

# Transcatheter Aortic Valve Implantation Assisted with Microcatheter: A New Method to Avoid Coronary Artery Obstruction

Xiang Chen<sup>1</sup>, Guo-Jun Chu<sup>2</sup>, Fei-Yu Wang<sup>2</sup>, Yu-Feng Zhu<sup>2</sup>, Ben Zhang<sup>3</sup>, Xian-Xian Zhao<sup>2</sup>, Yong-Wen Qin<sup>2</sup>, Jun-Bo Ge<sup>1</sup>

<sup>1</sup>Department of Cardiology, Zhongshan Hospital, Fudan University, Shanghai 200032, China

<sup>2</sup>Department of Cardiology, Changhai Hospital, Second Military Medical University, Shanghai 200043, China

<sup>3</sup>Department of Cardiothoracic Surgery, Guangzhou General Hospital of Guangzhou Military Area, Guangzhou, Guangdong 510010, China

Xiang Chen and Guo-Jun Chu contributed equally to this study

## Abstract

**Background:** Lack of fluoroscopic landmarks can make valve deployment more difficult in patients with absent aortic valve (AV) calcification. The goal of this article was to evaluate the feasibility and effectiveness of transcatheter implantation of a valved stent into the AV position of a goat, assisted with a microcatheter which provides accurate positioning of coronary artery ostia to help valved stent deployment.

**Methods:** The subjects were 10 healthy goats in this study. A microcatheter was introduced into the distal site of right coronary artery (RCA) through femoral artery sheath. A minimal thoracic surgery approach was used to access the apex of the heart. The apex of the left ventricle was punctured; a delivery catheter equipped with the valved stent was introduced over a stiff guidewire into the aorta arch. We could accurately locate the RCA ostia through the microcatheter placed in the RCA under fluoroscopy. After correct valve position was confirmed, the valved stent was implanted after rapid inflation of the balloon. The immediate outcome of the function of the valved stents was evaluated after implantation.

**Results:** All ten devices were successfully implanted into the AV position of the goats. Immediate observation after the procedure showed that the valved stents were in the desired position after implantation by angiography, echocardiogram. No obstruction of coronary artery ostia occurred, and no moderate to severe aortic regurgitation was observed.

**Conclusions:** When the procedure of transcatheter implantation of a balloon-expandable valved stent into the AV position of goats is assisted with microcatheter positioning coronary artery ostia, the success rate of operation can be increased in those with noncalcified AV.

**Key words:** Aortic Valve Replacement; Stent Disposition; Stent Migration; Percutaneous

## INTRODUCTION

Aortic valve (AV) disease is common among elderly individuals, and its prevalence increases with age.<sup>[1]</sup> Transcatheter AV implantation (TAVI) has developed as the standard of care for inoperable patients with severe symptomatic calcific aortic stenosis and is recommended by clinical practice guidelines.<sup>[2,3]</sup> But native AV regurgitation is a contraindication to TAVI, and the standard of care remains surgical AV replacement.<sup>[4]</sup> This is because the absence of fluoroscopic landmarks in the noncalcification AV may lead to increased risk for stent valve dislocation in TAVI.

In the present study, we placed a microcatheter in the coronary artery as a mark. These techniques can help to ensure accurate positioning of the ostia of the coronary artery and improve the success rate of valve stent implantation.

## METHODS

### Aortic valve stent and delivery device design

The valve stent and delivery device [Figure 1] were produced by Lepu Medical Technology Co., Ltd. (Beijing, China), according to our design and instructions. The balloon-expandable valve stent was constructed from cobalt-chromium alloy and bovine pericardium. The stent was cut in a cylindrically shaped mesh configuration with laser engraver machines. Fresh bovine pericardium was tailored into three bioprosthetic valves after sterilization,

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**Address for correspondence:** Dr. Jun-Bo Ge,

Department of Cardiology, Zhongshan Hospital, Fudan University,  
Shanghai 200032, China

E-Mail: gjb20130901@sina.com

decellularization, and decalcification. Then, the pericardial tissues were sutured to the distal end of the stent by 7-0 polypropylene thread (Johnson and Johnson, New Brunswick City, NJ, USA). A polyethylene terephthalate fabric was used to cover the dense stitching around the one-third segment of the valve stent and served as a gland pouch to effectively reduce perivalvular leakage.

The stent delivery system was comprised of an outer sheath and stent delivery catheter [Figure 2]. The proximal segment of a stent delivery catheter could be an inflatable balloon. The outer sheath and stent delivery catheter were integrally connected to form one component. The valved stent could be compressed to the balloon and be withdrawn into the outer sheath by retracting the delivery catheter. The tip of the delivery catheter had a conical smooth transition made with silica gel material to allow implantation of the delivery catheter by performing apical puncturing. The stent delivery system could be classified into 20-, 23-, and 26-mm sizes, according to the types of the size of the balloons.

### Experimental animals

Ten healthy goats (6 male and 4 female), weighing an average of  $23.5 \pm 1.65$  kg, were obtained from the Marine Animal Medical Research Institute. Animal studies were approved by the local hospital ethics committee. All animals received care in compliance with the Guide for the Care and Use of Laboratory Animals ([www.nap.edu/catalog/5140.html](http://www.nap.edu/catalog/5140.html)). Anesthesia for each goat was initiated by an intramuscular injection of 10 mg/kg ketamine after 8 h of fasting, followed by an intravenous (IV) injection of propofol ( $0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ). The airway was maintained by endotracheal intubation and a respirator.

### Valve stent implantation

The electrocardiogram and oxygen saturation were monitored throughout the whole operation. The bilateral femoral artery and right femoral vein were punctured, and each inserted with a 6-Fr leak-proof sheath. Heparin 50 U/kg IV was administered. The temporary pacing lead was introduced into the apex of the right ventricle via the femoral vein sheath. A 6-Fr pigtail catheter was delivered via left femoral

artery sheath. Left ventricular (LV) and aortic angiographic procedures were performed to show the coronary traveling, determine the best imaging position, and measure the diameter of the aortic annulus [Figure 3a]. The valve stent size was selected according to the diameter of the AV ring, and then was compressed to the balloon of the delivery catheter using a stent compressor. The diameter of the selected stent was 2–3 mm larger than the diameter of the animal AV ring. A 6-Fr three-dimension (3D) right catheter was used to cannulate the right coronary artery (RCA) via right femoral artery sheath. A 0.014-inch 190 cm BMW angioplasty guide wire was used to cross into the distal RCA. Thereafter, a microcatheter was positioned the distal RCA over the guide wire [Figure 3b]. Then the guide wire was withdrawn, and the 3D right catheter was placed far from the ostia of RCA.

Transapical access was gained through a left anterolateral minithoracotomy in the fourth intercostals space, and purse-string sutures with 4-0 prolene were applied to the LV apex. The apex of the left ventricle was punctured, and a stiff guidewire was inserted into the descending aorta on fluoroscopy. A 20-Fr delivery device was inserted into the left ventricle from the heart apex over the stiff guidewire. The outer sheath was fixed when it had penetrated 3–4 cm into the ventricle according to the calibration on it. Then the delivery catheter with the loaded prosthesis was advanced through the native valve into the ascending aorta under fluoroscopic guidance. Not needing the aortic angiography, we could accurately locate the location of the ostia of RCA by means of the microcatheter placed in the RCA under fluoroscopy. We located the upper edge of valve stent close below the ostia of RCA with the guidance of the microcatheter [Figure 3c].

Aortic annulus was moved up and down as in a normal heartbeat. Stent positioning at this time could not be accurate. Ventricular temporary rapid pacing could slow down the velocity of blood flow from the left ventricle and reduce the movement amplitudes of the aortic annulus. Arterial pressure of goat was significantly reduced (arterial pressure  $<50$  mmHg) by 250–300 beats/min of rapid pacing as confirmed by performing a pressure monitoring after temporary pacing. The stent position was determined again on fluoroscopy; then, the valve stent was expanded and released by injecting the balloon with a contrast agent diluted 5:1 [Figure 3d]. The contrast agent was extracted when the valve stent was opened fully. Temporary pacing was stopped, the delivery catheter was extracted, and then purse sutures were used for ligature. Subsequently, the position of the valve stent and performance of the artificial valve were assessed by aortic angiography [Figure 3e and 3f].

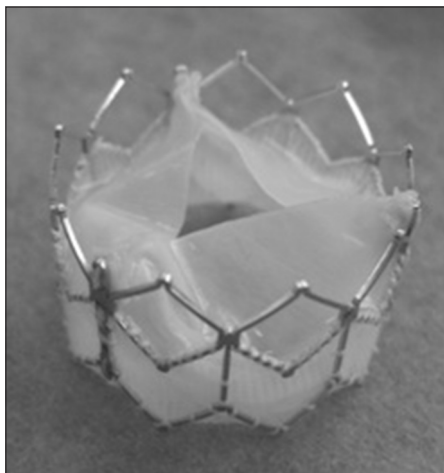


Figure 1: Prosthetic aortic valved stent.

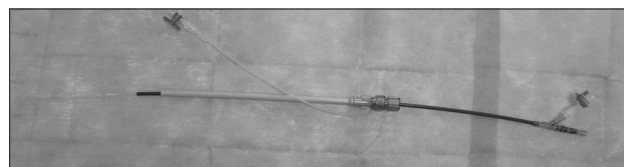
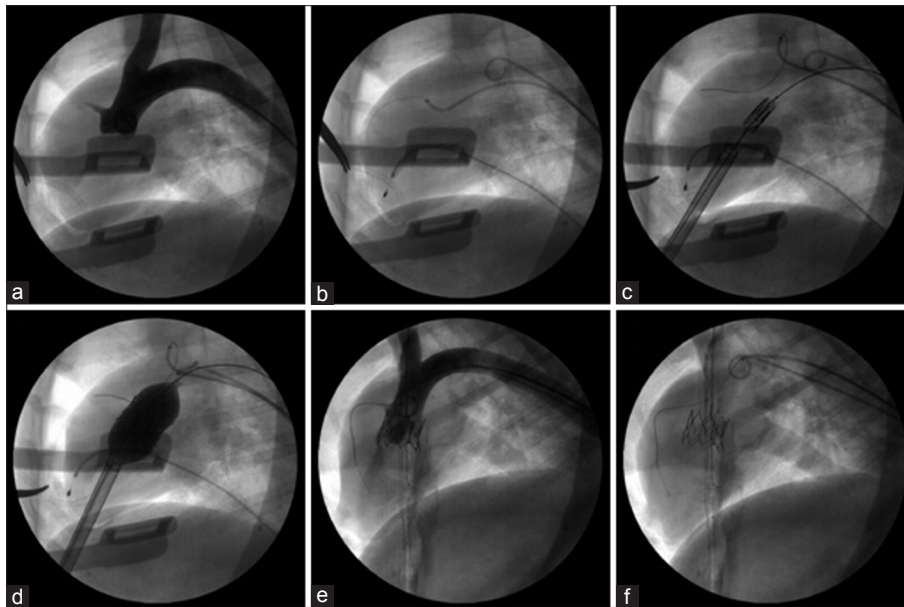


Figure 2: Delivery system of stent.



**Figure 3:** Transcatheter aortic valve implantation assisted with microcatheter; (a) Aortic angiography were performed to measure the diameter of the aortic annulus; (b) A microcatheter was positioned the distal right coronary artery over a guide wire; (c) Delivery device was inserted into left ventricular from the heart apex; (d) The valve stent was expanded and released by injecting the balloon with a contrast agent; (e and f) The performance of the artificial valve were assessed by aortic angiography.

### Postoperative treatment

The chest was closed if no active bleeding was observed in the thoracic cavity. After the sheaths of the femoral artery and vein had been removed, the hemostasis of bilateral femoral artery was performed by applying direct pressure to puncture points for 15 min. Propofol was not used until 15 min before the end of the operation. After the operation, IV injections of 0.5 mg atropine and 1 mg neostigmine were administered to reverse muscle relaxation, and 160–320 million units of penicillin were administered as an anti-inflammatory agent. The tracheal catheter of the experimental goat was removed when autonomous respiration and blood pressure were recovered. Penicillin was administered for 7 days to prevent infection, and then low-molecular-weight heparin and aspirin were administered for 3 and 90 days, respectively. The wound was disinfected daily with iodine. After 2 weeks, the sutures were removed.

### Evaluation of valve stent implantation

In each case, the location and function of the prosthetic AV were detected by aortic root angiography and transthoracic echocardiography immediately after the operation. One randomly selected goat was euthanized 2 h after successful implantation for macroscopic inspection at necropsy. The general health status, including eating, defecation, and activities, of the goats were observed. The performance of the prosthetic AV, including perivalvular leakage and aortic regurgitation (AR), was evaluated based on findings from transthoracic echocardiography 1 month after operation.

### Statistical analyses

All the statistical analyses were performed using the SPSS 18.0 software package (SPSS Inc., USA). The measurement

data were indicated as mean  $\pm$  standard deviation (SD). The data from the different groups were analyzed using a repeated-measures method. A *P* value  $< 0.05$  was considered statistically significant.

### RESULTS

The interventional procedure was completed successfully in all 10 goats; no AV block or other complications related to the operation were detected. The mean valve stent diameter was  $21.18 \pm 1.28$  mm; the operation duration and X-ray exposure time were  $128.90 \pm 10.67$  min and  $14.40 \pm 3.44$  min, respectively [Table 1]. In each case, the aortogram [Figure 3e] and transthoracic echocardiography [Figure 4] immediately after implantation revealed that the valve stent was implanted at a desired position, no obstruction of coronary artery ostia occurred, and no regurgitation or paravalvular leakage was observed. Two goats had mild perivalvular leakage; no moderate – gross regurgitation or paravalvular leakage were observed. One goat (No. 6) was sacrificed 2 h after successful implantation to allow observation of the position and function of the valve. The cardiac anatomy of the sacrificed animal showed that: The valve stent was well “anchored” against the aortic wall with desired position, the upper edge of the valve stent was lowered from coronary artery ostia by 1–2 mm, the lower edge of the valve stent was far away from the mitral valve, and the functions of the coronary artery and mitral valve were not affected. The other nine goats survived for more than 1 month with normal diet and activity. Transthoracic color Doppler ultrasound at 1 postoperative month showed normal position of the prosthetic valve with no evidence of stenosis and insufficiency apparent, trans-prosthetic valvular flow velocity was normal.

**Table 1: Data of the operational experiment animals**

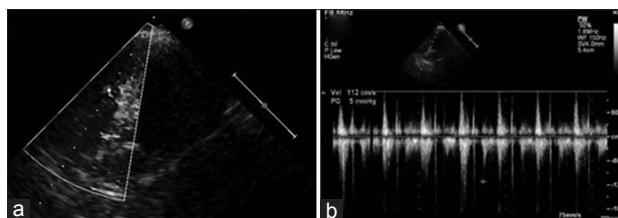
Number	Body mass (kg)	Aortic ring diameter (mm)	Stent diameter (mm)	Operation time (min)	Radiographic time (min)
1	28.2	23.1	26	142	19
2	29.3	22.8	26	138	17
3	28.4	21.5	26	145	20
4	27.5	20.8	23	133	16
5	28.1	20.8	23	128	15
6	25.2	19.2	20	124	13
7	26.9	19.8	23	118	11
8	27.5	20.2	23	129	14
9	28.3	22.3	26	113	10
10	29.1	21.3	26	119	11
Mean	27.85	21.18	24.20	128.90	14.60
SD	1.18	1.28	2.10	10.67	3.44

SD: Standard deviation.

## DISCUSSION

Transcatheter aortic valve implantation has become the standard of care for extreme-surgical-risk patients with symptomatic severe aortic stenosis and an alternative to surgery for those at high risk.<sup>[5]</sup> But according to recent guidelines, AR without the aortic calcified stenosis is still considered a contraindication to TAVI. Technical key points of TAVI include precise positioning and release of the stent valve prosthesis. The coronary arterial ostia would be obstructed if the valve stent were deployed too high; a too low position of the valve stent would induce the large paravalvular leakage or interfere with the function of the mitral valve, which would lead to poor prognosis. There are several reasons to explain why TAVI has not been used in patients with AR. One of the reasons is that the lack of fluoroscopic landmarks to outline the annulus position can make valve stent deployment more difficult in patients with noncalcified AR and result in stent mispositioning during TAVI procedures.<sup>[6,7]</sup>

Some fixed landmarks, such as sternal wires, pacing wire or vertebral bodies, may assist the location of valve stents during TAVI procedure in patients with absent AV calcification. Transesophageal echocardiography may help to show the valve stent and aortic annulus. Aortic angiography needs to be performed several times to locate the accurate position of the valve stent and aortic annulus during the operation, which may lead to the contrast agent overload and impair the kidney function. Another technique, in which two pigtail catheters were placed in two coronary sinuses, was useful to decrease the valve stent dislocation in TAVI for AR patients.<sup>[8]</sup> The Jena Valve prosthesis (Jena Valve Technology GmbH, Munich, Germany) features, a unique clip fixation mechanism of the native AV leaflets that may offer anchorage of the valve stent in the AVR during TAVI procedure.<sup>[9]</sup> Pasupati<sup>[10]</sup> used a metal loop to preimplant the stent into the ascending aorta of the AV through the peripheral vessel as a landmark of aortic sinus, and the metal loop may provide more friction between the stent and aortic wall, creating an additional anchor site.

**Figure 4:** Postoperative ultrasound; (a) No regurgitation or paravalvular leakage was found; (b) Trans-prosthetic valvular flow velocity was normal.

In this study, we developed a novel method to locate the coronary ostia by deploying a microcatheter in the coronary artery, which can help to ensure precise positioning and release the stent valve prosthesis. In procedures, we located the upper edge of the valve stent close below the ostia of RCA 1–2 mm with the guidance of the microcatheter under fluoroscopy. According to the result of the sacrificed animal's cardiac anatomy, we can see that the valve stent was deployed in optimal position, the native AVs were stuck between the annulus and stent, there was no observed obstruction of coronary ostia, and the lower edge of the valve stent was far away from the mitral valve. In this experiment, due to the precise release of the stent, the inferior edge of the stent was deployed only 2–3 mm lower than the aortic annular, and the conduction system of the heart was not affected. No atrioventricular conduction block occurred after operation. This technique can help ensure accurate positioning of valve stents while also reducing large contrast doses from multiple aortograms and decreasing contrast-induced nephropathy. Moreover, the procedure of TAVI assisted with a microcatheter is not complicated, and no complication related to the operation occurred during the study. A point to note in procedures is that the 3D right catheter should be removed from the ostia of RCA before the valve stent is implanted. Otherwise, the 3D catheter will damage the RCA ostia due to the pressure of the inflated balloon.

This study had several limitations. First, the animal cohort size was small and the follow-up time short. Second, the TAVI was performed in healthy animals with normal AVs. In the “realworld,” the anatomy of the AR is far more complicated than that of normal AVs.

In conclusion, experiment outcomes were promising without major complications during the operation or adverse events during early follow-up. This indicates the feasibility and safety of TAVI assisted with a microcatheter in noncalcified AR. We believe that the technique of microcatheter positioning of the coronary artery can elevate the veracity of valve implantation and reduce the complication of misposition of valve stent, which would provide a solution to valved stent position during TAVI procedure in patients with noncalcified AR.

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