European Heart Journal (1992) **13** (*Supplement E*), 85–90

Assessment of myocardial oxygen consumption (Vo_2) and systolic pressure–volume area (PVA) in human hearts

H. TAKAOKA, M. TAKEUCHI, M. ODAKE AND M. YOKOYAMA

1st Department of Internal Medicine, Kobe University School of Medicine, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe, 650, Japan

KEYWORDS: Ventricular function, myocardial oxygen consumption, pressure-volume relationship.

Several studies have recently reported that the relationship between myocardial oxygen consumption per beat (Vo_2) and left ventricular (LV) systolic pressure–volume area (PVA), which represents total mechanical energy generated by contraction, is linear and independent of loading conditions in excised, supported, and intact hearts. We assessed the Vo_2–PVA relationship in nine patients with heart disease. LV volume and pressure were measured simultaneously by conductance catheter and tip-micromanometer. Vo_2 was calculated from the difference between arterial and coronary sinus oxygen content, and coronary sinus blood flow measured by the thermodilution method. We obtained the linear relationship between Vo_2 and PVA by dextran infusions (median $r = 0.917$). The slope of the Vo_2–PVA relationship was $(1.82 \pm 0.66) \times 10^{-5}$ mlO_2 mmHg^{-1} ml^{-1} and the contractile efficiency, the reciprocal of the slope of the Vo_2–PVA relationship, was 40 ± 13%. The Vo_2 intercept, which reflects Vo_2 for non-mechanical work, was 0·0284 ± 0·0286 ml O_2 $beat^{-1}$. These results suggest that PVA is a good predictor of myocardial oxygen consumption and a powerful tool to evaluate the coupling of LV mechanical performance to energy use in human hearts.

Introduction

It was reported recently that the systolic pressure–volume area (PVA) correlates linearly with left ventricular (LV) oxygen consumption per beat (Vo_2) in excised, supported dog hearts[1–3] and intact dog hearts[4–6] (see Fig. 1). PVA is the area enclosed by end-systolic and end-diastolic pressure (P)–volume (V) relationships and the systolic P–V trajectory, and represents total mechanical energy consisting of both external work (EW) and mechanical potential energy (PE). When both Vo_2 and PVA were expressed in J $beat^{-1}$ 100 gLV^{-1}, the reciprocal of the slope of the linear Vo_2–PVA relationship was considered to reflect chemo-mechanical energy transduction efficiency (contractile efficiency) from excess Vo_2 above unloaded Vo_2 to PVA.

The conductance catheter technique allows accurate and continuous measurement of ventricular volume[7–11]. Using this method, the present study was undertaken to determine whether PVA linearly correlates with Vo_2 and thus whether it can serve as a powerful tool to assess the coupling between mechanical performance and energy utilization in human hearts.

Methods

PATIENT POPULATION

Nine patients, eight males and one female (mean age 56·4 ± 8·3 years; three with angina pectoris and six with old myocardial infarction) undergoing cardiac catheterization for the evaluation of ischaemic heart disease were enrolled in the study. Table 1 summarizes patient characteristics. Ejection fraction was 54 ± 20%, cardiac index 2·91 ± 0·54 $ml.min^{-1}.m^{-2}$ and heart rate 87·8 ± 4·4 $beats.min^{-1}$. Patients with acute myocardial infarction, valvular heart disease, idiopathic or ischaemic cardiomyopathy, or high-risk haemodynamic instability were excluded. No patient had dyskinetic LV wall motion. Complete, informed and written consent was obtained from each patient before the study, and no unfavourable complications occurred as a result of it.

CATHETERIZATION PROCEDURE

All diuretic and vasodilator medications were withheld for 24 h before the study. Nine French (F) introducer sheaths were placed into the right femoral artery and vein and the left subclavian vein by the Seldinger percutaneous technique. The patients underwent routine catheterization, including coronary angiography and left ventriculography, as previously described in detail[12,13]. After completion of routine catheterization, a 7F thermodilution Swan–Ganz catheter (Goodtech Inc., U.S.A.) was advanced to the pulmonary artery and a 8F micromanometer-tipped conductance catheter (Dräger Medical Electronics, Best, The Netherlands) was advanced into the LV through the femoral sheaths. A continuous slow infusion of heparinized saline was maintained through the lumen of the conductance catheter to prevent clotting. Subsequently, an 8F Webster catheter (Webster Labs, Baldwin Park, CA, U.S.A.) was advanced into the coronary sinus (CS) through the left subclavian sheath, as confirmed by contrast injection. The right atrium was paced with an electrodes-tipped Webster catheter at 80–90 $beats.min^{-1}$ (10–20 $beats.min^{-1}$ above baseline heart rate).

Correspondence: Motoshi Takeuchi, MD, 1st Department of Internal Medicine, Kobe University School of Medicine, 7-5-1, Kusunoki-cho, Chuo-ku, Kobe, 650, Japan.

0195–668X/92/0E0085 + 06 $08.00/0

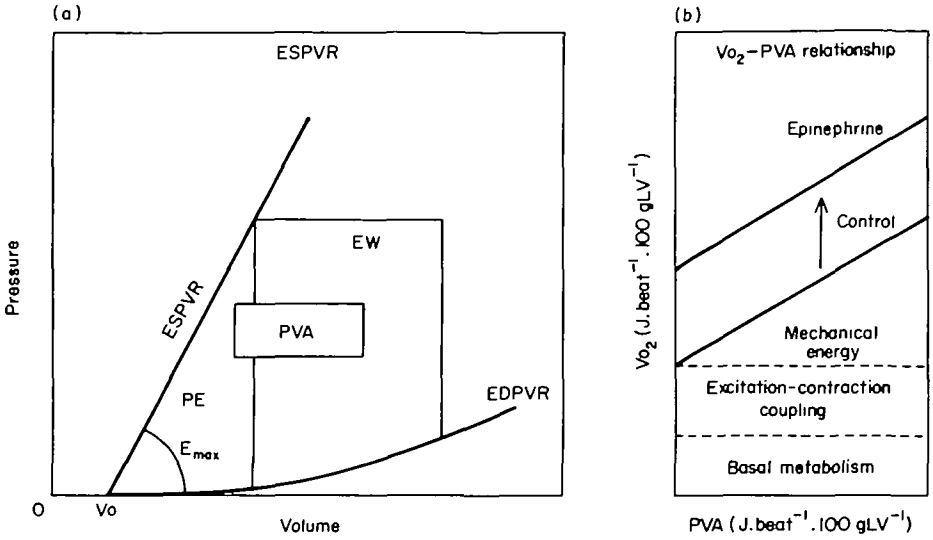

Figure 1 Panel (a): Diagram of the left ventricular pressure–volume relationship. The systolic pressure–volume area (PVA) is the area enclosed by the end-systolic (ESPVR) and end-diastolic (EDPVR) pressure (P)–volume (V) relationships and the systolic P–V trajectory. PVA represents total mechanical energy (TME), consisting of external work (EW) and mechanical potential energy (PE). E_{max}; the slope of the ESPVR, V_0; the volume-intercept of the ESPVR, Panel (b): Schematic diagram of the Vo_2–PVA relationship. Vo_2 correlates linearly with PVA in both control and augmented contractile states ($Vo_2 = a \cdot PVA + b$). The reciprocal of the slope of the Vo_2–PVA relationship (1/a) represents chemomechanical energy transduction efficiency (contractile efficiency) in excised, supported dog heart preparations. The Vo_2-intercept reflects unloaded Vo_2, consisting of Vo_2 for both excitation–contraction (E–C) coupling and basal metabolism.

VOLUME MEASUREMENT

The conductance catheter had eight platinum electrodes and was used to generate an electrical field (20 kHz, 30 μA RMS) in the LV between the electrodes at the apex and near the aortic valve. Sensing electrodes evenly distributed along the catheter measured conductances between five electrode pairs located within the LV. The conductances are summed and converted to the volume using a Leycom Sigma-5 signal conditioner-processor (Cardio Dynamics, Rijnsburg, The Netherlands). The volume (V) of the LV at any time is calculated as:

$$V(t) = 1/\alpha \cdot (L^2 \cdot \rho \cdot G(t) - \alpha Vc)$$

where $G(t)$ is the instant sum of the five conductances, α a dimensionless slope constent, L the distance between sensing electrodes, ρ the resistivity of blood and αVc the parallel conductance term to correct volume for the conductance of the surrounding tissues[7–11].

To determine αVc, 10 ml of hypertonic saline (5% NaCl) was injected as a bolus into the main pulmonary artery through the distal port of the thermodilution catheter, causing a transient increase in measured conductance, $G(t)$, without significantly altering cavity volume. The calculation of parallel conductance by the saline method assumes that actual volume and αVc remain constant[8–11]. In addition, to determine the gain constant, $1/\alpha$, we obtained the ratio of stroke volume (SV) determined by the thermodilution method to conductance catheter determined SV[11].

ASSESSMENT OF LV CONTRACTILITY

After completion of the calibration, a large balloon occlusion catheter (Baxter Healthcare Corporation, U.S.A.) was advanced to the right atrium (RA)–inferior vena cava (IVC) junction. To measure the P–V relationship, the balloon was rapidly inflated in the IVC just below the RA and pulled back to occlude venous return. P–V loops for the sequence of beats following reduction in LV preload, resulting in a 30–40 mmHg drop in LV systolic pressure, were recorded (8–10 beats) as shown in Fig. 2. Subsequently, the balloon was deflated and both pressure and volume rapidly returned to baseline. This procedure was repeated at least twice to obtain end-systolic P–V relationships (ESPVRs). The slope, E_{max}, and the volume intercept, V_0, of the ESPVR were obtained by the method previously reported by Kass *et al.*[11]. All volume-derived variables (E_{max}, Vo) were normalized for body surface area.

CALCULATION OF PRESSURE–VOLUME AREA (PVA)

PVA was calculated as an area bounded by end-systolic and end-diastolic P–V relationships and the systolic P–V trajectory of each beat, as shown in Fig. 2. The unit of PVA, mmHg·ml beat^{-1}, was converted and normalized for LV mass into a unit of energy, J beat^{-1} 100 gLV^{-1}, where 1 mmHg·ml is equivalent to $1{\cdot}33 \times 10^{-4}$ J. LV mass was assessed by the angiographic method of Rackley *et al.*[14].

MEASUREMENT OF MYOCARDIAL OXYGEN CONSUMPTION (Vo_2)

With the Webster catheter advanced into the coronary

Table 1 Mechanical and energetical parameters

No	Age	Diagnosis	Sex	Haemodynamics					ESPVR			Vo_2-PVA relationship			
				PAWP (mmHg)	CI ($l.min^{-1}.m^{-2}$)	EDVI ($ml.m^{-2}$)	ESVI ($ml.m^{-2}$)	EF (%)	E_{max} ($mmHg.ml^{-1}.m^{-2}$)	V_0 ($ml.m^{-2}$)	r	Slope ($mlO_2.mmHg^{-1}.ml^{-1}$)	Vo_2-intercept ($mlO_2.beat^{-1}.100\ gLV^{-1}$)	Eff (%)	r
1	69	OMI	M	14	1·93	150	121	26	2·50	67·7	0·987	0·0000257	0·009	25·90	0·723
2	56	AP	M	8	3·12	78	24	71	3·37	−2·1	0·992	0·0000166	0·021	43·79	0·917
3	64	AP	M	5	3·09	80	14	84	4·18	−30·7	0·848	0·0000179	0·007	37·10	0·837
4	56	OMI	M	6	3·61	79	37	58	1·67	−13·5	0·984	0·0000156	0·025	43·79	0·975
5	56	OMI	M	14	2·45	198	145	33	1·75	79·7	0·967	0·0000310	0·049	21·47	0·999
6	61	AP	F	4	2·78	86	21	79	5·36	11·0	0·984	0·0000086	0·091	65·62	0·911
7	46	OMI	M	15	3·42	118	72	50	4·23	28·2	0·961	0·0000190	0·043	34·97	0·839
8	58	OMI	M	5	2·53	102	54	47	5·14	24·2	0·999	0·0000150	0·004	44·19	0·999
9	42	OMI	M	5	3·27	111	76	42	2·56	24·0	0·963	0·0000146	0·007	45·51	0·999
mean	56·4			8·4	2·91	111·3	62·7	54·4	3·42	20·9	0·965	0·0000182	0·0284	40·26	0·911
S.D.	8·3			4·6	0·54	40·3	45·8	20·2	1·39	35·7	0·046	0·0000066	0·0286	12·79	0·096

PAWP, pulmonary artery wedge pressure; CI, cardiac index; EDVI, end-diastolic volume index; ESVI, end-systolic pressure index; EF, ejection fraction; ESPVR, end-systolic pressure–volume relationship; E_{max}, the slope of ESPVR; V_0, the volume axis intercept of ESPVR; r, correlation coefficient; Vo_2, myocardial oxygen consumption per beat; PVA, systolic pressure–volume area; Eff, contractile efficiency; OMI, old myocardial infarction; AP, angina pectoris.

sinus (CS), CS blood flow (CSF) was measured at least twice during a 30 s continuous injection of room temperature indicator (5% glucose) through the catheter lumen at a rate of 40 $ml.min^{-1}$ with the use of a Mark IV angiographic injector (Medrad Inc., U.S.A.). CSF measurements were performed with previously established methods[15, 16]. In all patients coronary venous blood was sampled from the distal port of the Webster catheter for oximetry. Myocardial oxygen consumption per minute, calculated as the product of CSF ($ml.min^{-1}$) and coronary arteriovenous oxygen content difference (vol%), was divided by heart rate to yield myocardial oxygen consumption per beat (Vo_2). The unit of Vo_2, ml $O_2.beat^{-1}.100\ gLV^{-1}$, was converted into a unit of energy, J $beat^{-1}.100\ gLV^{-1}$, where 1 ml O_2 is equivalent to 20 J.

STUDY PROTOCOL

After adequate placement of both the conductance and Webster catheters, blood resistivity, ρ, was measured and entered into the signal coordinator, and volume correction by αVc and $1/\alpha$ was performed. Subsequently, atrial (CS) pacing was started at a fixed heart rate. After steady-state haemodynamic conditions were established, P–V loops and Vo_2 were measured and transient vena caval occlusions (IVCO) were performed several times. This was followed by an infusion of dextran (100–200 ml per 5 min). After haemodynamic stabilization was confirmed, steady-state haemodynamics, P–V loops, and Vo_2 were measured. Volume loading was repeated two or three times, and the same measurements were performed at each volume loading stage. At the end of this protocol, IVCO was repeated. We measured ρ on each occasion that more than 400 ml dextran was infused and entered the new value into the signal coordinator.

To confirm that no myocardial ischaemia occurred during dextran infusion, blood was sampled from the CS and femoral arteries before and after dextran infusion, and lactate concentrations were measured. In addition, to confirm that there was no inotropic alteration during dextran infusion, blood was sampled from the femoral vein before and after dextran infusion, and catecholamine concentrations were measured.

CONTRACTILE EFFICIENCY

Linear regression analysis was performed to determine the slope (ml $O_2 \cdot mmHg^{-1} \cdot ml^{-1}$ but dimensionless after conversion to energy units) and the Vo_2 axis intercept (ml $O_2.beat^{-1}.100\ gLV^{-1}$) of each Vo_2–PVA relationship. The contractile efficiency was assessed as the reciprocal of the dimensionless slope of the linear Vo_2–PVA relationship according to Suga *et al.*[2].

STATISTICS

Comparisons of paired variables before and after volume loading in each run were performed by paired t-test. Linear regression analysis was performed to obtain Vo_2–PVA relationships. A value of $P < 0.05$ was considered statistically significant. Data are presented as mean ± S.D. unless otherwise indicated.

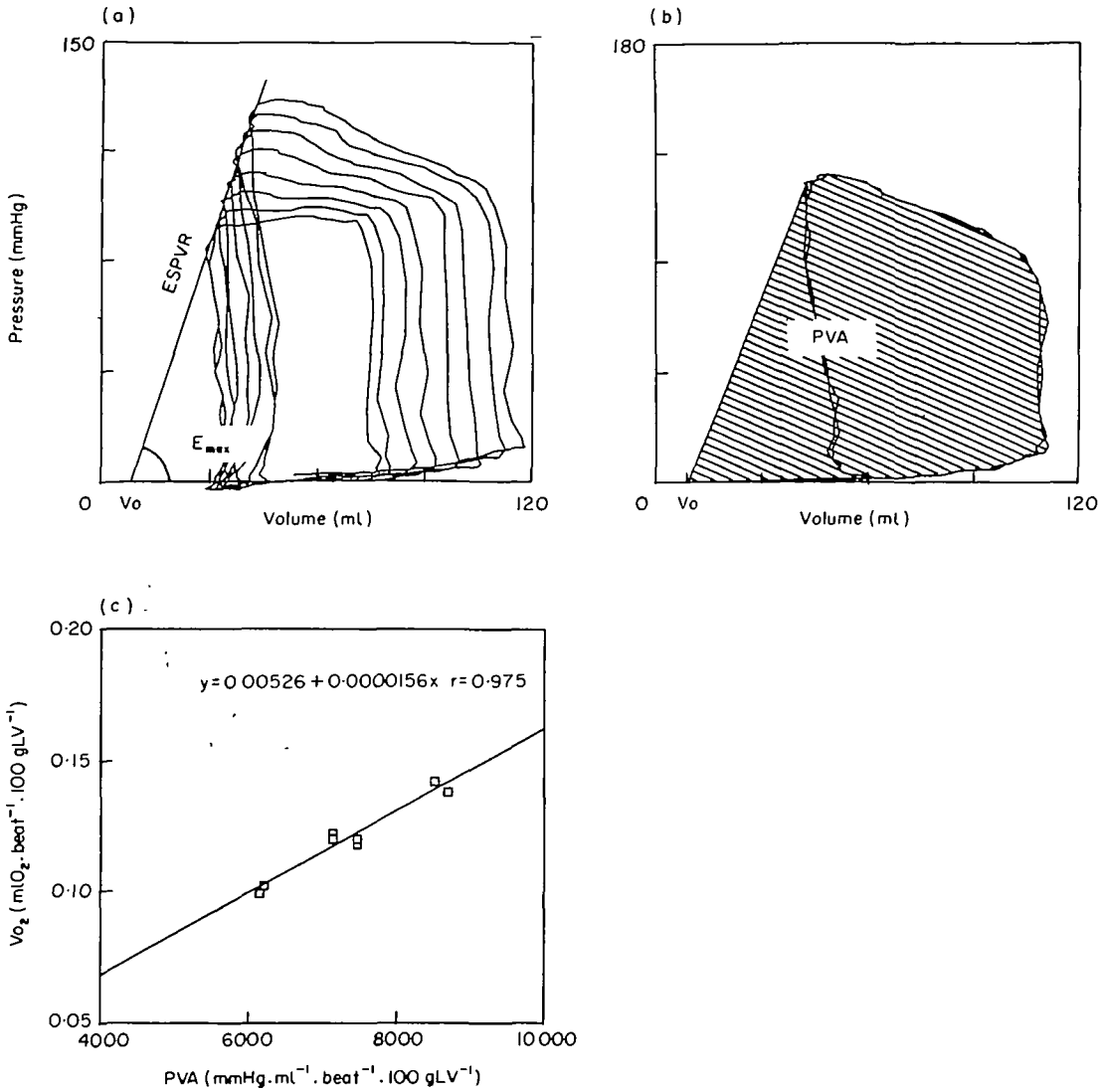

Figure 2 Panel (a): Representative pressure (P)–volume (V) loops obtained by the conductance catheter during inferior vena caval occlusion (IVCO). Panel (b): Representative P–V diagram to measure the systolic pressure–volume area (PVA). PVA was calculated using the V_0 obtained by IVCO and the systolic P–V trajectory of each steady-state contraction. Panel (c): We obtained a linear regression equation ($Vo_2 = 1{\cdot}56 \times 10^{-5}$ PVA + 0·00526). Correlation coefficient (r) was 0·975, contractile efficiency (Eff) 43·8% and the Vo_2-intercept 0·00526 ml O_2.beat^{-1}.100 gLV^{-1}.

Results

INFLUENCE OF VOLUME LOADING ON CARDIAC MECHANICS AND ENERGETICS

Volume loading resulted in significant increases in pulmonary artery wedge pressure (PAWP; 6·4 ± 4·1 to 18·4 ± 6·7 mmHg or 276 ± 184%, $P < 0{\cdot}001$), right atrial pressure (RAP; 2·9 ± 3·2 to 5·9 ± 3·6 mmHg, or 173 ± 176%, $P < 0{\cdot}005$), LV end-diastolic volume index (LVEDVI; 99·7 ± 42·9 to 114 ± 44·0 ml.m^{-2} or 15·8 ± 11·1%, $P < 0{\cdot}005$), CSF (156 ± 26·0 to 193 ± 38·0 ml.min^{-1}, or 23·5 ± 12·7%, $P < 0{\cdot}005$), PVA (6900 ± 2609 to 8726 ± 3555 mmHg · ml.beat^{-1} 100 gLV^{-1}, or 25·2 ± 10·8%, $P < 0{\cdot}005$) and Vo_2 (0·109 ± 0·032 to 0·134 ± 0·036 ml O_2.beat^{-1}.100 gLV^{-1}, or 18·9 ± 8·5%, $P < 0{\cdot}001$). There was no significant change in LV end-systolic pressure or heart rate.

INFLUENCE OF VOLUME LOADING ON CONTRACTILITY AND MYOCARDIAL ISCHAEMIA

We obtained a highly linear ESPVR and the correlation coefficient was close to unity in each heart (r = 0·965 ± 0·053, median r = 0·984). Normalized E_{max} (which went from 3·72 ± 1·43 to 3·69 ± 1·68 mmHg · ml^{-1}.m^{-2}; NS), normalized V_0 (from 20·9 ± 35·7 to 17·5 ± 31·9 ml.m^{-2}; NS), adrenaline (from 0·047 ± 0·075 to 0·037 ± 0·056 mg.ml^{-1}; NS) and noradrenaline (from 0·199 ± 0·117 to 0·168 ± 0·104 mg.ml^{-1}; NS) concentrations in the peripheral blood remained unchanged after volume loading . There were no changes in myocardial lactate extraction upon vol-

ume loading (from 34·5 ± 16·5 to 36·7 ± 16·2%; NS), administered and neither were there any ECG changes which might have suggested myocardial ischaemia.

ASSESSMENT OF VO_2–PVA RELATION

We measured multiple Vo_2-PVA points by volume loading with dextran infusions, and obtained highly linear regression lines for the Vo_2–PVA relationship in each patient; the correlation coefficient (r) was 0·911 ± 0·096 (median r = 0·917). The slope of the Vo_2–PVA relationship, the contractile efficiency and the Vo_2–intercepts were (1·82 ± 0·66) × 10^{-5} ml O_2 $mmHg^{-1} \cdot ml^{-1}$, 40·3 ± 12·8% and 0·0284 ± 0·0286 ml O_2 $beat^{-1}$, respectively. Table 1 summarizes various parameters of the Vo_2–PVA relation in all the patients.

Discussion

We investigated the relationship between Vo_2 and PVA in human hearts and found that the Vo_2–PVA relationship was linear and that contractile efficiency, i.e. efficiency from excess Vo_2 above unloaded Vo_2 to total mechanical energy, and Vo_2 for non-mechanical work could be assessed in human hearts.

Because accurate and repeated volume measurements are required to assess the Vo_2–PVA relationship, a technique such as biplane cineventriculography, which affects haemodynamics, LV size and contractility, is inadequate for this purpose. Furthermore, it is important for clinical application that the methodologies are safe, simple and reproducible. From these points of view, fast computed tomography[4] and radionuclide volumetric techniques[6] have been applied to assess the Vo_2–PVA relationship in the intact animal preparation. In the present study, we estimated LV volume using the conductance catheter as previously reported[17].

Volume corrections by parallel conductance, αVc, and gain constant, $1/\alpha$, are necessary to obtain accurate and absolute left ventricular volume measurements. Using these volume corrections, Baan *et al.*[8] compared LV volume during cardiac cycles measured by the conductance method with single plane cineventriculography in human hearts and found linear correlations. In a preliminary study[17] we compared LV volume measured by the conductance method with biplane cineventriculography in patients with LV wall motion asynergy and also found linear correlations. Moreover, using this method, Kass *et al.*[11] and Baur *et al.*[19] were able to assess the ESPVR and its slope, E_{max}, in human hearts.

Theoretically, PVA is an expression of total mechanical energy. The dimensionless ratio of PVA (in J $beat^{-1}$ 100 gLV^{-1}) to excess Vo_2 above unloaded Vo_2 (in J $beat^{-1}$ 100 gLV^{-1}) has been considered the ratio of total mechanical energy output to energy input used exclusively for mechanical contraction. This reflects the chemomechanical energy transduction efficiency of the contractile machinery, that is, contractile efficiency (see Fig. 1). Contractile efficiency appears to be independent of heart rate, preload, afterload, mode of contraction and acute change in contractility[2].

Suga *et al.*[2] reported that contractile efficiency was approximately 40% in excised, supported dog hearts. Goto *et al.*[3] have also reported that contractile efficiency was 40% in excised, supported rabbit hearts. In the present study, linear Vo_2–PVA relationships were able to be assessed in all patients, and contractile efficiency derived from these linear Vo_2–PVA relationships was 40 ± 13%. Contractile efficiency assessed in the present study thus closely approximates those in the excised, cross-circulated hearts.

A possible alteration in contractility due to volume loading might exist[18]. However, we did not detect any changes in heart rate, E_{max}, V_0 and catecholamine concentrations in the peripheral blood during volume loading in our patients. There was also a possibility of myocardial ischaemia during volume loading. However, there was no change in lactate extraction of the heart to indicate myocardial ischaemia. Although we could not fully exclude the possibility of regional subendocardial ischaemia,there was no detectable myocardial ischaemia which might influence the Vo_2–PVA relationship.

In summary, using the conductance catheter we investigated the Vo_2–PVA relationship in human LV. Our data suggest that in human hearts, PVA correlates linearly with Vo_2. This approach makes it possible to assess the contractile efficiency, efficiency from excess Vo_2 above unloaded Vo_2 to PVA, and Vo_2 for non-mechanical work in human hearts.

We acknowledge Kaoru Yoshizawa, Minoru Iwata (Taisho Biomed Instruments Co. Ltd., Japan) and Teruo Nakatsuka (Goodman Co. Ltd., Japan) for their technical assistance in our catheterization laboratory.

References

[1] Suga H, Sagawa K, Shoukas AA. Load independence of the instantaneous pressure-volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res 1973; 32: 314–22.
[2] Suga H. Ventricular energetics. Physiol Rev 1990; 70: 247–77.
[3] Goto Y, Slinker BK, LeWinter MM. Decreased contractile efficiency and increased nonmechanical energy cost in hyperthyroid rabbit heart. Circ Res 1990; 66: 999–1011.
[4] Chung N, Wu X, Balley KR, Ritman EL. LV pressure-volume area and oxygen consumption: evaluation in intact dog by fast CT. Am J Physiol 1990; 258: H1208–15.
[5] Nozawa T, Yasumura S, Suga H *et al.* Relation between oxygen consumption and pressure-volume area of in situ dog heart. Am J Physiol 1987; 253: H31–H40.
[6] Starling MR, Mancini GBJ, Montgomery DG, Gross MD. Relation between maximum time-varying elastance pressure-volume area and myocardial oxygen consumption in dogs. Circulation 1991; 83: 304–14.
[7] Baan J, Aouw Jong TT, Kerhof PLM *et al.* Continuous stroke volume and cardiac output from intraventricular dimensions obtained with impedance catheter. Cardiovasc Res 1981; 15: 328–34.
[8] Baan J, van der Velde ET, De Bruin HG *et al.* Continuous measurement of left ventricular volume in animals and humans by conductance catheter. Circulation 1984; 70: 812–23.
[9] Burkhoff D, van der Velde ET, Kass D, Baan J, Maughan WL, Sagawa K. Accuracy of volume measurement by conductance catheter in isolated, ejecting canine hearts. Circulation 1985; 72: 440–7.

[10] Kass DA, Yamazaki T, Burkhoff D, Maughan WL, Sagawa K. Determination of left ventricular end-systolic pressure–volume relationships by conductance (volume) catheter technique. Circulation 1986; 73: 586–95.
[11] Kass DA, Meidei M, Graves W, Brinker JA, Maughan WL. Use of a conductance (volume) catheter and transient inferior vena caval occlusion for rapid determination of pres ssure-volume relationships in man. Cathet Cardovasc Diagn 1988; 62: 1237–46.
[12] Takeuchi M, Igarashi T. Fukuzaki H *et al.* Single beat estimation of end-systolic pressure–volume relationships in human hearts. Circulation 1991; 83: 202–12.
[13] Takeuchi M, Fujitani K, Fukuzaki H *et al.* Effects of left ventricular asynchrony on time constant and extrapolated pressure of left ventricular pressure decay in coronary artery disease. J Am Coll Cardiol 1985; 6: 597–602.
[14] Rackley CE, Dodge HT, Coible YD, Hay RE. A method of determining left ventricular mass in man. Circulation 1965; 29: 666–71.
[15] Ganz W, Tamura K, Marcus HS, Donoso R, Yoshida S, Swan HJC. Measurement of coronary sinus blood flow by the thermodilution in man. Circulation 1971; 44: 181–95.
[16] Baim DS, Rothman MT, Harrison DC. Improved catheter for the regional coronary sinus flow and metabolic studies. Am J Cardiol 1980; 46: 997–1000.
[17] Odake M, Takeuchi M, Hayashi T. Determination of human left ventricular volume by conductance catheter (CC): a comparison with biplane cineangiography. Circulation 1989; 80 (Suppl): II–251.
[18] Lew WYW. Time-dependent increase in left ventricular contractility following acute volume loading in the dog. Circ Res 1988; 63: 635–47.
[19] Baur LMB, Schipperheyn JJ, Baan J *et al.* The influence of angiotensin converting enzyme inhibition on pump function and cardiac contractility in patients with chronic congestive heart failure. Br Heart J 1991; 65: 137–42.