

Initial Experience with the Toronto Root Bioprosthesis

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Background and aim of the study: The study aim was to assess the safety and efficacy of the Toronto Root bioprosthesis for aortic root or valve replacement during the early postoperative stages.

Methods: Between November 2000 and December 2002, the Toronto Root was implanted in 191 patients in 17 institutions. The patients' mean age was 65 years (range: 25 to 87 years) and 70% were males. The bioprosthesis was implanted as a full aortic root in 76% of patients, as a root inclusion in 9%, and in the subcoronary position in 15%. The sizes used in decreasing frequency were 27, 29, 25, 23 and 21 mm. Coronary artery bypass was performed in 25% of patients. Echocardiography was performed before hospital discharge and at six months postoperatively. Serum aluminum levels were monitored pre- and postoperatively as this metal is used in anticalcification treatment of the arterial wall of the porcine root. For the purpose of this study, follow up was closed at six months in all patients, and was complete.

Results: Eight patients died, though none of the

deaths was valve-related. Two patients required reoperation because of technical errors during implantation. Two patients developed endocarditis, one patient required surgical intervention, and two patients suffered cerebral transient ischemic attacks. All survivors experienced symptomatic improvement, and 97% were in NYHA functional classes I and II at six months postoperatively. Blood levels of aluminum were unchanged at follow up. The mean effective orifice area of all valves studied was 2.0 ± 0.8 cm², and the mean systolic gradient 7.0 ± 3.9 mmHg at six months postoperatively. No patient had more than trace aortic insufficiency.

Conclusion: Early experience with the Toronto Root bioprosthesis has shown it to be a safe and effective valve for aortic valve or aortic root replacement, with excellent hemodynamic characteristics, a low transvalvular gradient and a large effective orifice area.

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The Toronto Root bioprosthesis (St. Jude Medical, St. Paul, MN, USA) is an intact porcine aortic root which is fixed with glutaraldehyde under a pressure of <2 mmHg, and subsequently treated with ethanol and then aluminum to prevent calcification of the aortic cusps and arterial wall, respectively (1). The manufacturer refers to this anticalcification method as BiLinx. This bioprosthetic valve became available for clinical use in September 2002 in Europe, and is currently under investigation in the United States and Canada. No published data are available with regard to the valve's hemodynamic performance in the clinical set-

ting. Herein, the early clinical outcome and hemodynamic performance of the Toronto Root in patients participating in an observational clinical trial to assess the valve's safety and effectiveness as a bioprosthesis for aortic root or valve replacement are summarized.

Clinical material and methods

Patients

Ethics Review Board approval was obtained from each participating institution before the trial was commenced. Patients who required aortic valve or root replacement were asked to participate in this study, and their informed consent was obtained. The clinical characteristics of those patients enrolled between November 2000 and December 2002 are detailed in Table I. Details of participating institutions and principal investigators of the Toronto Root Bioprosthesis are listed in Appendix I.

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Surgical approach

Three different operative techniques were used for implantation of the Toronto Root, namely aortic root replacement (n = 150 patients), aortic root inclusion (n = 17), and modified subcoronary implantation (n = 24). The operative technique used for implantation varied according to the surgeon's preference and pathology of the aortic root. Operative data are shown in Table II.

Follow up

Patients operated on at institutions in North America underwent transthoracic echocardiography and blood testing prior to discharge from hospital, at six months later, and annually thereafter. Because of a limited follow up, only those results obtained from echocardi-

grams carried out prior to discharge (127 studies) and at six months (96 studies) were analyzed. Serum aluminum levels were also measured before and after surgery, as aluminum is used in the anticalcification treatment of the arterial wall of the porcine root.

For the purpose of the present report, the follow up was closed at six months postoperatively, but was complete.

Data analysis

The hemodynamic parameters obtained during echocardiography were expressed as mean \pm SD. Comparisons of the hemodynamic parameters and serum aluminum levels at discharge and at six months postoperatively were made using an unpaired Student's *t*-test.

Table I: Patient clinical characteristics.

Parameter	Value
Age (years)	
Mean \pm SD	65 \pm 13
Range	25-99
Gender ratio (M:F)	134:57
Electrocardiography	
Sinus rhythm	175 (92)
Atrial fibrillation	13 (7)
Pacemaker	3 (1)
Associated diseases	
Hypertension	107 (56)
Diabetes	13 (7)
Previous TIA or stroke	14 (7)
Carotid artery disease	10 (5)
Peripheral vascular disease	6 (3)
Renal failure	3 (1)
Hypercholesterolemia	56 (29)
Liver disease	6 (3)
Chronic obstructive lung disease	22 (11)
Previous cardiac surgery	
Aortic valve repair/replacement	6 (3)
Coronary artery bypass	3 (1)
NYHA functional class	
I	36 (19)
II	77 (40)
III	69 (36)
IV	9 (5)
Coronary artery disease	59 (31)
Left ventricular function	
Normal or mild dysfunction	132 (69)
Moderate dysfunction	47 (27)
Severe dysfunction	12 (6)
Aortic valve lesion	
Stenosis	72 (38)
Insufficiency	71 (37)
Mixed	48 (26)

Values in parentheses are percentages.
TIA: Transient ischemic attack.

Results

Postoperatively, eight deaths occurred among patients (seven operative, one late) during the first six months of observation. Four deaths were due to low cardiac output syndrome following surgery, and four were non-cardiac-related. There were no valve-related deaths. Two patients required reoperation due to technical errors occurring during implantation in the subcoronary position. In addition, two patients developed early prosthetic valve endocarditis: one of these was

Table II: Operative data.

Parameter	Value
Aortic valve pathology	
Degenerative	105 (55)
Bicuspid	57 (30)
Other congenital	23 (12)
Rheumatic	3 (1)
Bioprosthetic dysfunction	3 (1)
Aortic valve size (mm)	
21	5 (3)
23	30 (16)
25	43 (22)
27	63 (33)
29	50 (26)
Coronary artery bypass graft	48 (25)
Mitral valve repair	4 (2)
Aortic cross-clamp time (min)*	108 \pm 35 ⁺
CPB time (min)*	142 \pm 47 ⁺

Values in parentheses are percentages.

*Values are mean \pm SD.

+No statistical differences demonstrated among techniques used to implant the valve.

CPB: Cardiopulmonary bypass.

Table III: Echocardiographic data.

Parameter	Valve size (mm)					All
	21	23	25	27	29	
No. of patients						
At discharge	3	19	28	36	37	123
At 6 months	3	15	19	31	28	96
Peak gradient (mmHg)						
At discharge	23.5 ± 2.4	20.1 ± 9.7	22.1 ± 11.0	13.9 ± 7.3	14.9 ± 7.4	17.2 ± 9.9
At 6 months	23.4 ± 4.2	18.4 ± 9.8*	14.5 ± 6.6*	12.5 ± 8.8	10.9 ± 4.2*	14.0 ± 6.7*
Mean gradient (mmHg)						
At discharge	10.5 ± 1.1	10.3 ± 5.3	11.4 ± 7.4	7.2 ± 4.6	7.3 ± 4.5	9.2 ± 6.3
At 6 months	12.0 ± 4.6	8.5 ± 4.0*	6.9 ± 3.6*	6.1 ± 4.5	5.0 ± 2.0*	7.0 ± 3.9*
Effective orifice area (cm ²)						
At discharge	1.1 ± 0.3	1.4 ± 0.5	1.6 ± 0.5	2.1 ± 1.3	2.4 ± 0.9	1.9 ± 1.0
At 6 months	1.1 ± 0.4	1.6 ± 0.5*	1.9 ± 0.6*	2.0 ± 0.7	2.5 ± 0.9	2.0 ± 0.8

*p <0.05 in comparison with previous measurement.

successfully treated with antibiotics alone, while the second required reoperation with an aortic homograft. Two patients suffered transient ischemic attacks attributable to the aortic valve bioprosthesis.

Serum aluminum levels remained unchanged during the period of observation: the mean serum level was 4.40 ± 8.88 µg/l preoperatively, 5.40 ± 7.47 µg/l at discharge, and 3.88 ± 7.99 µg/l after six months (p = 0.4).

The echocardiographic data obtained from patients at discharge and at six months postoperatively are detailed in Table III. At discharge, echocardiography in 123 patients showed no aortic insufficiency in 95% and trace insufficiency in 5%. At six months, there was no aortic insufficiency among the 96 patients studied.

Discussion

The Toronto Root bioprosthesis is treated with ethanol and aluminum in order to retard calcification of the aortic cusps and of the arterial wall (1). Ethanol prevents calcification of the aortic cusps probably by extracting lipids and altering collagen structure (2-3), whilst aluminum chloride inhibits calcification of the arterial wall by its effects on elastin and a local reduction in activity of alkaline phosphatase (4). The Toronto Root is the only bioprosthetic valve which undergoes anticalcification treatment of the arterial wall. As calcification remains the main reason for premature valve failure in young patients (5-7), valves treated with anticalcification

Table IV: Comparison of early postoperative hemodynamic performance of the Toronto Root, the Toronto SPV and the Medtronic Freestyle bioprostheses.

Parameter/ Bioprosthesis	Valve size (mm)				All
	23	25	27	29	
Mean gradient (mmHg)					
Toronto Root*	10.3 ± 5.3	11.4 ± 3.6	7.2 ± 4.6	7.3 ± 3.9	9.2 ± 6.3
Toronto SPV*	4.8 ± 3.4	6.2 ± 3.4	6.0 ± 3.0	4.6 ± 2.3	5.5 ± 3.1
Medtronic Freestyle‡	12.3 ± 6.3	8.9 ± 4.9	7.6 ± 4.3	5.8 ± 3.3	10.2 ± 6.4
Effective valve area (cm ²)					
Toronto Root*	1.4 ± 0.4	1.6 ± 0.5	2.1 ± 1.3	2.4 ± 0.9	1.9 ± 1.0
Toronto SPV*	1.8 ± 0.4	1.7 ± 0.5	2.0 ± 0.4	2.2 ± 0.5	2.0 ± 0.5
Medtronic Freestyle‡	1.4 ± 0.6	1.8 ± 0.7	2.1 ± 0.7	2.3 ± 0.5	1.7 ± 0.7

Values are mean ± SD.

*Present study; †From Dellgren et al. (9); ‡From Del Rizzo et al. (8).

agents may be more durable in this age group. The Medtronic Freestyle bioprosthetic porcine root, which is treated with the anticalcification agent alpha-aminooleic acid, has been in use for a decade, and Kon et al. reported no valve failure at eight years in a series of 104 patients, though 87% of these were aged 65 years or more (7). The present authors have not documented any calcification or valve failure during the first decade after aortic valve replacement with the Toronto SPV bioprosthesis, which has no anticalcification treatment, in patients aged 65 years or more. Thus, further follow up of newer bioprosthetic valves is required to prove that anticalcification treatment does indeed retard calcification in humans as it does in experimental animals.

The hemodynamic performance of the Toronto Root bioprosthesis is very similar to that of the Medtronic Freestyle and Toronto SPV bioprostheses (8,9); comparative values of mean systolic gradient and effective orifice area for these bioprostheses soon after implantation are listed in Table IV. The gradients across stentless porcine valves are known to decrease during the first postoperative year, while the effective orifice area increases (8-10). This observation could not be documented for all valve sizes with the Toronto Root bioprosthesis, most likely because of the small sample size and the various operative techniques used for implantation.

Unlike the Toronto SPV bioprosthesis - which can be implanted only in the subcoronary position - the Toronto Root may be used for aortic valve replacement by implanting it in the subcoronary position, as well as for aortic root replacement. Although many surgeons favor the technique of aortic root replacement even in patients with a normal aortic root when stentless porcine valves are used (7), the present authors continue to favor subcoronary implantation in patients with a normal or minimally dilated aortic root, while reserving the technique of root replacement for those patients with a dilated aortic root. Even in the latter group, an attempt is made to preserve the patient's own root by implanting the Toronto Root inside the root, using the technique known as 'aortic root inclusion'. In order to prevent distortion of the xenograft root, the non-coronary sinus of the recipient is opened down to the level of the aortic annulus. It is believed that this technique should facilitate reoperation (if ever needed), whilst offering the same advantages of aortic root replacement. Nonetheless, evidence remains that the technique of aortic root replacement is associated with better flow characteristics than either subcoronary or root inclusion techniques (10). In addition, there has been no valve failure during up to eight years of follow up when the technique of aortic root replacement is used to implant the Medtronic Freestyle valve (7) - which is most likely the reason why most sur-

geons favor aortic root replacement over the aortic root inclusion technique.

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Meeting discussion

SIR MAGDI YACOUB (United Kingdom): I have two questions. First, was the age distribution of your patients 25 to 99 years?

DR. TIRONE E. DAVID (Toronto, Ontario, Canada): Yes. There is no age limitation for the trial - any patient who signed a consent can be included.

MR. YACOUB: So how many were there of a younger age?

DR. DAVID: I don't have the individual database, but in my unit we don't use the valve in patients aged under 60 - that is a personal choice, but I am only one of the contributors. We reserve a biological valve for patients aged over 60 unless they wish to have a bioprosthesis.

MR. YACOUB: Did the 99-year-old patient have a root?

DR. DAVID: Yes, that operation was done in Philadelphia.

MR. YACOUB: In looking at the calculated gradients, I am surprised to see that the Freestyle had a higher gradient. I assume that you lumped combined data from the subcoronary position and the root, because in the presence of a root a Freestyle has a gradient of zero.

DR. DAVID: Yes, you are correct. Unfortunately, I used the database as for the Toronto valve. It is a pre-market approval database.

MR. YACOUB: And there will be many subcoronary positions?

DR. DAVID: Absolutely. They are grouped together for the FDA, so I am using comparable data for all three valves. This is a multicenter trial - it includes root, inclusion technique, and subcoronary for the Toronto Root. It is the same PMA database as for the Freestyle valve.

MR. YACOUB: If it was a root, there will be no data?

DR. DAVID: It should have a lower gradient, yes. So for the Toronto Root, it separates subcoronary versus root replacement. Root replacement had no gradient, or a much lower gradient.

DR. W. R. ERIC JAMIESON (Canada): I have two questions. The first is related to the tissue annular dimensions and how they correlate with the manufacturer's documented size. I ask this because it is a question which is before the ISO right now.

DR. DAVID: All three valves - the Toronto valve, Toronto Root and Medtronic Freestyle - are metric on the outside diameter at the annulus. So, a 23 Toronto Root has an annulus of 23 mm. It is your decision to upgrade or upsize. In root replacement, you can often implant one or two sizes larger because the valve can be placed outside the annulus. Then, there will be zero gradient, as Mr. Yacoub mentioned. Whatever the blood sees is cusps. That is one way of avoiding mis-

match when there is a small aortic root. Very few humans, except for the congenital heart, have an outflow tract less than 16-17 mm - even in small, elderly ladies the outflow tract is 16-17 mm. If you place a 23 valve on the outside, it has a zero gradient in those patients. So root replacement can be used to prevent mismatch and avoid enlargement of the aortic annulus.

DR. JAMIESON: What is your recommendation now for mechanical conduits, homograft roots and stentless roots?

DR. DAVID: The patient decides. I continue to be a believer in biological valves. I chose to move to North America because I liked the freedom that North America provided to its citizens. Freedom is not only political freedom, it is personal freedom as well: to avoid anticoagulation, stay away from the doctors, do whatever you like to do without fear that you are going to exsanguinate at any time. I believe in biological valves, and if I were a middle-aged man who needed an aortic valve to be replaced today, then I wouldn't think twice. In my heart, a biological valve is the goal. Twenty years ago I felt the same way, so it's not a function of age. I know many surgeons can do reoperations well, so I look for a surgeon who can reoperate on me safely. I offer my patients mechanical and tissue first - if they decide on mechanical, the conversation ends. If they accept a tissue valve, I perform a Ross operation in patients aged under 40 to 45, but use one of these valves for patients aged over 45 to 50. I only use homografts for infective endocarditis, not for elective aortic valve replacement.

DR. GIULIO RIZZOLI (Italy): Your study was carried out to assess the safety of the valve, and you presented a mortality of 4%, which is quite reasonable. But six months is really the perioperative mortality?

DR. DAVID: Correct.

DR. RIZZOLI: Mr. Yacoub showed a 2% mortality with the root technique in his data. Did you search for the causes of your 4% mortality? Was it related to the patients' condition, to the technique, or to another factor?

DR. DAVID: None of the deaths was valve-related, but there were three technical errors. In the pre-market approval for the Medtronic Freestyle for root replacement the mortality is 14%. Mr. Yacoub is an exceptional surgeon who can perform root replacement with 2% mortality - not all of us can. In the STS database, the mortality for a root replacement is 10%, and in Toronto it is 4%. Not all surgeons can do root replacement with a mortality of 2% for all-comers - I don't think it is easily reproducible. That's why I asked Mr. Yacoub what will happen at reoperation, and he said it would be zero mortality.

Appendix I: Participating institutions and principal investigators of The Toronto Root bioprosthesis.

Center name	Location	Investigator
Baylor University in Dallas	Dallas, TX, USA	Robert Hebler Jr. MD
Deutsches Herzzentrum Munchen	Munich, Germany	Prof. Rüdiger Lange
Herzzentrum Leipzig GmbH	Leipzig, Germany	Professor F. W. Mohr
Iowa Heart Center	Des Moines, IA, USA	David Hockmuth MD
Kendall Medical Center	Miami, FL, USA	Joseph Lamelas MD
Lankenau Hospital	Philadelphia, PA, USA	Scott Goldman MD
Loyola University	Maywood, IL, USA	Mamdouh Bakhos MD
Maine Medical Center	Portland, ME, USA	Reed Quinn MD
Medizinische Hochschule Hannover	Hannover, Germany	Prof. A. Haverich
Ospedale Ca Foncello	Treviso, Italy	Carlo Valfre MD
Sacramento CVSM Group	Sacramento, CA, USA	James Longoria MD
Southwest Texas Methodist	San Antonio, TX, USA	J. Marvin Smith III MD
Toronto General Hospital	Toronto, ON, Canada	Tirone David MD
Universitätskliniken Homburg	Homburg, Germany	Prof. H.J. Schaefers
University Hospital Graz	Graz, Austria	Prof. Bruno Rigler
University of Pennsylvania	Philadelphia, PA, USA	Joseph E. Bavaria MD
Wake Forest University Hospital	Winston-Salem, NC, USA	John Hammon MD
