Aortic Valve Replacement and Concomitant Mitral Valve Regurgitation in the Elderly
Impact on Survival and Functional Outcome

Christopher J. Barreiro, MD; Nishant D. Patel, BA; Torin P. Fitton, MD; Jason A. Williams, MD; Pramod N. Bonde, MD, MS, FRCS; Vincent Chan, BS; Diane E. Alejo, BA; Vincent L. Gott, MD; William A. Baumgartner, MD

Background—The impact of mitral regurgitation (MR) on elderly patients (≥70 years) undergoing isolated aortic valve replacement (AVR) is not clearly defined. This study investigates the long-term effects of preoperative, moderate MR on survival and functional outcome in elderly AVR patients.

Methods and Results—A retrospective review identified 408 consecutive elderly patients who underwent isolated AVR from January 1983 to February 2004. The pathologic etiology of MR was determined on preoperative echocardiogram, and patients were stratified into no/mild MR (Group I; n = 338) versus moderate MR (Group II; n = 70). Follow-up was 95.1% complete. Functional outcome was evaluated using the Short Form-12 questionnaire. On univariate analysis, Groups I and II differed in incidence of previous myocardial infarction (13.9% versus 28.6%; \(P = 0.004\)), hyperlipidemia (18.7% versus 33.3%; \(P = 0.009\)), and congestive heart failure (50.0% versus 70.0%; \(P = 0.002\)). On multivariate analysis, moderate MR was an independent risk factor impacting long-term survival (\(P = 0.04\)). Actuarial survival at 1, 5, and 10 years for Group I was 93.8%, 73.3%, and 40.1% versus 92.3%, 58.2%, and 14.6% for Group II (\(P = 0.04\)). Available postoperative echocardiograms for Group II (\(n = 37\)) demonstrated improvement in MR in 81.8% of functional MR patients. However, MR persisted or worsened in 65.4% of patients with intrinsic mitral valve disease (myxomatous, calcific, or ischemic MR). Functional outcomes showed 77% of Group I versus 78.6% of Group II rated their health as good to excellent post-AVR.

Conclusions—Moderate MR is an independent risk factor impacting long-term survival in elderly patients undergoing AVR. Therefore, patients with intrinsic mitral valve disease should be considered for concomitant MV surgery. (Circulation. 2005;112[suppl 1]:I-443–I-447.)

Key Words: aging ■ valves ■ surgery ■ mitral valve ■ survival

Aortic valve replacement (AVR) is indicated for elderly patients (≥70 years) with significant aortic stenosis (AS). Concomitant mitral regurgitation (MR) is found in as many as 67% of patients being evaluated for AVR.1–5 However, simultaneous replacement of both the aortic and mitral valves significantly increases morbidity and mortality, particularly among elderly patients.6,7 Therefore, surgical intervention must be carefully considered and used selectively. Numerous studies have suggested that MR occurs as a consequence of altered ventricular performance associated with AS and will improve after isolated AVR.8 However, the evidence is conflicting. Furthermore, there is a paucity of studies addressing these issues in an elderly population, and there are no clear guidelines regarding the treatment of these patients. The purpose of this retrospective study was to determine the impact of preoperative MR on long-term survival and functional outcome of elderly patients undergoing AVR and to determine the degree of improvement in MR after AVR alone.

Methods

A retrospective review of 408 consecutive patients (≥70 years) who underwent isolated AVR from January 1983 to February 2004 was conducted following Institutional Review Board approval. All of the patients had a preoperative transthoracic echocardiogram grading the degree of MR as follows: none - no regurgitant color flow; mild - sustained color flow jet with a maximal jet area >5% and <20% of atrial area; moderate - maximal jet area >20% and <40% of atrial area; and severe - maximal jet area >40% or a color flow jet reaching the back of the atrium with associated systolic flow reversal in the pulmonary area. Patients were stratified into Group I (none/mild MR; \(n = 338\)) versus Group II (moderate MR; \(n = 70\)). Patients with severe MR necessitating a mitral valve procedure or undergoing concomitant coronary artery bypass (CAB) were excluded. The pathologic etiology of MR was determined from the preoperative echocardiogram reports. Thirty seven of 70 Group II patients had postoperative echocardiogram reports, which were reviewed to...
TABLE 1. Pathologic Etiology of Moderate MR in Group II Patients as Determined by Preoperative Echocardiogram

<table>
<thead>
<tr>
<th>Etiology of MR</th>
<th>Group II (n=70)</th>
<th>Group II (n=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxomatous MR</td>
<td>34.3% (24)</td>
<td></td>
</tr>
<tr>
<td>Calcific MR</td>
<td>28.5% (20)</td>
<td></td>
</tr>
<tr>
<td>Ischemic MR*</td>
<td>15.7% (11)</td>
<td></td>
</tr>
<tr>
<td>Functional MR†</td>
<td>21.4% (15)</td>
<td></td>
</tr>
</tbody>
</table>

*Ischemic MR, presence of CAD, and wall motion abnormality on echo.
†Functional MR, secondary to severe AS/LV dysfunction with no morphologic abnormality on echo.

determine the degree of change in MR. Echocardiographic follow-up was limited by the availability of postoperative reports because of the long study period.

Data collection included a review of medical records, echocardiograms, coronary catheterization data, and pathology reports. Mortality data were obtained from autopsy reports, death certificates, the Social Security Death Index, and physician records. Telephone interviews with patients, family members, or personal physicians were the primary modes of follow-up. Functional outcomes and quality of life were assessed using the Short Form-12 health questionnaire. Follow-up was 95.0% (321 of 338) complete for Group I versus 95.7% (67 of 70) for Group II, with a mean of 4.5 and 3.4 patient years, respectively.

Outcomes were analyzed using SPSS statistical software (version 11.5) and are reported according to guidelines for reporting morbidity and mortality after cardiac valvular disease operations. Univariate analysis of preoperative, operative, and postoperative variables was performed using Fischer's exact test and the t test of means. Binary logistic regression was used to determine independent variables predictive of mortality. A Hosmer-Lemeshow statistic was run to determine goodness-of-fit of our multivariable model. Actuarial survival was plotted using the Kaplan-Meier method, and the 2 groups were compared using a log-rank analysis. Data are presented as Group I versus Group II unless otherwise stated. Descriptive statistics are presented as mean±SD, and statistical significance was defined as a 2-tailed probability value <0.05.

Results

The 408 patient cohort consisted of 338 (82.8%) patients in Group I (none/mild MR) and 70 (17.2%) patients in Group II (moderate MR). The pathologic etiology of MR in Group II patients as determined by preoperative echocardiogram is presented in Table 1. Myxomatous degeneration of the mitral apparatus was the underlying etiology of MR in 34.3% of our patients. Other etiologies included calcific mitral disease (28.5%) and ischemia (15.7%). Ischemic MR was determined based on the presence of coronary artery disease (CAD) and a wall motion abnormality on echocardiogram resulting in poor leaflet coaptation. MR was considered to be a functional result of AS and LV dysfunction in 21.4%, where no morphologic abnormality was identified on echocardiogram.

The clinical characteristics of the 2 groups are summarized in Table 2. The mean ages of the patients were 77.0±4.9 and 78.1±5.4 years, respectively. The gender ratios of the 2 groups were similar. A mechanical aortic prosthesis was used in 31.7% versus 32.9%. A bioprosthetic aortic valve was used in 68.3% versus 67.1%. The 2 groups significantly differed with respect to only 3 preoperative characteristics: prior myocardial infarction (13.9% versus 28.6%; P=0.004), hyperlipidemia (18.7% versus 33.3%; P=0.009), and CHF (50.0% versus 70.0%; P=0.002). There were no differences between the groups in any other preoperative variables including hypertension, diabetes, chronic obstructive pulmonary disease, smoking, prior CAB, left ventricular ejection fraction (LVEF), and urgency of surgery (operation performed urgent/emergently).

Mortality data and postoperative complications are summarized in Table 3. The in-hospital mortality of Group II (7.1%) was almost twice that of Group I (3.8%), although not statistically significant. There was no difference in late mortality between the 2 groups (40.8% versus 41.4%). The incidence of postoperative complications including stroke, anticoagulant-related hemorrhage, infectious endocarditis, and thromboembolic events remained low and was similar between groups. Two patients in Group I and 1 patient in Group II required redo-AVR. The Kaplan-Meier survival curves of the 2 groups were similar initially but began to diverge at 2 years (Figure). Actuarial survival at 1, 3, 5, and 10 years was 93.8%, 83.9%, 73.3%, and 40.1% for Group I versus 92.3%, 71.0%, 58.2%, and 14.6% for Group II (P=0.04).

TABLE 2. Clinical Characteristics of Group I and Group II.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group I (n=338)</th>
<th>Group II (n=70)</th>
<th>Univariate P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>49.7% (168)</td>
<td>48.6% (34)</td>
<td>0.89</td>
</tr>
<tr>
<td>Female</td>
<td>50.3% (170)</td>
<td>51.4% (36)</td>
<td></td>
</tr>
<tr>
<td>Mean age, yrs</td>
<td>77.0±4.9</td>
<td>78.1±5.4</td>
<td>0.09</td>
</tr>
<tr>
<td>Prior MI</td>
<td>13.9% (47)</td>
<td>28.6% (20)</td>
<td>0.004</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>18.7% (62)</td>
<td>33.3% (23)</td>
<td>0.009</td>
</tr>
<tr>
<td>CHF</td>
<td>50.0% (169)</td>
<td>70.0% (49)</td>
<td>0.002</td>
</tr>
<tr>
<td>Hypertension</td>
<td>57.8% (192)</td>
<td>68.1% (47)</td>
<td>0.14</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19.9% (66)</td>
<td>20.3% (14)</td>
<td>1.0</td>
</tr>
<tr>
<td>COPD</td>
<td>16.0% (53)</td>
<td>14.5% (10)</td>
<td>0.86</td>
</tr>
<tr>
<td>Smoking</td>
<td>43.4% (144)</td>
<td>49.4% (31)</td>
<td>0.79</td>
</tr>
<tr>
<td>Prior CAB</td>
<td>11.4% (38)</td>
<td>15.7% (11)</td>
<td>0.31</td>
</tr>
<tr>
<td>LVEF</td>
<td>51.5±17.2</td>
<td>47.6±15.0</td>
<td>0.35</td>
</tr>
<tr>
<td>Urgency of surgery*</td>
<td>29.0% (98)</td>
<td>34.3% (24)</td>
<td>0.31</td>
</tr>
</tbody>
</table>

*Urgency of surgery indicates operation performed urgent/emergently.

TABLE 3. Morbidity and Mortality of Group I and Group II

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I (n=338)</th>
<th>Group II (n=70)</th>
<th>Univariate P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>3.8% (13)</td>
<td>7.1% (5)</td>
<td>0.21</td>
</tr>
<tr>
<td>Late mortality</td>
<td>40.8% (138)</td>
<td>41.4% (29)</td>
<td>1.0</td>
</tr>
<tr>
<td>Stroke</td>
<td>3.8% (13)</td>
<td>2.9% (2)</td>
<td>1.0</td>
</tr>
<tr>
<td>ARH</td>
<td>4.7% (16)</td>
<td>2.9% (2)</td>
<td>0.75</td>
</tr>
<tr>
<td>IE</td>
<td>0.9% (3)</td>
<td>1.4% (1)</td>
<td>0.53</td>
</tr>
<tr>
<td>TE</td>
<td>3.6% (12)</td>
<td>4.3% (3)</td>
<td>0.73</td>
</tr>
<tr>
<td>Redo-AVR</td>
<td>0.6% (2)</td>
<td>1.4% (1)</td>
<td>0.43</td>
</tr>
</tbody>
</table>

ARH indicates anticoagulant-related hemorrhage; IE, infectious endocarditis; TE, thromboembolism.
Multivariate analysis was conducted using binary logistic regression and is reported in Table 4. Moderate MR was identified as an independent risk factor predicting mortality ($P=0.032$; odds ratio $=1.428$; 95% CI, 1.032 to 1.976). In addition, diabetes mellitus and preoperative New York Heart Association (NYHA) class III/IV status were found to significantly impact mortality (Table 4). Other variables entered into our binary logistic regression included prior MI, prior CAB, diabetes, hypertension, hyperlipidemia, smoking, CHF, LVEF, and urgency of surgery. None of these was found to have a significant impact on mortality.

Both groups showed similar improvements in NYHA status and had good functional outcomes. Preoperatively, 12.3% of Group I was classified as NYHA I/II, which improved to 86.7% postoperatively. Similarly, 20.3% of Group II was preoperatively classified as NYHA I/II, which improved to 92.5%. When patients were asked about their general level of health postoperatively, the following data were obtained: for Group I, 77% (77 of 100) reported good-to-excellent health, 18% (18 of 100) reported fair health, and 5% (5 of 100) reported poor health; for Group II, 79% (11 of 14) reported good-to-excellent health, 21% (3 of 14) reported fair health, and 0% reported poor health. The majority of Group I (78%; 78 of 100) and Group II (93%; 13 of 14) also reported no-to-mild limitations of physical activity post-AVR, with only 22% (2 of 100) and 7% (1 of 14), respectively, reporting moderate limitations.

Seventy patients had preoperative moderate MR on echocardiography. Postoperative echocardiograms were available for 37 of 70 patients. MR was identified in 89.2% (33) of the postoperative echocardiograms with the following classifications: mild, 37.8% (14); moderate, 37.8% (14); and severe, 24.2% (9). No evidence of MR was seen in 10.8% (4). Therefore, in this limited echocardiographic follow-up of patients with preoperative moderate MR, moderate MR persisted or worsened MR. However, this difference was not statistically significant, which may be because of our limited postoperative echocardiographic follow-up. In addition, all 5 of the patients whose MR progressed from moderate to severe died with an average postoperative survival time of 2.9 years.

### Table 4. Independent Predictors of Late Mortality as Determined by Multivariate Statistical Analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Multivariate $P$ Value</th>
<th>Odds Ratio 95% CI Lower</th>
<th>Odds Ratio 95% CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate MR</td>
<td>0.032</td>
<td>1.43</td>
<td>1.032</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.032</td>
<td>1.799</td>
<td>1.052</td>
</tr>
<tr>
<td>NYHA III/IV</td>
<td>0.026</td>
<td>1.449</td>
<td>1.045</td>
</tr>
<tr>
<td>COPD</td>
<td>0.114</td>
<td>1.615</td>
<td>0.891</td>
</tr>
<tr>
<td>CHF</td>
<td>0.124</td>
<td>0.501</td>
<td>0.208</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.277</td>
<td>0.786</td>
<td>0.509</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.437</td>
<td>0.288</td>
<td>0.167</td>
</tr>
<tr>
<td>Prior CAB</td>
<td>0.491</td>
<td>1.273</td>
<td>0.640</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.720</td>
<td>1.005</td>
<td>0.979</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.742</td>
<td>0.927</td>
<td>0.591</td>
</tr>
<tr>
<td>Age</td>
<td>0.787</td>
<td>1.006</td>
<td>0.963</td>
</tr>
<tr>
<td>Surgical urge</td>
<td>0.853</td>
<td>1.082</td>
<td>0.468</td>
</tr>
<tr>
<td>Prior MI</td>
<td>0.903</td>
<td>0.964</td>
<td>0.529</td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease; MI, myocardial infarction.

Hosmer-Lemeshow: $X^2=4.915$; degrees of freedom $=8$; $P=0.767$; The Hosmer and Lemeshow goodness-of-fit test divides subjects into deciles based on predicted probabilities, then computes a $X^2$ from observed and expected frequencies. The $P=0.767$ is computed from the $X^2$ distribution with 8 degrees of freedom and indicates that the logistic model is a good fit. That is, if the Hosmer and Lemeshow goodness-of-fit test statistic is $>0.05$, we reject the null hypothesis that there is no difference between the observed and predicted values of the dependent; if it is greater, as we want, we fail to reject the null hypothesis that there is no difference, implying that the model estimates fit the data at an acceptable level.

### Table 5. Postoperative Degree of MR With Respect to the Etiology of MR in Group II Patients (N=37)

<table>
<thead>
<tr>
<th>Etiology of MR</th>
<th>No</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxomatous MR</td>
<td>20.0% (2)</td>
<td>30.0% (3)</td>
<td>30.0% (3)</td>
<td>20.0% (2)</td>
</tr>
<tr>
<td>Calcific MR</td>
<td>0.0% (0)</td>
<td>20.0% (2)</td>
<td>60.0% (6)</td>
<td>20.0% (2)</td>
</tr>
<tr>
<td>Ischemic MR</td>
<td>0.0% (0)</td>
<td>33.3% (2)</td>
<td>50.0% (3)</td>
<td>16.7% (1)</td>
</tr>
<tr>
<td>Functional MR</td>
<td>18.2% (2)</td>
<td>63.6% (7)</td>
<td>18.2% (2)</td>
<td>0.0% (0)</td>
</tr>
</tbody>
</table>

Barreiro et al AVR and MR in the Elderly I-445
Discussion

Clinically significant MR is often found in conjunction with severe AS. Although isolated AVR in elderly patients has been widely adopted with acceptable mortality rates, the operative risk increases significantly for a double-valve replacement. The role of concomitant mitral valve surgery at the time of AVR is controversial, and no clear guidelines exist. The improvement seen in the severity of MR after AVR in some patients reflects the functional nature of MR. However, a subset of patients still remains who continue to have significant MR after AVR. These patients may potentially benefit from surgical intervention. Our study sought to determine the impact of preoperative, moderate MR on elderly patients undergoing isolated AVR and to define the degree of persistence of significant MR post-AVR.

Our patient cohort was divided based on the degree of MR assessed on preoperative echocardiogram. A comparison of these 2 groups allowed us to determine the significance of moderate MR on patient outcomes. Our investigations demonstrated acceptable postoperative morbidity and mortality with similar improvements in NYHA classification and functional outcomes in both groups. However, patients with significant preoperative MR had a decreased actuarial survival at all of the time points. In addition, multivariate analysis confirmed that moderate MR was an independent risk factor impacting late mortality. This raises the question as to whether or not a concomitant mitral valve procedure might benefit these patients.

MR in elderly patients with aortic valve disease has many potential etiologies. It may either be a consequence of the ventricular dysfunction associated with AS or it may reflect intrinsic mitral valve dysfunction. Morphological changes in the mitral valve because of myxomatous degeneration, calcification of the mitral leaflets or annulus, chordal/papillary muscle rupture, or ischemic disease may benefit, to varying degrees, from surgical intervention. Therefore, determining the etiology of MR preoperatively is an important consideration for the cardiothoracic surgeon.

Based on the postoperative echocardiographic reports, only 21.4% of patients with significant MR could be categorized as functional (because of severe AS and LV dysfunction). Therefore, the large majority of patients had a morphological/intrinsic abnormality of the mitral valve, which could potentially benefit from surgical correction. In fact, our postoperative echocardiographic follow-up demonstrated that the majority of patients with myxomatous (50%), calcific (80%), and ischemic MR (66%) remained unchanged or worsened, whereas the majority of functional MR (82%) improved. This suggests, therefore, that morphological/intrinsic abnormalities of the mitral valve have a greater potential for benefit from surgical repair than functional MR.

There has been much debate in the literature regarding the improvement in MR after AVR alone. To determine the incidence of MR in patients undergoing an isolated AVR for severe AS, Tunick et al retrospectively assessed the echocardiograms of 44 patients both preoperatively and postoperatively. Sixty-one percent of patients were found to have MR preoperatively, whereas 68% had MR postoperatively. However, the degree of MR decreased in 60% of patients but remained unchanged in 27% and worsened in only 13%. Therefore, the severity of MR improved in a majority of patients with AS after isolated AVR. In another retrospective review by Christenson et al of 60 patients undergoing AVR and CAB or isolated AVR, patients with AS and MR showed improvement in their MR status as long as they did not have CAD or morphological changes in their mitral valve. Tassan-Mangina et al performed a prospective study of 30 patients with a normal LVEF. The majority of patients with moderate MR associated with AS showed early regression of MR after AVR, reflecting the functional aspect of their MR. In this particular study, mitral calcifications and left atrial dilatation were predictive of persistent MR.

Although the previously mentioned studies suggest improvement in MR after AVR alone, there are still a number of patients with persistent MR postoperatively. In addition, there are numerous studies with contradictory conclusions in the literature. The change in MR severity after AVR was assessed in a study of 27 patients by Brasch et al. In more than half of these patients (52%), there was no echocardiographic evidence of improvement. Therefore, the authors suggest that additional mitral valve surgery should be considered in patients with moderate-to-severe MR. In a more recent study of 250 patients from Washington University who underwent AVR, moderate-to-severe MR was identified preoperatively in 35 patients. Fifteen of these patients had persistence of moderate-to-severe MR and a survival of only 78% at 3 years versus 98% survival in patients with trivial or mild MR. Therefore, the authors suggest that moderate-to-severe MR be addressed at the time of AVR. These results coincide with the findings of our present study in which moderate MR persisted in 51.3% of the postoperative echocardiograms assessed. Based on our etiologic data, MR persisted or worsened in 65.5% of patients with intrinsic mitral valve disease (myxomatous, calcific, or ischemic MR), whereas 81.8% of functional MR improved after isolated AVR. We also demonstrated a 5-year and 10-year actuarial survival of 73.3% and 40.1%, respectively, in those with no-to-mild MR versus only 58.2% and 14.6% survival, respectively, in those with moderate MR.

Ischemic cardiac disease is one etiology of MR that could potentially benefit from concomitant revascularization in AVR patients, as opposed to mitral valve surgery. Wall motion abnormalities resulting from ischemic disease can lead to poor mitral leaflet coaptation and significant MR. Prior MI was found to be twice as common in the group with moderate MR, which would suggest a higher degree of ischemic disease in this population. However, binary logistic regression analysis did not identify prior MI as an independent predictor of late mortality. In addition, we did not detect any significant difference in the incidence of prior CAB between the 2 groups.

Identifying ischemia as the underlying etiology for the MR is important in the surgical decision-making process. Controversy exists regarding the role of mitral valve repair in ischemic MR. Ring annuloplasty for ischemic MR with CAD can achieve valve competence. However, recent studies have demonstrated the operative mortality, midterm survival, and functional outcomes to be similar in patients treated with...
mitral valve repair and CAB versus CAB alone. These data refute the potential benefit of concomitant mitral valve repair in this subset of patients, although there still remains controversy in this area. Therefore, every effort must be made to preoperatively identify the underlying etiology of MR so that unnecessary surgical intervention can be avoided.

AVR is the accepted therapy for elderly patients with significant AS. MR is often found in conjunction with AS and may act as a marker of impaired left ventricular function. Our study clearly demonstrates that significant preoperative MR is an independent risk factor for late mortality. We also acknowledge the significantly increased operative mortality of a double valve replacement. However, we believe that the persistence or worsening of clinically significant MR post-AVR in patients with intrinsic mitral valve disease prompts the consideration of concomitant mitral valve repair in these patients.

Acknowledgments

This study was supported in part by the Mildred and Carmont Blitz Cardiac Research Fund. Dr Barreiro is a Hugh R. Sharp Jr Research Fellow, and Drs Fitton and Williams are Irene Piccinini Investigators.

References

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_Circulation_. 2005;112:I-443-I-447
doi: 10.1161/CIRCULATIONAHA.104.526046

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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