Twenty-Year Single-Center Experience With the Medtronic Open Pivot Mechanical Heart Valve

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Background. Since May 1992 the Medtronic Open Pivot mechanical heart valve has been implanted routinely at the authors’ institution. The study aim was to analyze, retrospectively, the 20-year clinical results of the valve.

Methods. Between May 1992 and December 2011 a total of 1,520 valves was inserted into 1,382 consecutive patients (1,012 aortic, 473 mitral, 26 tricuspid, 9 pulmonary). The mean age of the patients was 61 ± 13.2 years. Preoperatively, 65% of the patients were in New York Heart Association (NYHA) class III or greater. Frequent comorbidities included atrial fibrillation (n = 419), coronary disease (n = 357), and diabetes (n = 255). The 99% complete follow-up totaled 10,527 patient-years (range 12 to 244 months).

Results. Ninety-day mortality was 5.2% (n = 73, 8 valve related). Of the 550 total deaths, 240 were cardiac and 36 valve related. Multivariate analysis selected age, NYHA III or greater, concomitant coronary revascularization, and respiratory insufficiency as risk factors for death. Renal failure was considered a risk factor in the aortic and atrial fibrillation in the mitral subgroup. Erratic international normalized ratio (INR), NYHA class III or greater, and non-sinus rhythm were risk factors for thromboembolism; likewise redo operations in the aortic subgroup. Erratic INR and age were risk factors for bleeding as were over-coagulation and coronary revascularization in the aortic subgroup and redo operations and renal failure in mitral patients.

Conclusions. This 20-year experience demonstrated excellent clinical outcomes with no structural valve failure. Odds ratio defined aortic patients as the lowest risk for adverse events. By contrast atrial fibrillation and elderly age, in combination with unstable anticoagulation, yielded the worst long-term results.


Since May 1992, the Open Pivot mechanical heart valve (OPMHV; Medtronic, Minneapolis, MN) was used at the University Hospital Ghent, when it first became commercially available [1]. In the open pivot design the leaflets slide over small convex spheres protruding into the valve housing in order to minimize flow disruption and turbulence, opposed to the classic hinge mechanisms with recesses or cavities. We also participated among other centers in the original Food and Drug Administration premarket study [2]. Subsequently, the clinical results of all consecutive OPMHV implants, as of 1992 with a minimum follow-up of 1 year, were analyzed retrospectively.

Material and Methods

Patients

Between May 1992 and December 2011 a total of 1,520 mechanical valves (1,012 aortic, 473 mitral, 26 tricuspid and 9 pulmonary), was inserted in 1,382 consecutive patients. The sites of implantation and sizes of all valves as the age distribution are shown in Figure 1. Overall, the mean age of all patients was 61 ± 13.2 years (range 3 months to 92 years). Preoperatively, 65% of the patients were highly symptomatic; these included 12 patients in New York Heart Association (NYHA) class V intubated and resuscitated. Calcific degeneration (71%) was the most commonly encountered aortic valve pathology. By contrast, 31% of the mitral and 55% of the tricuspid patients had a history of rheumatic valve disease still endemic in an important immigrant population. The most frequent comorbidities and characteristics of the patients are summarized in Table 1. Standard operative techniques were used as described in previous studies [1, 3]. This series included 272 (20%) redo valve operations, of which 17 were either second or third reoperations. In 142 patients (10%), a less-invasive approach, such as an upper sternotomy for aortic (n = 135) or a minithoracotomy for mitral valve replacement, was used. All patients were entered into a homemade database. The study was approved by the institution’s Ethical Committee (ECB6702006188) waiving the need for patient consent.

Statistical Analysis

As a measure of the early variability of the international normalized ratio (INR) value for each patient, an absolute value of the mean INR deviation recorded for each patient was employed. The INR was considered erratic if variability exceeded 1 standard deviation of the mean.
Variables entered into the risk factor analysis included the following: age as a continuous variable; gender; redo operations; rhythm; NYHA class; poor ventricular function; pulmonary hypertension; valve etiology; valve site; coronary artery bypass grafting (CABG); valve repair; chronic renal failure (CRF); chronic obstructive lung disease (COLD); paravalvular leakage; thrombosis; thromboembolism; bleeding; antiplatelet therapy, INR as a continuous variable; and erratic INR. Continuous variables were expressed as the mean ± standard deviation. The Student t test was used for parametric data and the Wilcoxon test for nonparametric data. The survival or event-free survival was analyzed using the Kaplan-Meier product-limit estimation. Predictors of early death were determined by logistic regression analysis. Univariate analysis selected age (p < 0.0001), redo operations (p < 0.0001), atrioventricular valve (p < 0.0001), NYHA class III or greater (p < 0.0001), and non-sinus rhythm (NSR) (p = 0.001), as overall risk factors for early death. In the subgroup analysis, pulmonary hypertension (p = 0.008) in mitral and concomitant CABG (p = 0.002) in aortic patients were considered independent risk factors. Multivariate analysis maintained atrioventricular valve position as the only significant risk factor (odds ratio [OR] 1.91, CI 1.88 to 1.97, p < 0.0001).

Follow-Up
Follow-up was 99% complete (range 12 to 244, average 112 ± 63.3 months), yielding 10,527 patient-years. Only 5 patients, all residing in foreign countries, were lost to follow-up. Fifty-eight patients were excluded from further follow-up; 17 patients after implantation of an additional valve, 2 patients underwent heart transplantation, while in 39 cases the original valve was replaced. In total, 887 (67%) of all survivors consulted the authors’ institution on a yearly basis. For the remaining, the clinical and laboratory data were acquired from general practitioners or specialists. A total of 106,665 INR values was obtained.
Twenty patients ceased anticoagulation; 8 because of repetitive hemorrhage and 6 patients were shifted to antiplatelet therapy due to advanced age, lack of compliance, or psychologic disorders. In the 6 remaining cases the decision was taken without evident reason.

Late Death

A total of 477 patients died during later follow-up (214 aortic, 179 mitral, 78 multiple valve, 5 tricuspid, and 1 pulmonary valve replacement). Forty-nine of these deaths (10%) had to be considered valve related, including sudden death (n = 20), anticoagulation-related hemorrhage (n = 14), prosthetic valve endocarditis (n = 7), thromboembolism (n = 5), and valve thrombosis (n = 3). In 6 patients the cause of death remained unknown. Other causes were cardiac related (n = 181) and noncardiac related (n = 244). Survival was highly significant (p < 0.0001) in favor of the aortic compared with the mitral valve group (Fig 2). Moreover, in the mitral valve group half of the patients (51%) died from cardiac failure compared with barely one-fourth in the aortic valve group (24%). Other valve subgroups (tricuspid and pulmonary) were too small to perform survival analyses. Age, NYHA III or greater, concomitant CABG, and COLD were maintained as overall risk factors for survival in multivariate analysis. Beside the former, in the aortic subgroup chronic renal failure was considered a truly independent risk factor while atrial fibrillation was the only additional risk factor in the mitral subgroup (Table 2).

Valve Thrombosis

A total of 29 episodes of valve thrombosis were recorded (5 aortic, 14 mitral, 6 tricuspid, 4 pulmonary). If stable on admission, patients (n = 20; 3 aortic, 8 mitral, 5 tricuspid, 4 pulmonary) were treated immediately with high doses of thrombolytics until the valves were successfully de-blocked (n = 15). Those patients in whom thrombolysis was unsuccessful (n = 5; 1 aortic, 2 mitral, 2 tricuspid) and those who were hemodynamically unstable (n = 9; 2 aortic, 6 mitral, 1 tricuspid) underwent urgent reoperation that resulted in the loss of 4 patients (2 aortic, 1 mitral, 1 tricuspid). In aortic patients incidences occurred (on average 90 ± 63.8 months after initial implantation) with all INR values in the subtherapeutic range of 1.0 to 1.4, in mitral patients (average 49 ± 43.7 months) with INR in the range of 1.0 to 2.9, and in tricuspid patients (average 28 ± 13.7 months) with INR in the range of 1 to 2.8. All but 1 incidence in pulmonary patients occurred less than 1 year after initial implantation with INR values between 1.1 and 2.3. In this young patient group all valves were successfully thrombolysed. In the tricuspid group all valves were replaced by bioprostheses, while all aortic and mitral patients received a new OPHMV. Independent risk factors for thrombosis were erratic INR (OR 0.958, CI 0.933 to 0.983, p < 0.0001) and right-sided valves (OR 0.091, CI 0.018 to 0.194, p < 0.0001).

Thromboembolism

A total of 126 episodes of embolism were recorded, including cerebrovascular accident (n = 73), reversible ischemic neurologic deficit (n = 2), transient ischemic attack (n = 41), and peripheral (n = 9) or coronary (n = 1)
embolisms. Average INR at the time of the incident was 1.7 ± 0.1, and most incidents occurred within the first 5 years (average 56 ± 60.8 months). Log-rank analysis showed a higher incidence of thromboembolism in the mitral group compared with the aortic group (Fig 3). Univariate analysis selected erratic INR ($p < 0.0001$), NSR ($p = 0.004$), NYHA class III or greater ($p = 0.005$), and mitral valve surgery ($p = 0.001$) as independent risk factors for thromboembolism. Multivariate analysis revealed erratic INR, NYHA class III or greater, and NSR as overall significant risk factors. Only redo operations in the aortic subgroup were considered an additional risk (Table 3).

Hemorrhage
A total of 106 events of major bleeding occurred during follow-up including cerebral (n = 35), gastrointestinal (n = 34), peripheral (n = 17), traumatic (n = 15), and intraabdominal (n = 5) hemorrhages. The average INR at the time of the incident was 3.8 ± 2.2. They occurred at random throughout the follow-up (average 71 ± 47.2 months). A total of 31 incidents occurred in combination with antiplatelet therapy. Log-rank analysis did not detect any difference between the aortic and mitral group (Fig 4). Univariate analysis selected age ($p < 0.0001$), erratic INR ($p < 0.0001$), NYHA class III or greater ($p = 0.004$), NSR ($p = 0.005$), redo operations ($p = 0.041$), and COLD ($p = 0.046$) as independent risk factors for bleeding, with a trend for pulmonary valve patients ($p = 0.052$). Multivariate analysis maintained erratic INR and age as significant risk factors with a trend for female gender. In the subgroup analysis higher INR values and CABG were considered risk factors for aortic patients, similar to redo operations and chronic renal failure in mitral patients (Table 4).

Composite Thrombosis, Embolism, and Bleeding
Only aortic and mitral subgroups contained sufficient data for statistical analysis. Average INR values recorded between 2 and 2.5 for aortic (Fig 5) and between 3 and 3.5 for mitral valves (Fig 6) resulted in the fewest number of combined adverse events.

Endocarditis
Twenty-two episodes of prosthetic valve endocarditis were diagnosed based on clinical and echocardiographic examinations; 4 patients succumbed to the disease, 3 were successfully treated with long-term intravenous antibiotics, and 15 patients were successfully reoperated and all received a new OPMHV (average of 65 ± 45.4 months).

Paravalvular Leakage and Hemolysis
Thirty-two patients presented with paravalvular leakage, of whom 7 presented with hemolysis, in the absence of endocarditis; 2 patients died before closure was attempted.
in 20 patients the leakage was successfully closed (18 open, 2 endovascular), and in 10 patients the initial valve was replaced.

Reoperation
Fifty patients were reoperated because of valve-related issues; paravalvular leakage (n = 20), endocarditis (n = 15), valve thrombosis (n = 14), and pannus formation (n = 2). Other operative indications included additional valve repair (n = 51), CABG (n = 19), and aortic aneurysm (n = 4).

Valve Structure Failure
To date, no structural valve deterioration has occurred in the entire series. A 3-month-old child outgrew her mitral prosthesis and was in need of a larger sized one.

Comment
The 20-year follow-up of this single-center OPMHV patient group was 100% complete for all patients residing in the country. The clinical results of this OPMHV series were at least comparable with other data published for mechanical valves similar to those used at the present authors’ institution during the same time frame [5].

Survival
Not surprisingly, incidences of early deaths were highest in the tricuspid (7% of the total) and mitral (6.5%) groups, as both atrioventricular valve positions also contained the sickest patients [6]. The overall long-term survival was quite acceptable in the entire series and comparable with that reported elsewhere [5, 7]. The results obtained were statistically superior in the aortic group compared with the mitral and multiple valve replacement groups. Matching curves for the overall population (2010 life expectancy = 80 years) showed better survival of aortic patients compared with citizens of the same age [8]. By contrast, mitral and tricuspid valves were considered risk factors for death although some authors reported fair midterm results in the mitral position [9]. The bias might lay in a higher incidence of rheumatic disease in our series. Apart from obvious risk factors for late death such as older age, poor ventricular function, and COLD, non-sinus rhythm and concomitant CABG also impair survival. Even in younger patients, atrial fibrillation is an important risk factor [10] and, indeed, a high statistical difference was found in survival between patients in sinus rhythm or not, in favor of the former [11]. Concomitant CABG definitely compromises survival even in series of elderly aortic bioprosthetic patients, according to some authors [12]. However, the causes of death in our elder patients were mainly non-valve related. Other authors reported excellent results with aortic mechanical valves in the elderly [13, 14]. This may refuel the discussion as to the choice between a mechanical or biologic prosthesis in elderly patients without the aforementioned comorbidities.

Thromboembolism
The incidence of thromboembolism in the present study corresponds favorably to that reported in other similar mechanical valve series [15]. A higher incidence of thromboembolism was detected in the mitral compared
with the aortic group, despite a lowering of the anticoagulation regime in the latter group. Only erratic INR and poor ventricular function were identified as significant risk factors for thromboembolism. Patients with an erratic INR were not correctly anticoagulated for their cardiac pathology; hence, the increase in incidents [16]. Those patients with decreased cardiac function and often enlarged ventricles are definitely more prone to thromboembolic events. In the aortic subgroup redo operations were considered a risk factor for thromboembolism. By contrast to other previous reports, NSR in case of correct anticoagulation was not maintained as an important risk factor even in combination with mitral valve surgery [17].

**Hemorrhage**

Mechanical valve patients, in general, carry a greater risk for anticoagulation-related hemorrhage than thromboembolic events and this is considered to be dependent on the type of anticoagulation regime [16, 18]. The incidences of hemorrhage in the present series compare favorably with those reported for other mechanical valve series, especially in the low intensive anticoagulation group. Only erratic INR and age were identified as significant risk factors. The latter highlights once again the vulnerability of older valve patients. Although aortic patients presented a significantly lesser incidence of bleeding compared with mitral patients, they had a 40% increased chance of bleeding if anticoagulation was outside the target zone. Moreover, in the aortic subgroup concomitant CABG and non-sinus rhythm were considered risk factors for bleeding. Bearing in mind that the age of aortic valve patients is likely to rise, with an increasing incidence of coronary revascularization and atrial fibrillation, care should be taken in order not to over treat the elderly. The addition of antiplatelet drugs might be useful in patients with a history of arteriosclerosis. As 31 incidents of hemorrhage occurred in combination with an antiplatelet therapy in predominantly elderly female patients, the usefulness must be evaluated individually for each patient [19].

**Adverse Events and Anticoagulation**

The key message remains anticoagulation control. Because most survivors progressed significantly during follow-up, this indicated that some of those patients became low risk over time and, as a consequence, required their anticoagulation regime to be adapted. Lower anticoagulation regimes definitely yield lower

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**Table 4. Multivariate Risk Factors for Bleeding**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>p Value</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
</tr>
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<tbody>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erratic INR</td>
<td>0.079</td>
<td>&lt;0.0001</td>
<td>0.037</td>
<td>0.167</td>
</tr>
<tr>
<td>Age</td>
<td>1.015</td>
<td>0.013</td>
<td>1.011</td>
<td>1.016</td>
</tr>
<tr>
<td>Gender</td>
<td>0.479</td>
<td>0.055</td>
<td>0.226</td>
<td>1.094</td>
</tr>
<tr>
<td>NSR</td>
<td>1.521</td>
<td>0.13</td>
<td>0.884</td>
<td>2.619</td>
</tr>
<tr>
<td>Aortic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erratic INR</td>
<td>0.078</td>
<td>&lt;0.0001</td>
<td>0.043</td>
<td>0.141</td>
</tr>
<tr>
<td>NSR</td>
<td>1.672</td>
<td>0.013</td>
<td>1.114</td>
<td>2.509</td>
</tr>
<tr>
<td>Age</td>
<td>1.038</td>
<td>0.019</td>
<td>1.006</td>
<td>1.072</td>
</tr>
<tr>
<td>INR</td>
<td>1.395</td>
<td>0.013</td>
<td>1.072</td>
<td>1.815</td>
</tr>
<tr>
<td>CABG</td>
<td>0.529</td>
<td>0.032</td>
<td>0.296</td>
<td>0.947</td>
</tr>
<tr>
<td>Gender</td>
<td>0.547</td>
<td>0.087</td>
<td>0.275</td>
<td>1.092</td>
</tr>
<tr>
<td>Mitral</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erratic INR</td>
<td>0.125</td>
<td>&lt;0.0001</td>
<td>0.040</td>
<td>0.394</td>
</tr>
<tr>
<td>Redo</td>
<td>0.312</td>
<td>0.038</td>
<td>0.104</td>
<td>0.940</td>
</tr>
<tr>
<td>CRF</td>
<td>0.114</td>
<td>0.047</td>
<td>0.013</td>
<td>0.975</td>
</tr>
<tr>
<td>Age</td>
<td>1.054</td>
<td>0.057</td>
<td>0.998</td>
<td>1.113</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; CI = confidence interval; CRF = chronic renal failure; INR = international normalized ratios; OR = odds ratio.
incidences of bleeding, as demonstrated in previous studies [20, 21]. Nevertheless, in our series aortic valve patients still carry more risk for anticoagulation-related bleeding as shown by the right-shift of the OR calculation curve. This means that there is still a significant difference between the intended (low) and real (too high) anticoagulation regimes. Because all aortic valve blockages occurred in patients completely off anticoagulation one cannot recommend the INR to drop below 1.5. For the non-aortic valves the focus still stands on the thromboembolic complications. Particularly valve thrombosis remains a serious problem when INR values are outside the target zones. Of all episodes of valve thrombosis encountered, 30% occurred in the right-sided position [22]. The odds of thrombosis were calculated fourfold in the right-sided position compared with the left. One has to realize that 1 out of 5 of all right-sided valves in a young patient group (mean age = 31 years) became blocked. It appears far more difficult to stabilize anticoagulation regimes in a young and sometimes non-compliant patient group [23]. For the mitral valve adverse events are quite acceptable if patients remain within the INR target range between 2.5 and 3.5. However, risk stratification will be strongly influenced by
increasing age (bleeding) or decreasing ventricular function (thromboembolism). It is for all these reasons that the use of a mechanical valve cannot be advocated if a correct and stable anticoagulation cannot be guaranteed.

**Study Limitations**

Initially prospective by nature during the FDA premarket study the main limitation of this single-center study is its retrospective nature. Although follow-up was almost complete, only 67% of all patients were examined routinely at the authors’ institution, with a possible under-reporting of adverse events for the remaining.

In conclusion, this series of OPMHV implants demonstrated good clinical results over a period of 20 years. Moreover, to date no valve structural failure has been identified. The position of the prosthesis is clearly important, with a poorer prognosis for patients receiving mitral or tricuspid valves. The low thromboembolic rate allows the maintenance of a low INR in a selected patient population (mainly aortic), with a good outcome and without increasing the incidence of thromboembolic events even in elderly patients. By contrast, right-sided valves are prone to thrombosis and require complete and rigorous anticoagulation especially in younger patients.

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**References**