One-Hundred Aortic Valve Replacements in Octogenarians: Outcomes and Risk Factors for Early Mortality

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Background and aim of the study: **Today, ageing of the western population is causing aortic valve surgery to be performed in elderly patients with increasing frequency. The study aim was to evaluate surgical outcome in octogenarian patients undergoing aortic valve replacement (AVR).**
Methods: **A total of 100 patients (mean age 82.1 ± 2.7 years; range: 80-95 years) who underwent AVR over a three-year period was reviewed. Concomitant coronary artery bypass grafting was performed in 34% of cases, and a bioprosthesis was implanted in 80%. The mean logistic EuroSCORE was 13.3%.**
Results: **Operative mortality was 8.0%. In multivariate analysis, a logistic EuroSCORE ≥13.5% (p = 0.02), cross-clamp time ≥75 min (p = 0.02) and postoperative acute renal failure were predictors for in-hospital mortality. Follow up was 100% complete; the mean follow up period was 10.6 months. At one year after surgery, the actuarial survival rate of those patients who survived surgery was 86.1%. Postoperative dyspnea at one month (p = 0.004) was the only predictor of short-term mortality.**
Conclusion: **Age in itself should not contraindicate surgery, and healthcare systems should be prepared to accommodate elderly patients who may require special resources.**

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As the average age of the western population continues to rise, cases of degenerative aortic valve disease are being identified with increasing frequency. Age can be perceived by the referring physician as a risk factor for cardiac surgery, and may deter any consideration of surgical treatment. In the present study the authors' experience with octogenarian patients undergoing aortic valve replacement (AVR) was reported, and an analysis made of surgical outcomes and risk factors with regards to early mortality.

Clinical material and methods

Patients

Between May 2003 and May 2006, a total of 100 octogenarian patients (mean age 82.1 ± 2.7 years; range: 80 to 95 years) underwent AVR at the present authors' institution. These patients represented 23% of the total number undergoing AVR at the author's institution during the same period. Preoperative, intraoperative and postoperative data were collected from a computerized database (Table I). The mean logistic EuroSCORE was 13.3%, while aortic stenosis was diagnosed in 75% of patients, aortic regurgitation in 8%, and a double lesion in 17%. None of the patients was bedridden.

Surgical technique

A median sternotomy was performed as a standard approach, and cardiopulmonary bypass (CPB) with mild systemic hypothermia utilized in all patients. Myocardial protection was achieved with antegrade, intermittent, cold blood cardioplegia and topical cooling. A mechanical prosthesis was implanted in 20% of the patients, and 80% received a biological prosthesis (10 of these latter prostheses were stentless). Concomitant coronary artery bypass grafting (CABG) was performed in 34 patients, with a mean number of 1.5 ± 0.7 grafts per patient.

Follow up

Patient status after hospital discharge was determined by hospital visit and telephone interview, and was 100% complete. The mean follow up period was 10.6 months (range: 1 to 29 months). All survivors were questioned to determine their post-surgical general

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health status, the presence of any cardiac-related symptoms, their physical activity, and any readmissions to hospital.

Definitions

The following definitions were adopted for the study. Renal failure: a baseline creatinine level of ≥2.0 mg/dl, or an increase ≥0.5 compared to the preoperative value. Urgent surgery: a need for AVR in patients whose hemodynamic condition was judged as requiring surgery within the first admission to the institution. Perioperative myocardial infarction was defined as a new Q-wave or a myocardial fraction of creatinine kinase >100 IU/l, in association with persistent ST segment elevation. Stroke was defined as any central neurological deficit persisting for >24 h. Postoperative respiratory failure was defined when assisted ventilation was required more than 48 h. Low cardiac output syndrome: a need for intra-aortic balloon pumping or inotropes for more than 30 min to maintain the systolic pressure >90 mmHg and cardiac index >2.2 $l/min/m^2$. Intestinal complication: intestinal hemorrhage or mesenteric ischemia requiring abdominal exploration. Postoperative bleeding: mediastinal hemorrhage requiring surgery. Sternal wound infection: wound complication requiring surgery. Postoperative hemorrhage: evidence of blood loss such as melena and nosebleed. Postoperative patient-prosthesis mismatch (PPM) was defined as none when the indexed effective orifice area (IEOA) was >0.85 cm^2/m^2, moderate when 0.65-0.85 cm^2/m^2, and severe when <0.65 cm^2/m^2. A history of hypertension, chronic obstructive pulmonary disease, diabetes mellitus was defined as present if indicated on medical records. Postoperative activity level was valued with a three-score assessment: level A, heavy, compatible with outdoor sport

*Table I: Operative patient data (n = 100).**

Operative data (n = 100)	Survivors (n = 92)	Non-survivors (n = 8)	p-value
Preoperative data (%)			
Female gender	47.8 (44)	50.0 (4)	1
Diabetes mellitus type II	9.7 (9)	0.0 (0)	1
Arterial hypertension	56.5 (52)	50.0 (4)	0.7
Chronic renal failure	17.3 (16)	12.5 (1)	1
Atrial fibrillation	19.5 (18)	12.5 (1)	1
LVEF <50%	21.7 (20)	12.5 (1)	1
NYHA class III-IV	46.7 (43)	100 (8)	0.005
Pulmonary hypertension	10.8 (10)	25.0 (2)	0.2
Activity level B	21.7 (20)	12.5 (1)	1
Aortic valve regurgitation	8.6 (8)	0.0 (0)	1
Intraoperative data (%)			
Logistic EuroSCORE ≥13.5%	20.6 (19)	62.5 (5)	0.01
Cross-clamp time ≥75 min	21.7 (20)	75.0 (6)	0.003
Concomitant CABG	34.7 (32)	25.0 (2)	0.7
Mechanical prosthesis	20.6 (19)	12.5 (1)	1
Stentless prosthesis	9.7 (9)	25.0 (2)	0.2
Urgency	6.5 (6)	12.5 (1)	0.4
Postoperative data (%)			
New-onset AF	36.9 (34)	12.5 (1)	0.2
Acute renal failure	21.7 (20)	75.0 (6)	0.003
Sternal wound infection	4.3 (4)	0.0 (0)	1
Stroke	2.1 (2)	12.5 (1)	0.2
Pacemaker	1.0 (1)	0.0 (0)	1
Respiratory failure	6.5 (6)	25.0 (2)	0.1
PPM: moderate	30.4 (28)	25.0 (2)	1
PPM: severe	14.1 (13)	12.5 (1)	1

*Analyzed using Fisher's exact test.
Values in parentheses indicate numbers of patients.
AF: Atrial fibrillation; IEOA: Indexed effective orifice area; LVEF: Left ventricular ejection fraction; PPM: Prosthesis-patient mismatch.

activities (running); level B, compatible with indoor activities (domestic jobs); and level C, bedridden patients (1).

Statistical analysis

Data were analyzed with the software package MedCalc®. All continuous variables were expressed as a mean or percentage. Operative data, presented as dichotomic variables, was analyzed with the two-tailed Fisher's exact test. As the logistic EuroSCORE was not normally distributed, it was converted into a binary variable. The 75% quartile mean value was taken as discriminatory value; hence, the outcomes of patients with a logistic EuroSCORE ≥13.5% were compared to those of patients with a lower score. The same analysis was conducted for cross-clamp times, but in this case the discriminatory value was 75 min. Any deterioration in activity level after cardiac surgery was also coded as a dichotomy variable: 1 was assigned to patients with a lower activity score, and 0 to those with the same or a better activity level than the preoperative status. Following their collection, all operative data from the computerized database were analyzed independently by two authors (S.U, R.S). Any variable with a p-value ≤0.05 in the univariate analysis was entered into the backward logistic regression model to identify independent risk factors for early and short-term mortality. Short-term survival rates were calculated using the Kaplan-Meier method.

Results

The mean CPB time was 91.6 ± 39.8 min, and the mean cross-clamp time 63.0 ± 19.3 min. The mean intensive therapy unit stay and mean hospital stay were 2.5 and 15.4 days, respectively. The overall operative mortality was 8.0% (n = 8). The mortality rate for isolated AVR was 9.2%, and for AVR + CABG was 5.8%. Causes of in-hospital mortality were low cardiac output syndrome (75.0%, n = 6), respiratory failure (12.5%, n = 1) and stroke (12.5%, n = 1). Among the survival group (n = 92), no patient presented with perioperative myocardial infarction or intestinal ischemia.

Univariate analysis identified four factors related to hospital mortality: preoperative NYHA class III or IV (p = 0.005), logistic EuroSCORE ≥13.5% (p = 0.01), cross-clamp time ≥75 min (p = 0.003), and postoperative acute renal failure (p = 0.003) (Table I). Of these variables, preoperative NYHA class was not an independent predictor of in-hospital mortality according to multivariate logistic regression analysis (Table II).

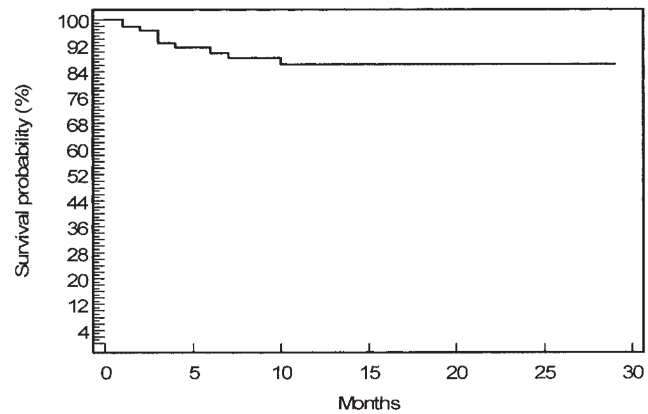

Figure 1: Kaplan-Meier survival curve following aortic valve replacement.

Among the group of 92 hospital survivors, 10 died during the follow up period; death was cardiac-related in all 10 cases (nine low cardiac output, one prosthesis endocarditis). Reoperation occurred only in one case due to endocarditis, and this patient died during the postoperative course. Among the 82 survivors, none was in NYHA functional class IV, 2.4% (n = 2) were in class III, and 97.6% (n = 80) were in class I/II. During the first 24 months of follow up the annual incidences of hemorrhagic events and stroke were 4.8% and 2.4%, respectively. None of these complications had any statistical correlation with warfarin treatment. Among the hospital survivors, 8.5% (n = 7) were readmitted because of atrial fibrillation (n = 1), pneumonia (n = 1), anemia (n = 1) and other non-cardiac pathologies (n = 4). The actuarial survival rate at 12 months was 86.1% (Fig. 1). Logistic regression analysis identified postoperative dyspnea at one month (p = 0.004; odds ratio (OR) 26.6; 95% confidence interval (CI) 2.8 to 248.9) as the only predictor of short-term mortality. During the follow up period, 95.1% of the patients (n = 78) maintained their preoperative activity level, and 4.9% (n = 4) reported a postoperative reduction in physical activity.

Table II: Independent predictors of in-hospital mortality by logistic regression multivariate analysis.

Patient variable	p-value	OR	95% CI
Cross-clamp time ≥75 min	0.02	9.6	1.3-67.0
Logistic EuroSCORE ≥13.5%	0.02	8.5	1.2-58.5
Postoperative ARF	0.01	13.7	1.8-101.6

ARF: Acute renal failure; CI: Confidence interval; OR: Odds ratio.

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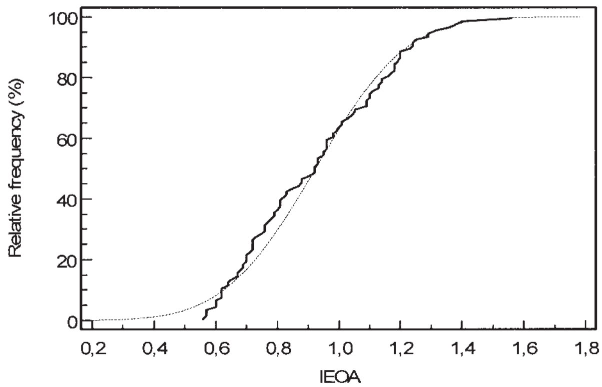

Figure 2: Cumulative frequency distribution of the indexed effective orifice area (IEOA) (solid line). The broken line indicates the normal distribution.

Patient-prosthesis mismatch

Details of the valve prostheses and EOA are listed in Table III. The median IEOA was 0.92 ± 0.23 cm^2/m^2; the frequency distribution of IEOA around the median value is shown in Figure 2; hence, severe postoperative PPM (IEOA <0.65 cm^2/m^2) was identified in 14 patients. No statistical difference was found between the PPM group and controls in terms of in-hospital and early mortality. Other outcomes such as intensive therapy unit stay, hospital stay, postoperative NYHA functional class and postoperative hemorrhage were not statistically different between the PPM and control groups.

Discussion

Murray and Lopez, in their projection study, reported in 1997 that during the next 13 years health trends will be determined by the ageing of the world's population (2). In fact, as the human lifespan increases, people aged over 80 years represent the fastest-growing section of the population in western countries (3). The consequence of this demographic data is that the prevalence of octogenarians with cardiovascular pathologies is growing. Indeed, it is estimated that up to 40% of octogenarians will experience cardiovascular disease in their lifetime (4).

Old people represent an heterogeneous population the age-span of which covers about 25 years (5). Recently, there has been a trend to define an "old" patient as one living in a western country and aged ≥80 years, but this definition cannot weigh any possible discrepancies between chronological and biological age. In addition to age, a physician should evaluate the patient's functional reserve which, in the elderly, might be limited by co-morbidities, though not necessarily so. A different view has been suggested by Bouma et al. (6), who showed how much the old age of the patient can influence the inclination of cardiologists to advise aortic valve surgical treatment among octogenarians. The majority of reports regarding octogenarian populations use a younger group as a control, but this has important limitations because of the different incidences of co-morbidities between the two populations (7). Hence, because of the above-mentioned factors, the evaluation of possible enhanced risks and possible reduced benefits of cardiac surgery in the elderly is complex (8).

Currently, the largest series on octogenarians undergoing AVR is the United Kingdom Heart Valve Registry study, which has incorporated 1,100 patients (9). This study reported a 30-day mortality of 6.6%, with actuarial survival of 89% at one year, 79% at three

Table III: Reported values of in-vivo effective orifice area (EOA, in cm^2) used in this study.

Valve prosthesis	No. of patients	Valve size (mm)						Reference
		19	21	23	25	27	29	
Mechanical								
CarboMedics	14	1.0	1.54	1.63	1.98	2.41	2.63	Pibarot et al. (21)
St. Jude Medical Regent	4	1.50	2.00	2.40	2.50	3.60	4.80	Bach et al. (22)
Bioprosthetic								
Mitroflow	41	1.6	2.03	2.42	3.04	-	-	*
CE Perimount	15	1.1	1.3	1.5	1.8	1.8	-	Pibarot et al. (21)
Epic	12	1.1	1.14	1.4	1.7	-	-	Walther et al. (19)
Mosaic	4	-	1.18	1.33	1.46	1.55	1.60	Thomson et al. (23)
Stentless								
Medtronic freestyle	2	1.15	1.35	1.48	2.00	2.32		Pibarot et al. (21)
Pericarbon freedom	8	-	1.7	1.9	2.0	2.2	2.4	Repossini et al. (24)

*EOA data provided by valve manufacturer.

years, 69% at five years, and 46% at eight years. More recently, Chiappini et al. (1) reported an in-hospital mortality of 8.5% among a population of 115 octogenarians. In the same study, actuarial survival at one and five years was 86.4% and 69.4%, respectively. In contrast, an in-hospital mortality of 16.7% was reported by Bloomstein et al. (10) among a study population of 180 septuagenarians and octogenarians.

The in-hospital mortality rate in the present series was 8.0% and, considering the high risk profile of the study population (mean logistic EuroSCORE 13.3%), this rate appeared acceptable. In the present series the cumulative survival rate was 86.1% at 12 months, which was is comparable with that reported previously, and showed good short-term results despite advanced patient age (11-13).

The results of previous studies have suggested that a prolonged CPB time, a small body surface area, left ventricular dysfunction, previous myocardial infarction, arterial hypertension and a body mass index >29 were independent predictors of early mortality among octogenarians (9,14,15). In the present series, a prolonged cross-clamp time, postoperative acute renal failure and a logistic EuroSCORE >13.5% were independent predictors of in-hospital mortality. Nevertheless - and as reported by others previously - CABG was not an independent risk factor of early mortality in the present population (15,16). In this series, mortality after AVR was 9.2%, and that for AVR + CABG was 5.8%; this difference in favor of the more complex procedure may be explained by the heterogeneity of the two groups.

In order to investigate the postoperative quality of life of patients, their perception of activity status was evaluated: consequently, 95% of the patients claimed to maintain the same preoperative activity level. Indeed, it can be assumed that in the present study population the activity level was independent of any cardiac symptoms in the majority of cases, and that the surgical procedure preserves this parameter of quality of life.

A significant percentage (14%) of the patients undergoing AVR were found to have severe PPM (IEOA <0.65 cm^2/m^2). Postoperative PPM is thought to reduce left ventricular mass regression and to produce poor postoperative results after AVR (17,18). However, no statistical correlation was identified between PPM and in-hospital mortality, short-term mortality, or postoperative symptoms. Previously, contradictory data have been reported concerning the impact of PPM on postoperative outcome (19,20), and several confounding variables, including the use of in-vitro EOA parameters, the time of EOA evaluation, and calcium antagonist treatment and prosthesis implant technique, might help to explain these discordances. A lack of any correlation between PPM and postoperative NYHA functional class in an octogenarian population has also been documented (21), though this may be related to the life style of elderly patients, whose physical activity may simply be not sufficiently intensive to show symptoms.

Study limitations

The main limitations of the present study related to its retrospective nature, although the sample population was also relatively small and not compared to a control group. In addition, the EOA data were not evaluated using echocardiography, but rather were acquired from previously reported studies.

In conclusion, the results of the present study confirmed that octogenarian patients account for a significant percentage of the total number of patients undergoing aortic valve surgery. Although this group of patients can be perceived as being of high risk, surgical management offers acceptable results. Age in itself should not be a contraindication for surgery, and healthcare systems should be prepared to accommodate this group of patients who may require special and expensive resources.

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