Sutureless replacement of aortic valves with St Jude Medical mechanical valve prostheses and Nitinol attachment rings: Feasibility in long-term (90-day) pig experiments

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Objective: Nitinol attachment rings (devices) used to attach mechanical aortic valve prostheses suturelessly were studied in long-term (90 days) pig experiments.

Methods: The aortic valve was removed and replaced by a device around a St Jude Medical mechanical valve prosthesis in 10 surviving pigs. Supravalvular angiography was done at the end of the operation. No coumarin derivate was given.

Results: No or minimal aortic regurgitation was confirmed in all surviving pigs at the end of the operation. Total follow-up was 846 days. In 4 pigs, follow-up was shorter than 90 days (28–75 days); the other 6 pigs did reach 90 days’ survival or more. Repeat angiography in 4 pigs at the end of follow-up confirmed the unchanged position of the device at the aortic annulus, without aortic regurgitation. At autopsy, in all pigs the devices proved to be well grown in at the annulus, covered with endothelium, and sometimes tissue overgrowth related to not using coumarin derivate. There was no case of para-device leakage, migration, or embolization. No damage to surrounding anatomic structures or prosthetic valves was found.

Conclusions: Nitinol attachment rings can be used to replace the aortic valve suturelessly with St Jude Medical mechanical aortic valve prostheses, without para-device leakage, migration, or damage to the surrounding tissues, in long-term pig experiments during a follow-up of 90 days or more. Refraining from anticoagulation in pigs with mechanical valve prostheses can lead to tissue overgrowth of the valve prosthesis. Further studies are needed to determine long-term feasibility of this method in human beings. (J Thorac Cardiovasc Surg 2011;141:1231-7)

Video clip is available online.

Hand-suturing is the current standard for attaching an aortic valve prosthesis to the anatomic aortic valve annulus. However, it consumes a relatively great deal of time, particularly in multivalve and combined procedures, and makes minially invasive valve surgery less favorable. The first valve prosthesis implanted in the human being by Hufnagel in 1952 (as reported by Hufnagel and Harvey) was a sutureless valve, and sutureless Magovern–Cromie valves were used for aortic and mitral valve replacements for many years. Currently, there is renewed interest in sutureless aortic valve implantation, mostly by mounting a biological aortic valve into a metal stent and compressing it into a catheter sleeve. However, with this technique the diseased valve is not removed, and current valves stents do not yet result in early outcomes comparable with surgically removed and replaced heart valves. Previously, we have shown that it is feasible to use Nitinol attachment rings to attach mechanical aortic valve prostheses solidly to the aortic valve annulus after removal of the original aortic valve in acute pig studies and that such rings can withstand a high pulling force. Our intention with this study was to investigate the long-term (90-day) outcome in pigs of using such Nitinol attachment rings to suturelessly replace the aortic valve by a St Jude Medical mechanical aortic valve prosthesis (St Jude Medical, Inc, Minneapolis, Minn) approved by the Food and Drug Administration (FDA).

MATERIALS AND METHODS

After extensive ex vivo and short-term in vivo testing, long-term in vivo experiments were performed in pigs from February 2007 until June 2010.
2009 (Figure E1) with Nitinol sutureless attachment rings around suturing-denuded 19- or 21-mm FDA-approved St Jude Medical demo mechanical aortic valve prostheses (device pigs). In the last experiments the aortic valve was replaced by an unchanged 19-mm FDA-approved St Jude Medical demo mechanical aortic valve prostheses using standard hand-suturing techniques (control pigs). The follow-up of the surviving 10 device and 1 control pigs ended in September 2009 and is described in more details.

Devices, Stretching, and Activation
The proprietary valve attachment rings (VARs) were manufactured from Nitinol memory metal (Endosmart GmbH, Stutten, Germany) and had a sinusoidal shape with a flexible upper and lower flange. The bare Nitinol ring was almost completely covered by textile (Jotec GmbH, Hechingen, Germany), while maintaining full valve rotatability (Figure 1, A and B, Video E1). After sterilization, the device was mounted on the applicator, and the flanges were manually stretched in iscd saline. Unintended early expansion during navigation at room temperature was prevented by placement of 1 to 3 stretching sutures through the textile covering of the flanges and fixation to the applicator, which was kept in iscd saline until its use. After positioning and rewarining, the ring fixed itself by clamping the valve annulus tissue between its upper and lower flanges. In the first 5 pigs in the device group, 21-mm St Jude mechanical aortic valve prostheses were used, and in the last 5, 19-mm St Jude mechanical aortic valve prostheses were used. VARs with a fixed upper flange and a flexible lower flange were also developed, with the advantage that larger unchanged mechanical or biological valve prostheses can be mounted on top of such rings (Figure E2, A and B, Video E2). A fixed upper flange can work as a self-blocking mechanism to facilitate “blind” navigation of the VAR to the annulus. However, in this series of experiments only rings with flexible upper and lower flanges were used.

Applicators
In 7 cases the device was mounted on an applicator with 2 separate holding arms (Kiki Ingenieursgesellschaft GmbH, Malsch, Germany) (Figure 2, A). In 1 case an applicator was used with a temperature-regulating fluid-recirculating closed circuit (Technische University Delft, Delft, The Netherlands) (Figure 2, B). Although this recirculating applicator proved feasible, it was not used more frequently because its large heads were obliterating the surgical view and damaging the aorta. Finally, a simple holding applicator was developed and used in 2 later cases, consisting of a holder with a ring sutured on top of the valve housing (Instrumentation Department, Catharina Hospital, Eindhoven, The Netherlands) (Figure 2, C).

Surgical Procedures and Postoperative Investigations
In anesthetized and ventilated young female pigs (mean weight, 74.8 kg; range, 68–77 kg), a median sternotomy was performed. After heparinization, the animal was placed on full bypass with arterial cannulation in the ascending aorta or aortic arch and venous cannulation with a single cannula through the right atrial appendage. Left ventricular (LV) decompression was achieved through the LV apex, the aorta was cross-clamped, and a single shot of cold St Thomas’ Hospital crystalloid cardioplegic solution was adminis-
by supravalvular angiography and/or autopsy. In the long-term survivors, in 2 cases the flanges started to expand too early, and in 5 cases the aortotomy tore out, leading to its complicated closure. In 4 cases the temporary stretching sutures broke off when we attempted to retract them, and they could not be removed completely. Once the device was in place, the actuation with warm saline, or recirculating applicator, worked instantly in all cases. In the surviving pigs in the device group the average aortic crossclamp time was 49.2 minutes (range, 39–75 minutes), and the average perfusion time was 77.9 minutes (range, 54–122 minutes). Closing the aorta took at least 30 minutes in all cases.

Late Outcome
Among the 10 pigs surviving long term in the device group, the mean follow-up was 84.6 days (range, 28–148 days), with a total of 846 days, while 1 surviving control pig was followed up for 90 days (Table 1). Four device animals did not reach the predetermined 90 days’ follow-up period. One pig was humanely killed after 28 days because of bacterial aortic valve endocarditis. One pig drowned accidentally after 62 days when it fell through a manhole cover. Two pigs were humanely killed because of congestive heart failure at 69 and 75 days. The other 6 device and 1 control pigs did reach the predetermined 90 days’ follow-up period.
After initial recovery from surgery, all animals behaved and grew normally. There have been no signs of thromboembolic complications or other valve-related complications. The surviving pigs in the device group showed an average weight increase of 407 g per day, with mean weight of 122 kg around 90 days’ survival.

Angiographic Examinations

In all device and control pigs (with the exception of 1 case in which it was technically not possible), supravalvular angiography was performed after weaning from bypass and confirmed that the device, with respect to the valve, was at its desired position at the aortic annulus and the coronary arteries were patent. Angiograms at surgery showed grade 0 aortic regurgitation in 3, grade 1+ in 5 (Figure 3, A), and grade 2+ in 2 surviving device pigs. It was not possible to differentiate whether regurgitation was caused by para-device leakage or by backflow through the demo valves used. In 4 of the device pigs and 1 control pig the supravalvular angiogram was repeated after 90 days of follow-up, just before the animals were humanely killed. In all 4 of these device pigs, the late angiogram demonstrated an unchanged nonmigrated position of the device at the aortic annulus, with grade 0 regurgitation (Figure 3, B) in 1 case and grade 1+ regurgitation in 3 cases. The control pig did show grade 1+ regurgitation at the operation and when humanely killed. In 1 device pig, only fluoroscopy was performed when the animal was humanely killed, and this demonstrated an unchanged device position and normal valve blade movements (Table 1).

Pathologic Examinations

Autopsy of the pig with endocarditis that was humanely killed 28 days postoperatively showed a normal position of the device, with vegetations at the ventricular side of the valve prosthesis, but without para-device abscesses. There was left ventricular hypertrophy (LVH), likely caused by vegetations that almost obliterated the valve ostium from below. Autopsy of the drowned pig 62 days after the operation revealed no abnormalities of the device at its annular position. Postmortem examination of the 2 pigs with

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<th>Grade AI</th>
<th>Tissue overgrowth</th>
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D = Device; C = control; AI = Aortic insufficiency; LV = left ventricular; LVH = left ventricular hypertrophy. Cause of death: 1 = humanely killed at end of follow-up, 2 = heart failure, 3 = accidental drowning, 4 = endocarditis. Autopsy: 0 = no gross abnormalities, 1 = large atrial septal defect, 2 = left ventricular and right ventricular hypertrophy, 3 = chronic heart failure with tissue overgrowth, 4 = chronic heart failure with broken stretching suture, 5 = endocarditis.

FIGURE 3. A, Peroperative supravalvular angiogram of device in aortic annular position, with grade 1+ aortic regurgitation. B, Supravalvular angiogram after 90 days, showing same device as in Figure 3, A, with grade 1+ aortic regurgitation.
FIGURE 4. A, Device after 94 days, from aortic side, with grade 1 tissue overgrowth. B, Same device as in Figure 4, A, from left ventricular side with grade 2 tissue overgrowth. C, Hand-sutured control valve, after 90 days, from aortic side with grade 1 tissue overgrowth. D, Same device as Figure 4, C, from left ventricular side with grade 2 tissue overgrowth.

DISCUSSION

This study demonstrates that Nitinol attachment rings around suture-denuded mechanical aortic valves remain well attached to the aortic valve annulus, without peri-device leakage or damage to the valve prosthesis or surrounding tissues, not only during acute pig studies, but also during follow-up of 90 days or more. A certain degree of tissue overgrowth of the devices was found, but not more than grade 2 at the aortic side in 90% and at the LV side in 70% of the cases, and not apparently different from the single control case. Similar tissue overgrowth has been described in pigs in which the mitral valve was replaced by a mechanical valve prosthesis and is related to level of anticoagulation with coumarin derivatives. High-dose anticoagulation results in low-grade tissue overgrowth with high mortality, and no coumarin derivatives, as in our study, results in high-grade tissue overgrowth with low mortality. Although peroperative angiography of our (demo) valves demonstrated grade 2+ aortic regurgitation in 2 cases, late angiographic examinations performed in 1 of these cases did show grade 1+ regurgitation, and at autopsy no para-device leakage was demonstrated in either. In animals that did not survive the operation there was no direct relation to the sutureless valve replacement method as such, but mainly to problems with closing the aortotomy. In a number of cases these problems were related to the device–pig mismatch, inasmuch as initially we had only one relatively large device with a 21-mm valve prosthesis and relatively thick textile covering available. Subsequently, smaller 19-mm valve prostheses were used, and the thickness of the textile covering has been further diminished. Deviations from the
operative protocol by trying to omit stretching sutures, guiding sutures, or annular sutures was another reason for early failures and part of our learning process. In a number of cases the stretching sutures broke off, potentially causing prosthetic valve malfunction. This method of temporarily stretching the flanges needs to be improved by mechanical means. Although the use of guiding and annular sutures was shown to be necessary in this pig model, that is not to say that all these will be required in human beings, in whom exposure of the aortic valve is better, diseased annuli stiffer, and more devices sizes will be available. In this series of experiments, only prototypes of attachment rings were used with both flexible upper and lower flanges. The valve prosthesis was positioned within the rings, which were placed within the annulus, potentially diminishing effective valve orifice, especially in small sizes. Other prototypes with fixed upper and flexible lower flanges have been developed as well. With this latter prototype it is possible to place an oversized, unchanged valve prosthesis on top of the fixed upper flange supra-annularly. Such prototypes have been successfully tested by us in the aortic position in vitro and in the mitral position during acute pig experiments (manuscript submitted to this Journal), but were not used in these experiments because of the small aorta size in our pigs. Currently, there is a strong interest in self-expanding, or balloon-dilated, catheter-based sutureless biological aortic valve implants that are mounted within a stent.6-10 These valve stents are implanted by radial expansion within the calcified remnants of the pre-balloon-dilated diseased valve and show high incidence of postprocedure regurgitation.7,8,14 Percutaneous balloon aortic valvuloplasty as such carries a high rate of serious complications, including cerebral.15 Balloon-dilatable stents will demonstrate no active radial expansion force once they have been dilated. Also, a self-expanding stent will exert zero radial expansion force once the valve prosthesis that is sutured within the stent has fully expanded. For this reason, certain valve stents are attached distally in the ascending aorta, away from the valve annulus,16 and it is common17 and recommended18 to oversize valve stents to diminish para-device leakage. This oversizing may result in less than full expansion of valve prostheses and, together with noncircular expansion within calcium,19 these factors may lead to nonlaminar flow, potentially resulting in accelerated structural valve degeneration. Durability of (balloon-dilated) valves within a stent is currently still uncertain. On the contrary, the attachment rings are sized according to the annular diameter of the completely removed diseased valve. The ring attaches itself by clamping the annulus in a longitudinal direction, without radial expansion, which allows use of fully expanded biological or mechanical valve prostheses with proven long-term durability.20

Valved stents have a high profile that, together with the valve dilation method as such, can cause damage to the mitral valve, coronary ostia, aorta, left ventricle, and conduc-

tion tissue.9 The continuous radial expansion of (oversized) self-expandable valved stents at the aortic annular level results in a 30% to 40% incidence of conduction abnormalities, necessitating subsequent pacemaker implantation.21 Recently, 2 self-expanding valved stents were introduced for clinical investigation. These stents have the advantage that they can be applied after surgical removal of the diseased valve,22,23 but further these products carry potentially the same disadvantages as self-expanding catheter-based valved stents. Many of these disadvantages may be prevented by using Nitinol attachment rings to replace heart valves suturelessly.

In addition to the authors, the following persons contributed to the Sutureless Aortic Valve Project (in alphabetical order): Benjamin Berreklouw (video registration, Son, The Netherlands), Sander Brunner (Resident Catharina Hospital, Eindhoven, The Netherlands), Guus Brueren (Cardiologist Catharina Hospital, Eindhoven, The Netherlands), Lawrence Cohn (Brigham and Woman’s Hospital, Boston, Mass), Guy van Dael (Audiovisual Department, Catharina Hospital, Eindhoven, The Netherlands), Trevor Dekker (Medtronic Nederland BV, The Netherlands), Bennie Driehge (cardiologist, UZG, Ghent, Belgium), Viovanca Elisabeth (Fontys, Eindhoven, The Netherlands), Cristina Firanescu (Resident Catharina Hospital, Eindhoven, The Netherlands), Harold Fischer (Endosmart GmbH, Stutensee, Germany), Martijn van Geldrop (Resident Catharina Hospital, Eindhoven, The Netherlands), Yme Groeneveld (EPS, The Hague, The Netherlands), Piet Heeakkers (Institution Catharina Hospital, Eindhoven, The Netherlands), John van de Hulst (Vasucut Nederland BV, The Netherlands), Willemsen Janssen (Edwards Lifesciences Nederland BV, The Netherlands), Astrid Jorna (St Jude Medical Nederland BV, The Netherlands), Henk van Kemenade (Van Kemenade Slaughterhouse, Asten, The Netherlands), Wim Krijnen (Krijnen Medical BV, Beesd, The Netherlands), Marleen Mansveld (Catharina Hospital, Eindhoven, The Netherlands), Marjan van Marle (Traffic, Son, The Netherlands), Marijke Mersman (Catharina Hospital, Eindhoven, The Netherlands), Hardy Mueller (Jotec GmbH, Hechingen, Germany), Maria Olieslagers (UZG, Ghent, Belgium), Martijn Oostendorp (Technical University Delft, Delft, The Netherlands), Wim van Renterghem (Mediaventures, Mellebeke, Belgium), Mike Roelofs (Audiovisual Department Catharina Hospital, The Netherlands), Gerda van Rijk-Zwikker (LUMC, Leiden, The Netherlands), Cees Schot (Instrumentation, Catharina Hospital, Eindhoven, The Netherlands), Pamela Somers (UZG, Ghent, Belgium), Carl Swindle (Edwards Lifesciences Ltd, Irvine, Calif), Erik Tio (Ethicon Nederland BV, The Netherlands), Christian Velten (Endosmart GmbH, Stutensee, Germany), Jos Verbeek (Instrumentation Catharina Hospital, Eindhoven, The Netherlands), Bernd Vogel (Endosmart GmbH, Stutensee, Germany), Frederik Weinberg (Kiki GmbH, Malsch, Germany), and Sarah Van de Wiele (UZG, Ghent, Belgium)

References


FIGURE E1. Operative research team: Maria Olieslagers, Sara van de Wiele, Stefaan Bouchez, Filip De Somer, Eric Berreklouw, and Bart Koene (left to right).

FIGURE E2. A, Unchanged 19-mm Edwards Perimount biological aortic valve prosthesis on top of textile-covered Nitinol attachment ring with rigid upper and flexible lower flange (device), in warm expanded shape (side view). B, Same device as in A, in cold stretched shape (side view).