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# Long-Term Outcome of Surgically Treated Aortic Regurgitation

## Influence of Guideline Adherence Toward Early Surgery

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**OBJECTIVES** The purpose of this study was to compare postoperative outcome in two groups of patients with chronic severe aortic regurgitation (AR): those operated on early and those operated on late according to the guidelines.

**BACKGROUND** The impact of earlier surgery for chronic severe AR as defined in guidelines has not been evaluated.

**METHODS** A total of 170 patients with chronic severe AR submitted to aortic valve replacement were prospectively followed up. Patients were divided in two groups depending on the clinical situation at the time of surgery. Group A were 60 patients who were operated on following guidelines advice of earlier surgery, and group B were 110 patients who were operated on late with regard to guideline recommendations.

**RESULTS** Follow-up was 10 ± 6 years (1 to 22 years). During follow-up 44 patients died, 7 patients (12%) from group A and 37 (37%) from group B ($p = 0.001$). The cause of death was non-cardiac in 11 patients, 2 (3%) in group A and 9 (8%) in group B. Cardiac deaths occurred in 33 patients, 5 (9%) from group A and 28 (28%) from group B ($p = 0.002$). Causes of death differed between groups A and B: heart failure or sudden death were significantly more frequent in group B (20 patients vs. 1 patient, $p = 0.001$). Overall survival in groups A and B was 90 ± 4% vs. 75 ± 8% at 5 years, 86 ± 5% vs. 64 ± 5% at 10 years, and 78 ± 7% vs. 53 ± 6% at 15 years, respectively ($p = 0.009$).

**CONCLUSIONS** Early operation as defined in the guidelines improves long-term survival in patients with chronic AR. (J Am Coll Cardiol 2006;47:1012–7) © 2006 by the American College of Cardiology Foundation

In recent years the natural history of chronic aortic regurgitation (AR) has been well described, and several studies have clearly shown the predictors of unfavorable outcomes (1–5). It has been shown that a decrease of the left ventricular ejection fraction (LVEF) at rest increases the probability of symptoms at a rate of 25% per year (5), an end-systolic diameter (ESD) >50 mm at a rate of 19% per year (5), and more recently that changes in LVEF and ESD predict clinical deterioration or death at an annual rate of 10% to 20% (6). On the other hand, postoperative outcome depends on preoperative symptoms, preoperative LVEF, and LV dilation (7–9). In the American College of Cardiology/American Heart Association (ACC/AHA) guidelines (10), surgery is considered a Class I recommendation in all symptomatic patients and in asymptomatic patients when LVEF at rest is lower than 49%, and a Class II recommendation in asymptomatic patients with ESD >55 mm. In the recommendations of the management of asymptomatic patients with valvular heart disease from the European Society of Cardiology (ESC) (11), surgery is recommended in severe AR with resting LVEF <50% or with enlarged ventricles end-diastolic diameter (EDD) >70 mm and ESD >50 mm.

The aim of these recommendations is to offer a favorable postoperative long-term course. Although guidelines have been available for some years, the real impact of earlier surgery as defined in guidelines has not been evaluated, and there is some concern about the real benefit of surgery in the asymptomatic patient (12–14).

In the present study we analyze the impact of adherence to guidelines recommendations regarding earlier surgery on the long-term postoperative outcome in a large series of patients who were operated on in a single institution for isolated chronic severe AR according to a predefined protocol established in 1982 (15), similar to the subsequent ACC/AHA and ESC guidelines, which were designed in the late 1990s.

## METHODS

**Study population.** A total of 170 patients with severe isolated chronic AR and without significant coronary heart disease were consecutively submitted to aortic valve replacement in our institution between 1982 and 2002 according to

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**Abbreviations and Acronyms**

ACC/AHA = American College of Cardiology/American Heart Association
AR = aortic regurgitation
EDD = end-diastolic diameter
EF = ejection fraction
ESC = European Society of Cardiology
ESD = end-systolic diameter
LV = left ventricular/ventricle
NYHA = New York Heart Association

a predefined protocol (15) that advised surgery for all symptomatic patients and asymptomatic patients when ejection fraction (EF) <50% and/or ESD is between 50 and 55 mm. No patient was denied surgery because of preoperative very severe LV dysfunction. Data regarding preoperative New York Heart Association (NYHA) functional class, symptoms, and echocardiographic parameters were analyzed. Patients were divided in two groups depending on the clinical situation at the time of surgery. Group A ("early" surgery) included asymptomatic patients with moderate degrees of LV dysfunction (LVEFs between 45% and 50% and/or ESDs between 50 and 55 mm) and patients in NYHA functional class II. Group B ("too late" surgery) included patients either severely symptomatic (NYHA functional class III and IV) or with an LVEF <45% or an ESD >55 mm. All patients were operated on by the same surgical team. After surgery all patients were prospectively followed up by a single cardiologist (P. T.) that followed both groups of patients in an exactly similar manner, with the same clinical visits and drug therapy orientation in case they had heart failure or any other problem. Regular visits were scheduled at three months and yearly thereafter, and echocardiograms were performed after one year and every five years. This study was approved by an institutional review committee and all subjects gave informed consent.

**Statistical analysis.** Descriptive analysis was performed with mean values ± SD and range for continuous variables and absolute and relative frequencies of patients in each category for categorical variables. Differences between study groups were evaluated with the use of unpaired Student *t* test for continuous variables and chi-square test for categorical variables. Paired *t* test was used when appropriate. The probability of survival during follow-up was calculated by Kaplan-Meier analysis; the survival curves obtained were compared with the log-rank test (Mantel-Cox). Two Cox models were developed to assess the relative risk of cardiovascular death and death due to heart failure or sudden death. An additional analysis was also performed with the same methodology considering the two study groups only on the basis of NYHA functional class (I to II vs. III to IV), irrespective of the LVEF or LV dimensions of the patients.

A two-tailed value of $p < 0.05$ was considered significant. Statistical analysis was performed with the statistical package SPSS 11.0 (SPSS Inc., Chicago, Illinois).

**Table 1.** Preoperative Characteristics of Study Groups

| | Group A n = 60 | Group B n = 110 | p |
|---|---|---|---|
| Age (yrs) | 47 ± 15 | 53 ± 14 | 0.025 |
| Gender (M/F) | 49/11 | 86/24 | NS |
| NYHA FC | | | |
| I | 26 (43%) | 27 (25%) | |
| II | 34 (57%) | 17 (15%) | |
| III | | 35 (32%) | |
| IV | | 31 (29%) | |
| EDD (mm) | 71 ± 7 | 75 ± 8 | 0.002 |
| ESD (mm) | 48 ± 6 | 55 ± 10 | 0.0001 |
| EF (%) | 54 ± 7 | 42 ± 10 | 0.0001 |

EDD = end-diastolic diameter; EF = ejection fraction; ESD = end-systolic diameter; FC = functional class; LV = left ventricle; NYHA = New York Heart Association.

## RESULTS

**Baseline characteristics.** The study population is 170 patients, 135 men and 35 women, ages from 14 to 78 years, with a mean age of 50 ± 14 years (median: 53 years). All patients over 45 years had a normal coronary angiography. Group A includes 60 patients: 26 (43%) were asymptomatic patients with moderate LV dysfunction, and 34 patients (57%) were in NYHA functional class II. Group B includes 110 patients: 44 had either an LVEF <45% or an ESD >55 mm with either no symptoms or moderate symptoms, and 66 patients had severe symptoms (NYHA functional class III or IV). Demographic characteristics of the whole series are shown in Tables 1 and 2. All patients received an aortic prosthesis, 101 (59%) mechanical and 69 (41%) biological.

**Table 2.** Preoperative Clinical Status and Left Ventricular Parameters of Study Groups

| | n | Age/Gender (yrs, Male/Female) | EDD (mm) | ESD (mm) | EF (%) |
|---|---|---|---|---|---|
| Group A, n = 60 | | | | | |
| NYHA FC I | 26 | 43 ± 17 (14–78) 24/2 | 72 ± 7 | 49 ± 6 | 54 ± 7 |
| NYHA FC II | 34 | 51 ± 13 (22–71)* 25/9 | 69 ± 7 | 47 ± 6 | 54 ± 7 |
| Group B, n = 110 | | | | | |
| NYHA FC I | 27 | 44 ± 13 (18–68) 23/4 | 74 ± 7 | 55 ± 7 | 43 ± 7 |
| NYHA FC II | 17 | 49 ± 14 (24–77) 15/2 | 76 ± 8 | 58 ± 7 | 41 ± 8 |
| NYHA FC III–IV | 66 | 57 ± 12 (27–77)† 46/18 | 75 ± 9 | 55 ± 12 | 42 ± 11 |

*p = 0.030; †p = 0.0001.
Abbreviations as in Table 1.