

Effects of Surgical Ventricular Reconstruction and Mitral Complex Reconstruction on Cardiac Oxidative Metabolism and Efficiency in Nonischemic and Ischemic Dilated Cardiomyopathy

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OBJECTIVES The aim of this study was to investigate the effects of surgical ventricular reconstruction (SVR) on cardiac efficiency as a surrogate marker for cardiac function and oxidative metabolism in patients with severe heart failure.

BACKGROUND Our new integrated overlapping left ventriculoplasty, modified SVR, combined with mitral complex reconstruction, reduce left ventricular (LV) volume associated with improvement of symptoms of heart failure.

METHODS Twelve consecutive patients with end-stage heart failure due to nonischemic dilated cardiomyopathy (DCM) (n = 6) and ischemic dilated cardiomyopathy (ICM) (n = 6) who underwent SVR were studied. Myocardial oxidative metabolism per gram of tissue was estimated by monoexponential clearance of ¹¹C-acetate positron emission tomography (K_{mono}). Forward stroke volume at the LV outflow tract was measured by echocardiography. Cardiac efficiency was estimated by the ratio of external work (stroke volume at the LV outflow tract index × systolic blood pressure × heart rate) to K_{mono} before and 1 month after SVR.

RESULTS After SVR, medians of New York Heart Association functional class significantly improved from 3 to 1.5 (p < 0.01) in both DCM and ICM patients. End-systolic and end-diastolic volume and LV mass significantly decreased in both groups. Stroke volume at the LV outflow tract increased from 43 ± 8 ml to 52 ± 11 ml (p = 0.028) in DCM patients, but not in ICM patients (49 ± 21 ml to 59 ± 26 ml, p = 0.12). K_{mono} × LV mass, as an index of global LV oxidative metabolism, decreased in DCM patients (13.6 ± 1.9 g/min vs. 8.6 ± 1.5 g/min, p = 0.03) and ICM patients (12.0 ± 3.4 g/min vs. 9.2 ± 1.0 g/min, p = 0.06). As a result, cardiac efficiency increased in all patients with DCM (3.34 ± 0.46 × 10E6 vs. 4.74 ± 0.88 × 10E6 mm Hg·ml·min/m², p = 0.03) and in 5 of 6 patients with ICM (4.54 ± 1.66 × 10E6 vs. 5.99 ± 2.11 × 10E6 mm Hg·ml·min/m², p = 0.12).

CONCLUSIONS Combined surgery with SVR and mitral complex reconstruction reduced LV volume in association with improvement of cardiac efficiency in patients with severe heart failure. (J Am Coll Cardiol Img 2011;4:762–70) © 2011 by the American College of Cardiology Foundation

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Recent advances in medical treatment including angiotensin-converting enzyme inhibitors and β -blockers as well as cardiac resynchronization therapy have been shown to be effective at improving the symptoms and prognosis in patients with severe heart failure (1-3). Despite these standard therapies, the mortality rate in these patients is still high. Heart transplantation is the most effective surgical treatment for patients with refractory heart failure. The

See page 771

shortage of the donor hearts has necessitated the development of alternatives such as surgical ventricular reconstruction (SVR). We developed overlapping left ventriculoplasty (OLVP), modified SVR without resection of left ventricular (LV) muscle, and mitral complex reconstruction (MCR), which have been shown to improve the symptoms in end-stage heart failure patients (4,5).

Noninvasive qualitative assessment of myocardial oxidative metabolism is possible by using ^{11}C -acetate as a metabolic tracer with positron emission tomography (PET). ^{11}C -Acetate is taken up by the myocardium, and the subsequent monoexponential clearance rate of ^{11}C -acetate from the myocardium (K_{mono}) correlates well with the myocardial oxygen demand (6). The work metabolic index (WMI), as assessed by external work per myocardial oxidative metabolism, has been used as an index of cardiac efficiency (7-9).

LV remodeling, the dilation of the LV cavity with a spherical shape, is commonly seen in patients with severe heart failure due to ischemic dilated cardiomyopathy (ICM) as well as nonischemic dilated cardiomyopathy (DCM) (10). In addition, concomitant mitral regurgitation reduces forward external work and further increases LV dilation due to volume overload (10). These hemodynamic features of a remodeled left ventricle produce increased wall stress associated with increased oxygen demand, low output, and low cardiac efficiency (8,9,11). Importantly, β -blockers, cardiac resynchronization therapy, and the correction of mitral regurgitation have been demonstrated to improve cardiac efficiency assessed by using PET (7,11).

Our surgery integrated with SVR and MCR can reduce LV volume and correct LV shape, which can reduce LV wall stress. However, the effects of our surgery on cardiac oxidative metabolism and efficiency have not been elucidated. Furthermore, the difference in its effects on the etiologies of heart

failure is unknown. We thus determined whether SVR could improve cardiac efficiency in patients with severe heart failure due to ICM and DCM by using PET and ^{11}C -acetate.

METHODS

We studied 12 consecutive patients (age 59 ± 10 years) at the Department of Cardiovascular Surgery, Hokkaido University Hospital, Sapporo, Japan. The study patients had heart failure symptoms with New York Heart Association (NYHA) functional class III or IV and an LV ejection fraction (LVEF) $\leq 40\%$. The causes of heart failure were DCM in 6 patients and ICM in 6 patients. Patients under continuous infusion of positive inotropes and who had an LV aneurysm due to previous myocardial infarction were excluded. Patients who had significant coronary artery stenosis ($>50\%$) as assessed by invasive coronary angiography had a diagnosis of ICM, and patients who had no known coronary artery stenosis or recognized etiology by myocardial biopsy received a diagnosis of DCM. The study was approved by the institutional ethics board of the Hokkaido University Graduate School of Medicine. Written informed consent was obtained from each patient. Each patient received the standard medical treatment for severe heart failure (Table 1). Three patients had diabetes mellitus and were effectively treated with sulfonylurea ($n = 2$) and acarbose ($n = 1$). β -blockers were discontinued to avoid the worsening of heart failure during the perioperative period (for 1 month), as previously described (12). Other medical therapy except β -blockers was adjusted by physicians according to the patients' volume status and blood pressure.

Operative procedure. OLVP is an SVR that we previously developed (Fig. 1A). In patients undergoing OLVP, the left ventricle was incised from the apex basally to the diagonal artery along the left anterior descending artery at a distance of 1 or 2 cm. The lateral margin was then folded and sutured to the interventricular septum with interrupted mattress and continuous sutures using felt strips. The suture line was determined using intraventricular sizers. After suturing the lateral margin, the septal margin was then sutured onto the lateral wall over the previous suture line in ICM

ABBREVIATIONS AND ACRONYMS

DCM = nonischemic dilated cardiomyopathy

ICM = ischemic dilated cardiomyopathy

K_{mono} = monoexponential clearance rate of ^{11}C -acetate from the myocardium

LV = left ventricular

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVM = left ventricular mass

LVESV = left ventricular end-systolic volume

MCR = mitral complex reconstruction

NYHA = New York Heart Association

OLVP = overlapping left ventriculoplasty

PET = positron emission tomography

SV_{LVOT} = stroke volume at left ventricular outflow tract

SVR = surgical ventricular reconstruction

WMI = work metabolic index

Table 1. Patient Characteristics and Surgical Procedures

Patient #	Age (yrs)	Sex	Diagnosis	Procedure	Medications at Baseline
1	55	M	DCM, MR, Af	OLVP, MAP, RF maze	Diuretic, spironolactone, amiodarone
2	64	M	DCM, MR, AR, TR, p/o CRT	OLVP, MAP, PMA, TAP, AVR	β -blocker, ARB, diuretic, spironolactone
3	60	F	DCM, MR, TR, Af	OLVP, MCR, TAP, RF maze	ARB, diuretics, spironolactone
4	69	M	DCM, MR, TR, pAf	OLVP, MCR, TAP, pulmonary vein isolation	β -blocker, ARB, diuretics, amiodarone, sulfonyleurea
5	77	M	DCM, MR, TR	Linear closure, MCR, TAP	β -blocker, ARB, diuretics, sulfonyleurea
6	37	M	DCM, MR, pAf	OLVP, MCR	β -blocker, ARB, diuretics, spironolactone
7	50	M	ICM, MR, TR, p/o CRT	OLVP, CABG, MCR, TAP	β -blocker, spironolactone
8	55	M	ICM, MR, TR	OLVP, CABG, MCR, TAP	β -blocker, ARB, diuretic, spironolactone
9	62	M	ICM, MR, TR, Af	OLVP, CABG, MCR, TAP, RF maze	β -blocker, diuretic
10	60	M	ICM, MR, TR	Linear closure, CABG, MCR, TAP	β -blocker, ARB, diuretic, spironolactone
11	63	M	ICM, MR, TR	OLVP, MCR, TAP	ARB, diuretic, acarbose
12	52	M	ICM, p/o CRT	OLVP, CABG, PMA	β -blocker, ARB, diuretics

Af = chronic atrial fibrillation; AR = aortic regurgitation; ARB = angiotensin receptor blocker (includes renin-angiotensin blocker and angiotensin-converting enzyme inhibitor); AVR = aortic valve replacement; CABG = coronary artery bypass grafting; CRT = cardiac resynchronization therapy; DCM = nonischemic dilated cardiomyopathy; F = female; ICM = ischemic cardiomyopathy; MAP = mitral valve annuloplasty; M = male; MCR = mitral complex reconstruction; MR = mitral regurgitation; OLVP = overlapping left ventriculoplasty; pAf = paroxysmal atrial fibrillation; PMA = papillary muscle approximation; p/o = post-operation; RF maze = radiofrequency maze; SVR = surgical ventricular reconstruction; TAP = tricuspid valve annuloplasty; TR = tricuspid regurgitation.

patients or over the free LV wall in DCM patients, resulting in the overlap of myocardial walls in the anteroseptal lesion. This procedure has advantages such as preserving cardiac muscle and the circumflex coronary artery without resection of the left ventricle compared with traditional SVR. More importantly, this technique can alter the dilated spherical left ventricle to the appropriate elliptical shape (4,5,12).

MCR is mitral annuloplasty that includes papillary muscle approximation and papillary muscle suspension, which is effective in treating mitral regurgitation caused by tethering of mitral leaflets (Fig. 1B). Papillary muscle approximation has been already proven to be an effective procedure to reduce the tethering of the mitral leaflets and to suspend the tips of papillary muscles from mitral annulus, helping to prevent future deterioration of tethering (4,5,12).

Measurement of oxidative metabolism by ^{11}C -acetate PET and echocardiographic studies were performed in all patients before and 1 month after surgery. All patients underwent ^{11}C -acetate PET scan and echocardiography within a week of each other.

Myocardial oxidative metabolism by ^{11}C -acetate PET. PET was performed using a whole-body scanner (ECAT/EXACT HR+, Siemens/CTI, Knoxville, Tennessee). A total of 740 MBq of ^{11}C -acetate was administered intravenously for 60 s under resting conditions, and dynamic PET was performed (10×10 s, 1×60 s, 5×100 s, 3×180 s, 2×300 s). PET data analysis was performed using dedicated software (9). The images were iteratively reconstructed and resliced along the short axis. Blood

pressure and heart rate were monitored during PET to calculate a rate-pressure product.

To compute a semiquantitative summed rest perfusion score of ^{11}C -acetate perfusion imaging in the early phase (5 min), a standard 17-segment, 5-point scoring system (0 = normal uptake, 1 = mild defect, 2 = moderate defect, 3 = severe defect, and 4 = absent tracer uptake) was used.

Cardiac oxidative metabolism per gram of tissue was determined from the monoexponential clearance rate of ^{11}C -acetate (K_{mono}), as previously described (9). To calculate the LV mass (LVM), the volume within the region of interest was computed by using dedicated software.

Echocardiography. Echocardiographic examination was performed by an experienced cardiologist or sonographers, and 2 experienced cardiologists reviewed their findings without knowledge of the PET data. Left ventricular end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF were measured from apical 2-chamber and 4-chamber views using the biplane disk-summation method according to American Society of Echocardiography Committee recommendations. Forward stroke volume was measured with pulsed-wave Doppler imaging on the LV outflow tract (SV_{LVOT}). Mitral regurgitation was graded by using color flow Doppler imaging according to American Heart Association/American College of Cardiology guidelines (13).

Global oxidative metabolism and WMI. Global cardiac oxidative metabolism was calculated by multiplying K_{mono} by the LVM. External work per minute was calculated by the following equation: SV_{LVOT} index \times systolic blood pressure \times heart rate at resting condition. The WMI was calcu-

lated as an index of cardiac efficiency by dividing external work per minute by K_{mono} , as previously described (7,8).

Statistical analysis. All measurements were expressed as mean \pm SD. Baseline characteristic data were compared by an unpaired *t* test between DCM and ICM patients. Baseline and follow-up data were compared by Wilcoxon single-rank tests. A *p* value <0.05 was considered a statistically significant difference.

RESULTS

Baseline characteristics. There were no operative deaths. All patients underwent SVR (OLVP in 10 patients and linear closure in 2 patients) (Table 1). As concomitant procedures, MCR was performed in 9 patients and mitral valve annuloplasty in 2 patients, maze procedures for chronic atrial fibrillation in 3 patients, pulmonary vein isolation for paroxysmal atrial fibrillation in 1 patient, tricuspid valve annuloplasty for tricuspid regurgitation in 9 patients, and coronary artery bypass grafting for coronary artery disease in 5 of 6 ICM patients.

Table 2 shows the baseline characteristics of the study patients. Before surgery, 10 patients were classified as NYHA functional class III and 2 patients as functional class IV. Marked LV dilation and severe mitral regurgitation were observed in 11 of 12 patients. The average LVEF was 25% and the average SV_{LVOT} was 46 ml.

Table 3 shows the baseline characteristics of subgroups of patients according to DCM and ICM. When the baseline characteristics were compared between groups, heart rate ($p = 0.029$) and rate-pressure product ($p < 0.001$) were significantly lower in DCM patients than in ICM patients. LVEDV, LVESV, LVEF, and SV_{LVOT} did not differ between groups. The degree of mitral regurgitation tended to be greater in patients with DCM than in those with ICM ($p = 0.076$).

On ^{11}C -acetate PET data analysis, the summed rest perfusion score was 10.3 ± 6.7 in all patients, and there was no significant difference between DCM patients and ICM patients (7.0 ± 4.2 vs. 13.7 ± 7.4 , $p = 0.09$). The LVM did not differ between DCM patients and ICM patients (300 ± 41 vs. 248 ± 58 g, $p = 0.11$). K_{mono} and $K_{\text{mono}} \times \text{LVM}$ were comparable between patients with DCM and ICM (K_{mono} : 0.045 ± 0.003 vs. 0.048 ± 0.007 /min, $p = 0.37$; $K_{\text{mono}} \times \text{LVM}$: 13.6 ± 1.9 vs. 12.0 ± 3.4 g/min, $p = 0.37$). The WMI tended to be lower in DCM patients than in ICM patients

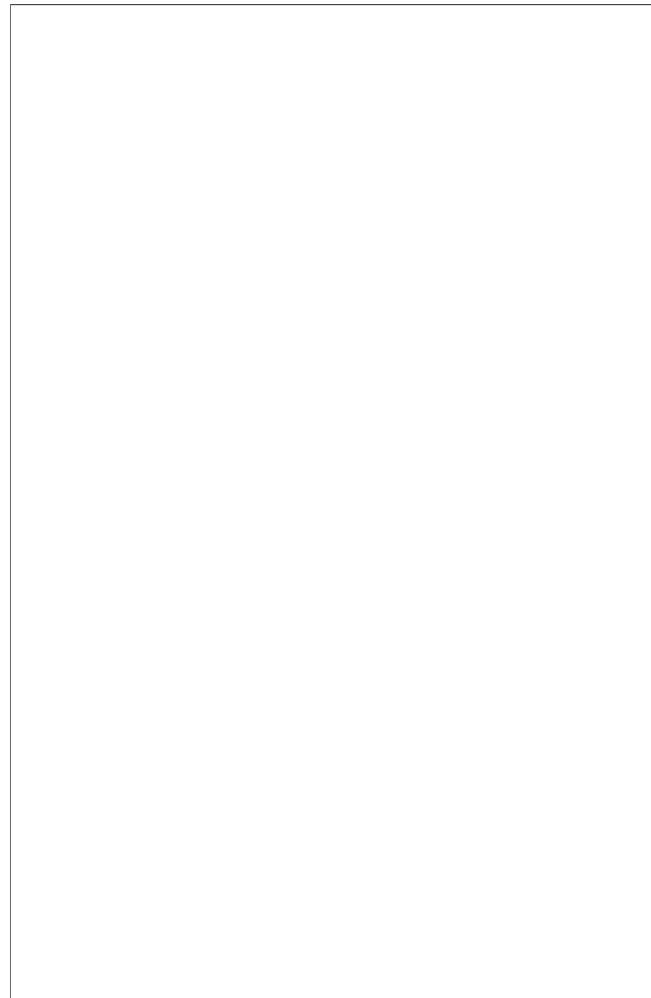


Figure 1. Scheme of Surgery

Procedure of overlapping left ventricular reconstruction (A) and mitral complex reconstruction (B). In addition to mitral annuloplasty and papillary muscle approximation (red arrow, upper middle image), papillary muscle suspension (red arrow, upper right image) is performed.

($3.34 \pm 0.46 \times 10^6$ vs. $4.54 \pm 1.66 \times 10^6$ mm Hg·ml/m², $p = 0.14$), which, however, did not reach statistical significance.

Effects of SVR on cardiac function and efficiency. After surgery, NYHA functional class was significantly improved in the study patients. Systolic blood pressure significantly decreased and heart rate significantly increased (Table 2). The rate-pressure product tended to be increased, which, however, did not reach statistical significance. LVEDV and LVESV significantly decreased in relation to the increase in SV_{LVOT} . Mitral regurgitation was decreased to minimal. Pulmonary artery systolic pressure significantly decreased. LVM significantly decreased from 274 ± 55 g to 191 ± 32 g ($p < 0.001$). K_{mono} did not change, whereas $K_{\text{mono}} \times \text{LVM}$

Table 2. Patient Characteristics Before and 1 Month After Integrated SVR in All Patients

Variables	All Patients (N = 12)		
	Before	After	p Value
NYHA functional class, median	3	1.5	<0.01
Hemodynamics			
Systolic BP (mm Hg)	102 ± 16	93 ± 9	0.011
Diastolic BP (mm Hg)	58 ± 12	59 ± 11	0.91
Heart rate, beats/min	69 ± 12	83 ± 18	<0.01
RPP, mm Hg × min ⁻¹	6,987 ± 1,416	7,635 ± 1,584	0.084
Echocardiographic findings			
LVEDV, ml	241 ± 76	150 ± 38	<0.01
LVESV, ml	174 ± 52	106 ± 35	<0.01
LVEF, %	25 ± 7	30 ± 6	0.20
Forward SV, ml	46 ± 15	56 ± 19	0.019
Mitral regurgitation	3.5 ± 0.9	0.6 ± 0.5	<0.01
Tricuspid regurgitation	1.8 ± 0.8	0.9 ± 0.9	0.021
PASP*	52 ± 15	41 ± 12	0.028

Values are mean ± SD or median. *PASP data were available in all nonischemic dilated cardiomyopathy patients and in 4 of 6 ischemic dilated cardiomyopathy patients.
BP = blood pressure; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RPP = rate-pressure product; SV = stroke volume; SVR = surgical ventricular reconstruction.

significantly decreased ($p = 0.001$) and the WMI significantly increased ($p = 0.015$) after SVR (Fig. 2).

When the effects of surgery were compared between groups, systolic blood pressure significantly decreased in ICM patients, but not in DCM patients (Table 3). Heart rate was significantly

increased in both groups. The rate-pressure product did not change in either group. LVESV and LVEDV by echocardiography significantly decreased in both groups. LVEF did not change in either group. SV_{LVOT} significantly increased in DCM patients, but not in ICM patients (Table 3). LVM was significantly decreased in both DCM patients (to 191 ± 27 g, $p = 0.001$) and ICM patients (to 190 ± 40 g, $p = 0.003$). K_{mono} did not change in either group, whereas $K_{mono} \times LVM$ was significantly decreased in patients with DCM ($p = 0.03$) and tended to be decreased in patients with ICM ($p = 0.06$). The WMI increased in all DCM patients and in 5 of 6 ICM patients (Fig. 2). Figure 3 shows a representative case.

DISCUSSION

The present study demonstrated that our new surgery integrating OLVP and MCR reduced LV volume and corrected the mitral regurgitation in end-stage heart failure patients with DCM and ICM. These surgical procedures may successfully aid in increasing the cardiac efficiency associated with the increase in forward external work and the reduction of global myocardial oxidative metabolism.

Effects of SVR and MCR on cardiac oxidative metabolism and efficiency. OLVP is a modified SVR technique without endoventricular patching and resection of viable myocardium. MCR with papillary muscle approximation and suspension is the most appropriate procedure for correcting tethered mitral valve

Table 3. Patient Characteristics Before and 1 Month After Integrated SVR in Patients With DCM and ICM

Variables	DCM (n = 6)			ICM (n = 6)		
	Before	After	p Value	Before	After	p Value
NYHA functional class, median	3	1.5	0.024	3	1.5	0.023
Hemodynamics						
Systolic BP, mm Hg	95 ± 9	91 ± 7	0.25	109 ± 18	95 ± 10	0.028
Diastolic BP, mm Hg	52 ± 11	55 ± 9	0.60	65 ± 8	63 ± 12	0.75
Heart rate, beats/min	62 ± 8	73 ± 13	0.043	76 ± 11	93 ± 17	0.027
RPP, mm Hg × min ⁻¹	5,853 ± 817	6,581 ± 1,231	0.17	8,120 ± 812	8,688 ± 1,158	0.35
Echocardiographic findings						
LVEDV, ml	263 ± 79	168 ± 43	0.028	219 ± 74	131 ± 24	0.028
LVESV, ml	189 ± 51	125 ± 40	0.027	159 ± 53	87 ± 17	0.028
LVEF, %	24 ± 7	26 ± 5	0.92	27 ± 8	34 ± 3	0.17
Forward SV, ml	43 ± 8	52 ± 11	0.028	49 ± 21	59 ± 26	0.12
Mitral regurgitation	4.0 ± 0.0	0.8 ± 0.4	0.020	3.0 ± 1.1	0.3 ± 0.5	0.026
Tricuspid regurgitation	1.8 ± 1.0	1.3 ± 1.0	0.28	1.8 ± 0.8	0.5 ± 0.5	0.038
PASP*	50 ± 17	40 ± 16	0.17	55 ± 12	43 ± 4	0.066

Values are mean ± SD or median. *PASP data were available in all DCM patients and in 4 of 6 ICM patients. Abbreviations as in Table 2.

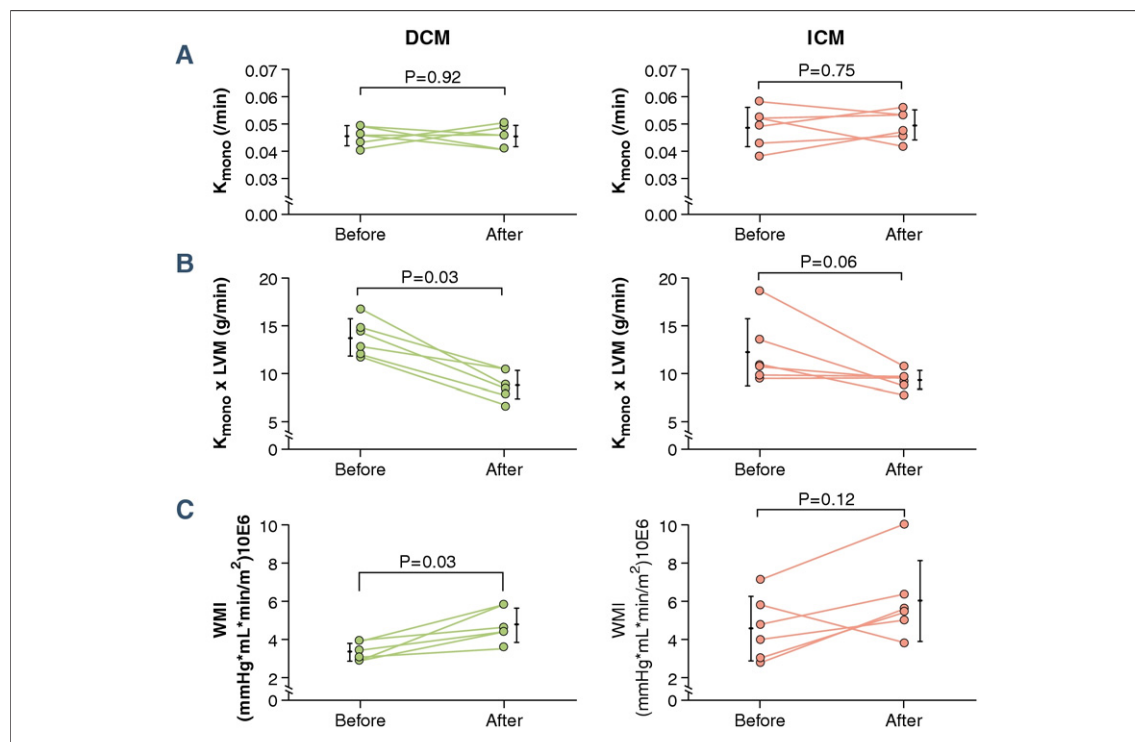


Figure 2. K_{mono} , $K_{\text{mono}} \times \text{LVM}$, and Work Metabolic Index Before and After Surgery

Monoexponential clearance rate of ^{11}C -acetate from the myocardium (K_{mono}), $K_{\text{mono}} \times$ left ventricular mass (LVM), and work metabolic index (WMI) before and after surgery. Effects of the surgery on K_{mono} (A), $K_{\text{mono}} \times \text{LVM}$ (B), and WMI (C) in patients with dilated cardiomyopathy (DCM) ($n = 6$, red circles) and ICM ($n = 6$, green circles). After surgery, K_{mono} did not change in either group, whereas $K_{\text{mono}} \times \text{LVM}$ was significantly decreased in patients with DCM and tended to be decreased in patients with ICM. The WMI increased in all patients with DCM and in 5 of 6 patients with ICM.

and maintaining the elliptical LV shape (4,5,12). We previously demonstrated that OLVP and MCR improved NYHA functional class, and the 1- and 3-year actuarial survival rates were 91% and 87%, respectively. The beneficial effects of OLVP and MCR on cardiac efficiency may contribute to a better outcome.

In the present study, the beneficial effects of SVR on the hemodynamics and echocardiographic findings were demonstrated. SV_{LVOT} increased only in DCM patients, which might be due to the greater degree of mitral regurgitation in DCM than ICM because the correction of mitral regurgitation by MCR can reduce volume overload in these patients.

Cardiac oxidative metabolism and efficiency have been used as a surrogate marker of cardiac dysfunction and failure (8). Dilated LV is associated with a greater wall stress and oxygen demand. Furthermore, the spherical LV shape is not effective for increasing cardiac output. In fact, as previously described (8), the WMI was decreased in dilated cardiomyopathy. In the present study, the observed

WMI before surgery was extremely low ($3.94 \pm 1.32 \times 10^6 \text{ mm Hg} \cdot \text{mL} \cdot \text{min} / \text{m}^2$) compared with that of a previous study ($5.31 \pm 2.15 \times 10^6 \text{ mm Hg} \cdot \text{mL} \cdot \text{min} / \text{m}^2$) in patients with LV dysfunction (LVEF = 31%) by Beanlands et al. (7), suggesting that our study population had more severe heart failure associated with poor cardiac efficiency.

Although oxidative metabolism was impaired in dysfunctional LV with myocardial infarction and remodeled LV associated with mitochondrial dysfunction (8,9), LV oxidative metabolism did not differ between ICM and DCM patients in the present study. The reason for the relative preservation of oxidative metabolism in ICM compared with DCM may be due to the comparable scar area in DCM and ICM because the patients with an LV aneurysm were excluded from our study and the semiquantitative myocardial perfusion score did not differ between groups. After SVR, K_{mono} did not change, suggesting that the anatomic changes in LV volume and shape after SVR and MCR maintain the functional state of myocardial oxidative metabolism per gram of tissue. This result is in

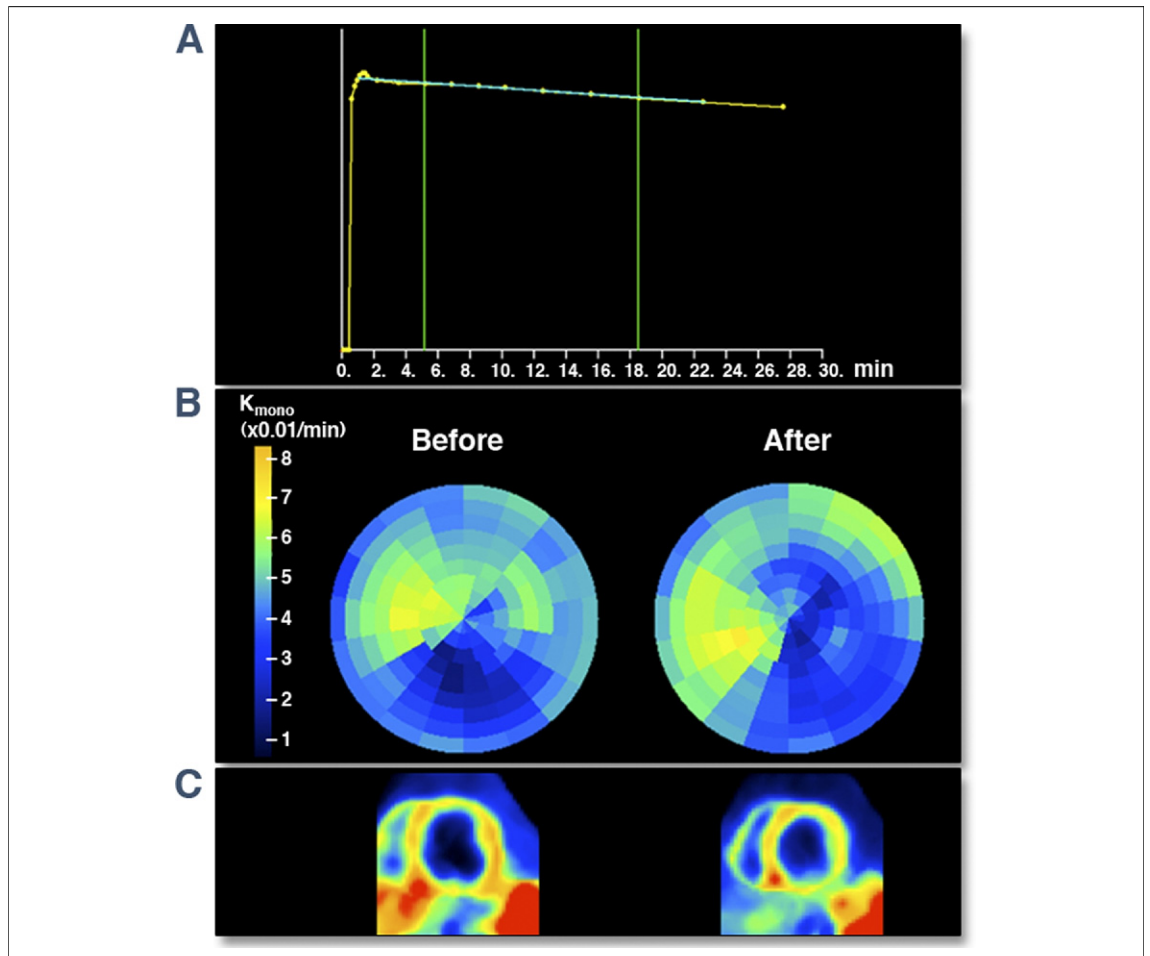


Figure 3. Representative Patient Who Underwent Surgery

A representative case (Patient #2 in Table 2). Monoexponential clearance rate of ^{11}C -acetate for the myocardium (K_{mono}) (A). Polar map of K_{mono} before and after surgery (B) and ^{11}C -acetate imaging (early phase) of short-axis view in the midlevel before and after surgery (C). K_{mono} value did not change, whereas left ventricular size decreased after surgery.

accord with a previous study that found that correction of mitral regurgitation did not change K_{mono} (11).

Previous studies demonstrated that advanced medical therapies could improve hemodynamics, systolic function, myocardial oxidative metabolism, and their integrated index, cardiac efficiency, in patients with heart failure (7,8,11). However, information about the effects of SVR on cardiac efficiency has been limited. The STICH (Surgical Treatment for Ischemic Heart Failure) trial demonstrated that SVR did not improve the prognosis in addition to coronary artery bypass grafting in patients with systolic dysfunction with an LVEF $\leq 35\%$ (14), indicating that SVR could not improve cardiac efficiency. However, it included only ICM patients who needed coronary artery bypass grafting and only 14% patients had moderate to severe

mitral regurgitation, whereas 11 of 12 patients (92%) in the present study had moderate to severe mitral regurgitation. In addition, their LVESV index was 82 ml, whereas it was 104 ml in our patients, suggesting that SVR might be more effective in patients with advanced LV remodeling and severe mitral regurgitation.

We included various procedures in addition to SVR and MCR, such as tricuspid valve annuloplasty, the maze procedure, and coronary artery bypass grafting. In particular, coronary artery bypass grafting may potentially affect cardiac oxidative metabolism in patients with ICM. However, their oxidative metabolism did not change after coronary artery bypass grafting in the present study, which has extended the previous findings that myocardial oxidative metabolism at rest is preserved in ischemic but viable myocardium (15). In addition, the effects

of tricuspid valve annuloplasty on the heart are unknown because we did not measure K_{mono} in right ventricular wall. However, this procedure may be less likely to affect oxidative metabolism in the LV wall.

Clinical implications. Low cardiac efficiency estimated by the WMI might be expected to closely relate with the progression of LV remodeling leading to cardiac death. Consequently, a decrease in wall stress associated with the improvement of cardiac efficiency may help to prevent the progression of LV remodeling over time, which, however, needs to be investigated in the larger population in the future.

SVR and MCR improved the WMI in all 6 patients with DCM and 5 of 6 patients with ICM, indicating that our new combined procedure can be used for both ischemic and nonischemic etiologies. One patient had mild LV dilation (LVEDV, 151 ml and LVESV, 113 ml) associated with a relatively preserved WMI (5.76×10^6 mm Hg·ml·min/m²), which was higher by 46% than the average value. This patient's WMI decreased to 3.76×10^6 mm Hg·ml/m² with an LVEDV of 102 ml and an LVESV of 71 ml after surgery, suggesting that patients with a preserved WMI and mild LV dilation may not be good candidates for our procedure. The optimal timing for our procedure and responders warrants investigation in a larger population.

Study limitations. There are several limitations to this study. First, the sample size of this study was small, but beneficial therapeutic effects of SVR on the WMI were demonstrated and statistically proved to be significant. Second, noninvasive assessment of external work estimated by the SV_{LVOT} could be underestimated in proportion to the magnitude of mitral regurgitating volume. Although we did not measure the mitral regurgitant WMI, the previous study demonstrated that regurgitant work was $0.705 \pm 0.176 \cdot 10E6$ (12% of the total WMI) in

patients with mitral regurgitation (34 ± 19 ml), indicating that the effects of mitral repair on the total WMI might be minimal even when the regurgitant WMI was considered in the present study. However, the WMI computed by the SV_{LVOT} and K_{mono} would be useful, especially in clinical practice. However, the WMI in DCM was likely underestimated compared with that in ICM because mitral regurgitation in DCM was more severe than that in ICM. The effect of mitral regurgitation on the WMI in severe heart failure needs to be investigated in a large population. Third, cardiac function and oxidative metabolism were examined at 1 month after surgery in the present study. Long-term results may be required to determine the changes in cardiac oxidative metabolism and efficiency more clearly. Fourth, β -blockers were discontinued during this study because administration of β -blockers often worsens heart failure in the perioperative period. This change in medication may complicate the effects of SVR on cardiac efficiency. However, the rate-pressure product did not change after SVR, suggesting that the effects of the discontinuing of β -blockers on myocardial oxidative metabolism might be small.

CONCLUSIONS

LV volume reduction and correction of mitral regurgitation by integrated surgery with SVR and MCR significantly improved cardiac efficiency in patients with end-stage heart failure, which was observed in both nonischemic and ischemic etiologies.

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REFERENCES

1. Krum H, Roecker EB, Mohacs P, et al. Effects of initiating carvedilol in patients with severe chronic heart failure: results from the COPERNICUS Study. *JAMA* 2003;289:712-8.
2. Young JB, Abraham WT, Smith AL, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. *JAMA* 2003;289:2685-94.
3. The CONSENSUS Trial Study Group. Effects of enalapril on mortality in severe congestive heart failure. Results of the Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS). *N Engl J Med* 1987; 316:1429-35.
4. 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.
5. Matsui Y, Suto Y, Shimura S, et al. Impact of papillary muscles approximation on the adequacy of mitral coaptation in functional mitral regurgitation due to dilated cardiomyopathy. *Ann Thorac Cardiovasc Surg* 2005;11:164-71.
6. Brown M, Marshall DR, Sobel BE, Bergmann SR. Delineation of myocardial oxygen utilization with carbon-11-labeled acetate. *Circulation* 1987; 76:687-96.
7. Beanlands RS, Nahmias C, Gordon E, et al. The effects of beta(1)-blockade on oxidative metabolism and the metabolic cost of ventricular work in patients with left ventricular dysfunction: a double-blind, placebo-controlled, positron-emission tomography study. *Circulation* 2000;102:2070-5.

8. Bengel FM, Permanetter B, Ungerer M, Nekolla S, Schwaiger M. Non-invasive estimation of myocardial efficiency using positron emission tomography and carbon-11 acetate—comparison between the normal and failing human heart. *Eur J Nucl Med* 2000;27:319–26.
9. Wu YW, Naya M, Tsukamoto T, et al. Heterogeneous reduction of myocardial oxidative metabolism in patients with ischemic and dilated cardiomyopathy using C-11 acetate PET. *Circ J* 2008;72:786–92.
10. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling—concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an International Forum on Cardiac Remodeling. *J Am Coll Cardiol* 2000;35:569–82.
11. Chow BJ, Abunassar JG, Ascah K, et al. Effects of mitral valve surgery on myocardial energetics in patients with severe mitral regurgitation. *Circ Cardiovasc Imaging* 2010;3:308–13.
12. Shingu Y, Yamada S, Ooka T, et al. Papillary muscle suspension concomitant with approximation for functional mitral regurgitation. *Circ J* 2009;73:2061–7.
13. Cheitlin MD, Alpert JS, Armstrong WF, et al. ACC/AHA Guidelines for the Clinical Application of Echocardiography. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Application of Echocardiography). Developed in collaboration with the American Society of Echocardiography. *Circulation* 1997;95:1686–744.
14. Jones RH, Velazquez EJ, Michler RE, et al. Coronary bypass surgery with or without surgical ventricular reconstruction. *N Engl J Med* 2009;360:1705–17.
15. Yoshinaga K, Katoh C, Beanlands RS, et al. Reduced oxidative metabolic response in dysfunctional myocardium with preserved glucose metabolism but with impaired contractile reserve. *J Nucl Med* 2004;45:1885–91.

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