Long-term Outcomes Following Reoperations for Stentless Aortic Valves.

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Abstract

Background: There is limited data on the long-term outcomes in patients who have undergone a reoperation following a failing stentless aortic valve. **Methods**: Between 2006-2016, a retrospective analysis was performed on 24 patients that underwent open aortic valve replacement surgery for a failed stentless aortic valve prosthesis at Health Sciences North, Sudbury, Ontario, Canada. The primary outcome was low mortality from cardiac related deaths after 5 years. **Results**: All patients underwent an insertion of a Medtronic Freestyle bioprosthesis implanted in the modified subcoronary technique for their initial operation. The interval from the first operation to the stentless redo surgery ranged from 6-13 years. Aortic valve reoperation was performed for structural valve deterioration in 96% (n= 23) of the cases. Reoperations involved a removal of the stented valve leaflets and stented valve-in-valve implantation in 20% (n= 5) of the cases, with the remaining cases requiring complete removal of the stentless prosthesis and aortic valve replacement. In those where a complete removal of the stentless valve was possible (n=19), there was no disruption of the native aortic root, and a 0% conversion to a Bentall procedure. There was no intraoperative mortality. The 30-day and 10-year operative mortality was 4% and 16%, respectively. **Conclusions**: Redo surgery for failing stentless valves can be done with relatively low-risk and with acceptable long-term outcomes without resorting to root replacement techniques.

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Running Head : Reoperations for Stentless Valves.

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AbstractBackground: There is limited data on the long-term outcomes in patients who have undergone a reoperation following a failing stentless aortic valve.**Methods**: Between 2006-2016, a retrospective analysis was performed on 24 patients that underwent open aortic valve replacement surgery for a failed stentless aortic valve prosthesis at Health Sciences North, Sudbury, Ontario, Canada. The primary outcome was low mortality from cardiac related deaths after 5 years.**Results**: All patients underwent an insertion of a Medtronic Freestyle bioprosthesis implanted in the modified subcoronary technique for their initial operation. The interval from the first operation to the stentless redo surgery ranged from 6-13 years. Aortic valve reoperation was performed for structural valve deterioration in 96% (n= 23) of the cases. Reoperations involved a removal of the stented valve leaflets and stented valve-in-valve implantation in 20% (n= 5) of the cases, with the remaining cases requiring complete removal of the stentless prosthesis and aortic valve replacement. In those where a complete removal of the stentless valve was possible (n=19), there was no disruption of the native aortic root, and a 0% conversion to a Bentall procedure. There was no intraoperative mortality. The 30-day and 10-year operative mortality was 4% and 16%, respectively.**Conclusions**: Redo surgery for failing stentless valves can be done with relatively low-risk and with acceptable long-term outcomes without resorting to root replacement techniques.**Introduction**: The Freestyle Stentless Porcine Valve has been used since 1993[1] as a third generation porcine valve. Compared to conventional stented bioprostheses, stentless valves provided better hemodynamics with a larger effective orifice area with respect to their valve size.[2] This allowed for improved left ventricular function secondary to left ventricular mass regression[3-5] and reduced incidences of patient-prosthesis mismatch. However, despite the advantages, historically the utilization of stentless valves has been controversial. The benefits in hemodynamics have been negatively influenced by the technical difficulty in implanting the valve, with a longer learning curve and longer ischemic time.[6] There are multiple options for implanting a Freestyle valve, including the root inclusion technique, an isolated complete subcoronary technique, or a full root replacement.[7]As the use of the stentless valve gained popularity, it was reasonable to accept that these valves would eventually degenerate, leading to stentless valve reoperations. In addition to the technical difficulty of implantation, reintervention is also widely regarded as a greater surgical challenge. Over two decades at our center, Health Sciences North, Sudbury, Ontario, over 300 Medtronic Freestyle stentless valves were inserted. Many patients did return for reoperations. Prior to the broad introduction of transcatheter aortic valve replacement (TAVR), all patients returned to the operating room for reintervention. Subesequent to 2016, with the introduction of catheter-based aortic valve replacement in our center, valve-in-valve TAVR soon evolved as another treatment option.[8] This option, however, also presented technical challenges, with the lack of radio-opaque markers to guide trans-catheter valve implantation. The objective of this study was to evaluate the short- and long-term outcomes of patients who underwent a stentless valve reoperation at our center, including their perioperative outcomes, operative mortality, and long-term survival following aortic valve reoperation following an initial implantation of a Medtronic Freestyle stentless valve.**Material and Methods**:**Study Approval and Design**: This study was approved by the Institutional Review Board at Health Sciences North (Sudbury, Ontario) and was in compliance with Health Insurance Portability and Accountability Act regulations. Operative reports and medical records were reviewed by a single cardiac surgeon (BB) to confirm that these patients all had received a Medtronic Freestyle stentless valve (Medtronic Inc., Minneapolis, MN, USA) for their initial operation and had received a reoperation for a failed stentless valve. Long-term survival was obtained through medical record review and supplemented with telephone calls with 100% follow-up of all patients. All reoperations for stentless valves were performed by the same team of cardiac surgeons (BB

and DJM).**Patient Selection:**From 2006-2016, all consecutive patients (N=24) who underwent open reoperative aortic valve replacement (AVR) for a failing stentless valve were enrolled in this study.**Operative Technique**: In all cases, surgery was performed via redo median sternotomy. Prior cannulation of the femoral artery or subclavian artery was used only when the right ventricle was in close proximity to the posterior table of the sternum. Cardiopulmonary bypass, with standard ascending aortic cannulation, the aortic arch or femoral artery and the right atrium or femoral vein, was used with systemic hypothermia of 32^0C. Myocardial protection was achieved with intermittent antegrade cold blood cardioplegia. All concomitant procedures were performed according to standard techniques. Intraoperatively, the size of the stentless valve inserted in the first operation often determined whether a valve-in-valve technique would be feasible. We found that larger stentless valves (size 25 or greater) often allowed for an adequately sized stented valve to be inserted after removal of the torn leaflet tissue and the pannus in the left ventricular outflow tract (LVOT). When the stentless valve was of a smaller size (size 23 or smaller), meticulous removal of the entire valve was necessary before an appropriately sized valve was inserted. In our practice, this decision to proceed with complete removal of the stentless valve , or perform a valve-in-valve was often made intraoperatively. Factors such as the amount of calcification of the stentless casing (particularly in the area of the noncoronary sinus, the quality of the native tissue, the proximity of the subcoronary suture line to the ostium of the coronaries, and the annular size of the stentless bioprosthesis played a role in this decision. Additionally, if the patient had significant comorbidities and the perceived length of time required on cardiopulmonary bypass to completely explant the entire stentless valve was considered too lengthy, we would choose a more conservative, quicker surgical strategy such as a valve-in-valve implant. When the stentless was particularly adherent to the native root, we found that starting the removal in the area of the non-coronary sinus was the most forgiving strategy. If the wrong tissue plane between the stentless valve and the native aortic root was entered here, a pericardial or bovine patch repair of the root could be performed more easily than in other areas of the disrupted root. Stentless extraction was typically a lengthy process, requiring great care and patience to preserve the integrity of the native aortic root, and with strict adherence to myocardial protection. Fine Penfield dissectors were employed for much of this process and supported with sharp dissection when necessary. Great caution was used in the subcoronary areas where the margin of the stentless bioprosthesis was extremely intimate with the ostium of the coronary arteries. Removal of the stentless valve in this area often left a ridge or flap of tissue near the inferior margin of the main coronary artery. In such instances this area was reinforced with several 7-0 prolene sutures. When a surgical valve-in-valve technique was performed, 4-0 Ethibond pledgeted sutures were used, and the fragile tissue of the remaining porcine annulus was avoided. In these instances the native aortic annulus was covered by the stentless sewing cuff and therefore not visible. Sutures were placed just below the inferior margin of the cuff and exited through the stentless valve sewing ring ensuring good anchoring of the stented prosthesis that was being implanted. Maintenance cold blood cardioplegia at 8-12 degrees Celsius was given selectively into the coronary ostia at twenty-minute intervals for the duration of the procedure.**Statistical Analysis**: Descriptive statistics were computed for the study cohort. Continuous variables were summarized by reporting the median and ranges. Categorical variables were reported as N (%) in frequency tables.**Results**: All patients (n=24) received a Freestyle Aortic Root Bioprosthesis for their initial operation due to disease from aortic valve pathology. All patients had their initial stentless surgery performed by the same surgeon at the Sudbury Regional Hospital, Sudbury, Ontario. All patients had their initial valve inserted with the modified subcoronary implantation technique. Preoperative status and comorbidities of the patients are outlined in Table 1. The stentless valve required reoperation on average after 9.8 years, with aortic insufficiency as the mode of failure in all cases except one. Intraoperative examination of the stentless valve and the aortic root revealed a linear tear at or near the base of one of the leaflets. The leaflets, although demonstrating remarkably little calcification, were extremely brittle with minimal traction or manipulation. There were no serious adverse events which occurred during re-sternotomy. All five patients who underwent the valve-in-valve technique received a biological tissue valve. 37.5 % (N=9) of patients required a concomitant procedure, predominantly coronary artery bypass grafting. Surgical variables and characteristics are outlined in Table 2. In patients where the stentless valve was explanted (N=15), the root was preserved in 100% of cases, with no need for a conversion to a Bentall procedure. Of the 24 patients who underwent this procedure, 10 received mechanical valves and

14 received a stented aortic prosthesis. In 5 of these patients, the stentless leaflets were removed, and the new valve was sutured to the native annulus (valve-in-valve technique). Urgent surgeries were required in 20.8% (n= 5) of the cases, mostly due to hemodynamic compromise or endocarditis. Mean cross-clamp time was 156 minutes. 30- day outcomes revealed no post-operative myocardial infarctions, or strokes, with only one patient suffering from new onset renal failure. Hospital length of stay averaged 7.5 days. The single in-hospital mortality was an immunocompromised patient presenting with Staphylococcus aureus endocarditis involving the Freestyle valve. Intraoperatively, the valve was successfully explanted, however the patient required a concomitant repair of a ventricular septal defect, reconstruction of the left ventricular outflow tract, and concomitant coronary artery bypass grafting to the left anterior descending artery. The patient had a significantly lengthy cardiopulmonary bypass run, with post-operative coagulopathy and left ventricular dysfunction, necessitating mediastinal re-exploration twice. The patient subsequently expired on post-operative day 5 of multi-system organ failure. Follow-up at 2 months post-operatively and then once annually was performed. All patients had improved functional status with all in NYHA Functional Classes I-II. None of the valve-in-valve patients had a measurable paraprosthetic leak and two of the patients ultimately required re-interventions on their replaced aortic valves. One patient had a TAVR procedure performed eightt years later, and one patient underwent a third sternotomy with a tissue aortic valve replacement. Procedural outcomes are detailed in Table 3. The 5-year mortality was 4% (n=1), who was the in-hospitality mortality identified above. The 10-year mortality was 16.7% (n=4). Causes of death included two patients with acute renal failure and encephalopathy, and one patient with Staphylococcus aureus endocarditis and acute renal failure. The 10-year all-cause mortality was 33% (n=8). Of these 4 deaths, 2 were secondary to metastatic cancers and 2 were listed as death secondary to multi-system organ failures.**Comment**: In this study, we summarized a retrospective review of a single surgical team's experience of reoperative surgery for failing, predominantly regurgitant, stentless valves. The primary findings of the study are as follows. The 30-day mortality was 4% (1/24) for all patients, and the long-term cardiac 10-year mortality was 16% (4/24) for all patients. The primary operative method involved complete explantation of the stentless xenograft, without incurring any damage to the root necessitating the need for a complete root replacement. In their own retrospective series, Borger and colleagues[9] reported an operative mortality of 11% with 63% of patients requiring aortic root replacements, despite specifically attempting to preserve the pre-existing native aortic root. In a similar study, Boning and colleagues[10] reported a 21% (5/24) 30-day operative mortality following their stentless reoperations, which was higher than the 4% operative mortality in their patients who had a stented aortic valve reoperation. Our only early mortality was in a patient who had an active infection of their stentless valve, highlighting the further complexity in removing not only the stentless valve, but adjacent structures which were involved in the infectious process. In our hands, while all attempts were made to completely remove the stentless valve, if annular dimensions were adequate in an otherwise relatively higher risk patient, a stented valve was implanted within the stentless casing. Similar to other centres[8], our reoperative approach to stentless valves has evolved over the years, with the potential role for valve-in-valve TAVR in this particular setting. However, several difficulties and potential complications still have to be considered with this approach: the initial implantation technique of the stentless valve, the bulky nature of the leaflet tissue, lack of annular calcification, device malpositioning due to lack of anatomic markers to guide landing zones and coronary obstruction.[11-13]Future studies will need to analyze the long term impact of valve-in-valve TAVR prior to committing to this approach for stentless reoperations as a primary approach.

Limitations:

The primary limitation of our study is its retrospective nature and small sample size. In combination with the small sample size, the very low event rate of major adverse events including death makes statistical analysis difficult. However, few studies report longitudinal and complete follow-up of all patients up to 10 years. While we acknowledge the limitations of this study, we still feel the results indicate that redo surgery for a failing stentless valve can still be considered a reasonable option with good long-term outcomes.**Acknowledgements/Disclosures:**None.**Author Contributions:**Bindu Bittira: Article concept and design, data analysis and interpretation, drafting of original article and critical revision, longitudinal data collection. Derek MacDonald: Article concept and design, data analysis and interpretation, drafting

of original article and critical revision, longitudinal data collection. Mohammed Shurrab: Critical revision of article. Stacey Santi: Data analysis and interpretation, review of article. Sarah Grieve: Data collection.**References**:

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Table 1. Population characteristics, preoperative status and comorbidities of patients who received stentless valve reoperation (N=24)

	N (%)	**N (%)**
Sex	Sex	Sex
Male	18 (75.0) 6 (25.0)	18 (75.0) 6 (25.0)
Female		
Smoking status	Smoking status	Smoking status
Smoker	7 (29.2) 17 (70.8)	7 (29.2) 17 (70.8)
Non-smoker		
Age/Age at death (years)	71.5 (median) (range 58-92)	71.5 (median) (range 58-92)
Age at first operation (years)	53.5 (median) (range 40-69)	53.5 (median) (range 40-69)
Age at second operation (years)	62.5 (median) (range 47-82)	62.5 (median) (range 47-82)
Time between first and second operation (years)	9.8 (average) (range 6-13)	9.8 (average) (range 6-13)

	N (%)	**N (%)**
New York Heart Association (NYHA) Functional Classification Scale	New York Heart Association (NYHA) Functional Classification Scale	New York Heart Association (NYHA) Functional Classification Scale
I	0 (0) 3 (12.5) 14 (58.3) 6 (25.0)	0 (0) 3 (12.5) 14 (58.3) 6 (25.0)
II	1 (4.2)	1 (4.2)
III		
IV		
n/a		
LV Grade (1-4)	LV Grade (1-4)	LV Grade (1-4)
1	18 (75.0) 6 (25.0) n/a n/a	18 (75.0) 6 (25.0) n/a n/a
2		
3		
4		
	No	**Yes**
Comorbidities	**N (%)**	**N (%)**
Hypertension	6 (25.0)	18 (75.0)
Cholesterol	13 (54.2)	11 (45.8)
Diabetes mellitus	22 (91.7)	2 (8.3)
Cerebrovascular accident (CVA)/Transient ischemic attack (TIA)	24 (100.0)	0 (0)
Chronic renal failure (CRF)	22 (91.7)	2 (8.3)
Coronary artery disease (CAD)	18 (75.0)	6 (25.0)
Peripheral vascular disease (PVD)	23 (95.8)	1 (4.2)
Atrial fibrillation	21 (87.5)	3 (12.5)
AI	1 (4.2)	23 (95.8)
AS	22 (91.7)	2 (8.3)
Endocarditis	22 (91.7)	2 (8.3)
Structural valve deterioration	1 (4.2)	23 (95.8)

Table 2 Surgical variables and surgical characteristics of patients who received stentless valve reoperation (N=24)

	No	**Yes**
	N (%)	**N (%)**
Surgical variables		
Urgent surgery	19 (79.2)	5 (20.8)
Elective surgery	5 (20.8)	19 (79.2)
Concomitant procedure	15 (62.5)	9 (37.5)
Mechanical valve	14 (58.3)	10 (41.7)
Tissue valve	10 (41.7)	14 (58.3)
Valve-in-valve	19 (79.2)	5 (20.8)
Intra-op Bentall procedure	24 (100.0)	0 (0)
Transfusion	4 (16.7)	20 (83.3)
Ventricular assist device (VAD)	24 (100.0)	0 (0)
Post-op myocardial infarct (MI)	24 (100.0)	0 (0)
Stroke	24 (100.0)	0 (0)
New onset renal failure	23 (95.8)	1 (4.2)
Permanent pace maker required	24 (100.0)	0 (0)

	No	**Yes**
Re-operation bleeding	22 (91.7)	2 (8.3)
Second re-op	22 (91.7)	2 (8.3)
Cross-clamp time (min)	155.7 (average) (range 72-319)	155.7 (average) (range 72-319)
Bypass time (min)	201.04 (average) (range 117-355)	201.04 (average) (range 117-355)

Table 3. Procedural outcomes in patients who underwent stentless valve reoperation (N=24)

	No	**Yes**
	N (%)	**N (%)**
Procedural Outcomes		
Intra-op mortality	24 (100.0)	0 (0)
In-hospital mortality	23 (95.8)	1 (4.2)
30-day mortality	23 (95.8)	1 (4.2)
5-year mortality	23 (95.8)	1 (4.2)
10-year mortality	20 (83.3)	4 (16.7)
10-year all-cause mortality	16 (66.7)	8 (33.3)
Hospital length-of-stay (days)	7.5 (range 2-20)	