The Heart Surgery Forum #2015-1252
18 (4), 2015 [Epub August 2015]
doi: 10.1532/hsf.1252

Online address: http://journal.hsforum.com

The St. Jude Toronto Stentless Bioprosthesis: Up to 20 Years Follow-Up in Younger Patients

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ABSTRACT

Background: A retrospective long-term evaluation of the St. Jude Toronto stentless bioprosthesis in patients aged 60 years or younger.

Methods: From 1994 to 1997, 50 patients underwent aortic valve replacement with the prosthesis. The patient mean age at surgery was 54.5 years (±6.3 years). Follow-up data was acquired by patient file research and telephone interviews. Morbidity and mortality were evaluated with time-to-event analyses using the Kaplan-Meier-method. The log-rank test was used to determine influencing factors for long-term survival and reoperation.

Results: Mean follow-up was 13.5 years (±6.3 years) with a total follow-up of 661.8 patient years and a maximum of 20 years. Follow-up was 97.8 percent completed. Associated procedures were performed in 12 patients (24 percent), including coronary artery bypass grafting, mitral valve replacement and replacement of the ascending aorta. Freedom from reoperation at 10 years and 15 years was 76.0 ± 6.7 percent and 44.1 ± 8.9 percent, respectively. Reoperations (N=26) began 4.4 years after implantation and were necessary due to valve degeneration with regurgitation (79.2 percent of the cases), stenosis (12.5 percent), endocarditis (4.2 percent), and sinus valsalva aneurysm (4.2 percent). The log-rank test revealed that only body mass index (BMI) of greater than 25 lowered freedom from reoperation, while renal dysfunction, diabetes mellitus and arterial hypertension did not. Overall long-term survival at 10 years and 20 years was 82.3 ± 5.7 percent and 49.9 ± 8.9 percent, respectively.

Conclusion: In younger patients, the Toronto-bioprosthesis provided reliable long-term survival despite limited durability.

INTRODUCTION

The St. Jude Medical (SJM) Toronto stentless aortic valve was introduced in 1991. It received the CE mark in 1995 and FDA approval in 1997. It is one of the first stentless aortic valves, offering a superior hemodynamic behavior facilitated by an enlarged orifice area compared with stented aortic valves [Kunadian 2007]. Due to this advantage, left ventricular mass regression [Walther 1999] and mid-term survival [Lehmann 2007] were significantly superior compared with conventional stented bioprostheses. In addition, an increased durability of the bioprosthesis could be expected, mediated by decreased mechanical stress on the cusps of the valve. Especially younger patients, in whom structural deterioration occurs faster [Hammermeister 2000] and the cumulated risk of reoperation leads to the recommendation of mechanical prostheses [Nishimura 2014], could benefit. Various studies showed controversial results regarding the durability of different stentless prostheses [Kobayashi 2011]. David et al reported optimal patient survival but suboptimal valve durability for the Toronto bioprosthesis, especially for patients under 65 years [David 2008]. However, detailed long-term results with the SJM Toronto stentless aortic valve in younger patients have not yet been published.

MATERIALS AND METHODS

From 1994 to 1997, 50 patients age ≤ 60 years underwent aortic valve replacement with the SJM Toronto bioprosthesis. A bioprosthesis was chosen in these patients due to contraindications to oral anticoagulation or due to patient preference. All patients gave written informed consent after detailed discussion. The operation was performed according to institutional standards [Konertz 1994; Sidiropoulos 1997]. After approval of the study by the local ethics committee, follow-up data was acquired by patient file research and telephone interview. All data was analyzed with IBM SPSS Statistics version 22. Descriptive statistics are reported as the mean ± standard deviation for continuous variables and as absolute frequencies and percentages for categorical variables, unless otherwise noted. Morbidity and mortality were evaluated with time-to-event analyses using the Kaplan-Meier method. Univariate curve comparisons were performed using the log-rank test. All P values were two-sided. Statistical significance was set at a P value of less than 0.05. To create a control group, age- and gender-matched survival estimates of the general German population were obtained from the "Human Lifetable Database" [Statistisches 1993].

Received April 28, 2015; accepted July 18, 2015.

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Table 1. Baseline Characteristics

Characteristic	Value	Fraction
Number of patients	50	
Mean age	54.5 (±6.3 years)	
Range	29 years-60 years	
Sex		
Male	39	78 percent
BMI	26.3 ± 4.0	
NYHA classification		
I	4	8 percent
II	15	30 percent
III	25	50 percent
IV	5	10 percent
Left ventricular ejection fraction	50.4 ± 15.3 percent	
Normal (>50 percent)	34	68 percent
Moderately impaired (30 percent-50 percent)	11	22 percent
Profoundly impaired (<30 percent)	5	10 percent
Active endocarditis	2	4 percent
Comorbidities		
Arterial hypertension	34	68 percent
Diabetes mellitus	6	12 percent
Renal dysfunction	26	52 percent
Dialysis	2	4 percent
Atrial fibrillation	1	2 percent
Chronic obstructive lung disease	5	10 percent
Peripheral arterial disease	4	8 percent
Pulmonic hypertension (systolic pressure > 60 mmHg)	10	20 percent
Coronary heart disease	17	34 percent
Ascending aortic aneurysm	12	24 percent

Table 2. Operative Data

Characteristic	Value	Fraction
Isolated aortic valve replacement	38	76 percent
Combined procedures	12	24 percent
Coronary revascularization	7	14 percent
Further valve procedure	4	8 percent
Replacement of ascending aorta	2	4 percent
Surgical approach		
Median sternotomy	46	92 percent
Partial upper sternotomy	4	8 percent
Operation time in minutes	253.3 ± 278.9	
Isolated procedures	192.0 ± 39.4	
Combined procedures	416.9 ± 509.4	
Cardiopulmonary bypass time	114.8 ± 38.8	
Isolated procedures	104.4 ± 24.8	
Combined procedures	142.8 ± 54.5	
Aortic cross clamp time	85.1 ± 26.2	
Isolated procedures	79.3 ± 24.2	
Combined procedures	100.5 ± 26.0	
Implanted valve sizes in mm	27.7 ± 1.4	
25	7	14 percent
27	18	36 percent
29	25	50 percent

RESULTS

Mean follow-up was 13.5 years (±6.3 years) with a total follow up of 661.8 patient years and a maximum of 20 years. Follow up was 97.8 percent completed. The patient mean age at surgery was 54.5 years (±6.3 years). Patient baseline characteristics are listed in Table 1. Operative data are presented in Table 2.

Freedom from reoperation at 10 years and 15 years was 76.0 percent ±6.7 percent and 44.1 percent ±8.9 percent, respectively (Figure 1).

Reoperation was performed in 26 cases, including two transarterial aortic valve interventions (TAVI), with the first procedure after 4.4 years. Indications were valve degeneration resulting in regurgitation in 79.2 percent of the cases and stenosis in 12.5 percent of the cases, respectively. Additionally, reoperations were caused by endocarditis in 4.2 percent of the cases and sinus valsalva aneurysm in 4.2 percent of the cases. Univariate analysis revealed only BMI greater than 25 ($P = 0.04$) as a factor associated with reoperation, while renal dysfunction, diabetes mellitus and arterial hypertension were not. Reoperations were associated with a hospital mortality of 3.8 percent.

Long-term survival at 10 years and 20 years was 82.3 percent ±5.7 percent and 49.9 percent ±8.9 percent, respectively (Figure 2).

Reduced survival occurred in patients with profoundly impaired left ventricular function ($P = 0.03$), chronic obstructive pulmonary disease ($P < 0.01$), or pulmonary hypertension ($P < 0.01$). Without these high risk patients, long-term survival at 10 years and 20 years was 87.9 percent ±5.7 percent and 59.0 percent ±10.1 percent, respectively (Figure 3). Comparison to the age- and gender-matched general German population revealed an impaired long-term survival after aortic valve replacement for the study population. However, for those patients without the above specified risk factors, long-term survival was very close to the general population (Figure 3).

DISCUSSION

The search for the ideal heart valve prosthesis in the adult patient is an ongoing and challenging issue. The ideal

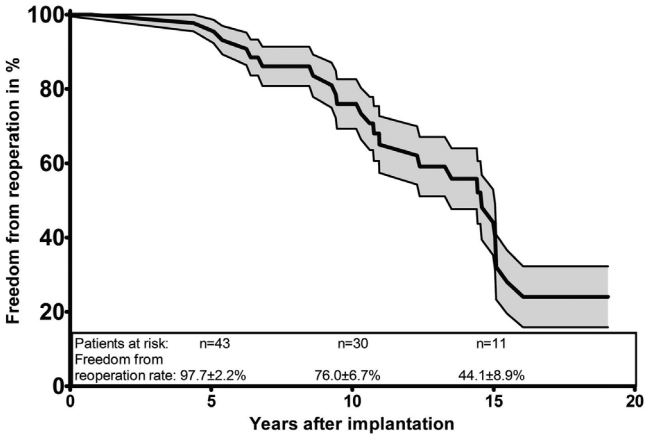

Figure 1. Freedom from aortic valve reoperation after implantation of the SJM Toronto (shaded area = standard error).

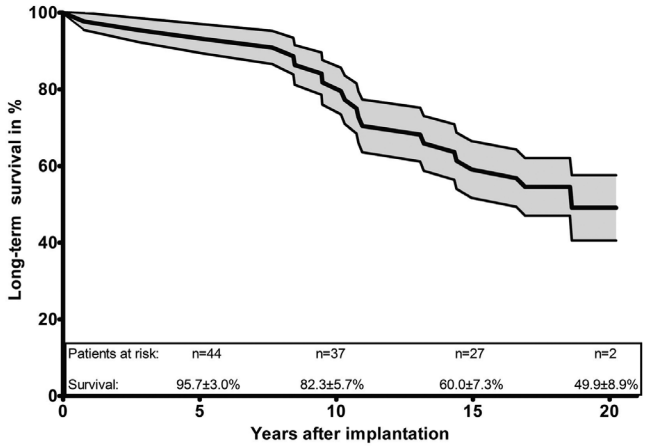

Figure 2. Long-term survival of the study cohort (shaded area = standard error).

device would be a simply, implantable prosthesis with excellent hemodynamic properties, unlimited durability and low thrombogenic potential so that anticoagulants are unnecessary. But no such device exists. Despite their high durability mechanical valves, lack biocompatibility with the consequence of thrombogenicity and pannus formation. Bioprostheses show better hemodynamics (particularly stentless aortic valves [Christ 2014]) and biocompatibility, but lack durability. Due to constant development of bioprosthetic valves in recent decades, durability has improved. Therefore, recent guidelines adjusted the recommendation for the implantation of biological aortic valves from 65 years to 60 years [Bonow 1998; Rahimtoola 2010].

Durability of bioprostheses is strongly dependent on the patient's age. The younger the patients are, the earlier the valve degenerates [Hammermeister 2000]. Published data regarding younger patients is divergent. For example, Hammermeister et al published freedom-from-reoperation rates at 10 years and 15 years in patients ≤60 years of 84 percent

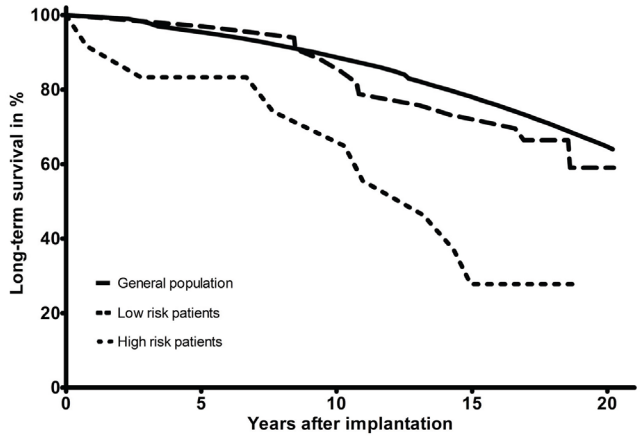

Figure 3. Long-term survival with risk adjustment (profoundly impaired left ventricular function, severe pulmonary hypertension, chronic obstructive pulmonary disease) compared to age- and gender-matched general population.

and 71 percent [Hammermeister 2000]. Valfre et al reported freedom-from-reoperation rates of the Hancock II bioprosthesis at 10 years and 15 years for in patients ≤60 years of 87.4 percent and 62.6 percent [Valfre 2010]. Welke et al published freedom-from-reoperation rates of the Carpentier-Edwards pericardial valve in patients aged 50 years until 65 years at 10 percent and 15 years of 68 percent and 41 percent [Welke 2011]. Recently, Une et al published long-term results of the Hancock II bioprosthesis with freedom-from-reoperation at 15 years of 60 percent for patients aged 50 years to 60 years [Une 2014]. For the Edward Prima Plus stentless bioprosthesis, our group showed a 10-year and 14-year freedom-from-reoperation rate in patients with a mean age of 53.1 years of 85.6 percent and 65.2 percent [Christ 2014] However, despite the divergence of this data, the results of the SJM Toronto in our study population are inferior. Of special concern is the early appearance of structural valve degeneration at 4.4 years after the operation with an almost linear curve progression of reoperations after this interval (Fig. 1). Despite this limited durability, long-term survival of the study cohort is comparable with other studies involving younger patients. For example, Oxenham et al [Oxenham 2003] published a 20-year survival for biological and mechanical prostheses of 31.1 percent and 28.4 percent, respectively; Ruel et al [Ruel 2007] reported 65.5 percent and 52.3 percent, respectively. Une et al published an actuarial survival after 20 years with a Hancock II bioprosthesis of 48.7 percent for patients age 50 years to 60 years [Une 2014]. Our group showed in a larger cohort with various stentless bioprostheses a 15-year survival of 55.8 percent [Christ 2013]. Long-term survival with the SJM Toronto in this report is within the range of these studies. The previously reported faster regression of left ventricular mass and concomitant recovery of left ventricular function after implantation of the SJM Toronto [Walther 1999] does not considerably support long-term survival in younger patients. Alternatively, the above described impaired durability may counterweight this advantage. However, the

comparison with other studies is restricted due to differences in composition of the study population, time of study-implementation, and type of implanted prosthesis. Therefore, comparison with the age- and gender-matched general population can be an appropriate way to evaluate long-term survival. Of course, this comparison also is influenced by the distinct study population. Severe co-morbidities, like profoundly impaired left ventricular function, chronic obstructive lung disease, and severe pulmonary hypertension have influenced long-term survival in this study. Additionally, Welke et al showed that older patients had an even superior life expectancy than their peers, while in younger patients a detrimental effect of aortic valve replacement on long-term survival was seen [Welke 2011]. Figure 1 shows the comparison of the study cohort with the age- and gender-matched general population and shows an impaired survival after implantation of the SJM Toronto. However, after excluding patients with severe comorbidities, patient survival is very similar to the general population (Figure 3). This fact reveals that the elevated risk of reoperation with the SJM Toronto does not impact long-term survival considerably, likewise Ruel et al had shown for stented bioprostheses [Ruel 2007]. Of course, the low hospital mortality after reoperations in the study cohort did influence this result extensively.

Standard therapy for aortic valve replacement in younger patients is still the mechanical heart valve [Rahimtoola 2010]. These valves are associated with lower reoperation rates, but higher rates of bleeding and stroke [Chiang 2014; Hammermeister 2000; Oxenham 2003; Ruel 2007] Long-term results of mechanical prostheses regarding survival tend to be comparable to bioprostheses [Chiang 2014; Hammermeister 2000; Oxenham 2003; Ruel 2007]. Regarding these similar survival rates even in younger patients [Chiang 2014], the different risks between mechanical and biological prostheses and their influence on survival seem to be counterbalanced. Consequently, biological prostheses could be used as an equivalent to mechanical prostheses in younger patients with respect to patient comorbidities and preference. Especially, if we keep in mind that by using more durable bioprostheses, long-term survival may rise even further. Additionally, one must consider the recent improvement and future development of TAVI. The concept of using bioprostheses in younger patients – and later TAVI in failing bioprostheses – is promising and should be endorsed.

Currently, a rapid development can be seen in the field of biological aortic valve prostheses, with newly introduced devices every year. The production of some devices was even stopped before long-term results were obtainable. But, long-term evaluation still is absolutely necessary and mandatory for every new device.

CONCLUSION

The SJM Toronto aortic bioprosthesis demonstrated a limited durability in patients aged ≤60 years. Despite this limitation, an acceptable long-term survival was found. This leads to the assumption that the cumulated risk of reoperation is not significantly lowering long-term survival. Even though the SJM Toronto showed limited durability compared with other bioprostheses, the use of bioprosthesis in general can be an alternative to mechanical valves in patients aged 60 years or younger, based on comparable long-term survival.

LIMITATIONS

The major limitation was the retrospective nature of our study, which could have led to an underestimation of the complication rates owing to patient misinterpretation or recall bias. Additionally, the composition and small size of the study population can lead to a bias of long-term results. Despite these limitations, one must consider the fact that a controlled randomized trial in young patients involving non-standard therapy is ethically very difficult to perform, if not impossible. Furthermore, the Toronto bioprosthesis is no longer commercially available. But, the long-term results of this study are helpful with clarifying therapeutic options in younger patients.

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