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 sutureless 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 derivates were 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 derivates. 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 sutureless 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)

Supplemental material is available online.

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 minimally invasive valve surgery less favorable. The first valve prosthesis implanted in the human being by Hufnagel in 1952 (as reported by Hufnagel and Harvey[1]) was a sutureless valve, and sutureless Magovern–Cromie valves were used for aortic and mitral valve replacements for many years.[2] 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.[3-8] However, with this technique the diseased valve is not removed, and current valved stents do not yet result in early outcomes comparable with surgically removed and replaced heart valves.[9,10] Previously, we[11] 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.[11] 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,[11] long-term in vivo experiments were performed in pigs from February 2007 until June

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Abbreviations and Acronyms
FDA = Food and Drug Administration
LV = left ventricular
LVH = left ventricular hypertrophy
VAR = valve attachment ring

2009 (Figure E1) with Nitinol sutureless attachment rings around suturering-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 prosthesis 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, Stutensee, 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 iced 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 iced saline until its use. After positioning and rewarming, 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 (Technical 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 crossclamped, and a single shot of cold St Thomas' Hospital crystalloid cardioplegic solution was administered. The aortic valve leaflets were completely removed. To compensate for mismatch between the diameter of the annulus and the device, having only one size prototype available per experiment, and the annular diameter being variable and flexible in young and healthy pigs, we placed a single circular annular suture. Because the view inside the small aorta was hindered by the device and applicator, and to give the device its optimal rotation, we used guiding sutures to assist in navigating the device to the annulus. These sutures were placed in the middle of sinuses, led through the textile covering of the VAR upper flange, and pulled during its positioning. After positioning, the annular suture was pulled and tied, and the stretching sutures were cut and retracted. The device was activated by warm (about 45°C) sterile saline over the heart in 5 cases, by circulation of warm saline through a recirculating applicator in 1 case, and by flushing the aorta with warm sterile saline in 4 cases. During reperfusion, inotropic and antiarrhythmic drugs were given, as indicated. Heart and valve function were evaluated by transesophageal echocardiography before bypass, before weaning off bypass, and after bypass in the initial cases. Supravalvular angiography was performed after perfusion through one of the carotid arteries by a cardiologist and was repeated under anesthesia before the pig was humanely killed in cases that reached 90 days' survival. Aortic regurgitation was graded by an independent cardiologist (Guus Breuren, MD) as 0 if absent and 1+ to 4+ if present.[12] During follow-up, the only anticoagulation given was 160 mg of acetylsalicylic acid twice a day and 75 mg of clopidogrel once a day. All animals underwent an autopsy, including macroscopic and histologic examination of the heart and organs. Position and function of the device were determined from both sides, and paravalvular leakage was sought with a 1-mm probe. Tissue overgrowth was graded as 0 if not covering the VAR's textile, 1 if covering the VAR's textile but not the valve ostium, 2 if covering less than 25%, 3 between 25% and 50%, and 4 more than 50% of the valve ostium. All long-term animal tests were approved along the Animal Research Ethics regulations of the institution. The animals received care in compliance with the European Convention on Animal Care and the Guide for the Care and Use of Laboratory Animals, as published by the US National Institutes of Health (NIH Publication No. 85-23, revised 1996).

RESULTS

Procedures and Early Outcome

In 13 device experiments and 1 control experiment the animals did not survive the operation or the first 24 hours thereafter, for different or combined reasons. In 3 cases, we could not place the device because it was too large (n = 2) or because a valve was damaged valve leaflet during loading (n = 1). Device–pig mismatch initially occurred often, because only 1 relatively large (21-mm valve) prototype was available, with a relatively thick self-made textile covering, which made implantation of the device impossible or very difficult, with irreparable damage of the aorta. In 5 cases there were difficulties with the aortotomy, with bleeding, or with compromised right coronary artery flow by the aorta closing sutures. In 4 cases we deviated from the operative protocol by trying to omit stretching, guiding, or annular sutures. Other problems included wrong sterilization method of the device in 2, accidental removal of the aortic cannula in 1, and retroperitoneal bleeding in another case. Also, 1 control animal did not survive as a result of a prolonged procedure owing to poor exposure of the aortic valve. There has been no early operative death directly related to the presence or action of the device, once implanted correctly. In all nonsurviving pigs in which the device could be implanted, the aortic annular position of the device has been confirmed