



ELSEVIER

Contents lists available at ScienceDirect

## Journal of Cardiology

journal homepage: [www.elsevier.com/locate/jjcc](http://www.elsevier.com/locate/jjcc)

## Original article

## Slope in preload recruitable stroke work relationship predicts survival after left ventriculoplasty and mitral repair in patients with idiopathic cardiomyopathy



Yasushige Shingu (MD, PhD), Suguru Kubota (MD, PhD), Satoru Wakasa (MD, PhD), Tomonori Ooka (MD, PhD), Hiroki Kato (MD, PhD), Tsuyoshi Tachibana (MD, PhD), Yoshiro Matsui (MD, PhD, FJCC)\*

Department of Cardiovascular and Thoracic Surgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan

## ARTICLE INFO

## Article history:

Received 9 September 2013  
Received in revised form 3 April 2014  
Accepted 16 April 2014  
Available online 18 June 2014

## Keywords:

Cardiomyopathy  
Mitral regurgitation  
Surgery

## ABSTRACT

**Background:** Left ventriculoplasty (LVP) and mitral valve plasty (MVP) are sometimes effective for patients with idiopathic dilated cardiomyopathy (DCM) who are not eligible for heart transplantation. Strict patient selection is warranted for these controversial procedures.

**Methods and results:** The subjects were 18 patients with idiopathic DCM and mitral regurgitation who had not been indicated for heart transplantation due to either older age or patient refusal, and who underwent LVP and MVP. Their mean age was  $57 \pm 14$  years and 50% were dependent on catecholamine infusion. The preload recruitable stroke work (PRSW) relationship and its slope (Mw) were estimated by a single-beat technique using transthoracic echocardiography. There were one 30-day mortality and six (33%) hospital deaths due to heart failure. The one-year survival rate was 50%. Left ventricular end-diastolic dimension (LVDD) decreased from  $77 \pm 11$  to  $68 \pm 11$  mm ( $p = 0.001$ ) whereas the ejection fraction did not change. Preoperative Mw was significantly higher in one-year survivors than that in non-survivors ( $54 \pm 17$  erg  $\text{cm}^{-3} 10^3$  vs.  $31 \pm 10$  erg  $\text{cm}^{-3} 10^3$ ,  $p = 0.005$ ). Preoperative LVDD was not different between the groups. The cut-off value of  $42$  erg  $\text{cm}^{-3} 10^3$  for Mw predicted one-year survival with high sensitivity (100%) and specificity (77%).

**Conclusions:** Mw, the slope in the PRSW relationship, may predict survival after LVP and MVP in patients with idiopathic DCM.

© 2014 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

## Introduction

The surgical strategy for patients with idiopathic dilated cardiomyopathy (DCM) and severe mitral regurgitation (MR) is controversial [1]. MR has a negative impact on the prognosis of patients with heart failure and a very low ejection fraction [2,3]. Mitral valve plasty (MVP) for patients with secondary severe MR and a low ejection fraction (<30%) is recommended in the American Heart Association (AHA) guideline (class IIb) [4]. However, early recurrence of significant MR and heart failure symptoms within 6 months have been reported in patients with

severely dilated left ventricle (LV) after down-sized mitral annuloplasty alone [5]. Thus, procedures in addition to mitral annuloplasty appear to be necessary for the large LV.

To eliminate recurrence of MR and heart failure symptoms in such high-risk patients, some groups, including ours, have developed several submitral procedures such as left ventriculoplasty (LVP) and reported acceptable midterm results [6–15]. Thus far, however, there exist no guidelines that recommend LVP concomitant with MVP, and Batista-type LVP is even a class III recommendation in the AHA guidelines [16]. We performed LV plasty for extremely large heart in 55 cases from 2004 to 2013, and one-year survival rate was 58%. From our experience, we believe this operation has a role in selected patients. Although strict patient selection is important for these controversial procedures, we do not have any reliable LV functional parameters for the prediction of responders to LVP and MVP that we can easily use in clinical practice [17].

\* Corresponding author at: Department of Cardiovascular and Thoracic Surgery, Hokkaido University Graduate School of Medicine, Kita 14, Nishi 7, Kitaku, Sapporo 060-8648, Japan. Tel.: +81 11 716 1161x6041; fax: +81 11 706 7612.

E-mail address: [ymatsui@med.hokudai.ac.jp](mailto:ymatsui@med.hokudai.ac.jp) (Y. Matsui).

We reasoned that load-independent contractile functional parameters would correlate with survival after operation. We demonstrate here that preload recruitable stroke work relationship is useful to predict survival after LVP and MVP in end-stage heart failure patients with idiopathic DCM and severe MR.

## Methods

### Patients' characteristics

Tables 1 and 2 show the patients' preoperative characteristics. The 23 consecutive cases included 18 idiopathic DCM patients with end-stage heart failure who underwent LVP and MVP from 2006 to 2013 (mean age,  $57 \pm 14$  years; 27–77 years). Five patients were excluded from the study due to lack of sufficient echocardiographic data. The diagnosis of DCM was based on the absence of significant coronary artery disease or primary valvular heart disease. The pathological findings of the LV muscle specimens obtained during surgery were also consistent with DCM in all cases. They all had New

York Heart Association (NYHA) class III or IV. Nine (50%) patients were dependent on catecholamine infusion just before operation. Intra-aortic balloon pumping in two patients and percutaneous cardiopulmonary support in one patient were needed just before the operation due to hemodynamic instability. While most patients used beta-blockers preoperatively, the use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers was relatively rare due to the low blood pressure and renal dysfunction. None of the patients had been registered for heart transplantation due to their age being over 60 years, which was the limited age in Japan at that time, in 11 cases and the patients' refusal in 7 cases. The University Ethics Committee approved the research protocol and informed consent was obtained from the subjects.

### Surgical procedures

To reshape the severely remodeled LV, we performed overlapping LVP without a patch as previously reported [10]. Briefly, we used a 72 ml silicone sizer to remodel the LV to a more ellipsoidal

**Table 1**  
Patients' clinical and echocardiographic characteristics of all 18 idiopathic dilated cardiomyopathy cases.

Age	Gender	NYHA class	CA Dependent	RF (Cr > 2.0)	AF	Echocardiographic data					
						LVDd (mm)	LVDs (mm)	LVEF (%)	DcT (ms)	MR grade	Mw (erg cm <sup>-3</sup> 10 <sup>3</sup> )
One-year survivors											
55	Male	3	Yes	No	Yes	88	81	34	135	4	56
67	Male	4	Yes	No	Yes	73	68	23	136	4	28
64	Male	3	No	No	No	80	70	24	144	4	46
60	Female	3	No	No	Yes	82	67	33	212	4	59
37	Male	3	No	No	No	69	54	31	231	4	43
52	Male	3	No	NO	Yes	83	79	21	125	4	41
63	Male	4	Yes	No	No	72	66	28	350	4	67
36	Male	3	Yes	No	No	89	76	40	244	4	88
27	Female	3	No	No	No	57	52	31	108	4	59
Non-survivors											
36	Male	4	Yes	Yes	No	94	87	10	100	3	21
69	Male	3	No	Yes	No	72	69	21	130	4	41
61	Male	4	Yes	No	No	88	85	17	82	4	17
59	Male	4	Yes	yes	Yes	85	74	32	NA	4	44
55	Male	4	Yes	No	No	80	74	24	115	4	33
67	Male	3	Yes	No	Yes	69	59	23	150	4	33
71	Male	4	Yes	Yes	No	62	58	14	120	4	18
77	Female	3	No	Yes	No	74	69	21	158	4	31
64	Male	3	No	No	Yes	73	70	27	96	3	37

AF, atrial fibrillation; CA, catecholamine; DcT, deceleration time; NYHA, New York Heart Association; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; Mw, the slope in the preload recruitable stroke work relationship; NA, not applicable; RF, renal failure.

**Table 2**  
Preoperative characteristics in dilated cardiomyopathy patients.

Variables	Total (n=18)	One-year survivors (n=9)	Non-survivors (n=9)	p-Value
Age	$57 \pm 14$	$51 \pm 14$	$62 \pm 12$	0.08
Male gender	15 (83%)	7	8	1.00
Atrial fibrillation	7 (39%)	4	3	1.00
Diabetes mellitus	5 (28%)	2	3	0.62
Renal dysfunction (serum creatinine >2.0 mg/dl)	5 (28%)	0	5	0.026
NYHA class III/IV	10/8	6/3	4/5	0.64
CRT-D implantation	7 (39%)	2	5	0.15
Catecholamine dependent	9 (50%)	3	6	0.35
Intra-aortic balloon pumping	2 (11%)	0	2	0.47
Percutaneous cardiopulmonary support	1 (6%)	0	1	1.00
Medications				
Amiodarone	11 (61%)	6	5	1.00
Beta blockers	16 (89%)	7	9	0.47
Angiotensin-converting enzyme inhibitors	5 (28%)	2	3	1.00
Angiotensin receptor blockers	7 (39%)	5	2	0.34

Values  $\pm$  standard deviation. CRT-D, cardiac resynchronization therapy-defibrillators; NYHA, New York Heart Association.

shape and to not reduce the LV cavity too much. The lateral wall was sutured continuously on the deep septal wall using 3-0 polypropylene sutures with specially designed large curved needles. After aortic declamping, the medial wall was then overlapped on the lateral wall using interrupted 4-0 polypropylene sutures. When myocardial fibrosis was evident only in the posterior part of the LV, we employed a Batista-type operation.

We performed MVP as a part of our original mitral complex reconstruction [14]. Briefly, papillary muscle approximation is a surgical method to join the entire papillary muscles side-by-side from the bases to the heads by three pledgeted mattress sutures of 3-0 polypropylene. We placed a subvalvular CV-4 ePTFE suture between the site of the chordal attachment of the approximated papillary muscles and the anterior mitral annulus. This suture was passed through the true-sized semi-rigid total annuloplasty ring [14].

#### Assessment of cardiac function by echocardiography

We used a Sonos 5500 ultrasound system (Philips Medical Systems, Andover, MA, USA) with a 3S transducer (3–5 MHz), a Vivid Seven system (GE/Vingmed, Milwaukee, WI, USA) with an M3S (2.5–3.5 MHz) transducer, or an Aplio system (Toshiba Medical Systems, Tokyo, Japan) with a 2.5 MHz transducer. These instruments were operated by experienced examiners who were blinded for the study. The following basic variables were measured from the parasternal long-axis view: LV end-diastolic (LVDD) and end-systolic dimensions (LVDS) (mm), left atrial dimension (LAD) (mm), interventricular septal thickness (IVST), and LV posterior wall thickness (LVPWT) (mm). On an apical long-axis image, the pulsed Doppler sample volume was located at the tip of the mitral valve leaflets to obtain the deceleration time (DcT) (ms) of the early transmitral flow velocity. The LV end-diastolic volume (EDV), end-systolic volume (ESV), and LV ejection fraction (LVEF) were measured using the modified Simpson method. The MR grade was determined by the proximal isovelocity surface area method or color Doppler images. In four cases, echocardiography was performed under dobutamine infusion (4–5 mg/kg/min). These four cases were not excluded because of very low Mw even with dobutamine. All values were averaged using three consecutive measurements.

#### Estimation of preload recruitable stroke work relationship

Stroke work in the heart with MR was calculated as we previously reported: (total stroke volume)  $\times$  (SBP – LAP) (ml mmHg), where SBP and LAP indicate systolic blood pressure and left atrial pressure, respectively [18]. Total stroke volume was calculated using the time velocity integral of pulsed Doppler at the LV outflow tract and mitral annulus level as follows: (forward stroke volume) + (regurgitation volume) (ml). LAP was estimated by continuous wave Doppler of the MR jet as follows: (systolic blood pressure) – (peak pressure gradient of the wave) (mmHg) [19].

The preload recruitable stroke work (PRSW) relationship and its slope (Mw), which is recognized as a load-insensitive index of contractile function, were estimated by a single-beat technique according to a report by Lee et al. [20]. Briefly, “Mw” was calculated as follows: (total stroke work)/[EDV –  $k \times$  EDV + (1 –  $k$ )  $\times$  LV wall] ( $\text{erg cm}^{-3} 10^3$ ). EDV was derived from the total stroke volume and LVEF. LV wall was estimated by the echocardiography-derived LV mass. Constant  $k$  was estimated by an equation:  $k = 0.0004 \times$  LV mass + 0.6408. This single-beat technique for Mw has been reported to be well correlated to that by the invasive catheter method for different LV sizes, LV mass, and the presence of regional wall motion abnormalities [20].

#### Validation of total stroke work by echocardiography alone using MR model in rat

To validate the key non-invasive parameter of total stroke work, we performed a pilot experiment using two male Sprague–Dawley rats (body weight, 300 g) obtained from Sankyo Labo Service Corporation (Tokyo, Japan). The use of animals was in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH publication no. 85–23, revised 1996) and the experimental protocols were approved by the local Animal Welfare Committee of the Hokkaido University, Japan. MR was created by damaging the mitral valve using 24G needles as previously reported [21]. Severe MR was confirmed by color Doppler. Four weeks after the procedure, animals were anesthetized with intramuscular ketamine and xylazine injection (45 and 4.5 mg/kg, respectively). The rats were examined in supine position by a Sonos 5500 ultrasound system with a 12-MHz phased array transducer and a 1.4F Millar catheter inserted through the right carotid artery and advanced into the LV. Signals of LV pressure and volume assessed by acoustic quantification mode in standard apical four-chamber view were simultaneously displayed in real-time mode in the monitor of the computer using a multichannel 16-bit analog-to-digital converter (PowerLab, ADInstruments, Sydney, Australia) and a data acquisition software (LabChart, ADInstruments). External total stroke work was automatically measured from the area of pressure–volume loops (TSW-loop) in the software at baseline and after bolus saline infusion of 2, 4, 6, 8, and 10 ml. The values from 10 consecutive cycles were averaged at each volume loading. At each loading condition, total stroke work by echocardiography alone (TSW-echo) was separately measured by the formula, (total stroke volume)  $\times$  (SBP – LAP) (ml mmHg), based on an assumption that pressure–volume loop is a square. These two different methods, TSW-loop and TSW-echo, were compared at each loading condition.

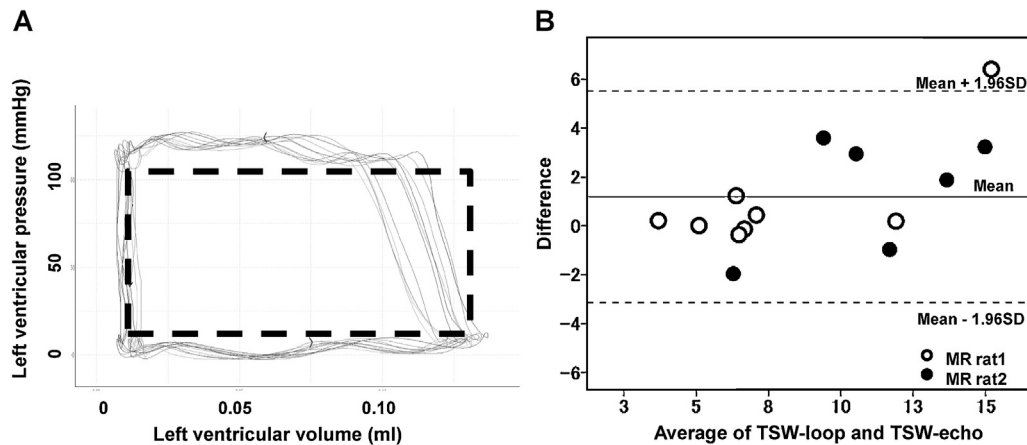
#### Statistical analysis

All the data are given as mean  $\pm$  standard deviation. Statistical analysis was performed with SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). Categorical data were compared by Fisher’s exact test. The Mann–Whitney  $U$ -test was used to compare the continuous variables between the groups and the Wilcoxon test to compare the preoperative and postoperative values. The receiver operating characteristic (ROC) curve was used to analyze the sensitivity and specificity of the parameters for detecting one-year survival. We selected the cut-off values that maximize sensitivity plus specificity. The area under the curve (AUC) was used to compare predictive parameters. The survival rate was analyzed by the Kaplan–Meier method and log-rank test. In the animal study, the Bland–Altman test was used to assess the limits of agreement and confidence intervals between the two methods, TSW-loop and TSW-echo. A  $p$ -value  $< 0.05$  was considered statistically significant.

## Results

#### Pilot experimental data

Mean total stroke work of different volume loading conditions was  $8.6 \pm 3.2$  ml mmHg and  $9.8 \pm 4.6$  ml mmHg by TSW-echo and TSW-loop, respectively. Linear regression analysis demonstrated a significant correlation between the two methods:  $y = 1.28x - 1.25$ ,  $r = 0.898$ ,  $p < 0.001$ . Fig. 1A shows representative consecutive 10 cycles of pressure–volume loop. Fig. 1B shows the Bland–Altman spots which also indicated good correlation between the two methods, with only one of the 14 measurements being over 1.96 SD.



**Fig. 1.** (A) Representative consecutive 10 cycles of pressure–volume loop (TSW-loop) and an assumed square for TSW-echo (dashed line). (B) Bland–Altman spots to assess the limits of agreement and confidence intervals between the two methods, TSW-loop and TSW-echo. MR, mitral regurgitation; TSW, total stroke work.

This indicates that TSW-echo in which the pressure–volume loop is assumed to be a square (Fig. 1A, dashed line) would be approximated to TSW-loop. We used TSW-echo for the calculation of Mw formula,  $TSW/[EDV - k \times EDV + (1 - k) \times LV \text{ wall}]$ , proposed by Lee et al. in which constant  $k$  was derived from human clinical data [20].

#### Operative data

All patients underwent mitral complex reconstruction including mitral annuloplasty and papillary muscle approximation as a part of LVP. There was no conversion to mitral valve replacement. Thirteen (72%) patients underwent LVP by overlapping and two patients (11%) by a Batista-type procedure. Tricuspid valve ring annuloplasty was performed in all cases and the MAZE procedure was conducted in five (28%). Cardiopulmonary bypass and aortic cross clamp times were  $235 \pm 61$  min and  $114 \pm 24$  min, respectively.

#### Comparison between one-year-survivor and non-survivor groups

There was one (6%) operative mortality within 30 days. There were six (33%) hospital deaths due to heart failure. The overall survival rates were 61% after 6 months and 50% 1 year after operation (one-year survivors,  $n = 9$ ; non-survivors,  $n = 9$ ).

Table 2 shows the differences in patients' preoperative characteristics between the one-year-survivor and non-survivor groups. Renal dysfunction (serum creatinine  $>2.0$  mg/dl) was more common in non-survivors than in one-year survivors. Age and preoperative medication were comparable between the groups.

Table 3 shows the differences in preoperative cardiac functional parameters between one-year survivors and non-survivors. In one-year survivors, the heart rate was significantly lower and DcT was significantly longer, which indicate lower LV filling pressure than in non-survivors. The preoperative LVEF, regurgitation, and

**Table 3**  
Preoperative cardiac functional parameters in dilated cardiomyopathy patients.

Variables	Total ( $n = 18$ )	One-year survivors ( $n = 9$ )	Non-survivors ( $n = 9$ )	$p$ -Value
Heart rate, bpm	$73 \pm 14$	$67 \pm 11$	$79 \pm 15$	0.042
Systolic blood pressure, mmHg	$88 \pm 10$	$88 \pm 11$	$89 \pm 10$	0.76
Diastolic blood pressure, mmHg	$53 \pm 10$	$50 \pm 9$	$56 \pm 10$	0.12
BNP, pg/ml	$1346 \pm 1041$	$1066 \pm 716$	$1628 \pm 1271$	0.35
Cardiac catheter data				
Cardiac index, L/min/m <sup>2</sup>	$2.0 \pm 0.4$	$2.1 \pm 0.5$	$1.9 \pm 0.3$	0.32
sPA, mmHg	$48 \pm 17$	$40 \pm 18$	$55 \pm 14$	0.07
PCWP, mmHg	$23 \pm 10$	$22 \pm 12$	$26 \pm 8$	0.86
Echocardiographic data				
LVDd, mm	$77 \pm 10$	$77 \pm 10$	$77 \pm 10$	1.00
LVDs, mm	$70 \pm 10$	$68 \pm 10$	$72 \pm 10$	0.43
IVST, mm	$9.3 \pm 1.0$	$9.7 \pm 0.9$	$9.0 \pm 1.1$	0.14
LVPWT, mm	$8.4 \pm 1.2$	$8.4 \pm 1.2$	$8.3 \pm 1.2$	0.85
LVEF, %	$25 \pm 8$	$29 \pm 6$	$21 \pm 7$	0.019
LAD, mm	$57 \pm 12$	$58 \pm 12$	$57 \pm 12$	0.70
DcT, ms	$155 \pm 68$	$187 \pm 79$	$119 \pm 26$	0.034
MR grade	$3.9 \pm 0.3$	$4.0 \pm 0.0$	$3.8 \pm 0.4$	0.15
Regurgitation volume, ml	$49 \pm 21$	$61 \pm 20$	$34 \pm 11$	0.011
Forward stroke volume, ml	$43 \pm 20$	$53 \pm 23$	$33 \pm 12$	0.040
Estimated LAP, mmHg	$24 \pm 14$	$18 \pm 7$	$30 \pm 17$	0.11
LVEDV, ml	$291 \pm 105$	$285 \pm 82$	$297 \pm 129$	0.97
LVESV, ml	$218 \pm 91$	$197 \pm 57$	$238 \pm 116$	0.83

Values  $\pm$  standard deviation. BNP, brain natriuretic peptide; DcT, deceleration time; IVST, interventricular septal thickness; LAD, left atrial dimension; LAP, left atrial pressure; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; LVPWT, left ventricular posterior wall thickness; MR, mitral regurgitation; PCWP, pulmonary capillary wedge pressure; sPA, systolic pulmonary artery pressure.

**Table 4**  
Changes in cardiac functional parameters in dilated cardiomyopathy patients.

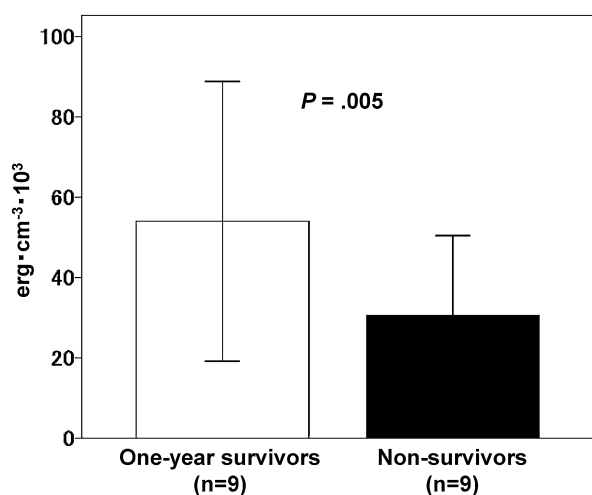
Variables	Total (n=15)		One-year survivors (n=9)		Non-survivors (n=6)	
	PreOP	PostOP	PreOP	PostOP	PreOP	PostOP
Heart rate, bpm	74 ± 15	84 ± 13*	67 ± 11	80 ± 13*	83 ± 14#	90 ± 12
SBP, mmHg	89 ± 11	87 ± 10	88 ± 11	89 ± 6	90 ± 12	83 ± 14
DBP, mmHg	53 ± 10	55 ± 7	50 ± 9	57 ± 4	58 ± 11	53 ± 10
<b>Echocardiography</b>						
LVDd, mm	77 ± 11	68 ± 11**	77 ± 10	67 ± 9**	77 ± 12	69 ± 10*
LVDs, mm	69 ± 11	61 ± 9**	68 ± 10	59 ± 7**	71 ± 12	64 ± 10*
LVEF, %	25 ± 8	23 ± 5	29 ± 6	26 ± 4	18 ± 5##	19 ± 5##
MR grade	3.9 ± 0.3	0.4 ± 0.5**	4.0 ± 0.0	0.2 ± 0.4**	3.8 ± 0.5	0.5 ± 0.5*
Forward stroke volume, ml	43 ± 21	47 ± 17	53 ± 23	57 ± 15	30 ± 8#	35 ± 12#
<b>SPECT</b>						
LVEDV, ml	351 ± 118	243 ± 81**	361 ± 80	250 ± 71*	337 ± 170	231 ± 102*
LVESV, ml	271 ± 118	188 ± 74**	265 ± 62	182 ± 49*	292 ± 183	198 ± 115
Reduction rate (LVEDV), %	–	29 ± 13	–	34 ± 14	–	23 ± 8
Reduction rate (LVESV), %	–	28 ± 16	–	33 ± 17	–	20 ± 13

Values ± standard deviation. DBP, diastolic blood pressure; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; OP, operation; SBP, systolic blood pressure; SPECT, single photon emission computed tomography. \* $p < 0.05$  and \*\* $p < 0.01$  vs. preOP values; # $p < 0.05$  and ## $p < 0.01$  vs. one-year survivors.

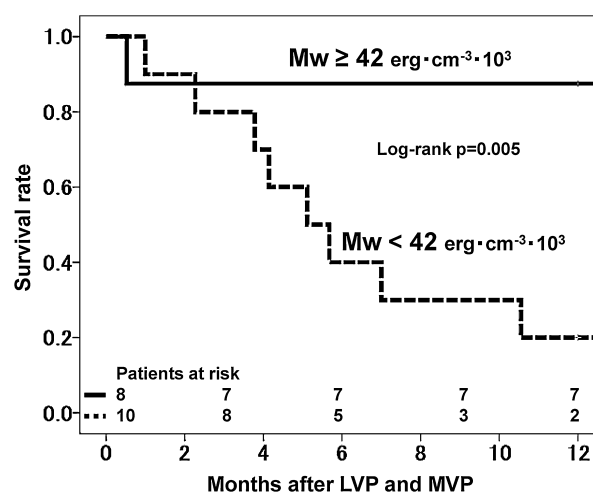
forward stroke volumes were significantly larger in one-year survivors than in non-survivors. LVDd and LV volumes were not significantly different between the groups.

Table 4 shows changes in cardiac functional parameters in one-year-survivor and non-survivor groups. The postoperative echocardiographic parameters were not applicable due to poor recording in three cases. The postoperative MR grade was mild or less in all cases. There was no reoperation due to recurrent MR during the follow-up (median, 11 months). In total, LVDd significantly decreased from  $77 \pm 11$  mm to  $68 \pm 11$  mm ( $p = 0.001$ ), although LVEF did not significantly change even with the elimination of significant MR (from  $25 \pm 8\%$  to  $23 \pm 5\%$ ,  $p = 0.51$ ), possibly because of concomitant LV volume reduction surgery. LVEF and forward stroke volume were significantly smaller in the non-survivor than in the one-year-survivor group both before and after surgery. LVESV did not significantly decrease after surgery and reduction rates were relatively low in the non-survivor group even though there was no statistical significance.

Fig. 2 shows preoperative Mw in PRSW, a load-insensitive index of contractile function in the one-year-survivor and non-survivor groups. Mw was significantly higher in one-year survivors than in non-survivors ( $54 \pm 17$  erg  $\text{cm}^{-3} \cdot 10^3$  vs.  $31 \pm 10$  erg  $\text{cm}^{-3} \cdot 10^3$ ,  $p = 0.005$ ).



**Fig. 2.** Preoperative Mw, the slope in the preload recruitable stroke work relationship, which is a load-insensitive index of contractile function, in one-year survivors and non-survivors who underwent left ventriculoplasty and mitral valve plasty.



**Fig. 3.** Survival curves by Kaplan–Meier analysis in those with higher Mw ( $\geq 42$  erg  $\text{cm}^{-3} \cdot 10^3$ ) and lower Mw ( $< 42$  erg  $\text{cm}^{-3} \cdot 10^3$ ). LVP, left ventriculoplasty; MVP, mitral valve plasty; Mw, the slope in preload recruitable stroke work relationship.

In the ROC curve analysis for prediction of one-year survival after surgery, AUCs were 0.982 ( $p = 0.002$ ), 0.929 ( $p = 0.005$ ), 0.884 ( $p = 0.013$ ), and 0.804 ( $p = 0.049$ ) for preoperative Mw, LVEF, MR volume, and deceleration time, respectively. The preoperative Mw was the best parameter to predict one-year survival after surgery. Mw-cut-off value of  $42$  erg  $\text{cm}^{-3} \cdot 10^3$  predicted one-year survival with sensitivity and specificity of 100% and 77%, respectively.

Fig. 3 shows survival curves determined by Kaplan–Meier analysis in those with “higher Mw” ( $\geq 42$  erg  $\text{cm}^{-3} \cdot 10^3$ ,  $n = 8$ ) and “lower Mw” ( $< 42$  erg  $\text{cm}^{-3} \cdot 10^3$ ,  $n = 10$ ). The patients with higher Mw tended to have a better survival rate than those with lower Mw (log-rank  $p = 0.005$ ). All but one patient with higher Mw survived with NYHA class of less than II (maximum survival, 5 years after surgery). On the other hand, in the group with lower Mw, more than half of the patients died of heart failure within 6 months after operation. There was no difference in preoperative characteristics except for LVEF in the higher and lower Mw group (Table 5).

## Discussion

We demonstrated that preoperative Mw, a load-insensitive index of contractile function, was a good predictor of one-year



**Table 5**  
Preoperative characteristics of patients with higher and lower Mw.

Variables	Higher Mw ( $\geq 42$ ) (n = 8)	lower Mw (<42) (n = 10)	p-Value
Age	50 ± 14	62 ± 12	0.06
Male gender	6	9	0.56
Atrial fibrillation	3	4	1.00
Diabetes mellitus	2	3	1.00
Renal dysfunction (serum creatinine >2.0 mg/dl)	1	4	0.31
NYHA class III/IV	5/3	5/5	0.66
CRT-D implantation	1	6	0.05
Catecholamine dependent	3	6	0.64
Intra-aortic balloon pumping	1	1	1.00
Percutaneous cardiopulmonary support	1	0	0.44
Medications			
Amiodarone	6	5	0.37
Beta blockers	6	10	0.18
Angiotensin-converting enzyme inhibitors	1	4	0.31
Angiotensin receptor blockers	4	3	0.63
Echocardiographic data			
LVDd, mm	78 ± 11	77 ± 9	0.83
LVDs, mm	68 ± 10	72 ± 10	0.46
LVEF, %	32 ± 5	20 ± 5	<0.001

Values ± standard deviation. CRT-D, cardiac resynchronization therapy-defibrillators; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; Mw, the slope in preload recruitable stroke work relationship; NYHA, New York Heart Association.

survival after LVP and MVP in patients with idiopathic DCM and MR, whereas LV size was not. This preliminary study will contribute to the decision-making for the indication and timing of LVP and MVP for patients with end-stage heart failure who are not eligible for heart transplantation.

Some groups, including ours, have been trying to develop submitral procedures and LVP in order to eliminate recurrence of MR and heart failure symptoms in high-risk patients [6–15]. A group from the Cleveland clinic reported midterm results of mitral valve surgery and LV volume reduction surgery (Batista operation) for patients with idiopathic DCM and end-stage heart failure [6]. The early mortality was 4% and one-year survival was 82%. They suggested that older age (>40 years) was the only predictive parameter for mortality, and that other functional parameters, including LV size and LVEF, did not correlate with survival after surgery. Suma et al. reported midterm results of mitral valve surgery in combination with selected LVP (Batista or septal anterior ventricular exclusion) for 95 patients with idiopathic DCM [22]. The three-year survival rates were 37% and 74% in patients with and without inotropic support before surgery, respectively. They suggested that preoperative inotropic dependency was the only contributing factor for mortality. Nonetheless, they did not find any cardiac functional parameters that predicted survival after operation. Thus far, therefore, there is no reliable functional parameter that we can easily assess in daily clinical practice to predict survival after LVP and MVP. In addition, there exists no demonstrable surgical strategy for patients with end-stage heart failure and significant MR.

The PRSW relationship and its slope, Mw, were estimated by a single-beat technique according to a report by Lee et al. [20]. This single-beat technique for Mw has been reported to be correlated well with that by the invasive catheter method for different LV sizes, LV mass, and the presence of regional wall motion abnormalities. A flat slope, low Mw, indicates that increased preload produces relatively little increase in stroke work because of reduced contractility. The relationship takes both preload and afterload into account and is applicable in a wide variety of cardiac diseases. In the current study, the preoperative Mw was the best parameter to predict one-year survival after surgery. Although LVEF was also a good parameter, we consider that PRSW would be more suitable for predicting prognosis of patients than LVEF

because PRSW considers LV developed pressure as well as stroke volume, which would reflect intrinsic LV capacity to pump. Although we need more evidence of efficacy in these preliminary procedures, we might consider LVP and MVP for idiopathic DCM patients with refractory heart failure before assist device implantation or heart transplantation when their Mw is greater than  $42 \text{ erg cm}^{-3} 10^3$ .

In this calculation of Mw, we need to determine the total stroke work in the heart with MR. We recently reported a noninvasive method for the estimation of total stroke work using transthoracic echocardiography, which is based on an assumption that the LV pressure–volume loop is approximated to a square [18]. Total stroke work was calculated as follows: total stroke work = (forward stroke volume + MR volume) × (LVSP – LVDP), which was further approximated to “(forward stroke volume + MR volume) × (SBP – LAP)”, where LVSP and LVDP indicate LV systolic and diastolic pressure, respectively. This formula is different from that reported by Chow et al. [23]: (forward stroke volume × SBP) + (MR volume × LAP). It is conceivable that regurgitant stroke work in MR should be calculated using LV pressure, but not LAP, as LV stroke work is always derived from “LV” pressure. In aortic valve stenosis, for example, we estimate LV stroke work from stroke volume multiplied by higher “LV” pressure, but not lower “aortic” pressure. Furthermore, we do not need the values of aortic and MR impedances for estimating LV stroke work. Aortic and MR impedances directly influence the forward and backward stroke volumes, respectively. The effect of different impedance is included in LV stroke work which is derived from LV stroke volumes.

### Limitations

The major limitation of this study is the small number of subjects. Second, the results in the current study are applicable only for MVP concomitant with LVP. Further study is necessary to examine the usefulness of Mw in PRSW for isolated MVP. Third, this study does not answer the question of whether volume reduction surgery in addition to MVP has any beneficial effect on LV function and such a surgery improves survival and functional status. A randomized trial with more subjects is necessary to determine this.

## Conclusions

Mw, the slope in the preload recruitable stroke work relationship, may predict survival after LVP and MVP in patients with idiopathic DCM and refractory end-stage heart failure, although further studies are necessary to validate its use.

## References

- [1] Nishigawa K, Tanemoto K. Restrictive mitral annuloplasty for functional mitral regurgitation in patients with end-stage cardiomyopathy. *Circ J* 2011;75:538–9.
- [2] Pecini R, Thune JJ, Torp-Pedersen C, Hassager C, Kober L. The relationship between mitral regurgitation and ejection fraction as predictors for the prognosis of patients with heart failure. *Eur J Heart Fail* 2011;13:1121–5.
- [3] Davoodi S, Sheikhatan M, Karimi A, Ahmadi SH, Goodarzynjad H, Fathollahi MS. Outcomes and long-term quality of life of patients with severe left ventricular dysfunction who underwent coronary artery bypass surgery. *Gen Thorac Cardiovasc Surg* 2012;60:202–12.
- [4] Bonow RO, Carabello BA, Chatterjee K, de Leon Jr AC, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS. American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular heart disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2008;52:e1–42.
- [5] Lee AP, Acker M, Kubo SH, Bolling SF, Park SW, Bruce CJ, Oh JK. Mechanisms of recurrent functional mitral regurgitation after mitral valve repair in nonischemic dilated cardiomyopathy: importance of distal anterior leaflet tethering. *Circulation* 2009;119:2606–14.
- [6] McCarthy JF, McCarthy PM, Starling RC, Smedira NG, Scalia GM, Wong J, Kasirajan V, Goormastic M, Young JB. Partial left ventriculectomy and mitral valve repair for end-stage congestive heart failure. *Eur J Cardiothorac Surg* 1998;13:337–43.
- [7] Kron IL, Green GR, Cope JT. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation. *Ann Thorac Surg* 2002;74:600–1.
- [8] Menicanti L, Di Donato M, Frigiola A, Buckberg G, Santambrogio C, Ranucci M, Santo D, Group R. Ischemic mitral regurgitation: intraventricular papillary muscle imbrication without mitral ring during left ventricular restoration. *J Thorac Cardiovasc Surg* 2002;123:1041–50.
- [9] Hvass U, Tapia M, Baron F, Pouzet B, Shafy A. Papillary muscle sling: a new functional approach to mitral repair in patients with ischemic left ventricular dysfunction and functional mitral regurgitation. *Ann Thorac Surg* 2003;75:809–11.
- [10] Matsui Y, Fukada Y, Naito Y, Sasaki S. Integrated overlapping ventriculoplasty combined with papillary muscle plication for severely dilated heart failure. *J Thorac Cardiovasc Surg* 2004;127:1221–3.
- [11] Langer F, Schafers HJ. RING plus STRING: papillary muscle repositioning as an adjunctive repair technique for ischemic mitral regurgitation. *J Thorac Cardiovasc Surg* 2007;133:247–9.
- [12] Rama A, Prashker L, Barreda E, Gandjbakhch I. Papillary muscle approximation for functional ischemic mitral regurgitation. *Ann Thorac Surg* 2007;84:2130–1.
- [13] Komeda M, Shimamoto T. Cutting secondary chordae and placing dual taut stitches between the anterior mitral fibrous annulus and the heads of each papillary muscle to treat ischemic mitral regurgitation without deteriorating left ventricular function. *J Thorac Cardiovasc Surg* 2008;135:226–7.
- [14] Shingu Y, Yamada S, Ooka T, Tachibana T, Kubota S, Tsutsui H, Matsui Y. Papillary muscle suspension concomitant with approximation for functional mitral regurgitation. *Circ J* 2009;73:2061–7.
- [15] Yamaguchi A, Adachi K, Yuri K, Kimura N, Kimura C, Tamura A, Adachi H. Reduction of mitral valve leaflet tethering by procedures targeting the subvalvular apparatus in addition to mitral annuloplasty. *Circ J* 2013;77:1461–5.
- [16] Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW. 2009 focused update incorporated into the ACC/AHA 2005 Guidelines for the Diagnosis and Management of Heart Failure in Adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation* 2009;119:e391–479.
- [17] Takahama H, Takaki H, Sata Y, Sakane K, Ino Y, Noguchi T, Goto Y, Sugimachi M. Exercise-induced ST. Elevation in patients with non-ischemic dilated cardiomyopathy and narrow QRS complexes: novel predictor of long-term prognosis from exercise testing. *Circ J* 2013;77:1033–9.
- [18] Shingu Y, Matsui Y. Did we misunderstand how to calculate total stroke work in mitral regurgitation by echocardiography. *Circ J* 2012;76:1533–4.
- [19] Gorcsan 3rd J, Snow FR, Paulsen W, Nixon JV. Noninvasive estimation of left atrial pressure in patients with congestive heart failure and mitral regurgitation by Doppler echocardiography. *Am Heart J* 1991;121:858–63.
- [20] Lee WS, Huang WP, Yu WC, Chiou KR, Ding PY, Chen CH. Estimation of preload recruitable stroke work relationship by a single-beat technique in humans. *Am J Physiol Heart Circ Physiol* 2003;284:H744–50.
- [21] Kim KH, Kim YJ, Ohn JH, Yang J, Lee SE, Lee SW, Kim HK, Seo JW, Sohn DW. Long-term effects of sildenafil in a rat model of chronic mitral regurgitation: benefits of ventricular remodeling and exercise capacity. *Circulation* 2012;125:1390–401.
- [22] Suma H, Tanabe H, Uejima T, Suzuki S, Horii T, Isomura T. Selected ventriculoplasty for idiopathic dilated cardiomyopathy with advanced congestive heart failure: midterm results and risk analysis. *Eur J Cardiothorac Surg* 2007;32:912–6.
- [23] Chow BJ, Abunassar JG, Asch K, Dekemp R, Dasilva J, Mesana T, Beanlands RS, Ruddy TD. Effects of mitral valve surgery on myocardial energetics in patients with severe mitral regurgitation. *Circ Cardiovasc Imaging* 2010;3:308–13.