Influence of Atrial Fibrillation on Outcome Following Mitral Valve Repair

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Background—To investigate the outcome of patients in atrial fibrillation (AF) following mitral valve repair, clinical and echocardiographic follow-up was undertaken in 400 consecutive patients who underwent mitral valvuloplasty from 1987 to 1999.

Methods and Results—The main indications for surgery were degenerative (81.4%), endocarditis (7.1%), rheumatic (6.6%), ischemic (4.6%), and traumatic (0.3%) mitral valve disease. After excluding 6 paced patients and 1 patient in nodal rhythm, we compared the outcomes of 152 patients in AF against 241 patients in sinus rhythm. For patients in AF versus those in sinus rhythm, more AF patients were older (mean age 67.2 ± 8.8 versus 61.9 ± 11.8 years, respectively; P < 0.001), more were assigned to a poorer New York Heart Association (NYHA) class (77.6% versus 66.0% in NYHA III/IV, respectively; P = 0.01), and more demonstrated impaired ventricular function (78.9% versus 46.2% with moderate or severe impairment, respectively; P < 0.001). For patients in AF versus those in sinus rhythm, there was no difference in 30-day mortality (2.0% versus 2.1%, respectively; P = 0.95), repair failure (5.4% versus 3.6%, respectively; P = 0.41), stroke (5.4% versus 2.2%, respectively; P = 0.11), or endocarditis (2.3% versus 0.9%, respectively; P = 0.27) on follow-up at a median of 2.8 years (interquartile range 1.1 to 6.0). On echocardiography, the proportion of patients with mild regurgitation or worse was 13.3% (AF patients) versus 10.8% (patients in sinus rhythm) (P = 0.70). Patients in AF versus those in sinus rhythm had lower survival at 3 years (83% versus 93%, respectively) and 5 years (73% versus 88%, respectively). Univariate analysis identified factors affecting survival as AF (P = 0.002), age > 70 years (P = 0.041), and poor ventricular function (P < 0.001). However, by use of a multivariate model, only poor ventricular function remained significant (P = 0.01).

Conclusions—AF does not affect early outcome or durability of mitral repair. The onset of AF may be indicative of disease progression because of its association with poor left ventricular function. (Circulation. 2001;104[Suppl I]:I-59-I-63.)

Key Words: arrhythmia • mitral valve • surgery
tients who were individually contacted and agreed to attend an outpatient clinic that was organized specifically for the present study. Clinical and echocardiographic follow-up data for patients who were not reviewed were obtained from cardiologists from the respective referral centers.

On admission to our follow-up clinic, an ECG was recorded on all patients. This was performed before interview and clinical examination by a cardiologist with a particular interest and experience in mitral valve disease (J.B.B.). Clinical assessment included evaluation of rhythm, degree of mitral regurgitation, frequency of endocarditis, stroke (defined as a sudden onset of neurological deficit lasting >24 hours), and repair failure (defined as the need for a second operation).

Transesophageal echocardiography was performed by an experienced echocardiographer (C.W.) on a Hewlett-Packard 2500 echocardiography machine to evaluate postoperative mitral valve and ventricular function. Both clinical and echocardiographic assessments of mitral regurgitation were performed independently and in a blinded fashion; mitral regurgitation was graded (if present) from 1 to 6, which was considered trivial, mild, mild-moderate, moderate, moderate-severe, and severe regurgitation, respectively. Preoperative left ventricular function was estimated by echocardiography and angiography by use of visual estimation and graded according to the extent of impairment ranging from 0 to 3, indicating no, moderate, and severe impairment, respectively.

Surgical Technique
Operations were performed by a single surgeon (F.C.W.). Operative evaluation of the mitral valve was undertaken to determine valve pathology, and function was assessed according to Carpentier’s categories. Repair techniques were individualized according to pathology and have been described previously. All patients were given warfarin after surgery, with a target international normalized ratio from 2.0 to 3.0. This was discontinued at 6 weeks for patients who were in sinus rhythm on follow-up.

Statistical Methods
Background data and procedural details are presented as mean±SD or frequencies (percentages). The patients were grouped according to preoperative rhythm (sinus or atrial fibrillation). Groups were compared for categorical variables using χ² or the Fisher exact test. Normally distributed and nonnormally distributed measures were compared by using the t test and Mann-Whitney test, respectively. The Wilcoxon signed rank test was used to compare preoperative and postoperative NYHA functional class for patients in preoperative sinus rhythm. Actuarial survival was calculated by the Kaplan-Meier method, and Cox regression analysis was used to assess the effect of preoperative rhythm, age, NYHA functional class, and ventricular function on survival. Statistical analyses were performed on SPSS for Windows, version 10.

Results
Of the 400 patients who underwent mitral repair, 6 were paced before surgery, and 1 was in a nodal rhythm. Therefore, we excluded these 7 patients, leaving 393 for analysis. Sixty-two patients died before review, and postoperative data were obtained from 299 survivors who attended our follow-up clinic. Information from the remaining 32 patients was obtained from referring cardiologists. The mean age of our study population was 63.9±11.0 years, and the causes for mitral regurgitation were degenerative (81.4%), endocarditis (7.1%), rheumatic (6.6%), ischemic (4.6%), and traumatic (0.3%) mitral valve disease.

Demographics, operative procedures, and outcome measures were compared in 241 patients who were in sinus rhythm and in 152 patients in atrial fibrillation. The sex distribution was similar in both arms of the study; 65.6% of the patients in sinus rhythm were male, and 62.5% of the patients who were in atrial fibrillation before surgery were male (P=0.53). Patients in atrial fibrillation were older, at a mean±SD age of 67.2±8.8 years compared with 61.9±11.8 years for patients in sinus rhythm (P<0.001). Preoperative NYHA class was significantly poorer, with 77.6% in either NYHA class III or IV compared with 66.0% of patients who were in sinus rhythm (P=0.01). Similarly, left ventricular function was also poorer in patients with atrial fibrillation; 78.9% had moderate or severe impairment compared with 46.2% of the patients in sinus rhythm (P<0.001) (Table 1).

Degenerative mitral valve disease was the most common cause of mitral regurgitation, and the distribution was similar in both groups. The proportion of patients with rheumatic mitral regurgitation was significantly higher in the atrial fibrillation arm versus the sinus rhythm arm (12.5% versus 2.9%, respectively; P<0.001), with the remaining causes equivalently distributed. Concomitant coronary artery bypass surgery and aortic valve replacement were performed in similar numbers in both groups of the study; however, the requirement for tricuspid valve repair was significantly higher in patients who were in atrial fibrillation versus those in sinus rhythm (4.6% versus 0.4%, respectively; P=0.006). The 30-day mortality of patients in atrial fibrillation was 2.0%, and this was comparable with 2.1% of patients who were in sinus rhythm (P=0.95). A summary of patient demographics and operative procedures is presented in Table 1.
On follow-up at a median time interval of 2.8 years (interquartile range 1.1 to 6.0), no significant differences were noted for repair failure, defined as the need for reoperation, which was 5.4% in patients with atrial fibrillation and 3.6% in patients who were in sinus rhythm ($P=0.41$). The proportion of stroke for patients with atrial fibrillation was 5.4% compared with 2.2% in patients who were in sinus rhythm ($P=0.11$). Endocarditis occurred in 2.3% of patients with atrial fibrillation and 0.9% of patients in sinus rhythm ($P=0.27$). For patients who were in atrial fibrillation before surgery, 81.0% remained in atrial fibrillation on follow up, with 17.2% converting to sinus rhythm. For patients who were in sinus rhythm before surgery, 10.2% were in atrial fibrillation on follow-up.

The discrepancy of NYHA functional class was no longer significant on follow-up, with 7.2% of patients who were in preoperative atrial fibrillation belonging to class III/IV compared with 3.7% of patients who were in preoperative sinus rhythm ($P=0.12$). A Wilcoxon signed rank test was performed and demonstrated significant improvement in NYHA class in both groups ($P<0.001$).

No differences were noted in the clinical assessment of the degree of postoperative regurgitation, with trace regurgitation as the most common result. On transesophageal echocardiography, trace regurgitation was also noted in 41.3% of patients who were in sinus rhythm and 42.5% of patients who were in atrial fibrillation ($P=0.13$). There was no significant difference in the proportion of patients who had more than mild regurgitation during the follow-up of patients who were in preoperative atrial fibrillation compared with sinus rhythm (13.3% versus 10.8%, respectively; $P=0.70$). Left atrial dimensions were significantly larger in patients who were in atrial fibrillation before surgery, and no differences were apparent when left ventricular end-systolic and end-diastolic dimensions were compared. These results are summarized in Table 2.

Kaplan-Meier analysis revealed that 3-year survival was lower for patients with atrial fibrillation (83%, 95% confidence limit [CL] 76% to 89%) compared with that for patients in sinus rhythm (93%, 95% CL 90% to 97%). At 5 years, the survival rate was 73% (95% CL 64% to 82%) of patients with atrial fibrillation compared with 88% (95% CL 82% to 93%) of patients in sinus rhythm. Univariate analysis confirmed that preoperative atrial fibrillation significantly affected survival ($P=0.002$, Figure 1). Additional factors that influenced survival were age ≥70 years ($P=0.041$, Figure 2) and poor ventricular function ($P<0.001$, Figure 3). Preoperative symptoms did not influence survival in our series when the survival of patients with NYHA class I/II was compared with the survival of patients with NYHA class III/IV ($P=0.443$). By use of a multivariate analysis, the only factor to influence survival was poor left ventricular function ($P=0.012$). The hazard ratio of patients with moderate to good function was 1.69 (95% CL 0.80 to 3.55), and that of patients with poor to good function was 3.31 (95% CL 1.49 to 7.37). The hazard ratio comparing patients in preoperative atrial fibrillation with those in sinus rhythm was 1.40 (95% CL 0.76 to 2.60, $P=0.28$), and the hazard ratio for patients aged <70 years compared with those aged ≥70 years was 1.26 (95% CL 0.70 to 2.28, $P=0.44$).

A subgroup analysis excluding patients with concomitant procedures was also performed to compare survival of patients with preoperative atrial fibrillation with patients in sinus rhythm. This was undertaken to eliminate the effect of concomitant disease. After the exclusion of 98 patients who

| TABLE 2. Postoperative Rhythm, Functional Class, Complications, and Echocardiographic Data |
|---------------------------------------------|-----------------|------------------|-----|
| Follow-up rhythm                           | Sinus Rhythm    | Atrial Fibrillation | $P$ |
| Survivors, n                               | 215             | 116               |     |
| Complications                              |                 |                  |     |
| Repair failure, n (%)                      | 8 (3.7)         | 7 (6.0)           | 0.40|
| CVA, n (%)                                 | 5 (2.3)         | 7 (6.0)           | 0.11|
| Endocarditis, n (%)                        | 2 (0.9)         | 3 (2.6)           | 0.27|
| Echocardiographic outcome                  |                 |                  |     |
| Echocardiogram performed, n (%)            | 213 (99.1)      | 113 (97.4)        |     |
| Degree of regurgitation                    |                 |                  |     |
| Nil, n (%)                                 | 47 (22.1)       | 17 (15.0)         |     |
| Trace, n (%)                               | 88 (41.3)       | 48 (42.5)         |     |
| Mild, n (%)                                | 55 (25.8)       | 33 (29.2)         |     |
| Mean LA size, cm (95% CL)                  | 4.7 (4.6-4.8)   | 5.9 (5.7-6.1)     | <0.001|
| LVEDD, cm (95% CL)                         | 5.4 (5.3-5.5)   | 5.6 (5.4-5.8)     | 0.31|
| LVESD, cm (95% CL)                         | 4.0 (3.8-4.2)   | 4.1 (3.9-4.3)     | 0.29|

CVA indicates cardiovascular accident; LA, left atrium; LVEDD, left ventricular end-diastolic diameter; and LVESD, left ventricular end-systolic diameter.

Figure 1. Survival by preoperative rhythm.
had ≥1 concomitant procedure, the 3- and 5-year survival of 81% (95% CL 73% to 89%) and 71% (95% CL 60% to 81%), respectively, for patients with preoperative atrial fibrillation was still significantly lower compared with 93% (95% CL 88% to 97%) and 89% (95% CL 82% to 95%), respectively, for patients in preoperative sinus rhythm (P < 0.001). Although univariate analysis revealed that preoperative atrial fibrillation significantly affected survival, once again, this did not achieve significance on multivariate analysis. The hazard ratio of patients in preoperative atrial fibrillation to those in sinus rhythm after excluding concomitant disease was 1.78 (95% CL 0.84 to 3.76, P = 0.125). Poor ventricular function remained an independent risk factor for mortality (P = 0.009).

**Discussion**

The results of the present study indicate that atrial fibrillation does not affect early outcome or durability after mitral valve repair. Although the presence of preoperative atrial fibrillation was associated with lower survival, this was not found to be an independent risk factor.

**Timing of Surgery for Mitral Regurgitation**

Traditional indications of NYHA class III/IV dyspnea and left ventricular dysfunction have resulted in poor outcome after surgery for mitral valve regurgitation. It has become increasingly evident that the timing of surgery is critical to the overall success of this procedure because early surgery has been associated with improved survival and lower morbidity.

Surveillance of disease progression by NYHA functional class has an inherent limitation of subjectivity. Moreover, deterioration of left ventricular function can progress inconspicuously. Left ventricular ejection fraction measured by echocardiography has been reported to be the most powerful predictor of late survival. Although monitoring of left ventricular function using ejection fraction (a load-dependent index) is the current standard, it may not be ideal. Patients with severe mitral regurgitation in the compensated state may still demonstrate normal values of ejection fraction despite impaired myocardial function as a consequence of reduced afterload.

**Atrial Fibrillation as a Marker of Disease Progression**

The onset of atrial fibrillation has been considered to be a decisive turning point in the course of mitral regurgitation and, therefore, may prove to be a useful marker for disease progression in patients with severe mitral regurgitation. Compared with patients in NYHA class I/II, a higher proportion of patients with mitral regurgitation in NYHA class III/IV has been observed to be in atrial fibrillation despite no significant differences in ejection fraction. Moreover, a longitudinal echocardiographic study has confirmed that the incidence of atrial fibrillation was significantly higher in patients with progression of disease severity despite no significant alteration in ejection fraction.

**Association of Atrial Fibrillation With Survival**

Preoperative atrial fibrillation has been identified to be an independent predictor of overall survival, and we report significantly lower 3- and 5-year survival rates of patients who were in preoperative atrial fibrillation compared with patients who were in sinus rhythm. However, multivariate analysis has identified poor ventricular function as the only independent risk factor for overall survival in our series. Differences in overall survival based on preoperative rhythm have not been consistent in other reports, and this may be due in part to heterogeneity of the study population or sample size limitations, as reported by the respective authors.

**Clinical Implications**

Before surgery, a higher proportion of patients in atrial fibrillation compared with those in sinus rhythm were in NYHA functional class III/IV. However, this difference was no longer apparent after surgery and is attributed to significant improvement in functional class for both arms of the study. Apart from symptomatic benefit, early surgery after the onset of atrial fibrillation may have a prognostic significance. Previous studies that have not demonstrated a difference in survival between patients in atrial fibrillation before surgery have identified trends toward lower survival in patients who remain in atrial fibrillation after surgery. However, these observations have been limited by power to demonstrate statistical significance. Because shorter duration of preoperative atrial fibrillation is associated with higher return to postoperative sinus rhythm, further work is required.
to determine whether a survival advantage can be gained by early operation before or soon after the onset of atrial fibrillation.

Presently, our criterion for mitral repair is the presence of severe mitral regurgitation on echocardiography. We consider proceeding to surgery even before the onset of symptoms, ventricular dysfunction, or atrial fibrillation. The survival of the 55 patients in our series who fulfilled these preoperative criteria was 98% (95% CL 90% to 100%) at a median follow-up interval of 2.0 years (interquartile range 0.9 to 5.1 years).

Limitations of the Study
The estimation of left ventricular function was undertaken semiquantitatively in our series. However, the technique of visual estimation is validated and has been adequate for good clinical risk stratification. Because longitudinal follow-up was not undertaken for each patient, we were unable to determine postoperative rhythm over the course of time.

Conclusions
Although atrial fibrillation does not affect early outcome or durability of mitral repair, the onset of atrial fibrillation may be a useful indicator of disease progression because of its association with poor left ventricular function. Early surgery before or soon after the onset of atrial fibrillation may confer a prognostic benefit and is justified in view of low operative mortality and good long-term outcome of mitral valve repair.

References
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