

Modification of a Hybrid Technique for Closure of Muscular Ventricular Septal Defects in a Pig Model

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ABSTRACT

Objective: Closure of muscular ventricular septal defects (mVSDs) beyond the moderator band is still a challenge for both surgeons and interventional cardiologists. We evaluated a new technique in a pig model for hybrid patch closure of mVSDs via 2 stab wound incisions in the left ventricle (LV) without cardiopulmonary bypass.

Methods: Ten pigs underwent left anterolateral thoracotomy to expose the LV. mVSDs were created via a stab wound incision of the lateral wall of the LV under epicardial echocardiographic control. The patch system was forwarded through a second puncture of the LV apex and positioned in front of the mVSD. The stapler for fixation of the patch was introduced through the same incision as used for VSD creation. Finally, the patch was attached to the septum with nitinol anchors under epicardial echocardiographic and fluoroscopic guidance. Finally, detailed echocardiographic evaluation was done. All hearts were explanted, and macroscopic evaluation was done, either immediately after patch implantation (n = 4) or after 90 days (n = 6).

Results: mVSD creation was successful in all pigs. Closure of mVSDs was successful in 8 of 10 pigs, as confirmed by echocardiography, hemodynamic measurements, and macroscopic examination. One patch embolized through the mVSD into the pulmonary artery because of insecure fixation, and 1 animal died during the procedure because of ventricular fibrillation. The final echocardiographic evaluation revealed good LV function and no damage to the valves.

Conclusions: Closure of mVSDs can be successfully performed in a hybrid technique on the beating heart with 2 stab wound incisions; however, further modifications need to be developed before clinical application.

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INTRODUCTION

Hybrid therapy is a new approach for the treatment of complex congenital malformations that combine surgical and interventional techniques. Early experience has shown that hybrid therapy may reduce operative times, decrease procedural complexity and operative trauma, avoid the use of cardiopulmonary bypass or deep hypothermic circulatory arrest, and improve procedural outcomes [Hjortdal 2002; Bacha 2005; Schmitz 2008].

Therapy for muscular ventricular septal defects (mVSDs) beyond the moderator band is still challenging. Both surgical and interventional strategies for mVSD closure still have their limitations. Therefore, the hybrid approach seems to be an alternative for the treatment of mVSDs.

We recently published a hybrid technique for patch closure of mVSDs from the left ventricle (LV) side [Kozlik-Feldmann 2008a]. In principle, a patch-delivery device consisting of a polyester patch and a nitinol frame was forwarded via the main carotid artery into the LV (Figures 1A and 1B).

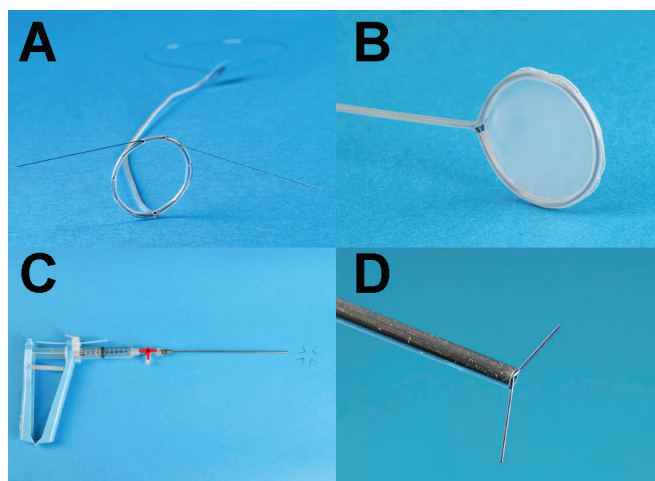


Figure 1. System for hybrid closure of muscular ventricular septal defects. A, Angled delivery system. B, Magnification of the tip of the straight tip delivery system with a polyester patch fixed to a nitinol frame. C, Custom-designed stapler instrument. D, Tip of the stapler instrument with a nitinol stapler.

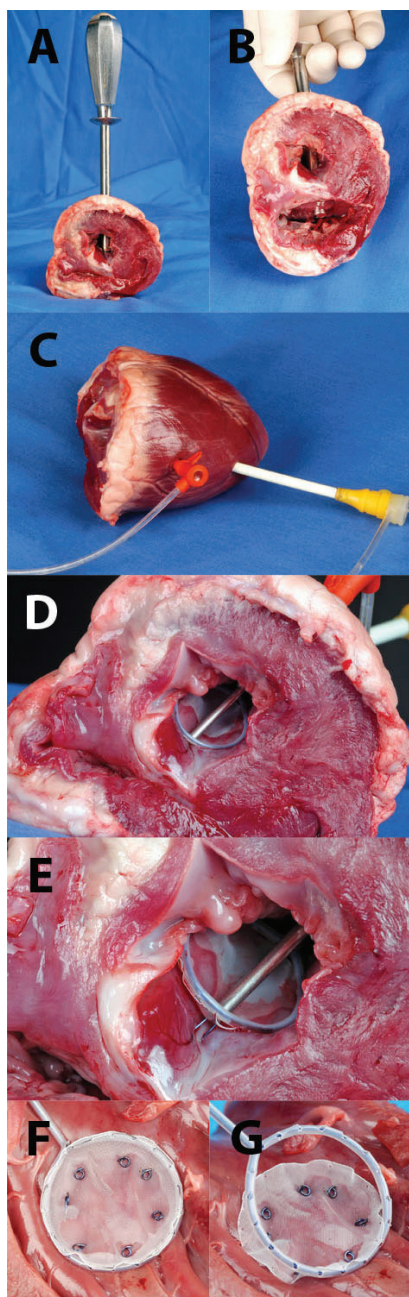


Figure 2. Demonstration of the principle of muscular ventricular septal defect (mVSD) creation and closure ex vivo. A, The punch instrument consisting of a trocar and a superimposed sharp hollow needle is forwarded through a left ventricular puncture toward the ventricular septum. B, After the trocar has been pulled back and the external tip of the hollow needle has been closed with a plug, the hollow needle is forwarded through the ventricular septum. C, The puncture used for VSD creation is used for inserting the 7F sheath for applying the nitinol clips. A second puncture close to the ventricular apex is made for the 11F sheath, through which the patch system is introduced. D, The patch system is introduced and deployed in front of the mVSD, and the nitinol frame stretches the polyester patch. E and F, Fixation of the patch with 8 to 10 nitinol anchors. G, After release of the nitinol wire, the frame is detached from the patch.

A specially designed stapler system was used via a LV puncture to fix the patch with 8 to 10 nitinol anchors (Figures 1C and 1D). Closure was done under epicardial echocardiographic and fluoroscopic control. Finally, the nitinol frame was detached from the patch. The general feasibility of this technique was shown in an acute pig model [Kozlik-Feldmann 2008b]; however, our study revealed several limitations of this strategy.

We therefore modified the technique. The patch system was forwarded into the LV via an additional apical stab wound incision. In this study, we report on our results of the evaluation of this modification in an animal model.

MATERIALS AND METHODS

Animals

Ten German Landrace pigs of either sex (20–30 kg) were used in an experimental protocol that was approved by the local Governmental Commission on the Care and Use of Animals (n = 10). They received care in compliance with the Guide for the Care and Use of Laboratory Animals. Experiments were performed in the laboratory of Surgical Research, Walter Brendel Centre for Experimental Medicine, at the Ludwig-Maximilians-Universität of Munich.

Anesthesia and Surgical Preparation

Anesthesia and surgical preparation were performed as described before [Kozlik-Feldmann 2008a, 2008b]. In brief, the main carotid artery and jugular vein on the right side were exposed surgically, the artery was cannulated with a 9F introducer sheath, and the vein was cannulated with an 11F introducer sheath. Arterial pressure and central venous pressure (CVP) were measured continuously. Thereafter, a left thoracotomy was performed in the fifth or sixth intercostal space. After opening of the pericardium, the heart was exposed with several stay sutures. The entire procedure was carried out without cardiopulmonary bypass. Two Teflon-armed purse-string sutures were applied on the LV wall for insertion of the VSD punch instrument and the stapler for the nitinol anchors.

Creation of mVSDs

mVSDs were created as described previously [Kozlik-Feldmann 2008b]. In brief, a custom-built punch instrument consisting of a trocar and a superimposed sharp hollow needle (Müller Instrumente, Tuttlingen, Germany) was used. Two purse-string sutures were applied on the LV wall, through which the instrument was inserted. The trocar was subsequently pulled back, and the open end of the hollow needle was closed with a plug. The hollow needle was forwarded toward the muscular septum under continuous 2-dimensional epicardial echocardiographic control (Sonos 5500; Philips Healthcare, Eindhoven, the Netherlands). After the tip of the hollow needle was positioned at the desired portion of the septum, the mVSD was created by rotating the needle continuously and pushing it through the septum (Figures 2A and 2B). Finally, successful creation of the mVSD was confirmed by echocardiography and oximetric measurement of the shunt volume by the Fick method.

Results with a Hybrid Technique for Muscular Ventricular Septal Defect (VSD) Closure in a Pig Model

Animal No.	Location of VSD	Outcome	Residual Shunting
1	Midmuscular	Successful closure	None
2	Midmuscular	Successful closure	Minimal
3	Apical	Death due to ventricular fibrillation before patch implantation	—
4	Midmuscular	Successful closure	None
5	Midmuscular	Successful closure	Minimal
6	Midmuscular	Patch embolized into pulmonary artery	Yes
7	Midmuscular	Successful closure	None
8	Midmuscular	Successful closure	None
9	Midmuscular	Successful closure	None
10	Midmuscular	Successful closure	None

Closure of mVSDs

The principle of the patch-delivery device and the custom-designed stapler for fixation have been described previously [Kozlik-Feldmann 2008b]. During this study, we modified the patch-delivery system and evaluated 45°- and 90°-angled patch-delivery devices.

The patch-delivery device was inserted into an 11F sheath and forwarded into the LV via a second LV puncture close to the apex. This puncture was also secured with 2 Teflon-armed purse-string sutures. After insertion, the patch was deployed in the LV and positioned in front of the defect under simultaneous fluoroscopic and epicardial echocardiographic guidance. The stapler was introduced through the 7F sheath inside the lateral LV wall. Subsequently, the patch was fixed to the septum with 8 to 10 nitinol minianchors under epicardial 2-dimensional echocardiographic and fluoroscopic guidance (Figure 4). After fixation was secured, the nitinol frame was detached from the patch by releasing the nitinol wires (Figures 2C, 2D, 2E, 2F, and 2G) and was drawn back into the sheath.

Hemodynamic Measurements and Echocardiography

Heart rate, arterial pressure, and CVP were measured and recorded periodically. The following hemodynamic parameters were obtained at baseline before thoracotomy: CVP, pulmonary artery pressure, and pulmonary capillary wedge pressure. An initial echocardiography assessment was performed to exclude heart defects. The same hemodynamic parameters were measured after shunt creation and closure of the defects. Blood samples were taken to measure shunt volume. Echocardiography was used to assess the diameter of the VSD.

After defect closure, echocardiography was performed to detect potential residual shunts and valve insufficiencies (Figure 3). Additionally, the residual shunt volume was evaluated by measuring the required hemodynamic parameters.

Macropathology

Hearts were explanted and evaluated macroscopically, either immediately at the end of the procedure (n = 4) or after 90 days (n = 6).

Statistical Analysis

Calculations were performed with SigmaStat software (Systat Software, San Jose, CA, USA). All values are presented as the mean $\pm$ SD. The paired Student *t* test was used to compare paired observations. A *P* value $<.05$ was considered statistically significant.

RESULTS**Creation of mVSDs**

A mVSD was successfully created in all animals (Figure 2). Two-dimensional echocardiography evaluations indicated the mean size of the iatrogenically created mVSDs was 8.2 ± 1.6 mm.

Closure of mVSDs

The defects were closed successfully in 8 of the 10 animals (Table). Moderate residual shunting was seen in 2 animals. This result was due to partly incorrect positioning of the patch. Figure 3 is a representative epicardial echocardiogram of a successfully closed mVSD without residual shunting. The mean number of nitinol anchors per patch was 8.5 ± 1.6 (range, 8-12). Closure of the mVSD was not successful in animal 9 because of technical difficulties. The patch could not be properly fixed, and it embolized through the mVSD into the pulmonary artery. Another animal died before patch implantation because of ventricular fibrillation.

Hemodynamics

Most pigs were hemodynamically stable at all time points and received no inotropic support during creation and closure of the mVSDs. The pulmonary artery pressure increased significantly after creation of the mVSD (from 21.4 ± 4.1 mm Hg to 29.2 ± 4.1 mm Hg; $P < .05$), and decreased after closure to 22.6 ± 6.6 mm Hg ($P < .05$). Pulmonary capillary wedge pressures also increased after creation of the defects (7.0 ± 3.6 to 11.0 ± 2.3 mm Hg; $P < .05$) but remained elevated after closure (10.7 ± 1.5 mm Hg).

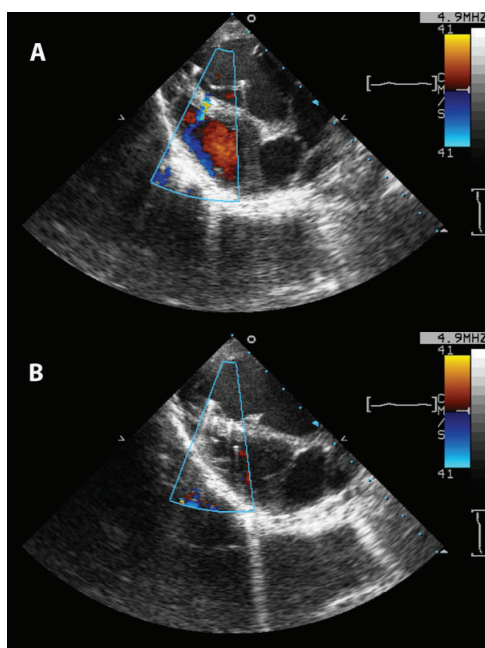


Figure 3. Echocardiograms made before and after fixation of the patch with 8 nitinol anchors. A, Long axis, before fixation. B, Long axis, after fixation. No residual shunting can be detected.

Macropathology

Figure 5 is an image of a representative explanted heart with correct placement of the patch over the defect. Correct placement was found in 8 of the 10 explanted hearts. Insecure fixation or dislodgement of the patch was seen in none of the cases. In animal 6, the patch embolized into the pulmonary artery. Animal 3 died of ventricular fibrillation before patch closure of the mVSD could be performed. In addition, macropathology assessment showed no damage to the valves in any of the cases.

DISCUSSION

Therapy for mVSDs beyond the moderator band is still challenging. Both surgical and interventional strategies for mVSD closure still have their limitations. Reoperation rates of up to 10% have been reported after surgery [Serraf 1992; Wollenek 1996; Kitagawa 1998]. Depending on the location of the defect, surgical exposure may be difficult. When the mVSD is approached through the right atrium and the tricuspid valve, visualization may be challenging because of hypertrophic right ventricular trabeculations. When the mVSD is approached through the atrial septum and the mitral valve, the angle to the septum sometimes makes it impossible to visualize the defect at all. The direct approach through the right of the free LV wall has also major disadvantages, because it is often associated with ventricular dysfunction, arrhythmias, and the development of apical aneurysms [Bacha 2005; Garcia-Valentin 2007]. Furthermore, such surgery requires the use of cardiopulmonary bypass, which may be associated with neurologic complications [Zeithofer

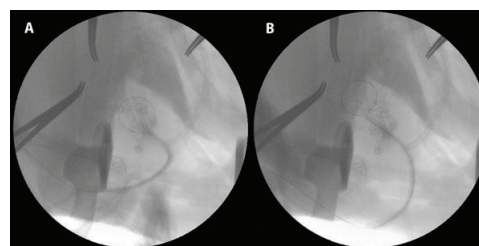


Figure 4. Angiograms before (A) and after (B) release of the frame from the patch.

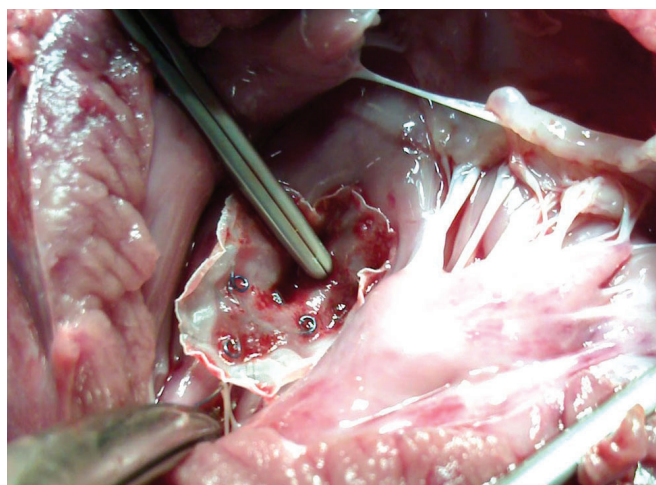


Figure 5. Macropathology. Examination of the explanted heart after iatrogenic creation of the muscular ventricular septal defect reveals adequate positioning and fixation of the patch.

1993; Bellinger 1999] or the development of a “systemic inflammatory response syndrome” [Madhok 2006].

Interventional closure of an mVSD may address some of these issues but has its own set of complications and disadvantages [Amin 2008]. Umbrellas, plugs, or coils for mVSD closure require reasonably sized insertion sheaths, which limit their application in very small children [Holzer 2004]. Furthermore, all devices currently on the market dilate the mVSD to its maximum in order to stay in place. The literature has indicated that continuous pressure on the circumference of the septal defect may cause late atrioventricular blocks, particularly for defects close to the bundle of His [Thanopoulos 2005].

There are some reports of off-pump closure of mVSDs with an Amplatzer device via a periventricular approach [Bacha 2005; Diab 2007; Garcia-Valentin 2007]. Besides the advantages, these authors reported valve injuries, device embolization into the aorta, rhythm disturbances, and device migration [Bacha 2005; Garcia-Valentin 2007].

The only remaining alternative for some patients is a palliative approach using a pulmonary artery band for postponement of either surgical or interventional closure of the mVSD.

Over the last decade, interest has grown in applying so-called hybrid techniques [Hjortdal 2002; Bacha 2005;

Schmitz 2008], in which surgical and interventional techniques are combined to reduce the morbidity associated with each separate technique. Most authors combine standard surgical and standard interventional techniques. Currently, the development of completely new approaches for pure hybrid application is rare; however, one example may be the development of the transapical approach for aortic valve replacement [Walther 2008].

We recently published a sole hybrid technique for mVSD closure in an acute and chronic pig model [Kozlik-Feldmann 2008a, 2008b]. Our goal was to fix a polyester patch with nitinol staples at the left side of the ventricular septum. We were in favor of the left side of the ventricular septum because its more planar shape (owing to fewer trabeculations) facilitates easier positioning of the patch in front of the mVSD and its fixation to the muscular septum. Furthermore, the blood pressure, which is typically higher in the LV than in the right ventricle, may help to press the patch against the septum, reducing the risk of residual defects.

Generally speaking, application of the fundamental principle worked; however, the technique as previously described had several disadvantages. First, the mVSD was approached with the delivery system through the main carotid artery; however, the use of the main carotid artery is not an acceptable option for applying this technique to humans. An alternative access site might be the femoral artery or, when a transseptal approach is used, the femoral vein; however, both pathways are very tortuous, making steering the patch system in front of the mVSD more or less impossible.

Second, retrograde passing of long sheaths through the aortic valve may cause damage to the valve leaflets. This complication, which was observed in the previous study, is a further argument against the femoral artery approach.

The alternative of a peripheral access might involve an additional stab wound incision in the LV apex. Given that the fixation system for the nitinol staples has to be passed through the free left lateral wall, trauma does not seem to be increased significantly when the patch system is passed through an additional 11F sheath into the LV cavum. As expected, this technique turned out to be much easier to apply. Because the pathway from the incision to the mVSD is short and straight, navigating the patch in front of the mVSD and fixing it with nitinol anchors was much easier.

Using 2-dimensional imaging to navigate a tool in 3-dimensional space turned out to be a challenge, however. Fluoroscopy or echocardiography alone was not able to guide the operator in placing the nitinol clips in the patch. On the one hand, fluoroscopy is not able to show the location of the mVSD, but the delivery system with the nitinol frame can be easily visualized. On the other hand, echocardiography can easily show the nitinol frame, the patch itself, and the mVSD. The clip applicator cannot be visualized, however, and determining the exact position of the patch in front of the mVSD in all 3 dimensions is nearly impossible with 2-dimensional echocardiography.

A potential option to improve visualization may be 3-dimensional echocardiography. This option has previously been described by Vasilyev et al in Boston [Vasilyev 2008]. Because we had no such system in our animal laboratory, we

tried to perform the operation with the same visualization tools that are available in most cardiac units.

There is one additional important issue. The hybrid technique for mVSD closure described above not only may be a future clinical application but also may work as a model for testing new patch materials. Anything that is flat and has a certain degree of stability can be fixed to the muscular septum with nitinol staples with this technique.

CONCLUSION

In conclusion, we demonstrated that our modified hybrid approach could close mVSDs adequately; however, some technical issues still need to be resolved before any clinical application can be considered. Furthermore, this technique can be used in an animal model for evaluating different patch materials for the closure of mVSDs.

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