Healing Study of Porcine Heart Transapical Wounds Closed Using a Remote Automated Suturing Technology

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Objective: A safe and reliable direct percutaneous approach for transapical access to the left ventricle would be a significant advance toward decreasing the invasiveness of intracardiac interventions. This report presents results from a surviving porcine beating heart model in which transapical access sites were closed using an automated suturing technique ultimately intended for percutaneous use.

Methods: Through an approved protocol including general anesthesia, the cardiac apex in 10 beating pig hearts was surgically exposed, permitting transapical passage of a 0.035-in guidewire and a 5.5F, 0.9-mL Fogarty balloon catheter. An automated suturing device was passed over the guidewire and the Fogarty onto the transapical access site. Two pledgeted horizontal mattress sutures were simultaneously placed concentrically around the apical access site with a single squeeze of the device's lever. A 25F dilator was passed into the left ventricle over the guidewire and subsequently removed. The sutures were then secured using pledgeted titanium knots. Chest wall and skin incisions were closed. The animals were recovered from anesthesia and resumed a normal diet.

Results: Under general anesthesia, the transapical access site of each animal was re-exposed, five at 1-week and five at 2-week intervals. Hemostasis was complete, and all wounds healed well.

Conclusions: The evaluation of transapical wound closures in this surviving porcine heart model demonstrates complete hemostasis and excellent healing through the use of this automated remote suturing technology.

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Transapical puncture of the left ventricle was first described in 1936 for use in angiography. It was not until the 1950s that this approach was used for diagnostic and hemodynamic assessments.[1] More recently, direct access to the left ventricle has evolved into an alternative approach for interventional cardiac therapies.[2–4]

Many surgical candidates in whom intracardiac procedures are indicated have significant comorbidities; as a result, open heart surgery with cardiopulmonary bypass may be associated with unacceptable morbidity and mortality. The use of transcatheter therapies, such as percutaneous femoral transarterial or transvenous access with subsequent transseptal puncture, may also be excluded in such patients because of difficulty with vascular access or the presence of prosthetic valves or Fontan circuits.[5] These minimally invasive approaches also have the potential for life-threatening complications due to remote access sites with tortuous pathways to the target lesion.[3,6,7]

Transapical access to the left ventricle allows for antegrade, shorter, and more direct access to the left ventricle of a beating heart compared with conventional techniques. The limitation of this approach is the need for primary site closure, most commonly by thoracotomy and direct suturing. High morbidity rates have been reported in previously investigated closure techniques and devices.[3–5,8]

We have reported results on the development and testing of a novel technology involving a remote automated transapical wound closure system in ex vivo porcine hearts, human cadavers, and beating hearts of nonsurviving pigs.[9] All automated apical closures were completely hemostatic and were as effective as hand-sutured closures tested in a comparative bursting pressure study. This research was undertaken to further evaluate the technology in a surviving porcine heart model, assessing ease of use, hemostatic ability, and postoperative histological evidence of wound healing.

METHODS

Animal Population

This study was approved by the Institutional Review Board for Animal Research. This study was conducted in a manner that

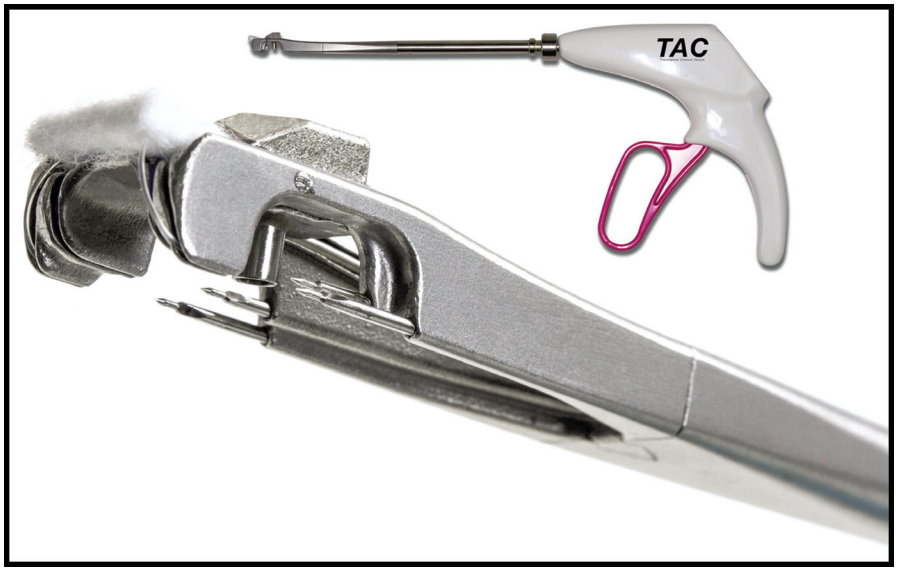

FIGURE 1. A side view of the automated suture placement device and an angled view of the tip of the device demonstrating the four needles traversing the empty tissue-engaging jaw.

does not inflict unnecessary pain or discomfort upon the animals, as outlined by the United States Public Health Service Policy on Humane Care and Use of Laboratory Animals and the Guide for the Care and Use of Laboratory Animals (1996), prepared by the Institute for Laboratory Animal Research of the National Academy of Sciences. Ten female swine, with a mean weight of 26 kg, ranging from 20 to 32 kg, were allocated to two groups: 1-week survival (n = 5) and 2-week survival (n = 5).

Initial Procedure

All animals were premedicated with ketamine, acerpromazine, atropine, and carprofen. After sedation, the animals were taken to the surgical suite and placed in supine position on a heating blanket, where isoflurane mask induction of anesthesia was performed. After the administration of lidocaine solution to the epiglottis, the animals were intubated with the appropriate size of endotracheal tube and mechanically ventilated while anesthesia was maintained. An intravenous line was placed in the ear, and cefazolin; amiodarone; and, if required, lidocaine were administered. In those animals undergoing a sternotomy, additional buprenorphine was given preoperatively.

The location of the apex in pig hearts is more medial compared with that in humans.[10] The location of the initial exposure varied in the early stages of the study as we attempted to identify the ideal approach in the pig. The procedure was performed through a left parasternal vertical thoracotomy in one animal, a left subcostal incision in one animal, a complete transverse sternotomy in two animals, and a left minithoracotomy with partial sternotomy in six animals. The last approach seemed optimal. In the earlier portion of the study, the pericardium was carefully opened and the apex was exposed. Later in the study, the pericardium was preserved in such a way as to allow it to be incorporated into the wound closures. One animal died upon opening the pericardium with Bovie because of ventricular fibrillation, but before cardiac manipulation, despite premedication with antiarrhythmics, and was therefore replaced with another animal to yield 10 survivors.

After exposure of the left ventricle, an 18-gauge intravenous catheter with an introducer needle was advanced perpendicularly into a fat-free portion of the left lateral anterior apex during diastole. Once a blood flash was observed, the needle was removed, and a "J"-tipped guidewire with an outer diameter of 0.035 in was inserted through the catheter, which was removed after adequate advancement of the guidewire into the ascending aorta. A custom-designed 8.3F dilator was used in three animals during the latter phase of the study. The dilator was passed over the guidewire and was used to enlarge the punctured pericardium/myocardium to allow for adequate positioning of tissue within the jaw of the suturing device. The dilator was subsequently removed, and a 5.5F Fogarty balloon catheter was passed over the guidewire through the apex and inflated within the left ventricle. Centered on the catheter, the TransApical Closure Device (LSI SOLUTIONS, Victor, NY USA) (Fig. 1) was guided onto the surface of the left ventricle.

The underlying myocardial tissue was mechanically aligned into the jaw of the suturing device. Pulling up on the Fogarty balloon while pushing the device tip down assisted in positioning and compressing the targeted tissue within the jaw. Deployment of the device allowed four integrated needles to simultaneously advance through the targeted tissue. Two needles oriented concentrically around both sides of the access site placed two specialized horizontal mattress sutures, one of 2-0 polypropylene and the other of 2-0 nylon, sharing a common distal preloaded four-holed Teflon pledget. Each suture was threaded through a separate CK Device (LSI SOLUTIONS; Fig. 2A) preloaded with a Teflon pledget, providing the ability to tension the horizontal mattress sutures, each now pledgeted on the proximal and distal sides of the wound, and to apply pressure to control bleeding at the access site.

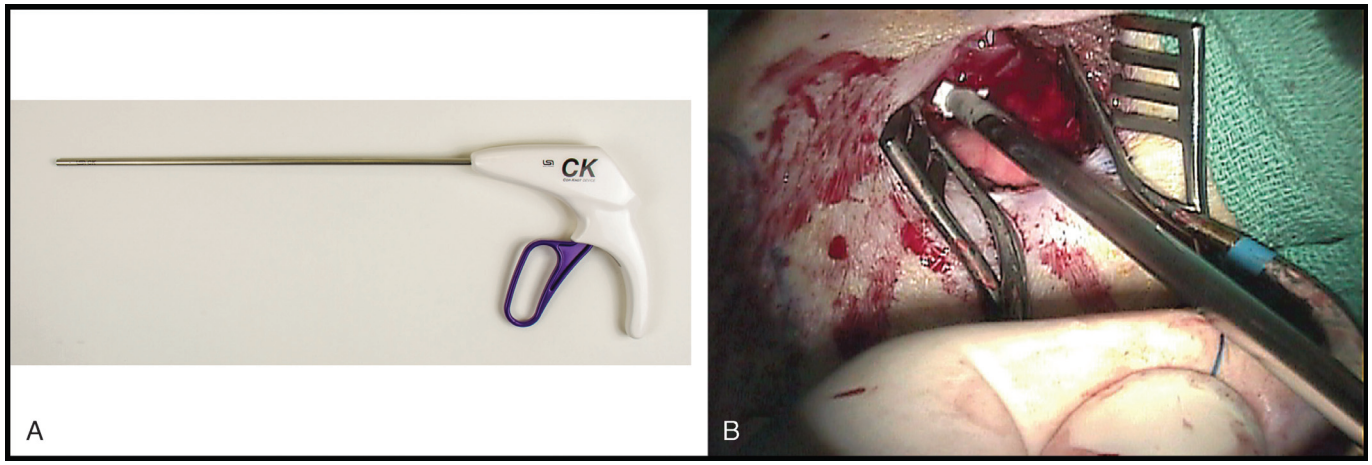

FIGURE 2. A, A side view of the automated knot device. B, The tip of the automated knot device preloaded with a pledget advancing to the access site for mechanical titanium knot placement.

After removal of the suturing device and the Fogarty balloon catheter, the apical access site was dilated with a commercially available 25F diameter dilator (Edwards Lifesciences, Irvine, CA USA). Once the dilator was removed, each of the pledgeted horizontal mattress sutures was fastened together using a CK Device deploying a mechanical COR-KNOT (LSI SOLUTIONS; Fig. 2B). All closure sites were hemostatic at the completion of the procedures.

In the four animals in which the pleural cavity was entered, the iatrogenic pneumothoraces were evacuated using suction and a catheter. Sternal, fascial, and skin incisions were sutured in layers. The animals were then recovered, housed, fed, and monitored daily. Skin wound dressings were not used.

Re-Exploration

Five animals were brought back to the operating room on postoperative day 7; and five animals, on postoperative day 14. On re-exploration, the animals were premedicated, positioned, and anesthetized, as described previously. Their hearts were exposed via a sternotomy in 9 of the 10 animals, whereas in one, we performed a subcostal clamshell approach. Hemostatic apical closure sites were observed in all beating hearts. The animals were then euthanized while under anesthesia using Beuthanasia-D or pentobarbital. The hearts/apical specimens were then harvested, with further dissection of the closure site for detailed viewing of wound healing on both epicardial and endocardial surfaces.

Histological Analysis

The hearts/apical specimens were then placed in formalin, sectioned, routinely processed, and embedded in paraffin. Serial 4-μm–thick sections were prepared for hematoxylin and eosin and Gömöri trichrome staining.

RESULTS

Initial Procedure

Transthoracic apical exposure was achieved without complication in 10 animals. Ventricular fibrillation with subsequent death occurred during apical exposure in one additional animal consequently excluded from the surviving cohort; although its heart had stopped beating, transapical access and site closure were still performed in this deceased pig to provide a closure site of nonsurviving control specimen. Transapical access to the left ventricle was accurately obtained using the Seldinger technique in 9 of the 10 eligible animals. In one, it seemed that the right ventricle was unintentionally entered because of abnormal cardiac anatomy and/or orientation; however, left ventricular access was successfully obtained on subsequent repositioning. All left ventricular access sites were dilated to 25F, and subsequent automated closure was achieved. All beating heart access sites were observed to be completely hemostatic (Fig. 3).

Once the cardiac apex was exposed, the average time from the beginning of the transapical access procedure at the commencement of the Seldinger technique to the end of the myocardial access site closure with the two titanium knots was approximately 12 minutes.

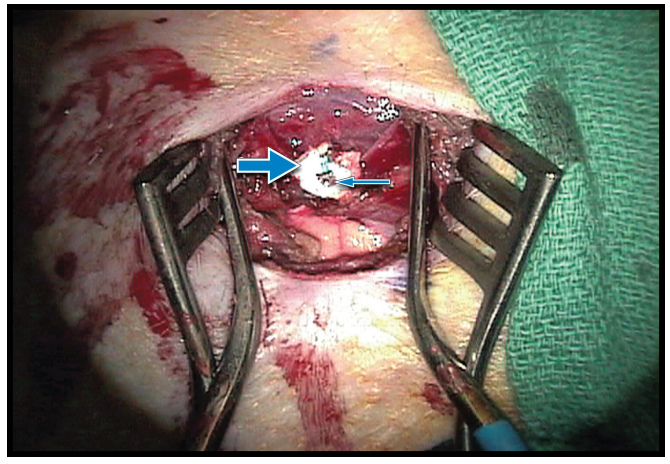

FIGURE 3. Complete hemostatic closure of the transapical access site with pledget (bold arrow) and titanium knot (thin arrow) in place at the completion of the initial procedure.

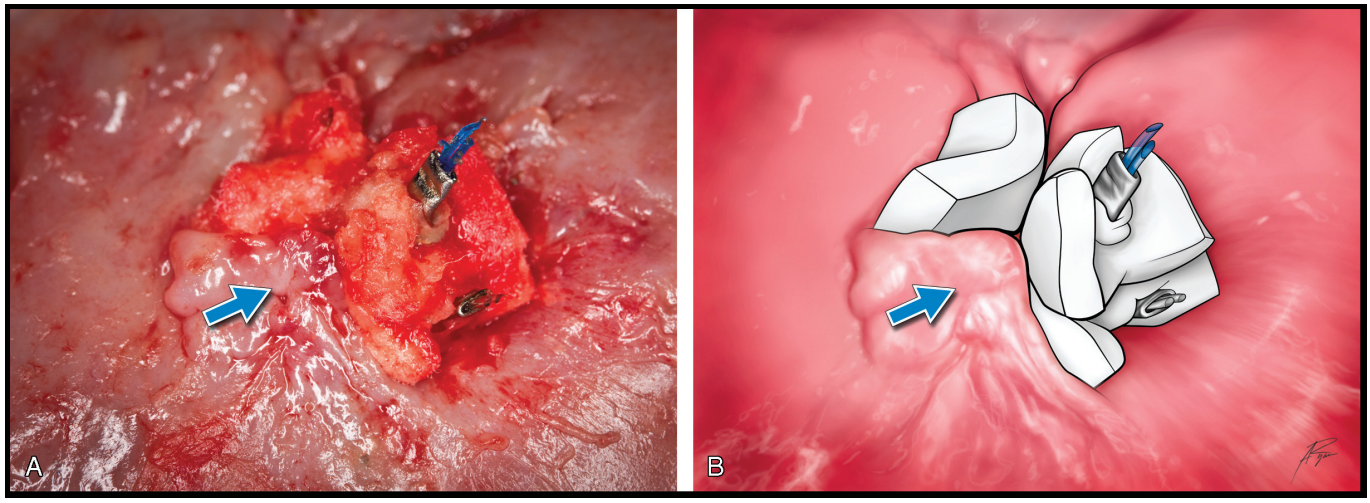

FIGURE 4. The epicardial surface after cardiac harvest on postoperative day 7 shown with the healing transapical access closure site (arrow) centered in the photograph (A). The accompanying illustration (B) highlights the pledgets and the titanium knots around the closure site (arrow).

Re-Exploration

The postoperative course was unremarkable in 8 of the 10 animals. Minor complications were identified in two: additional analgesia was required in one and a course of antibiotics was initiated in the other for signs of postoperative pneumonia. A minimal increase in mean weight to 27 kg was observed (range, 18–31 kg).

At the time of re-exploration, a small wound seroma was identified in one animal, and the chest wall exposure site in six animals demonstrated mild wound infection; however, there were no complications directly related to the myocardial apical closure site in any animal. Marked adhesion formation at the access site was observed in the four animals in which the pericardium was not incorporated into the site closure. All beating heart access sites remained hemostatic.

On further examination after cardiac harvest, no evidence of pseudoaneurysm formation was identified, and all closures demonstrated excellent tissue healing macroscopically at both 1- (Fig. 4) and 2-week intervals (Fig. 5).

The endocardial surfaces began to re-endothelialize within 1 week (Fig. 6A). Maturing, well-healed wounds were apparent by 2 weeks (Fig. 6B).

Histological Findings

The histological Gömöri trichrome staining analysis of the control specimen harvested immediately after completion

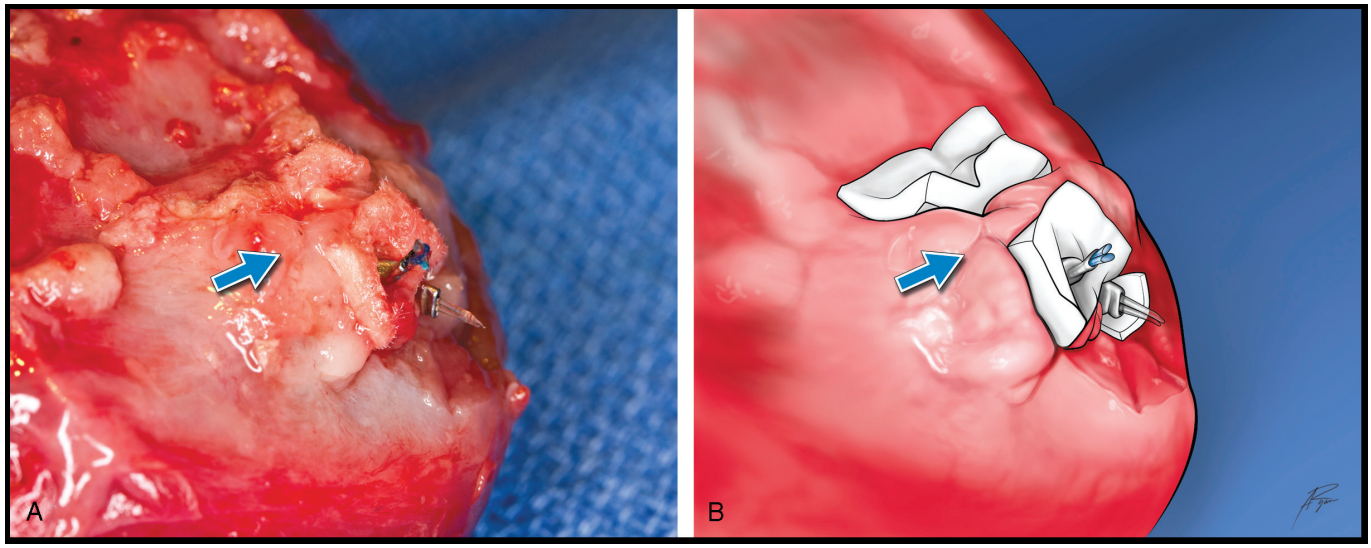

FIGURE 5. The epicardial surface after cardiac harvest on postoperative day 14 shown with the healing transapical access closure site (arrow) centered in the photograph (A). The accompanying illustration (B) highlights the pledgets and the titanium knots around the closure site (arrow).

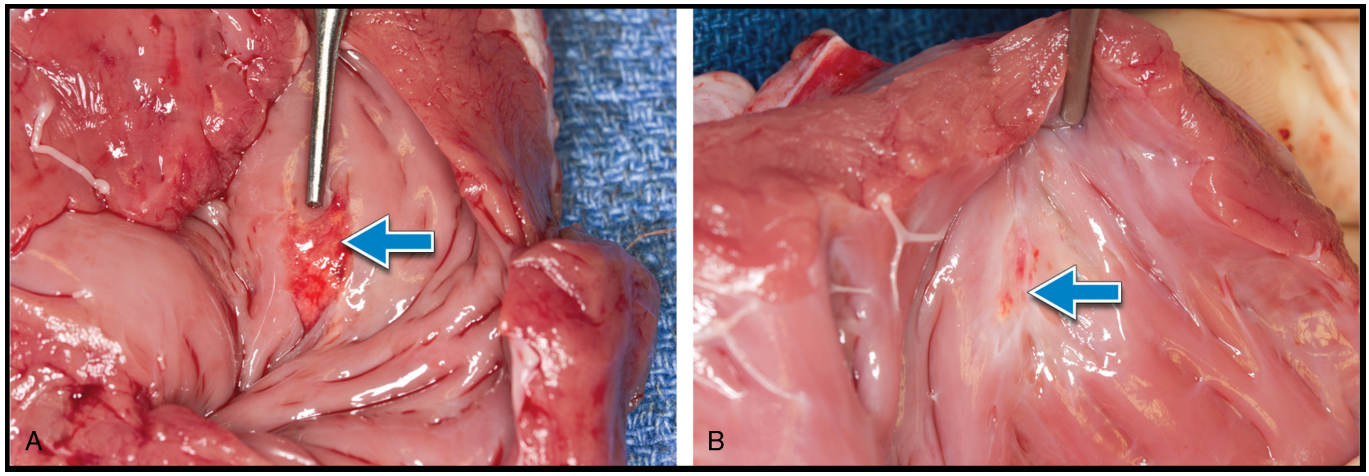

FIGURE 6. Re-endothelialized endocardial surface of the apical closure (bold arrow) on postoperative day 7 (A) and day 14 (B) with excellent healing and maturing closure site formation.

of the initial procedure in the deceased animal demonstrated excellent tissue apposition (Fig. 7A). On postoperative day 7, there was clear evidence of immature granulation tissue and mild collagen formation at the closure site (Fig. 7B). On postoperative day 14, there was maturing scar formation with moderate collagen deposition bridging the closure site cleft (Fig. 7C).

DISCUSSION

Percutaneous transapical puncture has been successfully used in the past for hemodynamic assessment and diagnostic purposes.[1] More recently, direct access to the left ventricle has been used to facilitate complex interventional procedures such as paravalvular leak and left ventricular pseudoaneurysm closure as well as for other structural cardiac interventions such as surgical delivery of transcatheter aortic valves.[2,3] Although these interventions may offer advantages over conventional open or femoral approaches in the high-risk patient, such procedures typically require larger-diameter sheaths. This requirement has been shown to result in high morbidity rates, ranging between 8% and 40%, due to pericardial bleeding or hemothorax, particularly when the access site is not primarily closed.[4,5,8] A recent report by Pitta et al,[8] describing 32 patients undergoing percutaneous left ventricular apical puncture, demonstrated a higher complication rate in those patients undergoing access for interventional than for diagnostic purposes (25% versus 13%). The most common complication was hemothorax (19%), thought to be the result of bleeding from the ventricular puncture site or a laceration of the coronary, pleural, or intercostal vessels. The authors concluded that there was a need for a safe and reliable method of closing such access sites.

To date, there is no validated safe and reliable method of closing a sizable percutaneous cardiac transapical access site, although various methods have been investigated. One of

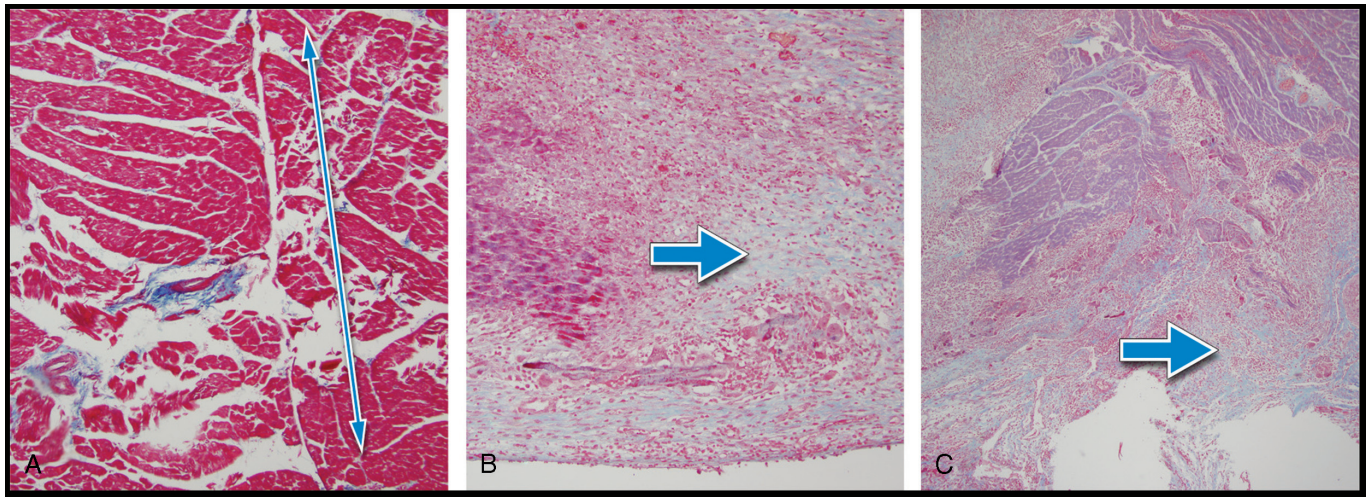

FIGURE 7. Gömöri trichrome stain at 4× magnification of a section through the transapical closure site. A, The control specimen identifying excellent immediate tissue apposition (left of the arrows). B, Immature granulation tissue and mild collagen formation (bold arrow) on postoperative day 7. C, Maturing scar formation with moderate collagen deposition bridging the closure site cleft (bold arrow) on postoperative day 14.

the first studies assessing direct closure of a ventricular access site formed by sheaths ranging from sizes 6F to 9F was performed by Lim et al.[4] Results demonstrated good success when horizontal mattress sutures to the superficial skin were performed after sheath removal in eight patients undergoing direct left ventricular access (n = 6) or right ventricular puncture (n = 2); only one patient developed hemothorax due to trauma of the intercostal vein.

Other closure techniques have been tested with some success. A survivor porcine study of seven animals was recently performed by Barbash et al[11] evaluating the safety and the feasibility of using a commercial collagen-based femoral artery closure device. Six of the seven animals accumulated a large pericardial effusion after closure, and, despite drainage, the large effusion recurred in half and was lethal in one. Jelnin et al[3] reported experience in 28 patients undergoing percutaneous transapical puncture for interventional procedures. A coil was used for access site closure in one patient and for a muscular ventricular septal defect occluder in another, and all other transapical accesses were closed using a duct occluder. Complications were observed in one patient, and the procedure proved to be fatal in another.

Our study demonstrated complete hemostatic closure of 10 access sites of beating hearts of surviving pigs that were initially dilated up to 25F. There were no procedure-related complications, and, at 1- and 2-week re-exploration, the closure sites were completely hemostatic, with evidence of both macroscopic and microscopic tissue healing. The high rate of chest wall wound infection is likely attributable to breed quality and/or farming conditions because six of the seven animals who underwent subsequent necropsy were identified to have significant pulmonary comorbidities, possibly affecting healing.

Our findings are limited by the short follow-up intervals of only 1 and 2 weeks. Late complications at the access closure site, therefore, cannot be excluded. Had we acquired specific pathogen-free animals, fewer complications may have been seen.

In conclusion, the automated apical access closure techniques and technologies developed for direct ventricular access and closure using the TransApical Closure Device (LSI SOLUTIONS) along with the CK Device and COR-KNOT (LSI SOLUTIONS) were demonstrated to be highly effective and reliable. This system provides immediate and reliable hemostasis of transapical access sites, with evidence of effective wound healing at both 1- and 2-week intervals. These successful results illustrating strong automated apical closures in the surviving porcine beating heart model encourage further evaluation.

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CLINICAL PERSPECTIVE

This article from Dr. Wilshire and her group from the University of Rochester investigated an automated suturing device for transapical access to assist in the performance of transcatheter valve replacement (TVR). This device was tested in 10 animals, which were then kept alive for 1 to 2 weeks. The entry site was dilated with a 25F dilator to simulate a TVR. In the surviving animals, all beating heart access sites remained hemostatic, and there was no evidence of pseudoaneurysm formation. Histologic examination showed excellent healing.

This is a timely experimental study. Bleeding and pseudoaneurysm formation remain rare but morbid complications of transapical access have prompted the search for other approaches for TVR such as transaortic, transsubclavian, and transcarotid. Although this is a small study with short follow-up, the findings are encouraging and support further evaluation of these devices.

