The Application and Teaching Value of a Ventricular Septal Defect Canine Model Established by Transcatheter Puncture

Wei Zhang,1* MD, Ya-wei Yang,2* MD, Xin-miao Huang,3 MD, Guo-jun Chu,3 MD, Tong Kan,3 MD, Ji-de Lu,1 MD and Yong-wen Qin,3 MD

Summary

This study aimed to improve and further explore a ventricular septal defect (VSD) canine model on the basis of the transcatheter puncture method and to evaluate its application and teaching value.

In order to lessen the complications of VSD closure, it is necessary to improve the currently available treatment devices using appropriate animal models.

In this study, we used 16 healthy adult canines as our models. After anesthesia, the VSD puncture was performed, followed by balloon dilatation of the perforation. VSD was confirmed by angiography. The venous-artery orbit was established, and the VSD was then closed once the catheter and occluder were across the defect.

Of the experimental canines, 14 of the 16 canines were successfully modeled, giving a success rate of 87.5%. The canines underwent an immediate creation of a venous-artery orbit for teaching practice and were implanted with an occluder during the procedure. After 4 weeks, 13 canines survived. As per our findings, most VSD types established by the puncture were perimembranous (10 of 13, 77%).

The current model has a high success rate. The model can not only avoid the risk of infection and hemodynamic disorders associated with an open thoracotomy, but can also be effectively used in evaluating the impact of occluders. It can also directly measure the parameters of the devices during the procedure, thus having a very high experimental and teaching value.

Key words: Heart septal defects, Thoracotomy, Congenital heart defects, Catheters, In vitro techniques

VSD has been identified as one of the most common congenital heart defects.1-3 Transcatheter closure of VSD was first reported by Lock et al. using a Rashkind umbrella device in 1987.2,4 With the development of technology and improvement of devices, transcatheter closure can become the preferred method for VSD treatment. However, VSD occluders, which are currently widely used in clinical practice, continue to have some unresolved complications, including complete atrioventricular block, valve damage, and hemolysis.3,5-7

In order to lessen these complications, it is thus necessary to improve the current devices by utilizing appropriate animal models. In addition, the procedure in itself has certain difficulties, often requiring the establishment of an arteriovenous track. To lessen the complications of such procedure, clinicians need to utilize animal models for practical training so as to reduce the “learning curve” when the technique is applied to humans.

The establishment of a VSD model through catheter puncture was first reported by Chinese scholar Hu et al. in 2004,6 the model had advantages as it was a convenient procedure and had only minor trauma, a high success rate, and a low incidence of complications. However, in that study, the VSD was blocked immediately after puncture; no clear statistical analysis was conducted in terms of the position of the VSD caused by the puncture, and no follow-up was conducted on the self-closing problem of the VSD established by balloon expansion after puncture. The evaluation data of that model were also found insufficient.

In this present study, we improved the VSD model on the basis of transcatheter puncture and further evaluated its applications and teaching value.
Methods

In total, we used 16 healthy adult experimental canines (12 males and 4 females), each weighing approximately 10-20 kg (16.41 ± 1.08 kg). This study was approved by our Institutional Animal Care and Use Committees of the Second Military Medical University (IACUC-SMMU) and was performed in accordance with our IACUC-SMMU guidelines and with China’s National Standard on Laboratory Animal Requirements of Environment and Housing Facilities (GB 14925-2001).

The canines were fasted for 6-8 hours before the start of the procedure. The experimental canines were anesthetized with 10% xylazine hydrochloride (0.03 mL/kg), together with 0.5 mg atropine sulfate administered as an intramuscular injection. After successful anesthesia, they were monitored using an electrocardiogram. The right femoral artery and femoral vein were then punctured, and sheaths were inserted to establish access for arterial pressure monitoring and venous fluid injections. The internal jugular vein was punctured, and a 5-French sheath was inserted, through which the ventricular septum punctures were performed.

VSD creation: A Swartz sheath and Brockenbrough puncture needle (St. Jude Medical, Minnesota) were delivered through a 0.32-inch J-guidewire to the right ventricular apex. With right anterior oblique 30° fluoroscopy, the Swartz sheath located in the right ventricular apex was slowly retracted to the level between the lower half to one-third of the ventricular septum, while adjusting the tip of the needle to face the septum under left anterior oblique 45° fluoroscopy. The tip of the needle was then slowly pushed out, and a dropout sensation was felt after penetrating the interventricular septum. The contrast agent was pushed through the tail of the catheter and could be seen dispersing in the left ventricle and aorta (Figure 1A).

An Inoue double half-guide wire (Toray Industries, Inc., Houston, TX) was inserted along the sheath and into the left ventricle, with a dilatation at the interventricular septum using a 6 mm polyethylene balloon for 10 minutes. VSD was confirmed by left ventricular angiography immediately after removing all catheters (Figure 1B). In vitro echocardiography was performed at 1-week follow-up after modeling.

Establishment of the venous-artery orbit: A 260-mm super-slide wire was inserted along the Swartz catheter into the left ventricle and passed through the aortic valve to the descending aorta. Then, a multi-function catheter was delivered into the descending aorta, through which the wire was snared by a goose snare through the right femoral artery (Figure 1C). Thus, after the wire was pulled out of the femoral artery sheath, the jugular
venous-ventricular septal defect-femoral artery orbit was established (Figure 1D).

**VSD closure:** The VSD was closed by the method previously described in detail. Briefly, once the catheter and occluder were across the defect, the left disk was deployed by pushing on the cable; then, the sheath and the cable were then pulled toward the VSD until a mild tension was felt. With gentle traction being maintained on the device, the sheath was withdrawn to release the right disk.

**Follow-up:** All canines were sacrificed and dissected when they arrived at the experiment end point as per the protocol of the occluder experiment; the distance from the edge of the occluder to the valves was measured to specify the type of VSD.

### Results

Of the experimental canines, 14 of the 16 were successfully modeled, giving a success rate of 87.5%. One of the dogs died of a pericardial tamponade caused by a puncture to the pericardium, while another dog had a sudden ventricular fibrillation during the puncture—a rapid push of 100 mg lidocaine given twice could not generate a sinus rhythm—and eventually died after being unable to defibrillate due to the lack of a defibrillator in the laboratory. Of the 14 canines successfully punctured, only 2 canines had non-severe pericardial tamponades.

The first three experimental canines had undergone an in vitro echocardiography 1 week after the successful modeling; unfortunately, no significant blood flow was observed. Those canines were re-punctured to complete the experiment. The remaining canines underwent an immediate creation of the venous-artery orbit for teaching practice and were implanted with the occluder during the procedure. No color Doppler ultrasound examination was performed before the occlusion. In one model, respiration and heartbeat stopped during the blocking process, and the anatomy showed that the entire cardiac tissue has blackened. It was considered to be death due to a very deep anesthesia, causing respiratory depression.

Four weeks after the experiment, 13 canines survived, and all the canines were sacrificed and dissected when they arrived at the experiment end point as per the protocol of the occluder experiment; thereafter, the distance from the edge of the occluder to the valves was measured (Figure 2). As per our findings, the distance from the edge of the occluder to the aortic valve was 2.3-7.8 mm (n = 13), with an average of 4.34 ± 1.70 mm, whereas the distance between the edge of the right ventricular side of the occluder and the tricuspid annulus was 0.6-4.1 mm (n = 13), with an average of 2.42 ± 0.93 mm, indicating that most VSD types established by puncture were perimembranous (10 of 13, 77%); the rest were muscular (3 of 13, 23%) (Table).

### Discussion

In this study, we present our experience of utilizing a novel VSD canine model, which has been identified to have a high success rate, reduce the risk of infection and hemodynamic disorders associated with an open thoracotomy, and effectively evaluate the impact of occluders. Animals with naturally occurring VSD such as Yucatan minipigs have a high valuation in training, but their numbers are limited, and the acquirement cost is high. Thus, VSD models prepared by surgical methods have been widely used; previous research reported that the success rate of modeling was 80-85%, and the short-term (2 weeks to 3 months) survival rate of experimental animals after successful modeling was 86-91%, showing good results.

In our study, the success rate was 87.5% (14 of 16), and the survival rate of experimental canines at 4 weeks postoperatively was 93% (13 of 14), comparable to surgical modeling. The success rate of modeling is not only related to the skill of the surgeon, but also to the trauma and experimental conditions, as surgical modeling requires opening of the thorax and pericardium, which thus increases the risk of infection and hemodynamic disorders, and is a test of the animal’s tolerance. In addition, surgical modeling places greater demands on the laboratory and necessitates postoperative rehabilitation, increasing the

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**Figure 2.** Type of VSD. A: Canine anatomy of the left ventricle at 4 weeks after closure of defect. B: Canine anatomy of the right ventricle at 8 weeks after closure of defect.
cost of the experiment. Compared to surgical modeling, this model not only avoids the aforementioned drawbacks, but also allows for simultaneous catheterization practice during modeling, allowing the surgeon to become familiar with the procedure while completing the occlusion experiment.

Of the human congenital types of VSD, 70-80% were determined to be located in the perimembrane. The Amplatzer perimembranous VSD occlude (AGA Medical, USA) has not been approved by the Food and Drug Administration (FDA) as it may result in high incidence of postoperative atrioventricular block. For further improvement of the device, more data are needed to evaluate the pressure of the device on the conduction bundle. Most of the VSD types established by model puncture in this experiment were perimembranous; thus, they could be effectively used to evaluate the impact of the occluder on the aortic valve, tricuspid valve, and conduction bundle.

**Limitations:** This approach also has its limitations; although a balloon was used for dilatation after the puncture, the color ultrasound has failed to reveal any significant perforating septal blood flow after 1 week, which could be attributed to the elastic contractile ability of the muscle, allowing it to close itself quickly. Therefore, the model cannot be used to test the blood flow-blocking ability of the device being used. However, most occluders contain multiple layers of polyester membrane to block the blood flow and promote thrombosis. This technology has already been used widely and often does not need to be verified. Besides, those canines need to be re-punctured, which greatly increases the time and the cost of the experiments. This disappointing result has also led us to give up to further observe self-closure in the subsequent experiments and instead focused on the simulation teaching and the evaluation value of VSD model. Therefore, the closure procedure was performed immediately after the establishment of the model. So we did not perform ultrasound examination after the model was established. The detailed echocardiographic data, such as left and right ventricular geometry characteristics, VSD size, estimated Qp/Qs, etc., were not available.

**Conclusions**

In conclusion, this present model has a high success rate and can be used to evaluate the effect of the occluder position on valves and conduction bundles, as well as for biocompatibility testing. More importantly, this model can be utilized to better understand the features of the occluders in real applications, such as hysteresis strength, elastic recovery ability, and release/recycle sensation, thus meeting the requirements for evaluation of new devices and teaching tasks.

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**Disclosure**

**Conflicts of interest:** None.

**References**


**Table. Distance from the Edge of the Occluder to the Valves (mm)**

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AV indicates aortic valve; TR, tricuspid ring; and SD, standard deviation.