Transapical Mitral Valved Stent Implantation

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Background. Transcatheter aortic and pulmonary valve replacement is currently being tested in human trials. Efforts to create a valved stent to replace the atrioventricular valves have shown limited success. This is due to their their complex anatomy and function.

Methods. A self-expanding valved stent was created for transapical replacement of the atrioventricular valve. Ten pigs underwent transapical off-pump mitral valved stent implantation. Data were gathered to assess the animals' hemodynamic stability for 60 minutes after implantation. The valved stent function was assessed by transesophageal echocardiography (TEE) and contrast left ventriculogram.

Results. All animals exhibited normal hemodynamics immediately after mitral valved stent implantation and maintained stability for the entire period of monitoring. Accurate positioning of the valved stent was established in all animals. Mild paravalvular regurgitation was found in three out of ten animals by TEE and in two animals during left ventriculogram. No left ventricular outflow tract obstruction was encountered.

Conclusions. Transapical off-pump mitral valved stent implantation is feasible in an acute experimental setting. Long-term function of the new valved stent remains to be established.

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Percutaneous and transapical implantation of aortic and pulmonary valved stents have shown promising results in humans. Currently, percutaneous approaches to treat mitral valve diseases are limited to repair techniques. These percutaneous repair techniques of the mitral valve have shown mixed results in clinical trials [1].

The feasibility of transcatheter mitral valved stent implantation has been solely reported by Ma and colleagues in 2005 [2]. Later that year, Boudjemline and colleagues [3] proved the feasibility of valved stent implantation into the tricuspid valve position. Both groups reported their difficulties with deploying and securing a valved stent in the atrioventricular position. The first obstacle is the lack of adequate echocardiographic visualization or fluoroscopic landmarks of the mitral valve apparatus for stent deployment. The second impediment is related to the left ventricular outflow tract (LVOT) obstruction, which results from the exclusive use of radial force to anchor the valved stent inside the mitral valve annulus. The third obstacle is related to the anatomy of the mitral valve apparatus, namely the presence of the chordae tendineae, which can interfere with complete expansion, accurate positioning, and anchorage of the valved stent. To date no other groups reported success in overcoming these difficulties.

After three years of in vitro testing of several prototypes of atrioventricular valved stents, followed by a series of preliminary in vivo testing in animals under cardiopulmonary bypass support, a working stent prototype was produced. The current study was designed to test the feasibility of transapical implantation of the new atrioventricular valved stent into the mitral position in animals without cardiopulmonary bypass support.

Material and Methods

A self-expanding valved stent intended for transapical implantation into an atrioventricular heart valve was constructed. The new valved stent has three components: (1) an atrial fixation system consisting of ultrathin high-density polyester covered metal springs (35 to 48 mm); (2) a ventricular body made of a nitinol self-expanding stent (Nitinol Devices & Components, Fremont, CA) that accommodates a bioprosthetic heart valve (diameter, 25 to 32 mm); and (3) a ventricular fixation system. Several different bioprosthetic valves have been sutured inside the ventricular component of the stent: one freshly isolated porcine pulmonary valve (23 mm external diameter), 3 bovine jugular valves (19 to 21 mm external diameter), three mitral and three aortic glutaraldehyde preserved porcine valves with external diameters ranging from 21 to 29 mm. The valved stent was folded and housed in a custom made front-loading delivery system (Fig 1A). The folded valved stents were 10 to 12 mm in diameter and 25 to 34 mm long. The data were gathered to assess the animal's hemodynamic stability for 60 minutes after implantation and to evaluate the new valved stent function. The latter was assessed by contrast ventriculogram and transesophageal echocardiography (TEE) at the time of implantation and after one hour. The TEE was initially performed to measure the maximum diameter of the mitral valve annulus and then was used to position the delivery system and guide the deployment of the new valved stent across the mitral valve. Mitral regurgitation and left ventricular outflow tract (LVOT)

Fig 1. (A) Shows a prototype valved stent partially loaded onto the deploying catheter. (B) Illustrates a deployed valved stent into the mitral position as seen from the left atrium.
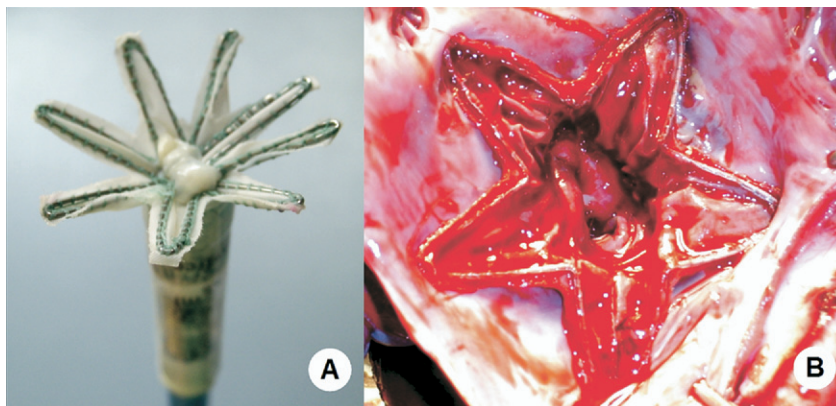
distortion by the newly placed stent were assessed by color flow Doppler and pulse wave Doppler.

Ten pigs, weighing between 45 and 55 kg, underwent transapical off-pump valved stent implantation. The first four valved stent implants were performed at the Schleswig-Holstein University in Kiel, Germany while the remaining six were performed at the University of Wisconsin, Madison, Wisconsin. The care received by animals at both institutions was in compliance with the 'Principles of Laboratory Animals' formulated by the National Society of Medical Research and the 'Guide for the Care and Use of Laboratory Animals' prepared by the Institute of Laboratory Animal Resources and published by the National Institute of Health (NIH publication 85-23, revised 1985). The institutional animal research ethics committee approved the protocol at both institutions.

A lower ministernotomy was performed under general anesthesia, electrocardiogram, and invasive blood pressure monitoring. The skin was incised 6 to 8 cm over the distal sternum. The xiphoid process was removed and the sternum was divided for less than 5 cm in the cranial direction. The pericardium was opened and a well was created by suturing the cut edges of the pericardium to the skin. A Finochietto retractor (GU Manufacturing Co. Ltd, London, UK) was placed and the heart apex exposed. Two rows of 3-0 polypropylene pledgeted felt pursestring sutures were placed around the left ventricular apex creating an area exposed for transcatheter access of 3 to 4 cm in diameter. A heparin bolus of 4,000 U was administered intravenously. The valved stents were unloaded from the introducer device after a two-stage procedure under TEE guidance. The left ventricular long axis was brought into view by TEE at a 0 degree angle and the atrial component of the stent was then partially deployed first by advancing the pusher toward the tip of the delivery system. During this phase of the procedure, the position of the delivery system was adjusted in order to have the atrial component of the partially deployed valved stent exactly above the mitral valve annulus. A 140 degree angle view was used for the subsequent valved stent positioning. The remaining part of the stent was deployed by retracting the delivery sheath while holding the pusher in place. A full TEE examination of the new valved stent was performed immediately after deployment and after one hour. Electrocardiogram, heart rate, and blood pressure were recorded continuously postimplantation. A contrast left ventriculogram was performed through the left ventricular apex after 60 minutes.

Results

Procedural data are listed in Table 1. All animals exhibited normal hemodynamics immediately after mitral

Table 1. Summary of Procedural Data

Implant Number	HR (BPM)		MAP (mm Hg)		MV Annulus (mm)	Surgical Access (min)	Stent Implant (sec)	Nr Attempts	TEE (MR)	LV Gram (MR)
	Baseline	1 hr	Baseline	1 hr						
1	85	92	65	58	25	45	204	3	Trace	None
2	82	87	62	67	22	36	245	2	Mild	Mild
3	85	95	55	57	21	38	161	2	Trace	None
4	88	96	57	52	24	33	109	1	Trace	None
5	80	90	95	65	27	32	180	2	Trace	None
6	86	79	90	72	24	35	150	3	Trace	None
7	93	94	96	78	21	39	120	2	Trace	None
8	85	83	82	71	22	32	90	2	Mild	None
9	78	92	91	62	22	22	110	3	Mild	Mild
10	83	86	80	64	25	25	100	1	Trace	None

HR = heart rate;   LV gram = left ventriculogram;   MAP = mean arterial pressure;   MR = mitral regurgitation;   MV = mitral valve;   TEE = transesophageal echocardiogram.
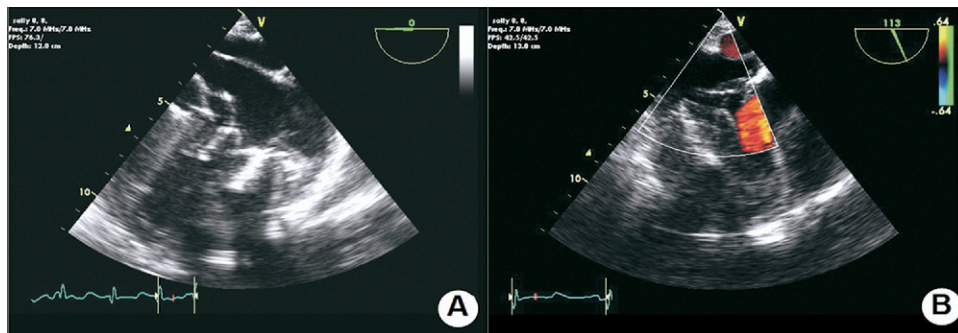
Fig 2. Transesophageal echocardiographic views of the mitral valved stent. (A) Shows the valved stent along left ventricular long axis view at a 0 degree angle. Note the visible valve leaflets inside the body of the stent. (B) Represents the color frame showing the unobstructed left ventricular outflow tract and its relationship with the new mitral valved stent.

valved stent implantation and maintained stability for the entire 60 minutes of monitoring. Atrial and ventricular ectopic beats occurred during preparation of apical access and during valve deployment in all animals. No sustained or hemodynamically relevant arrhythmias were recorded. The mean mitral valve annular diameter was 23.3 mm, ranging from 21 to 27 mm. Surgical preparation of apical access took an average of 33.7 minutes (range, 22 to 45 minutes). The mean time to deliver the valved stent across the mitral valve was 147 seconds (range, 90 to 245 seconds). There were between one and three attempts to adequately position and deploy the valved stent across the mitral valve annulus. Accurate positioning of the valved stent was established in all animals (Fig 1B and 2A). Mild paravalvular regurgitation was found in three out of ten animals by TEE. All bioprosthetic valves used were competent and had low transvalvular gradient (data not shown). Color as well as pulse Doppler tracing of the LVOT flow showed no evidence of obstruction (Fig 2B and 3B). No systolic anterior motion (SAM) of the anterior mitral valve leaflet was noted in all cases. Continuous wave Doppler flow through the new mitral valved stent was used to confirm the absence of mitral regurgitation (Fig 3A). As opposed to the TEE, ventriculogram showed paravalvular regur-

gitation only in two out of ten animals (Fig 4). There was no stent migration observed in this study.

Comment

In the current study most of the difficulties related to valved stent implantation in the mitral position were avoided. Transesophageal echocardiography allowed satisfactory visualization to guide the transapical mitral valved stent implantation. Radial force in the current stent design was used mostly for stent expansion and had only a minor role in anchoring the stent, which eliminated the risk of LVOT obstruction either directly or by SAM. In our experiments the chordae tendineae only interfered with the passage of the valved stent delivery system from the ventricular apex across the mitral valve into the left atrium. Once positioned in the left atrium the subsequent implantation steps were unaffected by the presence of the chordae tendineae. In this study we did not find it necessary to use rapid ventricular pacing or vagal maneuvers to aid implantation of the mitral valved stent or avoid its entrapment into the native mitral apparatus as suggested by others [2, 3].

In this study we chose a retrograde transapical delivery of the mitral valved stent through a lower ministernotomy in
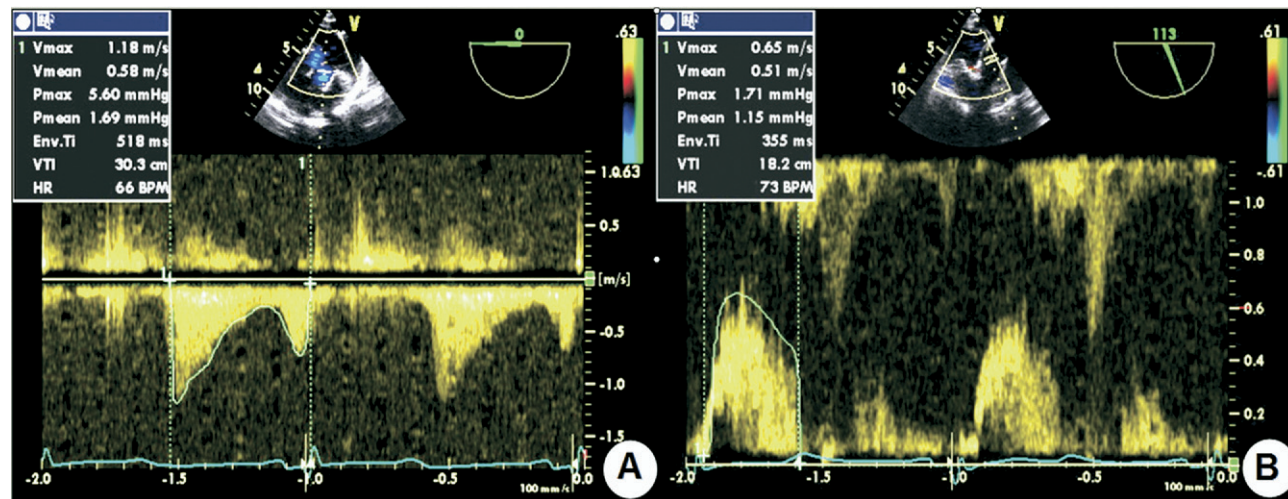

Fig 3. Transesophageal echocardiography Doppler examination of the mitral valved stent and left ventricular outflow tract (LVOT) flows. (A) Illustrates the amount of regurgitation (trace) on continuous wave Doppler exam to assess the forward flow through the mitral valved stent. (B) Shows the pulse Doppler exam through the LVOT showing unobstructed flow by the neighboring mitral valved stent.

Fig 4. Contrast left ventriculogram showing the position and competency of the mitral valved stent. (A) Illustrates mild paravalvular leak (arrow). (B) Shows no valvular or para-valvular regurgitation.
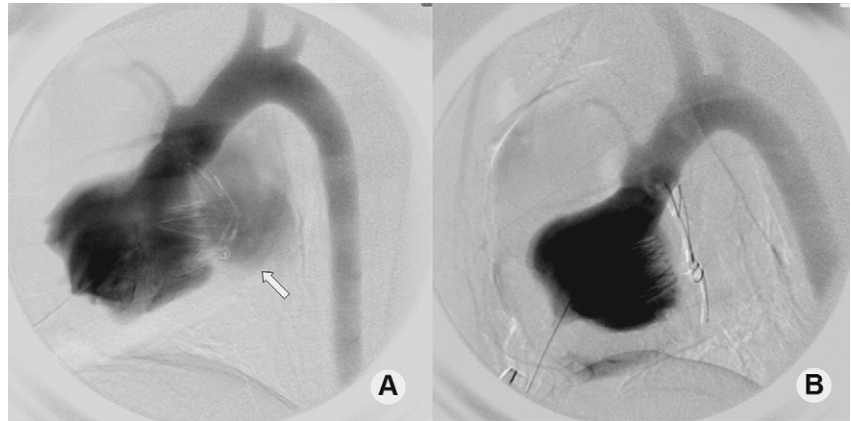
order to minimize bleeding and prepare the grounds for future survival experiments. We envision that with a higher level of engineering in manufacturing the valved stent could be delivered percutaneously by an antegrade transseptal approach. In our hands, the transapical approach was performed with ease and the implantation was successful in all cases despite multiple attempts. Each valved stent took between one and three attempts to correctly position it across the mitral valve. This was due not only to a steep learning curve related to transapical delivery under TEE guidance and determination of the best TEE angle for stent deployment but also due to the difficulties with obtaining satisfactory TEE visualization at all times. The TEE imaging in a swine model can be suboptimal at times because of the vertical position of the heart and occasional lung interposition between esophagus and the heart. After each attempt, the partially deployed valved stent was removed completely from the heart and the valved stent deployment sequence was reinitiated.

The first transcatheter mitral valved stent implantation was reported by Ma and colleagues [2]. A double crowned mitral valved stent was deployed in a swine model, using a left thoracotomy incision. The atrioventricular junction was marked epicardially with metal clips and the valved stent was subsequently deployed under fluoroscopic guidance through a pursestring suture placed into the left atrium. Their group reported no significant hemodynamic changes for 30 minutes after stent deployment, and an overall survival of 97.5 ± 56.3 minutes ranging from 40 to 180 minutes. Our study was not designed to assess survival. All animals maintained stable hemodynamics for 60 minutes postdeployment and no mortality was noted.

Boudjemline and colleagues [3] were the first to report percutaneous tricuspid valved stent implantation in eight ewes. Besides the acute results they also presented one month survival in four of the eight ewes implanted with a nitinol double disk valved stent covered with a polytetrafluoroethylene membrane. Through an antegrade femoral vein approach they guided the valved stent deployment under epicardial echocardiography through a small left thoracotomy. They reported no early or late valved stent migration. During their acute experiments the valved stent was entrapped into the tricuspid valve

chordae tendineae in one out of eight ewes. Boudjemline and colleagues [4] also described, for the first time, the concept of off-pump transcatheter valved stent implantation into a surgically implanted bioprosthesis. The surgically implanted valve carried radio opaque markers, which enabled accurate fluoroscopic valve deployment. This valve-in-a-valve concept was adopted by Walther and colleagues [5] who successfully implanted pericardial xenografts inside a surgically replaced bioprosthesis in the mitral and aortic positions in an acute setting in animals. The ease and accuracy of the valved stent in a valve implantation had led this group to already implement this concept in humans (personal communication, Thomas Walther, April 7, 2008).

One limitation of this study is the acute setting of its design. Moreover, the transcatheter mitral valved stent implantation was performed in healthy animals with normal mitral valves. This study demonstrates the feasibility of transapical beating heart valved stent implantation into a native mitral valve. The long-term function of the new atrioventricular valved stent remains to be established.

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