Apical closure device for transapical valve procedures†

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Abstract

OBJECTIVES: Transapical transcatheter valve procedures are performed through a left minithoracotomy and require apical sutures to seal the apical access site. The use of large-calibre devices compromises any attempt to fully perform the procedure with a thoracoscopic approach or percutaneously. We report our preliminary experience in animals with a new sutureless self-expandable apical occluder, engineered to perform transapical access site closure in a minimally invasive setting with large-size introducer sheaths.

METHODS: The apical occluder with extendable waist was implanted in six young pigs during an acute animal study. Under general anaesthesia, animals (mean weight: 62 ± 8 kg) received full heparinization (heparin: 100 UI/kg; activated clotting time above 250 s). Through a median sternotomy, a 21-Fr Certitude™ introducer sheath (outer diameter: 25 Fr) was placed over the wire into the cardiac apex. The delivery catheter carrying the constrained apical plug was inserted into the sheath and deployed under fluoroscopic control, whereas the Certitude™ was retrieved. After protamine infusion, we observed and recorded the 1-h bleeding with standard haemodynamic parameters. Animals were sacrificed, and hearts analysed.

RESULTS: Six apical closure devices were successfully introduced and deployed in six pig hearts through large-size apical sheaths at first attempt. In all animals, the plugs guaranteed immediate apical sealing and traces of blood were collected in the pericardium during the entire study period and no plug dislodgement was detected with normal systemic blood pressure (mean arterial mean blood pressure: 65 ± 7 mmHg). Post-mortem analysis confirmed the full deployment and good fixation of all plugs, without macroscopic damages to the surrounding myocardium.

CONCLUSIONS: This sutureless self-expandable apical occluder is a simple device capable of sealing large-size apical access sites (20–35 Fr) in an acute animal study. This approach is a step further towards less invasive transapical valve procedures in the clinical setting, and further animal tests will be performed to confirm the long-term efficacy and safety of this device.

Keywords: Transcatheter aortic valve replacement • Transapical valve replacement • Closure device • Percutaneous heart procedures

INTRODUCTION

Transapical transcatheter aortic valve replacement (TA-TAVR) is performed in high-risk patients with severe aortic or peripheral vascular disease. The ventricular apical access is reached through a left anterolateral minithoracotomy (7–10 cm) at the fifth intercostal space and, for the haemostasis, requires a double reinforced purse-string suture or multiple reinforced U-fashion stitches (at the moment, sheaths and delivery systems employed in TA-TAVR have an outer diameter ranging from 22 to 35 Fr). New transcatheter mitral valve therapies and structural heart procedures can be also performed via an apical access.

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Despite the advent of low-profile introducer sheaths and new delivery systems, the apical access remains a challenge having the risk of infection, myocardial damage, ventricular tear and life-threatening bleeding [1]. Moreover, the standard surgical apical access represents a limit for the development of video-assisted thoracoscopic TA-TAVR or truly percutaneous TA-TAVR.

On the other hand, recent reports have confirmed that structural heart disease, such as mitral or aortic paravalvular leaks, or left ventricular pseudoaneurysms, can be treated percutaneously through little apical access sites (using 6-Fr and, rarely, 12-Fr sheaths) closed by muscular ventricular septal defect (VSD) occluders, Amplatzer ductal occluders and Amplatzer vascular plug II (off-label use) [2, 3]. Therefore, during the past years, closure devices designed to be employed with transapical large-size introducer sheaths have...
been developed and tested: the Apica™ ASC device (Apica Cardiovascular, Galway, Ireland) CE-marked in August 2013; the CardioClose™ device (Entourage Medical Technologies, CA, USA); the TA PLUG device; the Permasel™ device (Micro International Device, PA, USA); and the CadiApex™ device (Cardiapex Ltd, Or Akiva, Israel) [4, 5]. However, at the moment, only few prototypes fulfil requirements for less invasive transapical valve procedures [5, 6]. After our previous experience with modified VSD occluders [7–10], we tested the safety and efficacy of a new percutaneous apical closure device, engineered for transapical valve procedures with large-size introducer sheaths.

**MATERIALS AND METHODS**

**Study design**

The study was carried out in an acute animal model, involving six young pigs and performed under general anaesthesia and full sternotomy during a time period of 3 months (2014).

The self-expandable apical closure device is placed in the apex through a last-generation 21-Fr introducer sheath: the safety of the device and its efficacy in sealing large-size apical access sites are tested with standard haemodynamic parameters. Bleeding from the apex is collected and measured during an observational period of 1 h. Animals are sacrificed to inspect the device and the interaction with the surrounding myocardium.

**The apical closure device**

The new apical closure device from Comed (Comed, Bolsward, Netherlands) is a device made of woven nitinol wires into two self-expandable round retention discs (inner disc of 18 mm diameter and outer disc of 16 mm diameter) with a connecting extendable waist of 10 mm diameter and 8 mm length (Fig. 1A and B). Owing to its adaptability (flexible device), the device is expected to occlude apical access sites ranging from a minimum diameter of 20 Fr to a maximum diameter of 35 Fr. The design is based on the concept that the apex contracts during the cardiac cycle (concentric contractions) and, therefore, apical occluders should not be too rigid or unflexible. Last but not least, this specific design allows a simple two-step manoeuvre for the deployment through large-size introducer sheaths under fluoroscopic control.

As regards the sealing property, the inner and outer discs present two membranes made of expanded Polytetrafluoroethylene that guarantee a mechanical occlusion of large-size apical access sites, and guarantee blood clotting for long-term haemostasis. With regard to the potential thromboembolic events, chronic animal tests will be performed.

**The delivery system for the apical closure device**

The Comed apical closure device is screwed to a wire and inserted into a 10-Fr size (outer diameter 13 Fr), 40-cm-long delivery system (Fig. 1C). This delivery system allows the placement of the device through large-size transapical introducer sheaths employed during the deployment of stent valves. During the present animal experience, we used a last-generation 21-Fr Certitude™ introducer sheath (Edwards Lifescience, Irvine, CA, USA) for Sapien 3 (outer diameter: 25 Fr).

**Animal preparation**

An acute in vivo evaluation was performed in six porcine experiments. Animals received care 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 protocol was approved by the Local Committee on Animal Research.

Six young pigs (mean weight: 62 ± 8 kg; mean body surface area: 1.4 ± 0.1 m²) were used for the study. After undergoing general anaesthesia with tracheal intubation and mechanical ventilation (ketamine 10 mg/kg, atropine 1 mg/kg and xylazine 0.1 mg/kg for premedication; propofol 4 mg/kg and isoflurane for anaesthesia induction; isoflurane 1.5–2.5% for maintenance anaesthesia), the right carotid artery and internal jugular vein were surgically exposed and catheters were placed to monitor the blood pressure (BP), the central venous pressure (CVP) and for blood sampling and infusion. Electrocardiography, arterial pressure, CVP and oxygen saturation were continuously monitored.

**The acute animal study**

**Preparation.** After full sternotomy and heparinization (Liquemine by Roche, Switzerland: 100 IU/kg), the cardiac apex was exposed, and punctured with a needle. Then, a standard guidewire was placed in the left ventricle followed by the insertion, over the wire, of a 21-Fr Certitude™ introducer sheath under fluoroscopic guidance (2–4 cm...
The two-step manoeuvre to deploy the closure device. The transapical access was established as described above. The first step is the inner disc deployment under fluoroscopic control: while the wire connected to the occluder remains still, the delivery system is pulled back until the inner disc is in contact with the apex (Fig. 2G and H). A tactile feedback and a fluoroscopic guidance confirm the manoeuvre. Step two is now performed. The introducer sheath and the delivery system are pulled back while the wire connected to the occluder is left in place: the outer disc opens outside the apex (Fig. 2I). Then, the wire is unscrewed and disconnected (Fig. 2J). See Video 1 for the two-step manoeuvre.

One-hour observational period. After having neutralized the heparin with protamine, blood in the pericardium is sucked and collected for 1 hour. During this time, haemodynamic parameters are maintained stable.

Statistical analysis

Variables are reported as mean ± 1 standard deviation.

RESULTS

Procedural success rate was 100% at first attempt in all animals. Immediate apical sealing was always obtained and no haemorrhagic events were detected. Haemodynamic parameters were stable during the procedures with mean heart rate of 93 ± 5 beats per minute and mean arterial mean BP of 65 ± 7 mmHg. During the 1-h observational period with normal haemodynamic parameters and after the protamine infusion, bleeding from sternum, mediastinum and heart, collected into the pericardium, was sucked and measured with an average of 16 ± 3.4 ml of blood lost per animal. Nevertheless, the majority of the bleeding episodes were from the mediastinum and the sternum. Post-mortem heart examination confirmed the good deployment of the devices without macroscopic myocardial injuries (Fig. 3).

To what my concern the risk of thromboembolic events, in all specimens we observed a strong fibrin thrombus without floating elements.

DISCUSSION

Standard surgical apical access remains a challenge in transapical valve procedures and limits the development of future percutaneous or video-assisted transapical TAVR. The launch of smaller introducer sheaths and low-profile delivery systems is a winning strategy but only the development of new apical closure devices will allow closed-chest transapical valve procedures.
the clinical experience with standard VSD occluders.

Further tests will be necessary to confirm this assumption, based on and a 3-month anticoagulation therapy or a double antiplatelet

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In fact, we can require further chronic animal tests to be confirmed. In fact, we can specify that the inner disc will be covered by fibrin. (B) Lateral view showing the apical closure device in place, with the inner (bottom) and the outer (top) discs well deployed. Myocardial injuries were not detected

Since 2006, we have performed animal tests using modified VSD occluders with large-size introducer sheaths, and we have collaborated to design and develop the new apical closure device from Comed. We believe that this occluder will fulfil important criteria required during less invasive transapical procedures: (i) the plug must guarantee apical access site sealing after the deployment and removal of the introducer sheath, without myocardial injuries or severe bleeding; (ii) the plug must be easy to deploy, safe (being always anchored to the delivery system until full release) and fully retrievable at any time; (iii) the plug must have very low thrombogenic characteristics.

After the described preliminary test, we can state that the closure device fulfils the first two characteristics, whereas the third one requires further chronic animal tests to be confirmed. In fact, we can speculate that the inner disc will be covered by neo-endothelium and a 3-month anticoagulation therapy or a double antiplatelet treatment will prevent thromboembolic events. Nevertheless, further tests will be necessary to confirm this assumption, based on the clinical experience with standard VSD occluders.

Comparing the new device with the Apica™ ASC system which is, at the moment, the only available CE-marked apical occluder, we can see major differences in size, design, engineering, and in the way the system anchors to the myocardium and occludes the access site [5, 11, 12]. At the moment, the Apica™ still requires a minithoracotomy and does not support thoracoscopic or percutaneous transapical valve procedures.

As far as different models of available stent valves are concerned, transcatheter valves placed through large-size introducer sheaths are privileged (i.e. the Edwards Sapien 3 THV). However, in the perspective of future fully percutaneous or video-assisted transapical-TAVR, sheathless stent-valve systems (i.e. the JenaValve) will also be employed but will require larger size introducer sheaths to convey the stent-valve delivery system at first and then the apical closure device, without the risk of cardiac tamponade.

A limitation of this study is the acute evaluation only and the fact that the procedure was performed through a full sternotomy in order to validate the safety and efficacy of the device. Moreover, the tests were performed in a limited number of pigs and the bleeding test was a 1-h observational test. Chronic animal tests (with a greater number of animals) performed through small minithoracotomies or in a full percutaneous setting will be performed soon and will focus on the device thrombogenicity, ventricular function, potential rhythm disturbances and bleeding tests longer than 24 h. In conclusion, the Comed device is safe in a standard animal model setting, and represents a step towards less invasive transapical valve procedures.

Conflict of interest: none declared.

REFERENCES