Percutaneous Transatrial Access to the Pericardial Space for Epicardial Mapping and Ablation

Running title: Scanavacca et al.; Transatrial access to the epicardial space

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Abstract:

**Background** — Puncture of the atrial appendage may provide access to the pericardial space. The aim of this study was to evaluate the feasibility of epicardial mapping and ablation through an endocardial transatrial access in a swine model.

**Methods and Results** — An 8F Mullins sheath was used to perforate the right (16) or left (1) atrial appendage in 17 pigs with a median size of 27.5Kg (Q1 25.2, Q3 30.0 kg). A 7F ablation catheter was introduced into the pericardial space to perform epicardial mapping and deliver RF pulses on the atria. The pericardial space was entered in all 17 animals. In 15 (88%) animals there was no hemodynamic instability (mean BP monitoring: initial: median 80, Q1 70, Q3 86; final: median 88, Q1 80, Q3 96, p=0.426). In these 15, a mild hemorrhagic pericardial effusion was identified and aspirated (median: 20ml/animal; Q1 15, Q3 30 ml) during the procedure and post mortem gross analysis found the atrial perforation was closed in these animals. In 2 of 17 (12%) animals there was major pericardial bleeding with hemodynamic collapse. On gross examination it was found that pericardial space was accessed via right ventricular perforation in one animal and the tricuspid annulus in the other. After the initial study, we used an occlusion device in three other animals (SJM, St Paul MN) to attempt to seal the puncture (two at RAA and one at RV). These 3 animals had no significant pericardial bleeding.

**Conclusions** — Transatrial endovascular RAA puncture may provide a potential alternative route for pericardial access. Further studies are needed to evaluate its safety with longer and complexes procedures before being applied in clinical settings.

**Key words:** transvenous, epicardial, mapping, ablation, atrial appendage, pericardial access, heart catheterization, pericardial effusion, paracentesis
Introduction

Subepicardial myocardial fibers may be the substrate for ventricular tachycardia (VT) in a significant portion of patients. Thus, combining endocardial and epicardial approaches may improve the success rate of VT ablations.¹⁻⁵ The most common technique to access epicardial substrate is through a non-surgical subxiphoid pericardial puncture; however, subxiphoid access is challenging for most electrophysiologists due to the significant potential risk of RV puncture.

An alternative that uses femoral access is to perforate the heart from the endocardial side. Verrier et al showed that the percutaneous approach via the right atrial appendage (RAA) provides a rapid and safe transvenous route to access the normal pericardial space.⁹,¹⁰ Subsequent studies have shown that RAA perforation may be useful to deliver a number of therapeutics ranging from drug delivery to implantation of pacemaker leads for cardiac resynchronization therapy.¹⁰⁻¹³ However, the feasibility of epicardial mapping and ablation via appendage perforation has not been explored. We sought to evaluate the feasibility of accessing and then maneuvering in the normal pericardial space through atrial appendage perforation. We also explored the possibility of using a closure device to close the puncture in a pilot study.

Methods

The experiments were performed according to a protocol approved by the scientific and ethical committee of our institution in accordance with the guidelines for good practices for the care in the laboratory animals.

Twenty pigs (median weight 27.5Kg, Q1 25.2, Q3 30.0Kg) were used in this study. The animals were fasted overnight and pre-anaesthetized using an intramuscular injection of 22 mg/kg of ketamine hydrochloride (Ketamine) and 0.3 mg/kg of midazolan (Dormonid). General anesthesia was performed with 10mg/kg intravenous thionembutal followed by inhaled halothane.
or isoflurane at 1% on mechanical ventilation. Peripheral venous access was obtained in the auricular region of the animals. Arterial blood pressure was recorded through a femoral arterial line. A 7F decapolar catheter was introduced into the coronary sinus via superior vena cava access. In addition a 7Fr quadripolar was temporarily placed at the HIS position via the femoral vein to mark HIS position on fluoroscopy. The quadripolar catheter was then removed for later use in the epicardium. Fluoroscopic images were obtained and recorded with a Philips radioscopic system. Intracardiac electrograms were filtered at band-pass settings from 80 to 500 Hz and displayed simultaneously with ECG leads I, II, III, on a multichannel recorder (EP Tracer, CardioTek, Maastricht, the Netherlands).

**Transatrial approach without closure (n=17)**

The feasibility of performing transatrial mapping and ablation without a closure device was tested in 17 animals (RAA=16; LAA=1). A long transeptal sheath (Preface Multipurpose Biosense Webster, Diamond Bar, CA or SL-1, St Jude Medical, St Paul MN, USA) was positioned into the RAA to access the pericardial space in 16 animals. A 7Fr quadripolar was placed via this long sheath at RAA position confirmed by standard fluoroscopic and electrograms recordings aspects (figure 1A). The quadripolar catheter was removed and a 5cc of contrast media (Ioxaglate Meglumine 320mg/ml) was injected to further confirm RAA position (Figure 1B). Then, a guidewire J shape 0.032 or 0.035 inches) and dilator were advanced inside sheath until the dilator distal was against RAA wall. The dilator was gently pressed against the RAA wall and the guidewire further advanced to perforate the RAA and to reach the pericardial space. No transeptal needle was used. Pericardial access was confirmed by positioning the radiopaque guidewire around the cardiac silhouette (figure 1C). The dilator was then advanced into the pericardial space followed by the long sheath. The dilator and guidewire were removed.
and the long sheath position confirmed by pericardial fluid aspiration and contrast injection (figure 1D). A non-irrigated ablation catheter with 4 or 8 mm distal tip (Biosense) was introduced into the pericardial space for mapping and ablation (figure 1D). In one animal, the left atrium was accessed by the transeptal approach and then left transatrial access to the pericardial space via LAA was attempted with the same technique applied through the RAA.

Using the ablation catheter, epicardial mapping was simulated by positioning the epicardial catheter in several epicardial areas of RV, LV, LA and RA. Next, RF applications were delivered (50W, 60°C for 60s) at the LA appendage or posterior-lateral wall of the RA. No ventricular ablation was performed due to concern of the high risk for VF induction in swine. Arterial pressure was continuously monitored and cardiac silhouette border movement checked periodically to identify a possible hemopericardium. Hemodynamic instability was defined as a drop in arterial BP of more than 20mmHg or if vasoactive drugs were needed to maintain BP above 60mmHg. The arterial blood pressure and heart rate, baseline and after removing the sheath from the pericardial space, were recorded.

**Post Ablation**

After ablation, the RF catheter was removed; a 6F pigtail catheter introduced in the pericardial space and moved throughout the space to remove any fluid or blood. Negative pressure was maintained continuously. The 8F long sheath was then withdrawn to RA and the pigtail under manual negative pressure for 5 additional minutes then removed. The arterial blood pressure and fluoroscopic cardiac border movement were monitored for 30min and then the animals were sacrificed.

**Transatrial access with closure device (n=3)**
In three animals, we performed the same transatrial access but closed the access hole with a patent foramen ovale closure device (“Premere”, St Jude Medical)\textsuperscript{14}. After mapping with ablation catheter, and draining fluid with pigtail we removed pigtail but left long sheath in pericardium. We then placed a guidewire via the sheath into the pericardium. The sheath was withdrawn into the heart and the PFO closure device placed via the guidewire as previously described for PFO closure \textsuperscript{14}.

**Sacrifice**

Sacrifice was performed by intravenous infusion of 20 ml of potassium chloride, the thorax was opened allowing access to the pericardial sac and pericardial bleeding was investigated and measured. The lesions as well as the atrial punctures were documented and microscopically examined after conventional histological processing.

**Statistical Analysis**

All variables were tested for normality using Shapiro-Wilk test. Procedure time, initial and final heart rates presented normal distribution and were expressed as mean±SD. Weight, initial and final mean blood pressure, and amount of bleeding did not present normal distribution and were expressed as median and first and third quartiles (Q1, Q3). Non-parametric Wilcoxon Signed Rank Test was used to compare paired variables without normal distribution. A P<0.05 was considered statistically significant.

**Results**

The data of all animals’ characteristics and clinical outcomes are presented on Table 1.

**Transatrial approach without closure (n=17)**

All 17 animals had pericardial access and 15 had successful simulated mapping and ablation. Mean time of procedure was 197.1±38.0 minutes. In 15/17 (88.2%) there was no
hemodynamic instability (mean BP monitoring: initial: median 80mmHg, Q1 70, Q3 86; final: median 88mmHg, Q1 80, Q3 96; P=0.06; median of differences: 4mmHg, Q1 0, Q3 16) or visual changes in the cardiac border movements on fluoroscopy.

The ablation catheter was introduced in the pericardial space; epicardial mapping and RF ablation were simulated. We performed a median of 8 (Q1 7, Q3 12) RF applications on the right and left atrium of the 15 animals that do not presented tamponade. There was an increase in the mean heart rate comparing the beginning and the end of the experiment (initial median: 100bpm, Q1 90bpm, Q3 105bpm; end median 120bpm; Q1 110bpm, Q3 130bpm; P<0.001; median of differences: 20bpm, Q1 0, Q3 36). A median of 20ml/animal (Q1 15ml, Q3 30ml) of pericardial serohemorrhagic fluid was identified and aspirated during the procedure.

In these 15 animals post mortem analysis detected the atrial access perforation in the RAA in 13 animals, in the right aspect of the atrial wall in one and in the LAA in one. Only a median of 6g (Q1 2g and 12g) of blood clot was found in the 15 animals without complications. Histological analysis demonstrated a fibrin thrombus occluding the endocardial side of the puncture orifice and extending irregularly through the path, with occasional complete contact between the orifice borders, probably due to myocardial fibers contraction around the perforation (Figure 2).

In two animals (12%) there was significant pericardial bleeding and cardiac tamponade. The first occurred in the animal number #3. Post mortem evaluation showed 155g of blood in the pericardial space and atrial perforation was identified outside the RA appendage at anterior aspect of the tricuspid annulus (Figure 3). The second tamponade occurred in the animal number #10. Post mortem evaluation revealed 201g of blood and perforation was identified at the RV outflow tract. Three and four RF applications were performed in animals #3 and #10, respectively. One interesting finding was that the weight of animals presenting tamponade was
higher than percentile 75 weighting 30Kg and 40Kg, respectively, animals #3 and #10.

**Transatrial access with closure device (n=3)**

The three procedures in which the cardiac perforation was repaired with the occlusion device were analyzed separately. The animals maintained hemodynamic stability during all procedure with no significant intrapericardial bleeding. Post mortem evaluation showed that the puncture was performed and closure device delivered at the RA in two animals, and RV outflow tract in one animal (Figure 4).

**Discussion**

We have shown that epicardial mapping and ablation are possible via a transatrial puncture in this pilot study. In most of our cases, a mild pericardial effusion without significant hemodynamic instability was identified although tamponade occurred in 12% of our cases. In those cases a closure device could be useful to prevent tamponade. This transvenous route might be a suitable access to map and ablate the epicardial surface of atria and ventricles for some electrophysiologists who do not feel comfortable accessing the pericardial space through the subxiphoid approach, and prefer to manipulate catheters via the transvenous access, but further studies are needed.

We suspect the mechanism of spontaneous RAA closure is the contraction of atrial myocardial fibers around the transatrial orifice against the catheter that avoids significant bleeding during the procedure. The hole may close up as catheters are slowly downsized. However, if this is true, patients with localized atrial scar at the access site might have continued bleeding since the scar would not contract. This fact may be important in patients with persistent AF or cardiomyopathies both of whom may have large areas of atrial scar. In our study, acute macroscopic and histological examinations showed impressive spontaneous reduction of the atria
perforation orifice after catheters withdrawal likely due myocardial fibers contraction located around the orifice perforation. Additionally, intramyocardial edema formed around the orifice borders propitiated conditions for a stronger contact between the borders, closing tight the orifice. However, it is possible this edema would reduce with time and that the puncture site might experience late bleeding. Microscopic evaluation also revealed a fibrin plug at the endocardial sites of the punctures that probably contributed to the absence of pericardial bleeding. These findings are in conformity with Verrier et al 9 and Waxman et al 10 reports that observed a fibrin clot at the endocardial site of the orifice in all of their histological samples leading to their conclusions that this fibrin plug would be the most important mechanism to prevent pericardial bleeding after the transatrial access.

In our study, the transatrial access failed in two cases when punctures were performed outside the RAA, one near the tricuspid annulus and another in the right ventricle free wall. In both cases, we had confirmed the sheaths positions in RAA with contrast infusion before making the perforation. We suspected that those sheaths came out dislodging from the RAA and fell into the right ventricle or the RA near the tricuspid annulus. Perforations at those places may not present as favorable conditions for spontaneous occlusion as the ones seen in the atrial appendages.

Interesting, the animal in which transatrial access was achieved through the LAA, did not present with pericardial bleeding. It is possible that the anatomy of the right and left atrial appendages in pigs favors for local thrombus formation when the catheter is downsized before being removed from the perforation. The role of intrapericardial negative pressure to avoid pericardial bleeding is still not clear. This maneuver has been performed together with downsizing the catheters in accidental atrial perforations during transeptal accesses to the left atrium and it was also performed in the present study. 15-17
Safety of the transatrial approach to the normal pericardial space

Verrier and colleagues originally described the transatrial pericardial access concept in 1998 in an experiment involving 19 animals (6 dogs and 13 pigs). In that study, a 21-gauge, hollow, radiopaque needle mounted at the tip of a 4F catheter and a soft, 0.014 guidewire were custom-fabricated to perform percutaneous approach from a femoral vein to pierce the right atrial appendage. Direct inspection after thoracotomy revealed no hemopericardium, laceration, or bleeding on catheter withdrawal. Those findings were confirmed in a subsequent study involving other 20 anesthetized pigs in which transatrial access was successfully accomplished within three minutes, without significant hemopericardial bleeding after 24hs and two weeks evaluations.

In our study, despite not using customized material, the findings were similar to those authors when pericardial access was obtained through the atrial appendage. We observed small pericardial effusion in 15/17 animals at the end of the procedure comparing to those authors, but it not preclude epicardial mapping and ablation. Milckelsen et al. also observed some pericardial effusion that was hemodynamically significant in four of the eight animals in which they were assessing the feasibility of inserting epicardial leads through the transatrial or transvenous (superior vena cava) route. They also used a non-customized and oversized material (8F or 9F sheaths) to access the pericardial space that might have facilitated the pericardial bleeding. In their study, there was no significant pericardial effusion at necropsy but moderate inflammatory reaction was observed in two chronic animals, which had exhibited significant pericardial bleeding during the procedure. These findings bring some kind of concern because intense pericarditis and even constrictive pericarditis has been reported in association with hemorrhagic effusions. In 2/17 animals there was massive bleeding with inability to
complete the procedure. However, significant pericardial bleeding has also been observed during the subxiphoid approach. It should be noted that this is our initial experience with this technique and it reflects our learning curve. It is possible with more experience we will have better results.

Limitations

This preliminary study has important limitations. First this is an experimental study performed in pigs and we cannot assume that human beings would have the same behavior. Second, we only evaluated the feasibility of positioning the ablation catheter in different areas of the atria and ventricles and delivering a few RF applications. It is possible that longer procedure times with more aggressive sheath manipulation would cause more bleeding or larger holes. Third, we did not use IV heparin, which is often needed in combined endocardial/epicardial VT ablations. Fourth, we did not perform any ablation on the ventricle so we cannot say that we would be able to get good lesions with this approach for VT ablation. Fifth, this was an acute study; a chronic survival study may show more bleeding. Sixth, we did not perform histological studies in every puncture sites, which could have given us insights into how strong the spontaneous closure is. Finally, although some electrophysiologists may be more comfortable manipulating catheters from the groin, it is possible that a majority of operators will not be comfortable with intentional cardiac perforation even if excellent data were obtained. Additionally, we did not compare the safety of a transatrial approach to a subxiphoid approach (the current standard) and thus can make no definite statements about the relative merits.

Conclusions

Transatrial endovascular RAA puncture may provide a potential alternative route for pericardial access. Further studies are needed to evaluate its safety with longer procedures,
ability to ablate the ventricle, and the use of closure tools before being applied in clinical settings.

**Funding Sources:** This study was supported by the Heart Institute (InCor), São Paulo Medical School University and Zerbini’s Fundation. Saint Jude Medical donated the three devices used in this study to occlude the perforations.

**Conflict of Interest Disclosures:** Dr Mahapatra SM is a consultant to STJ and a co-founder of EpiEP.

**References:**
6. Scanavacca M, Sosa E. Epicardial ablation of ventricular tachycardia in chagas heart


Table 1: Clinical data and clinical outcomes of all procedures.

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VF: Ventricular Fibrillation; LAA: Left Atrial Appendage; RAA: Right Atrial Appendage; TA: tricuspid Annulus; RV: Right Ventricle.
Figure Legends:

**Figure 1** – Transatrial access to the pericardial space in a pig model. A – Location of the ablation catheter in the right atrial appendage. B – Right atrial appendage angiography. C – Introduction of the guide wire into the pericardial space. D – Catheter (8mm-tip) introduction in the pericardial space.

**Figure 2** – Post-mortem macroscopic and microscopic aspects of transatrial puncture at the right atrial appendage without pericardial bleeding. (A) Macroscopic aspect of right atrial appendage perforation, red arrows show sites of RF lesions on RAA; (B) Microscopic aspects of right atrial appendage perforation.

**Figure 3** – Post-mortem macroscopic and microscopic aspects of accidental puncture at the tricuspid annulus that resulted in cardiac tamponade. (A) Epicardial view of accidental perforation at the tricuspid annulus; (B) Endocardial view of an accidental perforation slightly above the tricuspid annulus.

**Figure 4** – Macroscopic aspects of occlusion device at the RV.