Endovascular Reconstruction from Aortic Valve to Aortic Arch Using One-Piece Valved-Fenestrated Stent Graft with a Branch: A Proof-of-Concept Study

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ABSTRACT

Objective: To explore the feasibility of endovascular reconstruction of aortic root including aortic valve, sinus of valsalva and ascending aorta by a single stent-graft, a novel valved stent-graft with two fenestrae for preserving the coronary arteries was designed and performed in-vitro on a pig heart based circulation simulating system.

Methods: Pig hearts were harvested from 30 healthy adult female pigs weighing between 60-65 kilograms. Before sacrifice, all the pigs received aortic computed tomography angiography (CTA) examinations and morphologic parameters of aortic root were measured. Then we customized the valved stent-grafts according to the CTA measurements. After the pig heart was fixed on the special platform according to the original orientation and connected to the circulation system, the stent graft was delivered through transapical access and covered the segment from aortic annulus to proximal part of aortic arch under DSA (digital subtraction angiography) guidance. Then changes of coronary flow before and after the procedure and fenestration alignment with coronary ostia were analyzed.

Results: The overall technical success rate was 100%. The valve functions tested by ultrasound were in good condition under 120 mmHg circulation pressure. The flow of left coronary artery (LCA) did not decrease, but increased after the stent-graft implantation (340 ± 2.06 mL/min versus 288 ± 5.29 mL/min, $P < .05$). Similarly, the flow of right coronary artery (RCA) also increased (392 ± 9.17 mL/min versus 348 ± 8.01 mL/min; $P < .05$). The final angiography confirmed that both coronary arteries were patent. When generally observed from outer wall of valsalva sinus, both RCA and LCA orifices were aligned with the fenestrae. In 4 cases, the autologous valve leaflets blocked nearly 20% of the LCA fenestra's area, but the flow did not significantly decrease in these cases.

Conclusion: Stimulated on a pig heart-based circulation simulation system, the one-piece valved-fenestrated stent graft with a branch could be delivered via the transapical access and deployed accurately, which achieved endovascular reconstruction of aortic valve, sinus of valsalva and ascending aorta while preserving the coronary artery perfusion by fenestrations. More in-vivo experiments on animal models are mandatory to further verify its efficacy and safety.

INTRODUCTION

Aortic valve insufficiency (regurgitation) is a condition of valve dysfunction requiring surgical treatment, but with poor prognosis. Severe regurgitation in advanced-age patients could induce cardiac insufficiency, or even heart failure [Bonow 2016]. Elderly patients are always poor candidates for
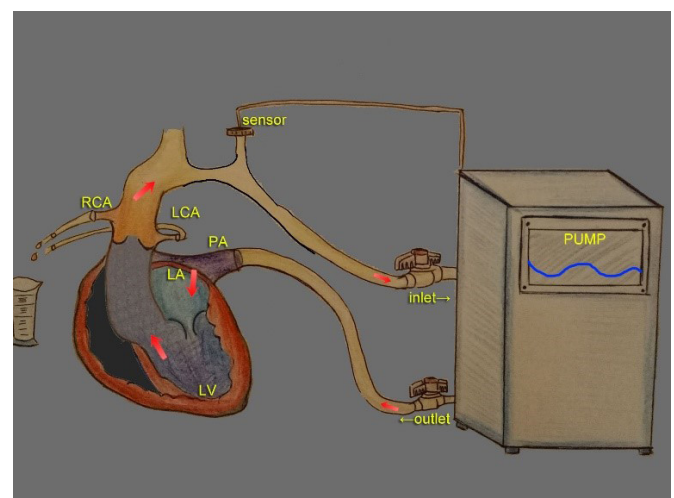
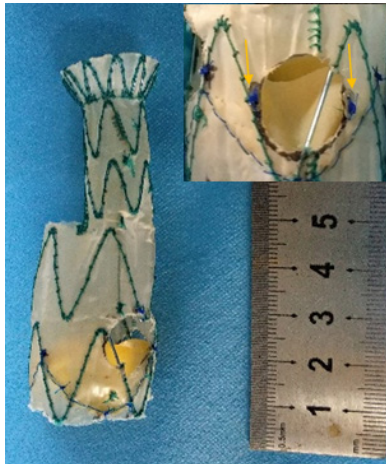Figure 1. In vitro installation schematic diagram.

Figure 2. The stent graft with its fenestrations and its "8" shape radioactive marks (arrow).
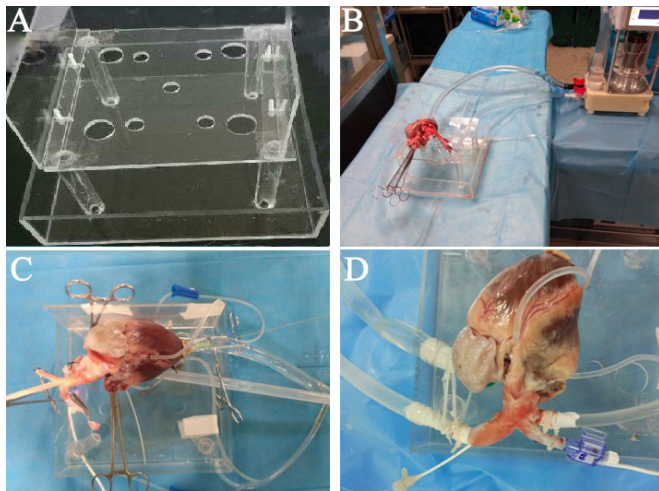

Figure 3. The experimental models successfully established. Special mounting plate for pig hearts (A). The pig heart-connected to the pump (B). The pig heart fixed on the plate appropriately (C). Fixed coronary artery lengthening tube by suture (D) (arrow).
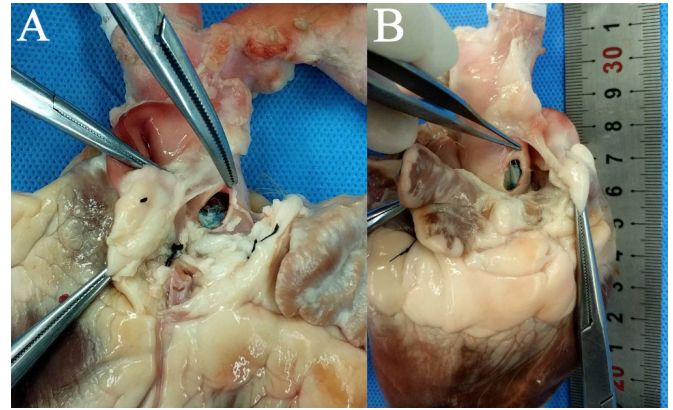

Figure 4. After the procedure, the fenestration was found right in the position. Left coronary artery fenestration (A) (arrow). Right coronary artery fenestration (B) (arrow).
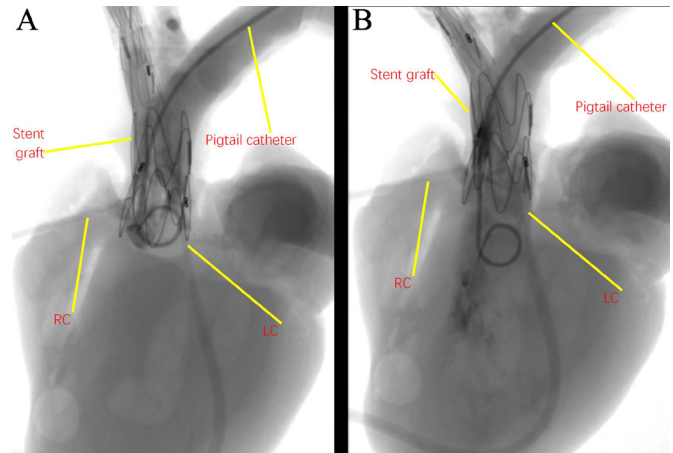

Figure 5. DSA showed the coronary flow was normal. The pigtail catheter was above the artificial aortic valve (A). The pigtail catheter was in the left ventricle (B).

open surgery. Transcatheter aortic valve implantation (TAVI) has become an important treatment option for aortic valve stenosis [Smith 2018], but currently there are no suitable endo devices specific for aortic valve insufficiency.

Aortic valve stenosis concomitant with ascending aortic aneurysm is a contraindication for TAVI [Mangieri 2017]. Self-expandable prostheses implantation can be performed only in patients with proximal aortic dimensions <45 mm [Chava 2017]. The long-term outcome of the balloon expandable valves in patients with thoracic aortic aneurysms has not yet been established [Eltchaninoff 2018].

Another critical condition involving both the ascending aorta and the aortic valve is Stanford type A aortic dissection with proximal entry tear located in aortic root. The dissection involvement may cause severe aortic regurgitation, which requires aortic valve replacement combined with

surgical replacement of the ascending aorta and coronary artery reconstruction [Feuchtner 2005].

If these conditions mentioned above occur in patients with high risk for open-surgery, it would pose a great clinical predicament, as these patients cannot receive a conventional aortic valve replacement due to the high risks, nor can they choose an endovascular treatment, due to the lack of suitable endo devices. The clinical outcomes of this subgroup of patients are far from satisfactory.

Successful transcatheter aortic valve implantation (TAVI) in extremely at-risk/inoperable patients has motivated efforts to develop technology that could provide endovascular management for both aortic valve and ascending aortic root pathology. To our knowledge, there is no research exploring the possibility of endovascular valved stent graft reconstructing the whole segment involving the aortic valve, sinus of valsalva, coronary arteries and ascending aorta because of the difficulty in in-vitro and in-vivo simulation. So we have made attempts to establish an in-vitro testing platform based
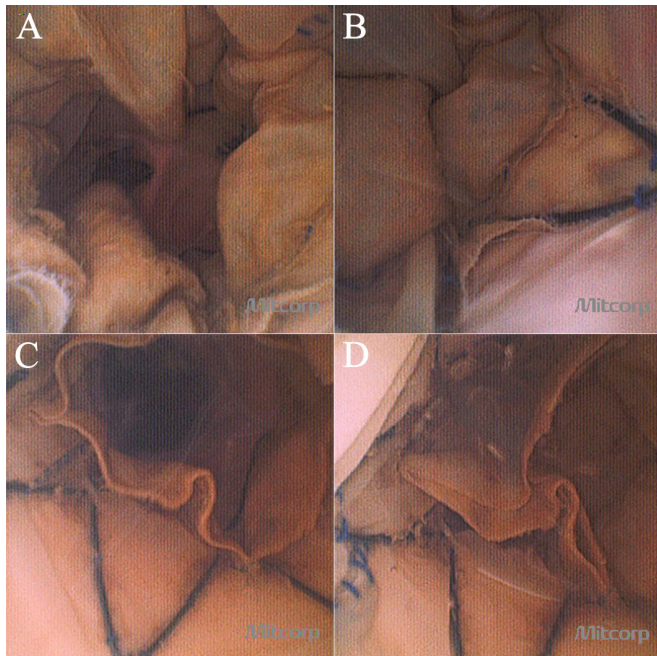
Figure 6. The endoscopy was placed both in the heart and the aorta to verify that the function of the artificial aortic valve worked well. In views of the heart side, the artificial aortic valve worked well (A, B). In views of the aorta side, the artificial aortic valve worked well (C, D).

Table. Changes in Coronary Flow before/after the Procedure

	Left coronary flow (mL/min)	Right coronary flow (mL/min)
Before procedure	288.10 ± 5.29	348.36 ± 8.01
	Left coronary flow (mL/min)	Right coronary flow (mL/min)
After procedure	340.28 ± 2.06	392.75 ± 9.17

on pig heart, which could simulate the process of endovascular procedures. Then, on the basis of our clinical practice of thoracic endovascular aortic repair (TEVAR) for ascending aortic pathologies and TAVI, we designed an endovascular valved-fenestrated-bifurcated stent graft and a set of corresponding delivering and positioning methods, thus reconstructing the segment from aortic valve to proximal aortic arch and preserve coronary arteries with two fenestrae; we explored its feasibility on the in-vitro circulation simulation system.

MATERIALS AND METHODS

Materials

1. Heart-aorta complex, harvested from female adult pigs weighing 60 ± 5 kg. Vascular branches on the aortic arch were preserved. Small branches of vessels were sutured or ligated, in case of fluid leaking. 2. Circulating pump (Maddie, Suzhou, China). It can connect to pressure sensors to control pressure and inject fluid intermittently and unidirectionally. Valved-fenestrated-bifurcated stent graft. We customized the valved-fenestrated-bifurcated stent grafts for the procedure accordingly. 3. Delivery system (Microport). 4. Other endovascular instruments like wire, short sheath, Drysheath, puncture needle, various catheter, contrast agent, etc.

Methods

Systemic preparation. As shown in Figure 1, the aorta, left atrium, and bilateral coronary artery were connected correctly, and all the leakages were sutured carefully. We did the purse-string suturing on the left ventricular apex in advance, as we would place a sheath via the transapical access [Wipper 2015].

According to the imaging and other data, we selected stent grafts with suitable diameters. The valve leaflets, made of bovine pericardium, were previously immersed in glutaraldehyde and sutured at the bottom of the stent graft; meanwhile, we calculated the angle and position of both of the two involved coronary arteries, designed the stent fenestrations and labeled several "8" shaped radioactive markers in specific locations where the fenestrae would be in special locations of the stent graft (Figure 2).

The valved stent graft was crimped and loaded into the delivery system in the Drysheath before the procedure.

Preoperative and postoperative evaluation. The coronary flow was measured before and after the procedure every 1 minute. Every step was repeated 3 times to get the mean parameter to avoid bias. Postoperative parameters were compared with preoperative parameters. After the procedure, the later parameter was compared with the previous one. In our experience, the coronary lengthening tubes need to be fastened before the procedure to avoid changes in the position or angle of the coronary arteries during the procedure. After the delivery, we performed an incision on the pig hearts to observe the stent fenestration alignment with coronary artery ostia.

Endovascular procedure. The cardiac apex was cannulated and the super-stiff guidewire was inserted. All the following steps were performed under the fluoroscopy: The guidewire was super-selected into the innominate artery. Calibrated pigtail catheter from the second branch of aortic arch was delivered into sinus of valsalva to perform the angiography to confirm the position of coronary arteries. The delivery system in the Drysheath was advanced through the apex access into the distal part of the ascending aorta and innominate artery. Then the Drysheath stayed in the ascending aorta, and the distal part of the stent graft contained in the soft sheath went into the innominate artery until the entire stent graft reached planned level.

We withdrew the Drysheath into the left ventricle; then the stent graft was in the semi-deployed situation as the diameter of soft sheath was 11 mm. We could then clearly see the position relationship among the "8" shaped radioactive markers. We adjusted the angle of fluoroscope where it could exhibit the tangent position of the left coronary artery, the longitudinal position of the stent graft, and the circumferential position of the fenestrae. Manipulating the circumferential position of the fenestrae was the most vital step of the procedure. We had to make sure two pairs of radio-markers overlapped: one pair

was the markers around the LCA, the other pair was the markers in the distal part of main body of the stent graft. After the stent graft reached the designated position both longitudinally and circumferentially and the pigtail catheter was withdrawn into the descending aorta, we pulled the yellow ring to withdraw the soft sheath to deploy the stent graft. Then we pulled the green ring to release the distal end of the limb section into the innominate artery. After the stent graft was fully deployed, angiography was performed to verify whether the coronary arteries were displayed or blocked. Finally, the Drysheath was withdrawn, the purse-string suturing was tightened, and the pigtail catheter was withdrawn.

In the end, an endoscopy (Mitcorp Mx500) was placed both in the heart and the aorta to verify the function of the artificial aortic valve.

Statistical analysis. All of the data are represented as mean ± SD. An independent sample t test was applied to compare sample means before and after implantation of the stent graft. $P < .05$ was considered statistically significant.

RESULTS

Thirty in vitro pig heart-based models were established successfully, with a 100% success rate (Figure 3).

After each stent graft delivery, the incision of the pig heart was performed and recorded. The stent fenestration alignment with coronary ostia is shown in Figure 4, and generally they were well positioned.

No significant decrease of coronary flow was detected. Instead, the flow increased to some degree ($P < .05$) (Table).

The DSA imaging showed that the coronary was filled with contrast agent, which suggested that the stent was generally well placed and the coronary flow was not affected (Figure 5).

The endoscopy showed the function of the artificial aortic valve was normal (Figure 6).

DISCUSSION

The in vitro pig heart-based model can simulate the in vivo circulation conditions. Advantages of this model include convenience, flow pressure adjustability, testability, and an anesthesia-free and sterilization-free procedure.

The establishment of the in vitro pig heart-based model provides convenience and possibility for better evaluation of stent configuration, releasing, and location. The repetition of an experiment only requires replacing the pig heart, which is fairly low in cost. Circulating pump with a pressure sensor can simulate in vivo blood pressure changes of pigs, which will ensure the simulations are nearer to the real in vivo conditions. In fact, there are currently no suitable devices that can directly evaluate the in vivo coronary microcirculation.

In order to test whether the coronary flow will be affected, we attached a lengthening tube to each coronary artery and fixed them to the heart and the heart-holding plate before the procedure to avoid changes in the position or angle of the coronary arteries during the procedure. The coronary

flow was measured before and after the procedure and the values were compared to estimate the exactness of fenestration alignment. Our experimental data showed no significant decrease but a certain degree of increase in coronary flow. This suggests that the stent graft implantation does not affect coronary flow, but actually improves it. This may be related to the presence of the valve on the stent graft, or the expansion of coronary arteries, among other possibilities, which need further studies.

Due to the anatomical relationship between the porcine aortic valve and coronary ostia, when the valve leaflets are forced to the aortic wall by self-expanding stent graft, left coronary ostia will be blocked, more than half of its area, by its own valve. That is why the effective area of coronary ostia was greatly reduced after the procedure [Gulyaeva 2012; Wang 2018]. So in respect to fenestration alignment with coronary ostia, we focused more on functional alignment than on anatomical alignment. We enlarged the fenestrae as wide as possible on the stent graft—to avoid procedure-related stenosis, or even blockage. Blockages can cause severe cardiac complications, or even death. Through the postoperative aortic dissection, we found that the existence of a minor bias in fenestration alignment is acceptable, because it will not affect the coronary flow as long as the fenestrae are generally well aligned with coronary ostia and not too far away from its correct position. Besides, the learning curve of this method is not too extended.

Compared with animal experiments in vivo, our method doesn't need anesthesia for animals, sterilization of instruments or advanced life support like ventilation. Therefore it's easier and more convenient to operate.

Conclusion

In summary, we have successfully established the in vitro pig heart-based model, on which we can easily and economically perform the simulation of stent graft delivering. The stent fenestration alignment with coronary ostia can be in good condition without significantly decreasing coronary flow. Simulated on a pig heart-based mock loop-like system, the one-piece valved-fenestrated stent graft with a branch could be delivered via the transapical access and deployed accurately, which achieved endovascular reconstruction of aortic valve, sinus of valsalva and ascending aorta while preserving the coronary artery perfusion by fenestration. As this is a proof-of-concept study, more in-vivo experiments on animal models are mandatory to further verify its efficacy and safety.

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