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Transvenous Access to the Pericardial Space: A Novel Approach to Epicardial Lead Implantation for Cardiac Resynchronization Therapy

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Abstract

Background: Percutaneous access to the pericardial space (PS) may be useful for a number of therapeutic modalities including implantation of epicardial pacing leads. We have developed a catheter-based transvenous method to access the PS for implanting chronic medical devices.

Methods: In eight pigs, a transseptal Mullins sheath and Brockenbrough needle were introduced into the right atrium (RA) from the jugular vein under fluoroscopic guidance. The PS was entered through a controlled puncture of the terminal anterior superior vena cava (SVC) (n = 7) or right atrial appendage (n = 1). A guidewire was advanced through the transseptal sheath, which was then removed leaving the wire in PS. The guidewire was used to direct both passive and active fixation pacing leads into the PS. Pacing was attempted and lead position was confirmed by cine fluoroscopy. Animals were sacrificed acutely and at 2 and 6 weeks.

Results: All animals survived the procedure. Pericardial effusion (PE) during the procedure was hemodynamically significant in four of the eight animals. At necropsy, lead exit sites appeared to heal without complication at 2 and 6 weeks. Volume of pericardial fluid was 10.8 ± 6.2 mL and appeared normal in four of the six chronic animals. Moderate fibrinous deposition was observed in two animals, which had exhibited significant over-procedural PE.

Conclusions: Access to the PS via a transvenous approach is feasible. Pacing leads can be negotiated into this region. The puncture site heals with the lead in place. Further development should focus on eliminating PE and performing this technique in appropriate heart failure models.

Introduction

Percutaneous access to the pericardial space (PS) may be useful for a number of therapeutic modalities ranging from drug delivery to implantation of medical devices. One useful example would be the implantation of pacemaker leads used in cardiac resynchronization therapy (CRT). The site of pacing strongly influences the sequence of contraction in the left ventricular (LV) wall.¹ Optimal positioning of the LV pacing lead is necessary to achieve maximum mechanical benefit from CRT.²⁻⁵ However, the standard approach to LV lead placement via the coronary sinus (CS) can be technically challenging in some patients. Variations in normal, abnormal and distorted venous anatomy can substantially interfere with LV lead positioning.

As a consequence, between 5 and 15% of the attempted LV lead implantations fail, approximately 9% of the CS-LV leads later become dislodged postimplantation and substantial number of patients receive little or no benefit from CRT, in part due to poor lead positioning.⁶

We are developing nonsurgical methods for accessing the PS and subsequently LV epicardial pacing sites that can be used when the conventional CS technique fails. The current study looks at the feasibility of using a catheter-based transvenous approach to epicardial lead implantation via controlled puncture of cardiac structures. We set out to show, in principal, that transvenous pacing leads could be advanced through select puncture sites in or near the heart leading into the PS and that the puncture site would heal with the lead in place.

Methods

All experimental procedures were reviewed and approved by the Animal Care and Use Committee of the National Heart, Lung and Blood Institute.

NIH mini-pigs ($n = 8$) of both sexes (42.3 ± 3.6 kg) were sedated with an anesthetic cocktail (0.1 mg/lb atropine sulfate (0.4 mg/mL), 1.0 mg/lb xylazine (100 mg/mL), 3.0 mg/lb ketamine HCL (100 mg/mL), 0.1 mg/lb butorphanol tartarate (10 mg/mL). Cefazolin (20–30 mg/kg IV) was administered prophylactically, at recovery and repeated 8 hours later ($n = 6$). In all animals, anal-gesia was achieved by placement of a fentanyl patch (50 mg/hr) peri-procedurally and administration of buprenorphine hydrochloride (6 mg/kg IV) as required. The animals were ventilated with a mixture of oxygen, medical air, and isoflurane (1–3%). A water-circulating blanket was used to maintain temperature at 38°C. All procedures were performed using aseptic techniques. A 6F sheath was introduced percutaneously or by surgical cut down into the right femoral artery to measure systemic arterial blood pressure. Dopamine (1–5 mcg/kg/min) was infused when mean arterial blood pressure fell below 80 mmHg. Oximetry, blood pressure, ECG, and level of sedation were monitored throughout the procedure.

A surgical cut down was performed to isolate the right jugular vein. Two guidewires were advanced through the vein into the inferior vena cava (IVC) under fluoroscopic guidance. A 5–7F pigtail catheter was inserted over the guidewire into the right atrium (RA) and a transeptal catheter (Medtronic, Mullins™, 8F 44 cm) was advanced into the IVC. Cine fluoroscopic views of the RA and superior vena cava (SVC) were performed using the pigtail catheter and manual injection of radiocontrast (10–20 mL). Cine images were reviewed and anatomic landmarks such as the RA appendage and the border of the RA and SVA in AP projection were noted. A controlled puncture was attempted at one of two sites. (See Fig. 1.) If the catheter could not be optimally positioned in the RA appendage, then the puncture was made at the anterior aspect of the terminal SVC (Fig. 2). In a single case, the procedure was modified to facilitate implantation of an active fixation lead by using a 9F peel away introducer sheath (SafeSheath® 25 cm 9F, Pressure Products), which was advanced into the PS over the 0.014" guidewire. The dilator and 0.014" wire were removed leaving the sheath in place, through which, a screw-in lead (CapSureFix™, 6.6F, Medtronic) was advanced into the PS, followed by sheath removal. The modified peel away introducer was then removed leaving the screw-in lead in place.

Pericardial effusion (PE) was estimated using change in fluoroscopic silhouette and change in mean arterial blood pressure. A sustained reduction of mean arterial blood pressure 20 mmHg was considered significant. Final lead position was documented by cine fluoroscopy. Epicardial pacing was attempted using an external stimulator. In one case angiography of the left coronary artery was performed while the lead was positioned on the left lateral wall. The proximal end of the lead was secured and the wound was closed in layers.

One group of animals were sacrificed acutely ($n = 2$), and the others at intervals of approximately 17 ($n = 3$) and 46 days ($n = 3$). Final lead position was confirmed by cine fluoroscopy. The incision site was reopened and the pacemaker lead was reconnected to an external stimulator, and pacing was attempted. The animal was euthanized. A postmortem examination was performed with special attention given to the lead puncture site and the PS. Tissue samples from the puncture site were fixed and embedded in paraffin. Histological slides (10 μm sections) were prepared using H&E and Masson trichrome staining.

Statistical Analysis

Continuous parameters were summarized using mean and standard deviation, and were compared using Student's *t*-test. A value of $P < 0.05$ was considered significant.

Results

The PS was successfully accessed through the terminal SVC ($n = 7$) and the RA appendage ($n = 1$). Both over the wire passive ($n = 7$) and active fixation pacing leads ($n = 1$) were used. The PS was entered through the terminal SVC ($n = 7$) and the RA appendage ($n = 1$). Coronary angiography was performed ($n = 1$) and relative epicardial lead position was assessed with attention to the venous filling phase. Fluoroscopic images from the implantation procedure are shown in Figure 3. Half the animals ($n = 4$) developed hemodynamic changes post-puncture that were treated with dopamine (initial dose: 1–3 mcg/kg/min). These animals ($n = 4$) were successfully weaned of dopamine within 28 ± 20 minutes. Blood pressure and heart rate remained stable over the course of the procedure ($n = 8$). On average ($n = 8$), the mean arterial blood pressure fell 2.0 ± 8.0 mmHg ($P = 0.048$), and heart rate slowed 11 ± 24 bpm ($P = 0.043$), from the time the arterial line was placed until removal. Capture of the ventricle was achieved in seven of the eight animals at implantation, (average threshold = 4.2 ± 1.2 mA, pulse width = 5 ms, R-wave 11.1 ± 3.7 mV). All animals were stable by the end of the procedure and recovered without further difficulty.

All leads ($n = 6$) remained in the PS over the recovery period (average duration 31 ± 15 days). In most cases, the lead position had changed when compared to the x-ray images at implant. Intermittent pacing was achieved in the majority ($n = 4$) of the chronic animals, (average threshold = 4.9 ± 1.1 mA, pulse width = 5 ms, R-wave 5.2 ± 2.6 mV). Inability to capture corresponded to ineffective lead position ($n = 1$) and significant fibrinous changes ($n = 1$) in the PS.

The animals were euthanized and autopsy was performed ($n = 6$). In the two nonsurvival studies approximately 10 mL and 30 mL of serosanguinous fluid and clotted blood was found in the pericardium. In the chronic group ($n = 5$) normal amounts of serous pericardial fluid were observed at necropsy, on average 10.8 ± 6.2 mL. In one case, a 15 mL serosanguinous effusions was observed. Filamentous fibrinous deposition in the PS was observed ($n = 2$) with adhesions present in one case. Significant effusions during the acute procedure seemed to predict abnormal pericardial findings at autopsy. Gross pathology of the exit sites acutely at 17 days and 46 days are illustrated (see Fig. 4). In all cases, the puncture site appeared well healed on gross inspection. Histology of the nonsurvival animal puncture sites showed disruption of the vessel layers and mural localized hematoma and fibrinous clot formation. In the 17-day group, fibroplasia, mesothelial and endothelial proliferation, neovascularization, some regions of discreet necrosis and mild chronic and active inflammation were observed. ($n = 3$). At 46 days ($n = 3$), the resolution of inflammation and findings consistent with organized scar formation were evident. (See Fig. 5.)

Discussion

We were able to introduce both passive and active fixation leads into the PS using the methods described above. Both puncture sites could be approached from the SVC. Both sites had easily identifiable anatomic landmarks that could be distinguished fluoroscopically. Both sites permitted entry into a fluid filled space (in contrast to a potential space) with an exit angle relatively parallel to the pericardium. Transient use of dopamine was necessary in only half the cases and was successfully weaned prior to recovery. All the animals recovered without further complication. The PS appeared relatively normal in the majority of animals at necropsy. The transit site into the PS from the terminal SVC and RA-appendage appeared to heal with the pacing lead in place in all six of the chronic study animals.

Currently, when standard transvenous lead placement is not possible or where the anatomy does not accommodate optimal lead positioning patients can undergo a number of alternative implantation procedures.⁷⁻¹¹ By far the most common option is to place LV leads directly on the epicardium, through sternotomy, modified sternotomy or any variety of laparoscopic techniques.¹² Surgical epicardial lead implantation has the advantage that direct access to the epicardium affords more freedom in selecting pacing sites. In addition, patients undergoing surgical implantation rarely need reintervention, due to the low incidence of lead dislodgement.¹³ However, surgical approaches can be very invasive. Patients often face a second separate procedure once the less-invasive conventional approach has failed. Surgical implantation is preformed under general anesthesia. The equipment and technical skills required are commonly outside the capabilities of clinical electrophysiologic services; therefore the surgical service must be consulted. These factors can lead to significant increases in the risk and cost associated with LV lead placement. Unlike most surgical alternatives the transvenous epicardial lead implantation technique could be performed immediately once the conventional approach has failed. This method would not necessarily require general anesthesia, additional incisions or surgical consultation.

Although the concept of transvenous access to the PS has been previously described¹⁴ this paper is the first to address introduction of permanent implantable medical devices via a controlled puncture. In addition, this is the first description of access to the PS by controlled perforation of the SVC. Verrier et al. published three studies where experimental catheters (4F) were advanced transvenously from the IVC into the RA; there a puncture the RA appendage was performed. Their method provided temporary access to the PS for the sampling or removal of fluid and administration of infusible therapies. These studies were repeated on animals in pulmonary hypertensive states and with aspirin.^{15,16} In all cases the puncture was well tolerated and sealed without complication. In our study the puncture was well tolerated but we did observe effusions as a result of our puncture. PE and tamponade are of great concern and can lead to significant clinical consequences.^{17,18} In most cases the bleeding associated with our puncture did not lead to further complications. In two cases, however, we observed diffuse fibrillar deposition in the PS at autopsy. (Both of these animals appeared to have moderate effusions during the transvenous puncture.) Constrictive pericarditis has been associated with pacing lead perforation and hemorrhagic effusion.¹⁹ We speculate that the hemepericardium produced during our procedure led directly to the pericardial changes witnessed. On the basis of our two acute studies we must assume that some degree of bleeding into the pericardium occurred in all cases. It is likely the mismatch in catheter size and the time required to exchange catheters over the wire contributed to the volume of the effusion. Minor modifications to the currently available catheters could significantly reduce or eliminate bleeding associated with this approach. Our catheter devices precluded ready access of the RA-appendage in these miniswine. The terminal SVC provided a much more accessible puncture site. This was due to the shape of the transseptal catheters we employed in this study; any approach to the RA-appendage from the superior veins requires a sharp turn once in the atrium. A different catheter

design may be more suitable to puncture RA-appendage. Punctures through more muscular structures, such as the RA-appendage, may also reduce the effusion.

Once the pacing lead was in the PS we were able to direct it to the left lateral wall with ease. However, we were unable to reliably pace the LV with the lead freely floating in the PS in all cases. In the single case where we attempted to implant an active fixation lead we were unable to direct the screw toward the myocardium. (We were unable to capture with this lead.) At this time we are not aware of any active fixation pacing leads on the market capable of right-angled fixation that can be advanced into the PS using this technique. We are currently developing pacing leads to complement our approach. In this study we also demonstrated the lead position relative to the coronary anatomy by angiogram. Presumably, active fixation devices could pose a potential hazard to vessels susceptible to puncture. Venograms of the CS are commonly performed during standard LV lead placement by implanting physicians. This procedure would provide similar anatomic information to guide pacing site selection.

Evaluating the integrity of the puncture site postimplantation was one of the principal aims of this study. The long-term effects of pacing leads spanning the RA have been studied in humans. Endocardial pacing leads are occasionally implanted using a surgical transatrial approach in patients with upper vein obstruction.²⁰ In these cases, the RA is visualized through sternotomy; pacing leads are passed through a small surgical incision into the RA and threaded into vascular space for standard endocardial implantation; a purse string suture is applied to secure the lead. Some patients who underwent this procedure have been followed for over 14 years. There are no reports of complications directly resulting from the RA incision or failure of the tissue surrounding the lead. However, most of our punctures were made through the terminal SVC. The changes we observed both grossly and with histological slides suggest that the SVC may be equally stable with long-term device implantation.

Limitations

There are significant differences between swine and human anatomy. Although, the anatomic structures we identified as puncture targets are relatively similar in humans important variations may exist. All implantations were made in healthy swine without significant pericardial abnormalities; it is likely that a large subset of CRT patients may have significant adhesions that could interfere with this and similar minimally invasive approaches to the PS. The long and short-term consequences of this procedure were not evaluated in heart failure models or under anticoagulant states. We did not quantitatively evaluate the acute effusion that occurred during the implantation procedure. The use of dopamine may have masked accurate assessment of the hemodynamic consequence from our puncture. Survival of the animal with the pacing lead in place was important to evaluate the healing process. Therefore, the transient use of dopamine was implemented. The instrumentation we employed was not optimal for this indication. Inappropriate catheter shape and size may have lead to greater effusion than would be expected with customized devices.

Conclusion

Recent figures estimate that over 50,000 biventricular pacing devices are implanted annually in patients hoping to benefit from resynchronization.²¹ It remains to be seen whether a catheter-based transvenous approach to epicardial lead implantation will facilitate optimal LV lead placement. More important, it remains to be seen whether it is safe to perform this procedure in the cohort of patients with heart failure. However, our work suggests that it may be possible. Unlike the current surgical epicardial implantation techniques this approach does not require a separate procedure, general anesthesia and could be performed by implanting physicians familiar with common catheter-based techniques. (Although, modifications to current pacing leads technology will be necessary to facilitate active fixation and bloodless entry into the PS.)

Furthermore, this approach may also be applicable to other indwelling devices where position in the pericardium might be desirable, such as implantable defibrillator leads or implantable infusion pump. Pacing leads can be positioned within the PS using a transvenous approach from the superior veins. The acute procedure is well tolerated despite effusion. The site of puncture heals with the chronic lead in place. Future studies will address catheter and lead design, safety and efficacy of this approach.

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Figure 1.

These two drawings illustrate the sites of controlled perforation utilized in this study. Exit site A is the terminal anterior SVC near the superior sinus of the PS. Exit site B is the right atrial appendage. The dotted line represents the projected path that the pacing lead might follow.

Figure 2.

The Mullins[™] transseptal catheter and needle (Brockenbrough[™], 18 gauge 44 cm, Medtronic) is positioned near the puncture site. (See panel A.) Radiocontrast is injected through the needle to confirm the location of the catheter during puncture. The puncture is made by advancing the needle the lumen of the catheter; the catheter is then passed into the PS. (See panel B.) Successful entry into the PS is confirmed by injection of radio contrast. A 0.014 wire is advanced through the lumen of the needle and into the PS. (See panel C.) The catheter and needle then removed leaving the 0.014 guidewire in place. (See panel D.) At this point two different methods for delivering pacing leads into the PS can be employed. Panels E and F illustrate the method used most often in this study. A pacing lead (Attain[™] OTW 5F, Medtronic,) is then advanced over the guidewire into the PS. (See panel E.) The guidewire was withdrawn leaving the pacemaker lead in the PS. (See panel F.)

Figure 3.

The three panels above show fluoroscopic images of an over the wire pacing lead that was advanced through the terminal SVC and positioned on the left lateral wall. Angiography of the left coronary system provides reference in the RAO (A), AP (B) and LAO (C) projections. The lead was maneuvered after the AP projection was acquired to a more basal position seen in panels B and C.

Figure 4. These photographs show pacing lead exiting the terminal SVC and entering the PS in an acute case (A), at 17 days (B) and 46 days (C). At both 3 and 6 weeks the exit sites appeared stable and relatively normal.

Figure 5.

The figure above shows an oblique slice of the puncture site in one animal (46-days postimplant) at $2.5\times$ magnification. The blue arrow indicates the general direction of the pacing lead as it transited from the venous space into the PS. (The lead was removed for processing.) The H&E stained slide on the left shows resolution of inflammation and well-organized tissue surrounding the pacing lead. The image on the right is the corresponding trichrome-stained tissue.