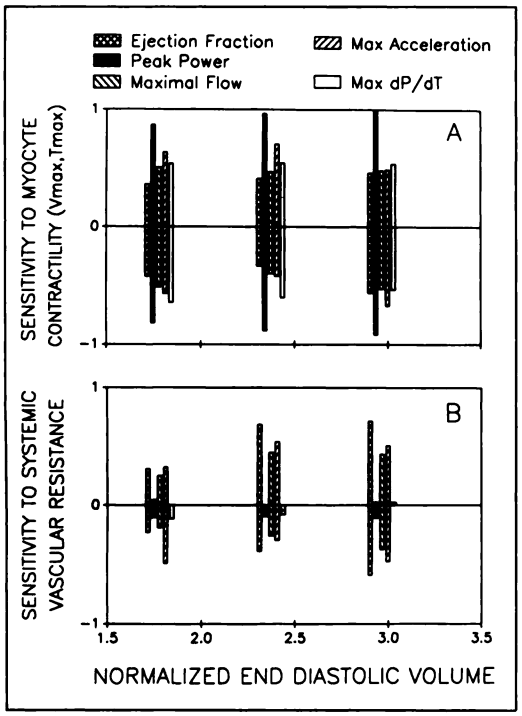

FIGURE 6. (A) Comparative assessment of the effect of change in contractility on several mechanical performance indices. Sensitivity to contractility at three different levels of preload is presented by bar graphs. Percent change in each index divided by percent change in contractility is defined as sensitivity. (B) Comparative assessment of the effect of change in SVR on several mechanical performance indices. Sensitivity to SVR at three different levels of preload is presented by bar graphs. Percent change in each index divided by percent change in SVR is defined as sensitivity to SVR.

dition, for calculation of power, we are interested in pressure at peak flow. This value occurs in all patients at an early stage, when the pressure curve is linear and well defined. Another possible source of error may originate from the volume measurements. The ERNA time-activity curve has a limited temporal resolution, allowing measurement of 7–8 average volume points during the initial phase of ejection. This measurement was validated by comparison with Doppler flow measurements. A good correlation was found between the two independently derived flow measurements. However, because of the presence of noise in the Doppler signal during exercise, we could not validate flow measurements at peak exercise. The issue of normalization of peak power to EDV or EDV^2 is not yet adequately resolved. Normalized peak power was expressed in watts/ml. The ideal way of normalizing peak power is not yet established. Based on experimental work in dogs, Kass et al. initially observed that normalization to EDV only partially eliminates preload dependence, whereas normalization to EDV^2 completely eliminates preload dependence (*15*). However, in a subsequent human study, the same group found that cardiac peak power correlates linearly with end-diastolic volume in human studies (*16*). They further suggested that for studies involving EDV >130 ml, normalization to EDV rather than EDV^2 is appropriate. Moreover, in the initial animal study, preload was markedly reduced by volume depletion, which is somewhat unphysiological. This may partly explain these differences observed by the same group of investigators. In intact humans, dynamic exercise results in a slight increase, if any at all, in EDV. At this stage, we feel it would be appropriate to realize that normalization of peak power to EDV or EDV^2 remains somewhat empirical, although we chose EDV for normalizing the peak power in this study. To what extent can the information derived from the open-chested dog model be extrapolated to human studies is not clear. In this study, we chose to normalize peak power to EDV. However, further confirmation of this approach is required. The presented data are derived from qualitatively good studies; studies of poor quality were excluded from data analysis. This occurred in approximately 20% of the studies.

CONCLUSION

Cardiac peak power is a relatively afterload-independent index of contractility. Clearly, further studies are necessary. Measurement of cardiac peak power should allow measurement of the contractile reserve and ventricular pumping ability in patients with coronary artery disease and has the potential for assessing contractile reserve in patients with depressed left ventricular function. This index may add a new dimension to the assessment of cardiac performance during exercise in patients with varying degrees of impaired left ventricular function. It may find particular value in evaluating therapeutic interventions in patients with heart failure and ventricular dysfunction.

APPENDIX

The mathematical model is based on myocytes directional distribution (*30*) and collagen spacial distribution (*31*). The uniaxial properties of myocytes and collagen fibers are represented by phenomenological relations, based on experiments with passive myocardium and activated papillary muscle. The myocyte contraction depends on two distinct contractility indices: maximal isometric stress (T_{max}) and maximal velocity of shortening (V_{max}).

Solving the nonlinear conservation laws of the model results in ventricular deformation variables and estimates of ventricular pressure and flow. Ejection pressure and flow were used to calculate peak power. The model was successfully used to obtain realistic simulation of ventricular contraction during ejection and the isovolumic phases (*32*). Using this model, the sensitivity of peak power, ejection fraction, peak flow velocity, maximal acceleration and maximal dP/dT to myocyte contractility was evaluated (*33*). The arterial system was simulated by a windkessel model using physiological values of the parameters of the arterial system provided by Beyar and Seidman (*34*).

In the sensitivity analysis, contractility was changed by ±20% and the resulting change in the investigated parameters was estimated. The same procedure was used for changes in SVR, which was changed by ±25%. Percent change in each of the investigated indices divided by percent change in contractility or SVR was defined as sensitivity. Sensitivity of the global indices of ventricular performance to contractility and to SVR at three different levels of preload is presented graphically in Figure 6. Three patterns of contractility modulations have been simulated, changes in

T_{max}, changes in V_{max} and simultaneous changes in both. It was found that peak power has a high sensitivity in the whole range of simulated preloads, to both positive and negative changes in contractility, while the other indices had lower sensitivities with strong dependence on preload. In addition, when T_{max} and V_{max} were changed simultaneously, an additive effect on peak power alone was observed. As shown in Figure 6A peak power showed the highest sensitivity to the change in contractility and was least affected by the change in SVR (Fig. 6B) at all three levels of preload. It is noteworthy that peak power demonstrated maximal sensitivity (±1) at all three preload levels, meaning that percent change in contractility equaled percent change in power.

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