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Limitations of Closing Percutaneous Transthoracic Ventricular Access Ports Using a Commercial Collagen Vascular Closure Device

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Abstract

INTRODUCTION—Closed-chest access and closure of direct cardiac punctures may enable a range of therapeutic procedures. We evaluate the safety and feasibility of closing percutaneous direct ventricular access sites using a commercial collagen-based femoral artery closure device.

METHODS—Yorkshire swine underwent percutaneous transthoracic left ventricular access (n=13). The access port was closed using a commercial collagen-based vascular closure device (*Angio-Seal*, St Jude Medical) with or without prior separation of the pericardial layers by instillation of fluid into the pericardial space (“permissive pericardial tamponade”). After initial nonsurvival feasibility experiments (n=6); animals underwent one-week (n=3) or six-week follow up (n=4).

RESULTS—In naïve animals, the collagen plug tended to deploy outside the parietal pericardium, where it failed to accomplish hemostasis. “Permissive pericardial tamponade” was created under MRI, and accomplished early hemostasis by allowing the collagen sponge to seat on the epicardial surface inside the pericardium. After successful closure, six of seven animals accumulated a large pericardial effusion 5±1 days after closure. Despite percutaneous drainage during 6-week follow-up, the large pericardial effusion recurred in half, and was lethal in one.

CONCLUSIONS—A commercial collagen based vascular closure device may achieve temporary but not durable hemostasis when closing a direct left ventricular puncture port, but only after intentional pericardial separation. These insights may contribute to development of a superior device solution. Elective clinical application of this device to close apical access ports should be avoided.

Keywords

Transapical; Heart rupture; Tamponade; Paravalvular leak; Valve repair

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Introduction

Percutaneous transthoracic ventricular access is used for diagnostic catheterization when crossing aortic and mitral valves is hazardous (1–3). More recently transapical ventricular access has been used for therapeutic applications (4–6), most notably for surgical delivery of transcatheter aortic valves (7).

Percutaneous access complication rates are low in patients with prior cardiac surgery using small-diameter catheters (1–3). However, non-surgical withdrawal of larger-caliber ventricular access sheaths may cause life-threatening pericardial bleeding or hemothorax (6). Limited clinical reports suggest non-surgical closure of right ventricular (8) and descending thoracic aorta (9) perforations may be feasible using a collagen-based device (*Angio-Seal*) intended for hemostasis of femoral artery access sites.

Safe and effective closure of percutaneous direct ventricular access would allow non-surgical access for therapeutic procedures from a direct transthoracic route. Conversely, off-label clinical use of vascular closure devices to obtain non-surgical closure after ventricular puncture has been associated with life-threatening complications [Personal communication, RJL]. The aim of the present work was to evaluate the safety and feasibility of “closure” of percutaneous direct left ventricular access using a commercial femoral artery closure device, in naïve swine.

Methods

ANIMAL PROCEDURES

Animal procedures were approved by the institutional animal care and use committee and conducted according to contemporary National Institute of Health guidelines. Thirteen naïve Yorkshire swine (40 ± 10 kg) were allocated to three groups: non-survival feasibility, (n=6); one-week survival (n=3); and extended survival up to 6 weeks (n=4).

Anesthesia was induced with ketamine, midazolam, and glycopyrrolate, and maintained with inhaled isoflurane and mechanical ventilation. A femoral artery and vein were accessed percutaneously, and a subxiphoid pericardial catheter placed under fluoroscopy for pericardial fluid instillation and drainage. Animals were treated with aspirin and unfractionated heparin to a target activated clotting time of 250 seconds immediately before closure.

Feasibility experiments (n=3) were performed in an open chest after sternotomy with intact or resected pericardium, under direct visual guidance. The ventricular cavity was accessed with an 18G needle (E-Z-EM, Westbury, NY), exchanged over a 0.035” guidewire for an introducer sheath (*Check-Flo*, Cook Medical, Bloomington, IN). The closure device was deployed under direct visualization.

Closed chest, direct transthoracic puncture of the left ventricle (n=10) was performed under real-time magnetic resonance imaging (MRI) guidance (10) from a sub-xyphoid approach. Introducer sheaths were advanced over a 0.035” nitinol guidewire (*Glidewire*, Terumo, Somerset NJ) into the left ventricular cavity.

COLLAGEN-BASED DEVICE FOR VENTRICULAR CLOSURE

An unmodified commercial vascular closure device (*Angio-Seal VIP*, St Jude Medical, Minnetonka, MN) was used to close percutaneous transthoracic ventricular access ports. This application is not suggested in the manufacturer’s Instructions for Use (11). The device components include a cylindrical polylactide and glycolide copolymer (PLGA) endovascular

foot ($10 \times 2 \times 1$ mm) suspended in midsection by a degradable glycolic acid polymer suture. Analogous to femoral artery closure, the foot is positioned at the endocardial side of the target structure, and then a bovine-derived collagen sponge is advanced a variable distance along the suture and compressed against the puncture hole (12).

For Yorkshire swine (35 ± 4 kg), the endocardium-to-skin distance is 4.8 ± 0.37 cm in this series, and the para-apical left ventricular myocardial thickness is 7.6 ± 0.2 mm. For closure of percutaneous transthoracic ventricular access, the left ventricular sheath was exchanged for the 8 Fr Angio-Seal sheath. Next the 8 Fr Angio-Seal device was advanced over a 0.035" nitinol guidewire (*Glidewire*, Terumo Corp., Somerest NJ) into the ventricular cavity. Next, the endovascular "foot" was deployed and retracted against the endocardium. Finally, the collagen sponge then was advanced to abut and seal the myocardial puncture (Figure 1).

PERMISSIVE PERICARDIAL TAMPONADE

To avoid entrapping the parietal pericardium with the collagen plug, the epicardium and parietal pericardium were separated by injecting intrapericardial normal saline via a separate pericardial catheter, thus inducing "permissive pericardial tamponade". Pericardial separation was confirmed by real-time MRI and instantaneous hemodynamic monitoring allowing a temporary fall in systolic arterial blood pressure by approximately 50% to allow Angio-Seal closure. Immediately after Angio-Seal deployment, the instilled pericardial saline was aspirated.

FOLLOW UP

Immediately after closure, serial MRI scans were performed and hemodynamics were monitored continuously for three hours. Follow up studies at 1, 2-, 4- and 6-week time points included cardiac MRI. When moderate or larger pericardial effusions were detected, they were drained percutaneously from a sub-xiphoid approach.

CARDIAC MAGNETIC RESONANCE IMAGING

MRI was conducted at 1.5T (*Espre*, Siemens Healthcare, Erlangen, Germany) using the standard posterior matrix and body matrix phased array coils (Siemens). Geometry and function measurements used ECG-gated, segmented, breath-held, balanced steady state free precession imaging; Typical acquisition parameters were TR/TE, 3.6/1.8 ms; flip angle, 65° ; field of view, 300×244 mm; matrix, 256×127 pixels; slice thickness, 8 mm; bandwidth, 1085 Hz/pixel. Parallel imaging with an acceleration factor of two was used to keep breathhold times under 15 seconds. Real-time MRI was performed using balanced steady state free precession imaging with multiple (typically three) slices with the following parameters (10): TR/TE, 3.2/1.6 ms; flip angle, 45° ; field of view, 340×255 mm; matrix, 192×144 ; bandwidth, 789 Hz/pixel; generating $1.8 \times 1.8 \times 6$ -mm voxels.

Results

PERICARDIAL SEPARATION IS REQUIRED FOR EFFECTIVE CLOSURE

Non-survival feasibility experiments were conducted in six animals to test a range of introducer sheath sizes (16-Fr, n=1; 14-Fr, n=4; 9-Fr, n=1).

In open-chest animals with an intact pericardium, the Angio-Seal collagen plug consistently deployed outside the parietal pericardium. Thereafter, the suture was observed to "tether" open the transmyocardial tunnel and the collagen plug was observed to be separated from the epicardial surface and therefore unable to apply hemostatic pressure. This led to overt pericardial bleeding in two of three animals, and immediate tamponade and shock in one.

In closed-chest animals, “permissive pericardial tamponade” was created by instilling 267 ± 81 ml of saline immediately prior to Angio-Seal deployment. This maneuver effectively separated the visceral and parietal pericardium in all animals (Figure 2a), allowed the collagen sponge to enter the pericardial space, and allowed the deployment of the Angio-Seal directly onto the epicardial surface. The instilled fluids were aspirated immediately following the Angio-Seal deployment (Figure 2b). Using this approach, Angio-Seal consistently achieved hemostasis (n=3) evident on immediate necropsy in the non-survival cohort.

We found that the Angio-Seal foot (10mm) tended to pull completely through the puncture hole when used to close a 14- and 16-Fr introducer sheath. Therefore we used 10 Fr for all survival experiments.

ACUTE SUCCESS OF COLLAGEN-BASED CLOSURE OF PERCUTANEOUS TRANSTHORACIC VENTRICULAR ACCESS

Survival experiments were performed in seven animals using a 10-(n=6) or 12-fr sheaths (n=1). Among these, permissive pericardial tamponade technique consistently allowed successful percutaneous deployment of the Angio-Seal at the ventricular access site. Appropriate delivery was verified by real-time MRI by pulling and pushing the heart while still connected to the Angio-Seal device [Video 1; Online supplement].

Animals remained hemodynamically stable during all phases of the procedure. Heart rate and mean blood pressures were, respectively, at baseline, 93 ± 25 min⁻¹ and 57 ± 6 mmHg; after puncture 99 ± 9 min⁻¹ and 47 ± 5 mmHg; after Angio-Seal closure 87 ± 28 min⁻¹ and 56 ± 12 mmHg; and at 3 hour follow 90 ± 18 min⁻¹ and 54 ± 9 mmHg. No significant ventricular arrhythmias were detected during the entire procedure.

During the immediate (3-hour) observation period, no significant pericardial fluid was detected or aspirated (Figure 3a, d).

Recovery from the procedure was uneventful for all 7 animals.

LATE FAILURE OF COLLAGEN-BASED CLOSURE OF PERCUTANEOUS DIRECT VENTRICULAR ACCESS

All follow-up animals (n=7) underwent serial MRI surveillance for pericardial fluid accumulation. Six of seven animals accumulated a large pericardial effusion 5±1 days after closure (Representative images in Figures 3b, e), and therefore underwent percutaneous needle aspiration for drainage of bloody fluid. All were hemodynamically stable, two euthanized as planned, and four survived for further observation. Pathology examination indicated that the Angio-Seal collagen sponge was appropriately located inside the puncture site (Figure 4).

Among the extended follow up group (n=4) a large pericardial effusion recurred in 2 of the 4 animals (Figure 3c and 3f respectively), one of which was identified at 2 weeks and was euthanized, and one animal that died unexpectedly; Necropsy indicated a large chronic pericardial effusion associated with a patent puncture hole. The other 2 animals were followed up to six weeks with repeated imaging and showed no evidence of repeated accumulation of pericardial fluid.

Discussion

We find that a commercial collagen-based vascular closure device can achieve temporary hemostasis for closure of a direct transthoracic myocardial access port, but that it provides

insufficiently durable hemostasis. Failure to deploy the epicardial plug component inside the pericardial space may lead to ineffective hemostasis. MRI provided insight into a mitigation approach: temporary (“permissive”) pericardial tamponade effectively separates the visceral and parietal pericardial layers to allow the hemostatic collagen sponge to reach the epicardial surface.

Percutaneous transthoracic left ventricular access will be useful for a spectrum of interventional procedures including trans-apical aortic valve replacement (7), treating prosthetic paravalvular leak (5), investigational mitral valve repair (4), and left ventricular radiofrequency ablation of ventricular arrhythmias (6). These share a need for a large, rigid, or other geometrically constrained access port to deliver equipment to a target. Current practice requires direct surgical exposure, and placing apical sutures under direct visualization by a skilled surgeon prior to left ventricular puncture (13,14).

In our experiments, early hemostasis probably reflects the ability of the swollen *Angio-Seal* collagen sponge to suppress bleeding along the left ventricle puncture site. Nevertheless, bloody pericardial fluid re-accumulated after only a few days, likely reflecting slow continuous ooze. We believe the following failure modes may have contributed to this process. First, the myocardial hole may have been tethered open by the foot or suture, analogous to what we observed when the sponge deployed outside the pericardium. Second, repeated high pressure myocardial contraction creates a different device environment from the intended peri-vascular position of the device. For example myocardial contraction may displace the collagen sponge otherwise retained by friction. Accordingly, it is possible the device underwent mechanical failure or rapid biodegradation.

We do not believe other potential failure modes contributed to late hemostatic failure in this experiment, such as exit or erosion of the rigid 10mm foot through the puncture tract, non-orthogonal or other maldeployment of the foot along an endocardial trabeculation, or cardiac ejection of the device.

A more robust closure system might include some of the following features. We find a separate pericardial catheter valuable to separate the pericardial layers but also as an emergency drain. A closure bailout mechanism, such as a guidewire, probably should remain until hemostasis is assured. Direct imaging guidance, unconstrained by ribs and imaging windows, is invaluable in assuring procedure success. An enhanced closure device itself may incorporate features such as a hemostatic material inside the myocardial channel, enhanced occlusive hoods for the endocardial or epicardial surfaces, features to protect left ventricular structures from injury or entrapment, and alternative closure mechanisms such as sutures or staples. Finally, we have learned that avoiding parietal pericardial entrapment is probably important for hemostasis, at least in a “naïve” pericardium.

Our findings are limited in that we use a device designed for vascular and not myocardial closure, and we test in an animal model with different thoracic anatomy from humans. Animals remained fully anticoagulated during deployment of the closure device, in order to test this procedure in a stressed condition. We are aware that anticoagulation reversal prior to puncture site closure could potentially improve device effectiveness. An additional limitation is the use of an 8 Fr *Angio-Seal* to close a site larger than 8 Fr. The 8 Fr *Angio-Seal* device has been shown to be effective for closure of 10 Fr and even some 12 Fr vascular punctures (15,16). Left ventricular mural elasticity is greater than femoral artery elasticity, and should accommodate a smaller closure device. Nevertheless our experience has provided insight into requirements for successful engineering of a tailored left ventricular closure device.

CONCLUSIONS

The *Angio-Seal* commercial degradable collagen vascular closure device may provide temporary initial hemostasis after percutaneous transthoracic left ventricular entry. Visceral-pericardial separation, through temporary permissive tamponade, proved useful to deliver the hemostatic sponge directly to the epicardial surface in naïve animals. However, the commercial device is prone to subacute and late pericardial effusion or tamponade and should be avoided for elective clinical applications. This experience will be useful to engineer an enhanced percutaneous left ventricular closure solution.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviation list

MRI Magnetic resonance imaging

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Figure 1. Sketch of Angio-Seal deployed at the left ventricular wall

The Angio-Seal foot is located on the endocardial side; the collagen sponge seals the myocardial puncture from the epicardial side. The two components are held together by suture inside the trans-myocardial channel thus maintaining hemostasis.

Figure 2. Permissive pericardial tamponade

Real-time MRI demonstrates infusion of saline into the pericardial space through a pericardial catheter. The effect is (a) temporary separation of parietal (arrow) and visceral pericardium by the instilled fluid (asterisk). (b) After Angio-Seal deployment, all pericardial fluid is immediately aspirated. See Video 1.

Figure 3. Consecutive magnetic resonance assessment of pericardial and pleural accumulation following left ventricular closure

Coronal plane images of the heart and chest from two representative swine. Figures a-c demonstrate a case of mid-term (5 days) and late failure (>2 weeks) of Angio-Seal to maintain hemostasis. Figures d-f demonstrate a case of mid-term failure but late success in achieving hemostasis. As shown in the images, at the completion of the acute phase of the experiments (3 hours; a and d) there is minimal pericardial fluid and no pleural fluid. However at 6 days follow up there is accumulation of pericardial fluid (b and e respectively). At 2 weeks some of the animals have re-accumulated pericardial fluid (after pericardial fluid drainage at 6 days) as represented at slide (c), while others are free of pericardial fluid, as represented in slide (f).

Figure 4. Pathologic examination of 6-day Angio-Seal closure device in the left ventricular free wall

(a) Six day old Angio-Seal collagen plug that was deployed percutaneously to close direct left ventricular access. The residual suture is still present; the sponge (S) is located inside the pericardial space (double headed arrow), underneath the parietal pericardium (PP) and directly against the visceral pericardium (VP). (b) Hematoxylin & eosin stain of a transverse section of the puncture hole shows the suture (arrow) with the collagen sponge filling the area of the puncture tract. Higher power slide of the suture (dashed box on slide 4b); polarization filters reveal a spectral pattern from the suture polymer (c). High power field of the myocardium around the puncture site shows area (width of approximately 2,200 μ) of myocardial necrosis adjacent to the puncture itself. This area is bordered by inflammation (d).