Mitral Valve Repair for Medically Refractory Functional Mitral Regurgitation in Patients With End-Stage Renal Disease and Advanced Heart Failure

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Background—Information regarding patient selection for mitral valve repair for chronic kidney disease or end-stage renal disease (ESRD) with severe heart failure (HF) as well as outcome is limited.

Methods and Results—We classified 208 patients with advanced HF symptoms (Stage C/D) undergoing mitral valve repair for functional mitral regurgitation into 3 groups: estimated glomerular filtration rate ≥30 mL/min/1.73 m² (control group, n=144); estimated glomerular filtration rate <30 mL/min/1.73 m², not dependent on hemodialysis (late chronic kidney disease group, n=45), and ESRD on hemodialysis (ESRD group, n=19; preoperative hemodialysis duration 83±92 months). Follow-up was completed with a mean duration of 49±25 months. Postoperative (1-month) cardiac catheterization showed that left ventricular end-systolic volume index decreased from 109±38 to 79±41, 103±31 to 81±31, and 123±40 to 76±34 mL/m², in the control, late chronic kidney disease, and ESRD groups, respectively. Left ventricular end-diastolic pressure decreased, whereas cardiac index increased in all groups with no intergroup differences for those postoperative values. Freedom from mortality and HF readmission at 5 years was 18%±7% in late chronic kidney disease (P<0.0001 versus control, P=0.01 versus ESRD), and 64%±12% in ESRD (P=1 versus control) as compared with 52%±5% in the control group (median event-free survival, 26, 67, and 63 months, respectively).

Conclusions—Mitral valve repair for medically refractory functional mitral regurgitation in patients with advanced HF yielded improvements in left ventricular function and hemodynamics irrespective of preoperative renal function status. Patients with ESRD showed favorable late outcome in terms of freedom from mortality and readmission for HF as compared with those with late chronic kidney disease. Further studies are needed to assess the survival benefits of mitral valve repair in patients with ESRD and advanced HF. (Circulation. 2012;126[suppl 1]:S205–S213.)

Key Words: cardiomyopathy ▪ chronic kidney disease ▪ end-stage renal disease ▪ functional mitral regurgitation ▪ mitral valve repair

Heart failure and end-stage renal failure (ESRD) requiring dialysis are major health problems in Japan, as in the United States. Heart failure and chronic kidney disease (CKD) share a number of major risk factors, including hypertension and diabetes mellitus, and a substantial proportion of patients with advanced heart failure have impaired renal function.1 Heart failure is the leading cause of mortality in patients with CKD or ESRD, whereas impaired renal function is strongly associated with poor outcomes in patients with chronic heart failure.2 Moreover, kidney dysfunction per se is a risk factor for developing left ventricular (LV) remodeling and heart failure.3,4

Ischemic or nonischemic dilated cardiomyopathy is frequently complicated by functional mitral regurgitation (MR) as a consequence of LV remodeling progression. Medically refractory severe functional MR has a strong negative impact on survival of patients with CKD or ESRD and advanced heart failure. An increasing number of patients with ESRD has led to increased referrals of patients on dialysis for surgical repair of functional MR and other concomitant procedures.5
The EuroSCORE II calculator (www.euroscore.org/calc.html) shows that impaired renal function (ie, creatinine clearance <50 mL/min) off dialysis is a major risk factor for postoperative mortality in patients undergoing cardiovascular surgery, and patients with ESRD on dialysis are sometimes considered to be a relative contraindication to surgical intervention for medically refractory functional MR because other risk factors are commonly associated with this condition. Thus, surgical indication and patient selection for repair of functional MR in patients with CKD or ESRD are controversial, and risk stratification is not supported by the online STS Risk Calculator (http://209.220.160.181/STSWebRiskCalc261/de.aspx). Furthermore, long-term outcomes of patients with CKD or ESRD after surgery have not been sufficiently reported.6

We investigated the outcomes of patients with ESRD and advanced heart failure who underwent a restrictive mitral annuloplasty and other concomitant procedures for medically refractory severe functional MR.

**Patients and Methods**

Between August 1999 and July 2010, 226 consecutive patients with advanced cardiomyopathy were referred for surgical treatment of medically refractory severe or moderate-to-severe (regurgitant volume >30 mL/beat) functional MR and concomitant surgical procedures. Patients who underwent an emergency operation or with recent myocardial infarction (<3 months) were excluded; thus, 208 (166 men, 42 women; 65±10 years old) were analyzed in this retrospective study. Functional MR was caused by restrictive leaflet motion secondary to global severe LV dilatation (Type IIIb MR, Carpenter’s classification) in all. Patients with organic MR, rheumatic mitral disease, or aortic valve disease were excluded. All had advanced (Stage C/D) heart failure symptoms and severe LV remodeling (ejection fraction [EF] <40%, end-systolic volume index >60 mL/m²).

Our institutional ethical committees approved this study and written informed consent for the procedures was obtained from each patient before surgery.

**Patient Stratification Based on Preoperative Renal Function**

Estimated glomerular filtration rate was calculated by the Modification of Diet in Renal Disease equation.7 Eight patients had an estimated glomerular filtration rate of ≥90 mL/min/1.73 m² (CKD Stage 1), 136 an estimated glomerular filtration rate of 60 to 89 or 30 to 59 mL/min/1.73 m² (CKD Stage 2 or 3), and 45 an estimated glomerular filtration rate of 15 to 29 or <15 mL/min/1.73 m² (CKD Stage 4 or 5: late CKD group). Nineteen patients had ESRD on hemodialysis (ESRD group), whereas 144 with CKD Stage 1 to 3 served as the control group.

Hemodialysis was introduced due to progression of diabetic nephropathy in 11, glomerular nephritis in 3, glomerular sclerosis in one, and unknown in 2 patients. Maintenance dialysis had been given for an average of 83±92 months (range, 3–300 months) before surgery. Patient characteristics for the 3 groups are presented in Table 1.

**Echocardiography**

Two-dimensional and Doppler transthoracic echocardiography examinations were performed before and 1 month after surgery, and annually thereafter. Measurements included LV end-diastolic dimension, LV end-systolic dimension, and LVEF. Systolic pulmonary artery pressure (PAP) was calculated by adding the value for right ventricular systolic pressure, derived from tricuspid regurgitation, to estimated right atrial pressure.8,9 The inferior vena cava (IVC) dimension was measured through a subcostal approach. It was previously reported that IVC dimension is an accurate predictor of continuous variables and is associated with clinical outcome.10

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=144)</th>
<th>Late CKD (n=45)</th>
<th>ESRD on HD (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y*</td>
<td>64±10</td>
<td>68±9</td>
<td>64±6</td>
</tr>
<tr>
<td>Males</td>
<td>119 (83%)</td>
<td>33 (73%)</td>
<td>14 (74%)</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.65±0.18</td>
<td>1.62±0.17</td>
<td>1.57±0.16</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>II</td>
<td>13 (9%)</td>
<td>4 (9%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>III</td>
<td>112 (78%)</td>
<td>32 (71%)</td>
<td>15 (79%)</td>
</tr>
<tr>
<td>IV</td>
<td>19 (13%)</td>
<td>9 (20%)</td>
<td>3 (16%)</td>
</tr>
<tr>
<td>Etiologies of cardiomyopathy*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>103 (72%)</td>
<td>34 (76%)</td>
<td>15 (79%)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>41 (28%)</td>
<td>11 (24%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Uremic cardiomyopathy</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>Duration of preoperative HD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>83±92</td>
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</tbody>
</table>

**Comorbidity**

Hypertension

<table>
<thead>
<tr>
<th></th>
<th>79 (55%)</th>
<th>28 (62%)</th>
<th>8 (42%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperlipidemia</td>
<td>58 (40%)</td>
<td>18 (40%)</td>
<td>4 (21%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>61 (42%)</td>
<td>24 (53%)</td>
<td>11 (58%)</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>11 (8%)</td>
<td>3 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>12 (8%)</td>
<td>5 (11%)</td>
<td>3 (16%)</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>21 (15%)</td>
<td>8 (18%)</td>
<td>4 (21%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>45 (31%)</td>
<td>12 (27%)</td>
<td>6 (32%)</td>
</tr>
<tr>
<td>History of ventricular arrhythmia</td>
<td>26 (18%)</td>
<td>11 (24%)</td>
<td>3 (16%)</td>
</tr>
</tbody>
</table>

| Previous cardiac surgery | 13 (9%) | 4 (9%) | 1 (5%) |
| Previous CABG | 9 (6%) | 3 (7%) | 0 (0%) |
| Previous PCI | 61 (42%) | 21 (47%) | 4 (21%) |

<table>
<thead>
<tr>
<th>Laboratory examination</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td>Creatinine, mg/dL*</td>
<td>1.1±0.3</td>
<td>2.2±0.6</td>
<td>7.7±3.1</td>
</tr>
<tr>
<td>eGFR, mL/min/1.73 m²*</td>
<td>57±19</td>
<td>23±5</td>
<td>7±3</td>
</tr>
<tr>
<td>Hemoglobin, g/dL*</td>
<td>13.1±2.1</td>
<td>11.3±2.2</td>
<td>10.4±1.4</td>
</tr>
<tr>
<td>Brain natriuretic peptide, pg/mL*</td>
<td>643±498</td>
<td>645±284</td>
<td>2335±1432</td>
</tr>
</tbody>
</table>

| Medications            |                |                 |                  |
| Beta-blockers          | 96 (67%)       | 29 (64%)        | 10 (53%)        |
| ACE inhibitors         | 46 (32%)       | 16 (36%)        | 3 (16%)         |
| Angiotensin II receptor blockers | 48 (33%) | 13 (29%) | 2 (11%) |
| Diuretics*             | 116 (81%)      | 34 (76%)        | 5 (26%)         |

| Surgical data          |                |                 |                  |
| Mitral annuloplasty ring size | |                  |                  |
| 24 mm                  | 69 (48%)       | 27 (60%)        | 13 (68%)        |
| 26 mm                  | 64 (44%)       | 17 (38%)        | 5 (26%)         |
| 28 mm                  | 11 (8%)        | 2 (2%)          | 1 (6%)          |
| Mitral annuloplasty alone | 54 (38%) | 21 (47%) | 3 (16%) |
| Mitral annuloplasty+CABG | 45 (31%) | 12 (27%) | 9 (47%) |
| Mitral annuloplasty+SVR | 21 (15%)       | 6 (13%)         | 2 (11%)         |
| Mitral annuloplasty+ CABG+SVR | 24 (17%) | 6 (13%) | 5 (26%) |

Continuous variables are summarized as the mean±SD. CKD indicates chronic kidney disease; ESRD, end-stage renal disease; HD, hemodialysis; NYHA, New York Heart Association; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; ACE, angiotensin-converting enzyme; SVR, surgical ventricular reconstruction.

*P<0.05 (one-way analysis of variance).
right atrial pressure and useful for monitoring volume status in patients with heart failure.10

Cardiac Catheterization
Cardiac catheterization was performed before and 1 month after surgery. Before left ventriculography, LV systolic pressure, end-diastolic pressure, pulmonary capillary wedge pressure, systolic and mean PAP, and right atrial pressure were measured. Using biplane cine-ventriculography, LV end-diastolic volume, LV end-systolic volume, and LVEF were determined. Cardiac output was measured by the thermodilution method. Volumes and cardiac output were indexed by body surface area.

The purposes of cardiac catheterization and its invasive nature were explained in detail to all patients, and only those who gave informed consent underwent catheterizations. The indications for postoperative catheterization were not selective and the procedure was performed by a cardiologist under appropriate hydration conditions. Preoperative coronary arteriography was performed in all 208 patients, whereas serial left ventriculography and hemodynamic measurements were performed in 154 (74%) and 109 (52%), respectively.

Surgical Procedures
All operations were performed with bicalve cannulation, mild hypothermic cardiopulmonary bypass, and meticulous myocardial preservation with intermittent cold blood cardioplegia. Coronary artery bypass grafting was generally performed first. The approach to the mitral valve was generally through a superior transseptal method. The mitral valve was repaired using a restrictive mitral anuloplasty technique with an undersized ring.11 Ring size was determined after careful intraoperative measurements of the height of the anterior leaflet and intertrigonal distance and then down sizing by 2 to 3 sizes. No other adjunct procedures were performed on the valve itself. Surgical ventricular reconstruction was performed when a broad anteroapical or anteroseptal asynergy (akinesis or dyskinesis) was demonstrated by left ventriculography and a postoperative LV end-diastolic volume index >90 mL/m2 was anticipated. Our criteria for adding surgical ventricular reconstruction to restrictive mitral anuloplasty were mainly based on 2 previous investigations.12,13

Perioperative Management for Patients With Hemodialysis
Hemodialysis was performed in all patients with ESRD 12 to 24 hours before surgical intervention. During surgery, an extracorporeal ultrafiltration method was used to appropriately maintain volume status. Hemodialysis was routinely resumed on the second postoperative day or earlier if volume overload or hyperkalemia was present.

Clinical Follow-Up
Every 6 months to 1 year, each patient was assessed in the department as well as by their primary cardiologist. Functional status was assessed according to New York Heart Association criteria and plasma brain natriuretic peptide (BNP) level. The primary study end point was mortality during follow-up, and the second was defined as the composite of mortality and readmission for heart failure. Diagnosis of postoperative recurrent heart failure was based on clinical symptoms, physical signs, or radiological evidence of pulmonary congestion.

Clinical follow-up examinations were completed for all patients (100%) with a mean duration of 49±25 months (range, 4–126 months) for survivors. The cumulative follow-up period was 728 patient-years.

Statistical Analysis
Continuous variables are summarized as means±SDs or SEs when describing data presented in a figure and categorical variables as frequencies and proportions. For the continuous variables, comparisons between 2 groups were made using an unpaired t test. Comparisons among 3 groups were made using one-way analysis of variance. For categorical variables, 3 groups were compared using Fisher exact or a Kruskal-Wallis test. Correlations between continuous variables were tested with Pearson correlation coefficient (r). Hemodynamic data (LV end-diastolic volume index, LV end-systolic volume index, LVEF, LV end-diastolic pressure, mean PAP, cardiac index) were analyzed using an analysis of covariance model, including factors for the corresponding baseline value as the covariate, group, and interaction between them. Functional (plasma BNP) and echocardiographic (LV end-diastolic dimension, LV end-systolic dimension, LVEF, systolic PAP) data over time after surgical intervention were analyzed using a mixed-effects model for repeated measures, including factors for the corresponding baseline value, group, time, and interaction between group and time. The following covariance structures were considered: unstructured, compound symmetrical, first-order autoregressive, and Toeplitz. The covariance structure that provided the best fit according to Akaike information criterion was used in the analysis. Assessment time points were treated as categorical factors. The analysis of covariance and mixed-effects models included adjustments for age, etiology of cardiomyopathy, with or without diuretics, and laboratory examination findings, which showed significant differences among the groups (Table 1).

The linearized mortality rate was computed by dividing the number of patients experiencing an event by patient-years at risk. Survival and adverse event-free curves were estimated using the Kaplan-Meier method, and compared using an overall log-rank test, followed by a post hoc pairwise log-rank test. The association of group with adverse events was examined using Cox proportional-hazards models with adjustments for all other covariates presented in baseline demographics, echocardiographic, and surgical data (see the online-only Data Supplement Appendix). Factors obtaining a probability value <0.05 in the univariate Cox proportional hazards analysis were then entered appropriately into the multivariate fashion. Results are summarized as hazard ratios and 95% CIs. Multiplicity in pairwise comparisons was corrected by the Bonferroni procedure. All probability values are 2-sided and values of P<0.05 were considered to indicate statistical significance. Statistical analyses were performed using JMP 7.0 (SAS Institute, Cary, NC), SAS statistical software (Version 9.2; SAS Institute), and SPSS (Version 17.0; SPSS Inc).

Results
Clinical Outcomes
Overall hospital mortality was 6.3% for all patients and 6.3%, 6.7%, and 5.3% for the control, late CKD, and ESRD groups, respectively, with no intergroup differences.

Among 195 operative survivors, 49 late deaths occurred during the follow-up period with a linearized mortality rate of 6.8% per patient-year. Patients with ESRD tended to die from infectious or bleeding disorders rather than cardiac causes, whereas those with late CKD died more often from cardiac-related causes such as heart failure or sudden death than the ESRD group (Table 2). Actuarial survival at 2 and 5 years was 66±7% and 45±8% in late CKD and 78±10% and 70±12% in ESRD compared with 87±3% and 77±2%, respectively, in the control group (median survival, 40, 67, and 118 months, respectively; Figure 1). Patients with late CKD had a worse postoperative survival (P<0.0001 versus control group), whereas patients with ESRD had nearly comparable overall survival as compared with the control (P=0.27 versus control). Similarly, freedom from mortality and readmission for heart failure at 2 and 5 years was 50±8% and 18±7% in late CKD (P<0.0001 versus control, P=0.01 versus ESRD) and 72%±11% and 64%±12% in ESRD (P=1 versus control) as compared with 77%±4% and 52%±5%, respectively, in the control group (median event-free survival, 26, 67, and 63 months, respectively; Figure 2).

The Cox proportional hazards model with adjustments for baseline demographics, echocardiographic, and surgical data showed that late CKD (hazard ratio, 2.6; 95% CI, 1.6–4.2;
P/H11021 0.0001) but not ESRD on hemodialysis (hazard ratio, 1.0; 95% CI, 0.5–2.3; P/H11005 0.91) was associated with postoperative adverse events defined as mortality and readmission for heart failure.

Pre- and Postoperative Hemodynamic Data
From baseline to 1 month after surgery, LV volumes were substantially decreased in all groups with no intergroup differences in regard to the postoperative values (interaction effects P/H11022 0.05, group effects P/H11022 0.05; Figure 3). LVEF changed from 26%/H11006 8% to 32%/H11006 12%, 25%/H11006 7% to 26%/H11006 10% and 24%/H11006 7 to 33%/H11006 8% in the control, late CKD, and ESRD groups, respectively, providing evidence that patients with late CKD showed less improvement in LVEF than the other 2 groups (interaction effect P/H11005 0.027). LV systolic pressure did not change, whereas LV end-diastolic pressure was decreased in all groups. Systolic and mean PAP were decreased in all groups, whereas right atrial pressure did not change. Cardiac index increased from 2.5±0.7 to 2.8±0.6, 2.4±0.5 to 2.6±0.6, and 2.9±0.7 to 3.1±0.8 L/min/m² in the control, late CKD, and ESRD groups, respectively. These findings suggested that improvements in LV function and hemodynamics could be obtained at 1 month after surgery, irrespective of preoperative renal function status, with no substantial intergroup differences for those postoperative values.

Serial Echocardiographic Data
LV dimensions were decreased and LVEF was increased at 1 month after surgery in all groups (Figure 4), with subsequent changes in each group apparently distinctive. In the control, these improvements (LV reverse remodeling) persisted during the 2-year follow-up period. As compared with the control group, patients with ESRD showed further decreases in LV dimensions and improvement in LVEF during the follow-up period. In contrast, patients with late CKD showed a gradual reincrease in LV dimensions and less improvement in LVEF than the other groups (interaction effects P/H11021 0.05 for all).

From baseline to 1 month after surgery, systolic PAP was decreased from 46%/H11006 13 to 33%/H11006 11, 49%/H11006 18 to 35%/H11006 12, and 49%/H11006 14 to 34%/H11006 8 mm Hg in the control, late CKD, and ESRD groups, respectively, showing nearly identical systolic PAP values at 1 month for the 3 groups. The systolic PAP value at 2 years after surgery was 36%/H11006 14 mm Hg in the control and 33%/H11006 11 mm Hg in the ESRD group, suggesting that improvement in systolic PAP was nearly completely sustained over time in those 2 groups. In contrast, patients with late CKD showed a gradual reincrease in systolic PAP and had a high PAP value (44%/H11006 18 mm Hg) at the 2-year follow-up examination.

IVC Dimension
Mean IVC dimension at the latest examination was significantly greater in the late CKD group as compared with the others (Figure 5).

Symptoms and Serial BNP Level
Among patients in 3 study groups, the proportion with New York Heart Association Class I heart failure (no symptoms)
increased and the proportion with Class III or IV heart failure decreased from baseline to the last follow-up visit (91%–15% for the control, 91%–33% for the late CKD, and 95%–17% for the ESRD group, respectively; Figure 6). The symptoms improved by an average of 1.1, 0.7, and 1.2 New York Heart Association classes in the control, late CKD, and ESRD groups, respectively (P=0.054 for the difference among the 3 groups in the change from baseline).

Plasma BNP concentration in the control group was decreased at 1 month after surgery and this improvement was sustained during the 2-year follow-up period. As compared with the control, patients with late CKD showed less improvement in plasma BNP value over time, whereas those with ESRD showed remarkable improvement in that value at 1 month and a gradual improvement thereafter (interaction effect P=0.001; Figure 7).

**Relationship Between IVC Dimension and Plasma BNP Concentration**

There was a significant positive correlation between BNP level and IVC dimension at 1 (r=0.47, P<0.0001) and 2 (r=0.44, P<0.0001) years after surgery (Figure 8).

**Discussion**

The major findings can be summarized as follows: (1) restrictive mitral annuloplasty for advanced cardiomyopathy could be performed for high-risk patients with late CKD or ESRD with an acceptable early mortality comparable to that seen in the control; (2) postoperative (1-month) cardiac catheterization resulted in a substantial decrease in LV volume and improvement of hemodynamic status with no intergroup differences for those postoperative values; (3) patients with ESRD had nearly comparable...
postoperative outcomes as compared with the control and significantly better outcomes than the late CKD group in terms of freedom from mortality and readmission for heart failure; and (4) patients in the control and ESRD groups showed further improvements in plasma BNP level during the 2-year follow-up period as compared with the late CKD group.

The 5.3% rate of early mortality seen in the patients with ESRD is favorable as compared with that in previous reports, including 20 studies with a total of 863 patients on chronic hemodialysis who underwent various cardiac procedures. Furthermore, the overall survival rate seen in our patients with ESRD is satisfactory given that outcome in patients with heart failure requiring regular hemodialysis is extremely poor with a 3-year survival rate <15% after hospitalization for chronic heart failure.

There are limited data available regarding acute hemodynamic changes after a restrictive annuloplasty in patients with

![Serial echocardiographic findings. CKD indicates chronic kidney disease; ESRD, end-stage renal disease; HD, hemodialysis; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; PAP, pulmonary artery pressure. Data are presented as mean±SE.](http://circ.ahajournals.org/doi/abs/10.1161/CIRCULATIONAHA.112.000005)
ESRD. Chang et al\textsuperscript{16} reported favorable short-term results of 5 patients with chronic hemodialysis undergoing mitral valve repair for “uremic cardiomyopathy” that mimicked the pathophysiological disorder in patients with dilated cardiomyopathy resulting from chronic volume overload. Their echocardiographic findings showed that LV end-diastolic volume decreased from 168 ± 20 mL at baseline to 113 ± 36 mL, whereas LV end-systolic volume decreased from 91 ± 38 mL to 52 ± 26 mL after mitral valve repair for uremic cardiomyopathy, similar to that seen in our patients with ESRD. Importantly, cardiac catheterization in the present study allowed confirmation of improvements in LV volume and function as well as other hemodynamic parameters including LV end-diastolic pressure, mean PAP, and cardiac index, irrespective of preoperative renal function status. Furthermore, our serial echocardiographic examinations extending over 2 years revealed that the sustained improvements in LV function (reverse LV remodeling) and hemodynamics seen in patients with ESRD were comparable to those in the control group, indicating the efficacy of surgical intervention in patients with ESRD.

Plasma BNP concentration may be a useful biomarker of heart failure and provide prognostic information.\textsuperscript{17} Sustained improvements in BNP level in the control and ESRD groups may indicate that relief of heart failure obtained immediately

![Figure 5](image-url). IVC dimension at latest follow-up examination. CKD indicates chronic kidney disease; ESRD, end-stage renal disease; HD, hemodialysis; IVC, inferior vena cava. Comparisons among 3 groups were made using one-way analysis of variance followed by the post hoc pairwise unpaired t test. Data are presented as mean±SE.

![Figure 6](image-url). Heart failure symptoms at baseline and at the last follow-up visit. CKD indicates chronic kidney disease; ESRD, end-stage renal disease; HD, hemodialysis.

![Figure 7](image-url). Serial changes in plasma BNP levels. BNP indicates brain natriuretic peptide.
after surgery was sustained over time, possibly accounting for the better outcome than seen in the late CKD group. In contrast, plasma BNP in patients with late CKD was decreased at 1 month after surgery along with a substantial decrease in LV volume confirmed by left ventriculography; however, that value remained substantially high at all follow-up time points, suggesting abnormal hemodynamics and unfavorable functional status despite significant MR improvement in the patients with late CKD.

Finally, we found a significant difference in the late outcome between the late CKD and ESRD groups despite no intergroup differences in postoperative LV and hemodynamic function, except for LVEF. Patients with ESRD exhibited a smaller IVC dimension than those with late CKD at the latest follow-up examination and also had higher rates of freedom from mortality and readmission for heart failure as compared with those with late CKD. Because IVC dimension is an indicator of volume status in patients with heart failure, our findings regarding IVC dimension led us to speculate that volume management for the ESRD group was performed more appropriately than for the late CKD group during the follow-up period. Indeed, it is more difficult to control body fluid volume balance in patients with renal dysfunction not receiving hemodialysis than in those with ESRD on hemodialysis. Our speculation may also be supported by the positive correlation found between BNP level and IVC dimension after surgery, indicating that the increased plasma BNP levels might have been partially caused by LV volume overload. Furthermore, the lower rate of mortality due to heart failure seen in patients with ESRD may be accounted for by adequate fluid removal and volume management. Our data suggested that the favorable late outcome seen in patients with ESRD, as compared with those with late CKD, was not mainly attributed to the surgical intervention itself, but rather adequate postoperative volume management. Therefore, we consider that postoperative volume management is important for better outcome in patients with functional MR and advanced cardiomyopathy; thus careful and meticulous monitoring of volume status is mandatory, especially for patients with late CKD.

Study Limitations
This study was retrospective in nature and investigated a small number of subjects; thus, any conclusions are limited. In particular, the sample size for ESRD on hemodialysis is very small and may have involved biased sampling, which might have led to the result showing no difference in survival between the patients with ESRD and control subjects. Inclusion of patients with different etiologies for heart failure and patients who had undergone concomitant surgical intervention such as coronary artery bypass grafting or surgical ventricular reconstruction might have influenced the results. However, such concomitant procedures are usually required for sick patients with a similar clinical and pathophysiologic status despite the etiology of LV dysfunction. We only analyzed patients with functional MR secondary to advanced cardiomyopathy considered suitable by referring cardiologists to undergo restrictive annuloplasty. No information is available regarding the number of patients not referred for surgical intervention during the same time period, because of the extremely high risk considered by their primary care physician.

It remains controversial whether patients with end-stage heart failure and functional MR can benefit from mitral valve repair. In our study, patients with normal or mildly impaired renal function (control group) and those with ESRD on hemodialysis showed improvements in LV volume and function, decreases in plasma BNP level, and a satisfactory overall survival rates. Our results from meticulous follow-up examinations, including invasive cardiac catheterization at 1 month after surgery as well as sequential BNP levels, show that mitral valve repair improved hemodynamics and symptoms in those patients. However, the lack of an untreated control group did not allow us to investigate the survival...
benefit conferred by mitral valve repair in patients with ESRD on hemodialysis. Additional randomized studies with higher numbers of patients and longer follow-up periods are necessary to confirm our results.

**Conclusion**

Mitrail valve repair for medically refractory functional MR and Stage C/D heart failure yielded improvement in LV function and hemodynamics with an acceptably low hospital mortality, irrespective of preoperative renal function status. Patients with ESRD showed favorable late outcome in terms of freedom from mortality and readmission for heart failure as compared with those with late CKD. Further studies are needed to assess the survival benefit of mitral valve repair in patients with end-stage renal disease and advanced heart failure.

**Sources of Funding**

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**Disclosures**

None.

**References**

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