Mechanical Valve Prosthesis is a Valid Option for Aortic Valve Replacement in the Elderly

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Background and aim of the study: **Thromboembolism and hemorrhage related to anticoagulation remain a major concern in elderly patients with mechanical valves. Clinical results following isolated aortic valve replacement (AVR) with tilting disk and bileaflet prostheses in patients aged over 70 years were analyzed and compared with results in patients aged <45 years.**

Methods: **Between January 1980 and August 2002, 319 consecutive older patients (group A) and 497 young patients (group B) underwent isolated AVR. Preoperative clinical data, early and late mortality, valve-related complications and data related to anticoagulation status (including mean INR and mean interval between INR assays) were compared between groups.**

Results: **Hospital mortality was lower in group B (3.4%) than in group A (10.7%; p <0.0001). Twelve-year actuarial survival was lower in older patients (54% in group A versus 78% in group B; p <0.001). The two groups showed similar 12-year actuarial freedom from hemorrhage (99.6% versus 99.5%; p = 0.69), endocarditis (99.6% versus 98.43%; p = 0.25) and perivalvular leak (99.6% versus 97.9%; p = 0.21). However, actuarial freedom from thromboembolism was lower in older patients (98.8% versus 99.7%; p = 0.041).**

Conclusion: **Despite lower rates of long-term mortality and thromboembolism (the latter because of advanced atherosclerosis) in group A, there were no differences in rates of other valve-related complications. Hence, older age cannot be considered a contraindication to implantation of mechanical valves in the aortic position.**

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With the exponential growth of the geriatric population in the Western World, the number of older patients referred for open-heart operations has markedly increased during the past decade. Aortic valve disease is the most common heart valve disease in aged patients. Controversies persist about the best valve substitute in older patients as, although the use of bioprostheses for heart valve replacement is well established, concerns are still raised about their durability, even in the elderly. At the present time it is unknown whether the benefits of superior structural integrity of modern bioprostheses - which should reduce the rate of reoperation - outweigh the risks of anticoagulant-related complications. On the other hand, the use of mechanical valves in the elderly is controversial, due to the need for life-long oral anticoagulation (1). Some authors (2-5) support bioprosthesis implantation in order to improve the patients' quality of life, whereas others (6-12) encourage the use of mechanical valves, accepting some incidence of anticoagulation- related complications in return for a satisfactory long-term freedom from reoperation.

The debate has also focused on the higher incidence of thromboembolic and hemorrhagic complications in the elderly due to a lower compliance to oral anticoagulation (6,8). These well-designed studies have introduced some biases, however; for example, patient selection for each prosthetic model was not randomized in some studies (6,8), while one series included patients with associated coronary artery or mitral valve disease (13). Other series considered patients with early-generation mechanical valves (1,3,4), and the targeted INR was not always specified (1,3,4). Finally, previous clinical investigations comparing results with mechanical prostheses between an elderly and a young population enrolled patients aged 65-75

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years, resulting in an age gap of only 10 years between the elderly and young populations (1,14).

Consequently, the aim of the present study was to assess the risks of valve- and anticoagulant-related complications in patients aged over 70 years by comparing long-term results of this age group with those obtained in patients aged less than 45 years.

Clinical material and methods

Study design and data acquisition

Between January 1980 and August 2002, 816 isolated aortic valve replacements (AVR) were performed at the authors' unit. An institutional policy was taken, based on surgical experience, to implant almost exclusively mechanical prostheses. Hence, tilting disk valves were mainly used between 1980 and 1995, and bileaflet valves between 1987 and 2002, with an overlap of both types during 1987 to 1995. Postoperatively, the patients were examined at 15 days, one month and six months, and annually thereafter.

Follow up data were collected between July and September 2002. The follow up methodology was approximately 60% prospective and 40% retrospective. All patients discharged home following cardiac surgery were scheduled to return to the outpatient clinic at least yearly. Any event which occurred since surgery was recorded into a dedicated follow up database.

When the decision was made to begin this project, the database was initially checked and the most recent follow up data for 56% of the patients were collected. For patients lost to follow up, or in whom the most recent examination was conducted more than six months ago, patient status was checked by telephone call to the patient, or to their physician. In situations where patients died during the follow up period, the closest relative was interviewed in order to determine the modality and cause of death.

Events were defined according to the relevant guidelines for reporting morbidity and mortality after cardiac valve operations (2).

Information was available for all patients; thus the follow-up was 100% complete. The mean follow up period was 61.2 ± 45.6 months (range: 1 to 264 months).

Patient selection

Patients who had only undergone isolated AVR were included in this study; those with associated coronary artery disease, mitral valve disease or type A aortic dissection were excluded.

The study population included 319 patients aged >70 years (group A; 35 patients with tilting-disk, 284 with bileaflet prostheses). Data obtained during the follow up were compared with those obtained from a similar cohort of 497 consecutive patients aged <45 years (group B; 262 patients with tilting-disk, 235 with bileaflet valves). Indications for surgery and the clinical characteristics of the patients are listed in Table I.

Surgical technique

Valve replacement was always performed by the same four surgeons, and the surgical technique remained substantially the same during the study period.

A standard cardiopulmonary bypass was performed in all cases. Until January 1990, bubble oxygenators

Table I: Patient preoperative data.

Parameter	Group A	Group B	p-value
Age (years)*	73.2 ± 2.9	36. 83 ± 10.12	0,0001
Male 230	354	0.456	
Female	89	143	0.398
Aortic stenosis	156	240	0.686
Aortic regurgitation	25	46	0.218
Mixed	138	211	0.458
Bicuspid valve	33	52	0.378
Atrial fibrillation	27	15	0.08
LVEF (%)*	47 ± 12	49 ± 9	0.1
Preoperative NYHA class			
III	199	301	0.311
IV	49	71	0.198
Emergency operation	21	33	0.540
COPD	95	44	0.0001
Diabetes	89	15	0.0001
Chronic renal failure	15	22	0.465

*Values are mean ± SE.
COPD: Chronic obstructive pulmonary disease; LV: Left ventricular ejection fraction.

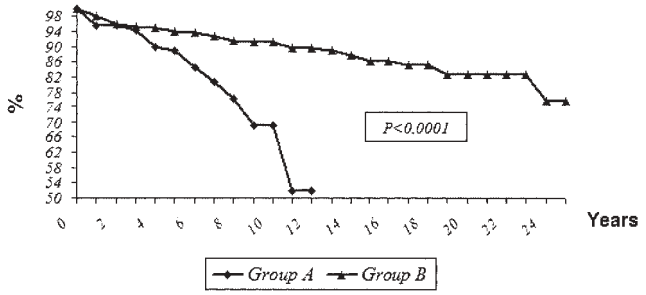

Figure 1: Twelve-year survival calculated using the Kaplan-Meier method.

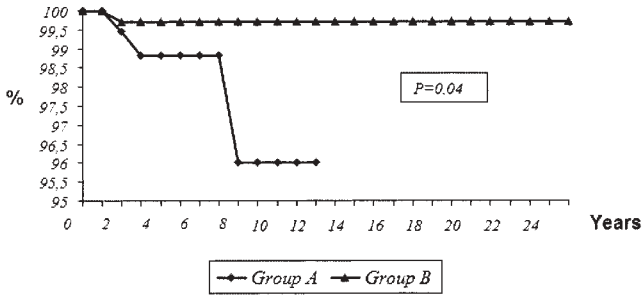

Figure 2: Twelve-year freedom from thromboembolism calculated using the Kaplan-Meier method.

were used, but since then hollow-fiber membrane oxygenators have been used routinely. Myocardial protection was achieved with mild systemic hypothermia (26°C), antegrade crystalloid cardioplegia and topical cooling using Shumway's technique. Kirsh cardioplegia was used until March 1981, but since then St. Thomas' Hospital 1 solution has been employed in all cases. Cardioplegia was infused through the aortic root in patients with predominant aortic stenosis, but delivered through direct cannulation of the coronary ostia in patients with valve regurgitation. All prostheses were inserted in the intra-annular position, using unpledgeted, interrupted simple Tevdek 2-0 stitches. Tilting disc valves were oriented with the main orifice toward the non-coronary sinus, whereas bileaflet valves were placed with their axis perpendicular to the septum. Free leaflet mobility was always evaluated on the completion of implantation. The mean aortic cross-clamp time was 68 ± 18 min (range: 35 to 120 min).

Anticoagulation management

All patients were given oral anticoagulants. Anticoagulation with warfarin was started on the second postoperative day. The therapeutic anticoagulation level was an International Normalized Ratio (INR) of 2.8 ± 0.8. An INR assessment was performed at least once each month. Among patients, 70% were controlled in the authors' hospital anticoagulation clinic, 20% in two private satellite hospitals which adopted the same anticoagulation policy, and 10% were controlled by their own physician who had been trained to follow the present authors' anticoagulation policy.

All data relating to the anticoagulation status of each patient were recorded on a computer, and the mean (±SE) INR value and time interval between each INR assessment were calculated. New hospital admissions for either cardiac or non-cardiac causes were also recorded.

Statistical analysis

Continuous data were expressed as mean ± SE, and compared using Student's *t*-test. Discrete variables were compared using the chi-square test.

Actuarial estimates of morbid events were calculated using Kaplan-Meier life-table analysis, and 95% confidence limits for the distribution function were calculated according to the Greenwood formula. A log-rank test was performed to ascertain differences between the two groups. Data were analyzed using SPSS software (version 10.0), including life-tables and survival function.

Results

The overall in-hospital mortality was 6.3% (51/816 patients). In group A, hospital mortality was 10.7% (n = 34), with causes of death being low output syndrome (n = 10), respiratory failure (n = 12), multi-organ failure

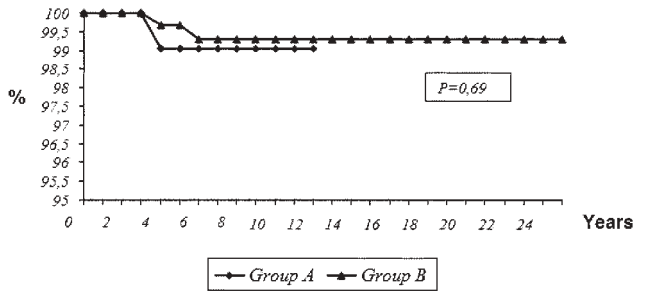

Figure 3: Twelve-year freedom from bleeding calculated using the Kaplan-Meier method.

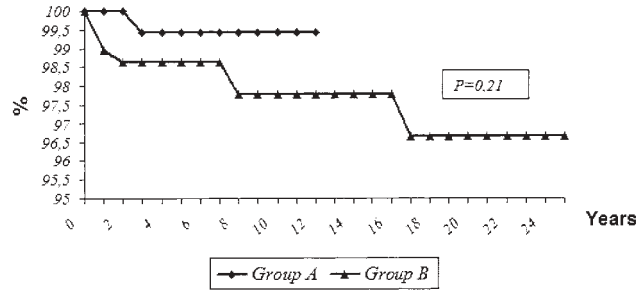

Figure 4: Twelve-year freedom from non-structural dysfunction calculated using the Kaplan-Meier method.

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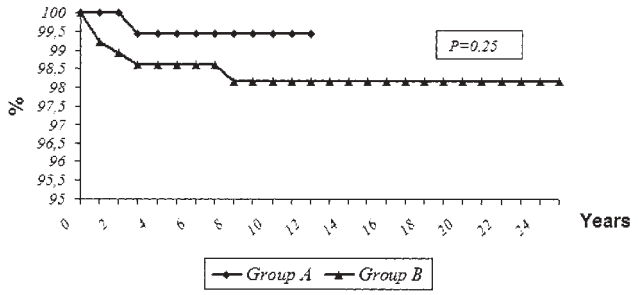

Figure 5: Twelve-year freedom from endocarditis calculated using the Kaplan-Meier method.

(n = 5), sepsis (n = 2), acute renal failure (n = 2) and ventricular fibrillation (n = 3).

In-hospital mortality in group B was 3.4% (n = 17; p = 0.0002); causes of death were low output syndrome (n = 5), respiratory failure (n = 3), multi-organ failure (n = 4), acute renal failure (n = 4) and ventricular fibrillation (n = 1).

With regard to late mortality, 91 patients died during the follow up period (33 in group A, 58 in group B). Twelve-year Kaplan-Meier survival proved to be significantly lower in group A than in group B (p <0.001) (Fig. 1).

Causes of late death in group A included cancer (n = 10), chronic lung disease (n = 6), sudden death (n = 8), progressive dementia (n = 2), pulmonary embolism following hip surgery (n = 1) and cirrhosis (n = 6). By comparison, 13 patients in group B died from cancer, 18 from cirrhosis, eight from sudden death, 10 from chronic lung disease, six from chronic renal failure, and three from trauma following a car accident.

With regard to thromboembolic complications, three patients in group A had a stroke, whilst one patient in group B had a retinal embolism. The 12-year freedom from thromboembolism was 98.88 ± 0.008% in group A and 99.74 ± 0.009% in group B (p = 0.041) (Fig. 2). However, when stratifying the population according to valve substitutes, all events occurred in patients with bileaflet valves, and Kaplan-Meier-estimated freedom from thromboembolism was 98.74 ± 0.006% in group A and 99.50 ± 0.003% in group B (p = 0.15).

One case of gastric hemorrhage (0.4%) was observed in group A, whilst one cerebral bleed and one colorectal bleed were observed in group B (0.5%). Hence, the 12-year freedom from hemorrhage was 99.63 ± 0.009% in group A and 99.48 ± 0.05 in group B (p = 0.69) (Fig. 3). These results were confirmed also in the subgroups of tilting-disk (100% freedom in group A; 99.45 ± 0.04% in group B; p = 0.72) and bileaflet valves (99.58 ± 0.007% freedom in group A; 99.5 ± 0.04% in group B; p = 0.77).

The mean interval between each INR control was 18.39 ± 1.90 days for group A and 21.78 ± 1.86 days for group B (p = 0.219), while the mean INR values in these groups were 2.14 ± 0.239 and 2.16 ± 0.211, respectively (p = 0.914).

With regard to non-structural dysfunction, one patient in group A and eight patients in group B experienced prosthetic valve dehiscence requiring valve replacement. However, freedom from perivalvular leak was similar in the two groups (99.63 ± 0.007% and 97.92 ± 0.004% in groups A and B respectively; p = 0.21) (Fig. 4). Similar results were observed for the tilting disc valve (100% freedom in group A; 96.17 ± 0.02% in group B; p = 0.35) and bileaflet valve (99.58 ± 0.005% freedom in group A; 99.50 ± 0.004% in group B; p = 0.99) subgroups. No cases of hemolysis were recorded in either group.

One patient in group A (0.37%) and six patients in group B (1.56%) developed postoperative endocarditis which required redo surgery. The 12-year freedom from endocarditis was 99.63 ± 0.003% in group A and 98.43 ± 0.002% in group B (p = 0.25) (Fig. 5). Within the tilting disk valve subgroup, freedom from endocarditis was 100% in group A and 97.80 ± 0.03% in group B (p = 0.44); the respective values in the bileaflet valve subgroup were 99.58 ± 0.001% and 99.00 ± 0.002% (p = 0.53).

Discussion

Prolonged life expectancy, wide diffusion of echocardiography and better survival following open-heart surgery have led to an increase in the number of patients requiring AVR in older age. The most suitable cardiac valve substitute in elderly patients remains a matter of debate, though out-of-range oral anticoagulation has been considered as a source of embolic and hemorrhagic complications in patients aged over 70 years (2-5).

Although good results have been reported with porcine valves, the overall durability of biological prostheses remains unknown despite improvements in design, fixation techniques and anti-mineralizing treatments. In fact, bioprostheses carry a higher incidence of reoperation than bileaflet prostheses (15). A prolonged life expectancy increases the likelihood of bioprosthetic degeneration in the very old patient, forcing reoperation for prosthetic valve replacement to be carried out at an extremely advanced age. Moreover, increased rates of calcium metabolism in the elderly may lead to early calcification of the bioprosthesis, especially for those patients in renal failure.

Although most studies have reported better results with bioprostheses than with mechanical valves in older patients (3-5), they have all introduced bias in their methods of selecting older patients as candidates to receive a mechanical valve.

Although bileaflet prostheses have shown excellent long-term durability, good hemodynamic performances and a low incidence of valve-related complications, several studies have reported a high incidence of hemorrhagic and thromboembolic complications in older patients receiving oral anticoagulant therapy (16,17). In one study of 565 patients taking warfarin for a variety of indications, age >65 years was found to be an independent risk factor for bleeding, with a cumulative incidence of bleeding at 48 months of 13% in those aged <65 years and 35% in those aged >65 years (18). However, these authors did not specify the target INR, and the rates of bleeding appeared much higher than were seen in the present study. In the report by Cannegieter et al. (19), a total of 1,608 patients who had mechanical valves and were receiving warfarin had an increased risk of bleeding with age. The incidence of bleeding was 2.5% per patient-year for those aged <50 years, 2.8% for those aged 50-69 years, and 5.6% for those aged >70 years.

Unfortunately, some studies did not specify the INR target (1,3,4), whereas other large series had an INR target of 4.5 (5,6). Moreover, evaluation of the incidence of valve-related embolic complications in elderly patients may be inaccurate because of the presence of risk factors for embolism other than the valve prosthesis.

The results of the Stroke Prevention in Atrial Fibrillation Study (3) showed that patients aged over 75 years who were receiving anticoagulation and had an INR <3 had a risk of bleeding similar to that of younger patients. In contrast, elderly patients with a target INR >3 had a three-fold increase in the rate of bleeding (3). These findings were confirmed by Burr et al. (20) in a series of 2,376 patients in whom the risk of bleeding was related to the intensity of anticoagulation, and not age. Other authors were unable to show any difference in terms of bleeding between series of patients who were either younger or older than 65 years (21). However, Horstkotte et al. (22) reported a low incidence of hemorrhagic and thrombotic complications in patients with bileaflet valves after adopting a low-intensity anticoagulation protocol.

Although in both patient groups of the present study, a low incidence of thromboembolic and hemorrhagic events was observed, the difference between the groups never reached statistical significance. The low complication rates encountered could be explained by the low thrombogenicity of bileaflet valves, the adoption of low-intensity anticoagulation, and an accurate control of patients in the anticoagulation clinic by a multi-specialty team. Nevertheless, a higher rate of thromboembolism which reached statistical significance was found among the elderly patients; this may be explained by the natural history of atherosclerotic disease, which often causes cerebral ischemic events in the elderly population. Unfortunately, it is difficult to identify whether a mechanical valve is the source of embolism when it is implanted in a patient with atherosclerotic disease. Furthermore, the study by Davies et al. (13), which incorporated patients with coronary artery disease and systemic atherosclerosis, may have overestimated the incidence of embolic complications. Nonetheless, the Kaplan-Meier-estimated freedoms from thromboembolism and bleeding measured in the present study were higher than those reported by Grunkemeier et al. (23). On the other hand, there is recent evidence emerging that meticulous control of anticoagulation (24) and low intensity anticoagulation with current generation bileaflet valves (25) can achieve very good clinical results.

A higher freedom from late mortality was also found among the younger patients of the present study, and this was consistent with findings published elsewhere (16). At the same time, no difference could be shown with regard to valve-related complications between young and elderly populations which had undergone AVR with a mechanical valve. Similar rates of complications were observed between the tilting disk and bileaflet valves, indicating that 'newer does not mean necessarily better'.

Study limitations

Among the limitations of the present study, the retrospective design may have increased the risk of missing events. Annual visits or interviews during follow up may have allowed patients time to forget symptoms which were compatible with a transient ischemic attack, or any other minor complication which might be relevant to the final outcome. The comparison of two groups with two different types of valve substitute may be of major concern, although the surgical technique, the surgeons and the anticoagulation policy utilized remained unchanged during the study period. The present series comprised a well-selected group of patients without coronary artery disease, and a follow up of almost 22 years. Moreover, no further bias was introduced by the choice of prosthesis, as the authors' policy was to implant exclusively tilting-disk valves until 1995, and bileaflet valves thereafter.

In conclusion, the study findings supported the use of mechanical heart valve prostheses in the elderly population, bearing in mind that life expectancy among these patients has increased in recent years. Consequently, the implantation of a mechanical valve, even in older patients, might avoid the risk of reoperation at a very advanced age.

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