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ORIGINAL RESEARCH

VENTRICULAR TACHYCARDIA - NEW TECHNIQUES

Feasibility of Transatrial Access for Epicardial Ablation

Evaluation of 2 Different Techniques in Swine

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ABSTRACT

BACKGROUND The subxiphoid pericardial access is technically difficult and has a considerable rate of complications, thus transatrial access may be an alternative.

OBJECTIVES This study sought to assess the feasibility and safety of this strategy regarding periprocedural period and after 1-week follow-up.

METHODS The investigators performed epicardial mapping through transatrial puncture in 20 swine. Animals were divided into group A, in which aspiration of the sheath was performed to maintain negative pressure after the withdraw of the catheters, and group B, in which a device (Konar-MF VSD Occluder) was delivered to occlude the right atrial appendage perforation. Bleeding was investigated immediately and 1 week after.

RESULTS Access was safe in 19 of 20 animals (95%) with small amount of bleeding (6.4 ± 6 mL). In group A (n = 10), 1 animal presented hemopericardium right after the puncture. In the other 9, epicardial ablation was performed and 60.0 ± 28.0 mL of blood was aspirated without events. After 1 week, fibrin-hemorrhagic pericarditis was identified in 3 animals. In group B (n = 10), reaching the epicardial surface was possible in all animals. An adequate position of the prosthesis was obtained in 90% (9 of 10). One death occurred in the immediate postoperative period, secondary to pneumothorax. After 1 week, postmortem analysis showed absence of pericardial bleeding and a normal-appearing pericardium in the 8 animals with adequate prosthesis position.

CONCLUSIONS Transatrial access allows epicardial mapping and ablation. Sheath removal after negative pressure contributes to achieving acute bleeding control but does not prevent its occurrence. The use of the device prevents bleeding and hemorrhagic pericarditis. (J Am Coll Cardiol EP 2023;9:2315–2328) © 2023 by the American College of Cardiology Foundation.

Since the epicardial ablation technique, by direct subxiphoid puncture, was described in 1996,[1] it has been established as the strategy of choice to reach the epicardial space, thus enabling the mapping and ablation of this area. However, the technical complexity and complications resulting from this access, mainly caused by inadvertent puncture of the right ventricle, have continued to occur,

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

RAA = right atrial appendage

reaching 20% of the procedures conducted in the most experienced services.[2,3] In addition, some difficult scenarios such as chagasic megacolon or even pericardial adhesions may contraindicate its performance. Thus, new strategies to access the pericardial space gained interest in clinical use.[4-7]

Different groups have evaluated transatrial access experimentally, but only with acute observations in nonheparinized animals; a systematic evaluation of techniques to occlude the transatrial access port has not yet been performed.[8-10] Therefore, our study evaluated for 1 week the use of 2 techniques—negative pressure by aspiration of the sheath and occlusion of the atrial orifice with a specific device—to seal the access hole at the end of the procedure in heparinized animals.

METHODS

EXPERIMENT PROTOCOLS. This preclinical study was approved by the Ethics Committee for the Use of Animals (University of São Paulo) and the Scientific Committee (Instituto do Coração da Faculdade de Medicina da Universidade de São Paulo).

Twenty animals were used and separated into groups A (10 animals; only the pericardial space sheath was removed, maintaining negative pressure) and B (10 animals; the occlusion device was positioned in the hole where the sheath passes through the right atrial appendage [RAA]). Epicardial right and left ventricles were explored, followed by the atria (Supplemental Figure 1) where 5 radiofrequency applications on average were performed on the posterior wall of the left and right atria (50 W, 60 seconds). Epicardial ventricular radiofrequency applications were not performed because of the high incidence of ventricular fibrillation in our previous experiences in swine.

At the end of the procedure, the animals were awakened from anesthesia, sent for observation for 24 hours in the vivarium, and then taken to the farm. After 1 week, they returned to the laboratory to be sacrificed. Then, an evaluation of the presence of hemopericardium and an anatomopathological study of all cases were performed (**Central Illustration**).

A detailed step-by-step description of the procedure can be accessed in the Supplemental Appendix.

STATISTICAL ANALYSIS. All variables were analyzed for normality of distribution using the Shapiro-Wilk test. Numeric variables with normal distribution were presented as mean $\pm$ SD and were compared using Student's t-test. A P value <0.05 was used to indicate statistical significance. For data analysis, the SPSS software (version 25.0, IBM Corp) was used.

RESULTS

GROUP A: TRANSATRIAL PUNCTURE WITH ASPIRATION OF THE SHEATH (NEGATIVE PRESSURE). In the 10 animals, reaching the epicardial surface was possible with a mean procedure time of 140.0 $\pm$ 9.0 minutes. Hemodynamic instability did not occur in 9 animals, with a mean arterial pressure of 73 $\pm$ 3 mm Hg at baseline and 74 $\pm$ 4 mm Hg at the end. The mean heart rate was 97 $\pm$ 4 beats/min at the beginning and 107 $\pm$ 3 beats/min at the end of the procedure (**Table 1**).

After transatrial puncture (excluding the animal that died), a volume of fluid was aspirated into the pericardial space (7.0 $\pm$ 5.0 mL). At the end of the mapping (60 minutes), blood was aspirated (7.0 $\pm$ 6.0 mL); after the sheath was removed, another volume of blood was aspirated (60.0 $\pm$ 28.0 mL), maintaining the Judkins right 6-F catheter associated with continuous negative pressure in the pericardial space (30 minutes) (**Figure 1**). After removal of the sheath to the right atrium with the maintenance of the Judkins 6-F catheter, the time to stop bleeding was 10 $\pm$ 5 minutes.

Animal 6 evolved with rapid deterioration in hemodynamic status after transatrial puncture, followed by a stop in cardiac silhouette movement. Despite rapid aspiration of >300 mL of blood, cardiac arrest occurred in asystole 10 minutes after transatrial puncture; postmortem analysis revealed laceration of the RAA as the cause of death (**Figure 2**).

The 9 surviving animals were taken to the farm without significant changes of behavior. All animals gained weight in the period (initial weight: 24.1 $\pm$ 1.40 kg; final weight: 27.4 $\pm$ 1.65 kg).

One week later, the animals returned for evaluation of cardiac contractility by radioscopy, and it was maintained similar to the previous silhouette during the procedure. On re-evaluation, the heart rate was 98 $\pm$ 5 beats/min.

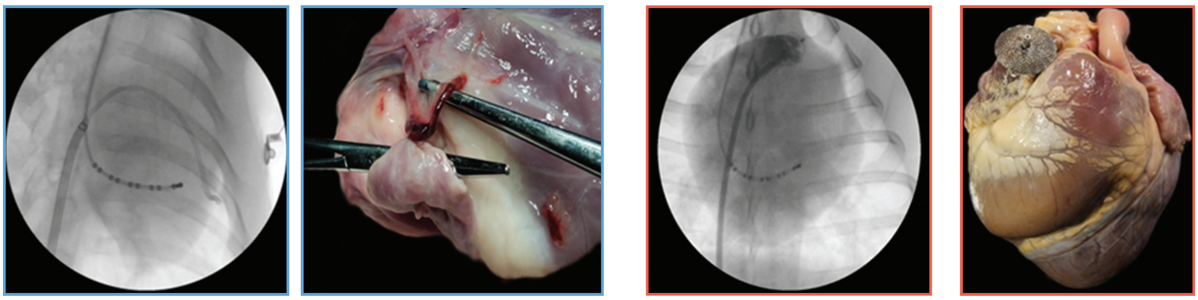
Transesophageal echocardiography was performed on animals 7 and 9, during the procedure and before sacrifice, with no evidence of pericardial effusion in both animals. All animals were sacrificed after and sent for postmortem analysis.

In 6 animals, postmortem analysis showed an absence or minimal amount of blood, with a usual-appearing pericardial space, without adhesions, with the animals presenting thrombus at the perforation

CENTRAL ILLUSTRATION Feasibility of Transatrial Access With 2 Techniques

A Maintenance of Negative Pressure

B Use of Occlusion Device



A: 90% successful and safe transatrial access.
3/9 animals developed fibrin-hemorrhagic pericarditis after 1 week.

B: 100% successful and safe transatrial access.
90% adequate position of the prothesis.
Absence of fibrin-hemorrhagic pericarditis with adequate position of the prothesis.

Chokr MO, et al. J Am Coll Cardiol EP. 2023;9(11):2315-2328.

Transatrial access allowed epicardial mapping and ablation in both groups. Sheath removal after negative pressure (A) contributed to achieve acute bleeding control, but the addition use of an occlusion device (B) prevented bleeding and post-hemorrhagic pericarditis.

site and localized pericarditis around the perforation (Figures 3A and 3B). In 3 animals (3, 5, and 9), an intense inflammatory reaction was identified, with a pattern of fibrinohemorrhagic pericarditis (Figure 3C). In the group with the usual pericardium, histological analysis revealed thrombosis formation (near the puncture site on the path from the endocardium to the epicardium) and fibrin deposits associated with fibrosis near the perforation hole (Figure 3D); in the fibrinohemorrhagic pericarditis group, neovascular formation, fibrinous pericarditis, and mesothelial cell reactivity were observed in areas distant from the perforation.

The total volume of blood aspirated during the procedure was higher in the 3 animals that developed fibrinohemorrhagic pericarditis (103.0 $\pm$ 25.0 mL and 50.0 $\pm$ 20.0 mL; $P = 0.011$).

All animals gained weight relative to the observation period on the farm. However, the group without pericarditis had a greater gain relative to the group with fibrinohemorrhagic pericarditis (3.60 $\pm$ 1.36 kg and 0.66 $\pm$ 0.57 kg, respectively; $P = 0.009$).

After 1 week of observation, the mean heart rate remained elevated in the group with pericarditis compared to that in the group in which intense inflammation was not observed (116.0 $\pm$ 7.2 beats/min and 89.0 $\pm$ 7.7 beats/min, respectively; $P = 0.001$).

Regarding the influence of the animal's weight on bleeding, a statistically significant difference was not observed, although death occurred in the swine with the lowest body weight (18.0 kg; $P = 0.183$) and with the smallest heart (120.0 g).

GROUP B: OCCLUSION OF TRANSATRIAL PUNCTURE WITH AN OCCLUDER DEVICE. In all 10 animals, reaching the epicardial surface was possible with a mean procedure time of 149 $\pm$ 15 minutes (Table 2). The mean blood pressures were 67 $\pm$ 3 mm Hg at beginning and 67.0 $\pm$ 3.5 mm Hg at the end of the procedure and the mean heart rates were 110 $\pm$ 16 beats/min at the beginning and 106 $\pm$ 16 beats/min at the end. As in the group A, systematic mapping of the entire epicardial surface was performed, and 5 radiofrequency applications on average were performed on the left and right atria (50 W; 60 seconds).

After the transatrial puncture, the mean volume of fluid aspirated into the pericardial space was 4.5 $\pm$ 1.6 mL. At the end of the mapping (60 minutes), the volume of blood aspirated was 5.5 $\pm$ 2.0 mL.

At the end of the procedure, proper positioning of the occluding prosthesis (Konar-MF VSD Occluder, Lifetech Scientific) was obtained in 90% (9 of 10) of the animals (Figure 4). Prosthesis embolization to the epicardium occurred in animal 7.

Animal 6 evolved with a rapid deterioration of the respiratory pattern while still in the hospital vivarium, followed by cardiac arrest about 12 hours after the end of the procedure. Thoracic fluoroscopy revealed a mediastinal shift to the left secondary to

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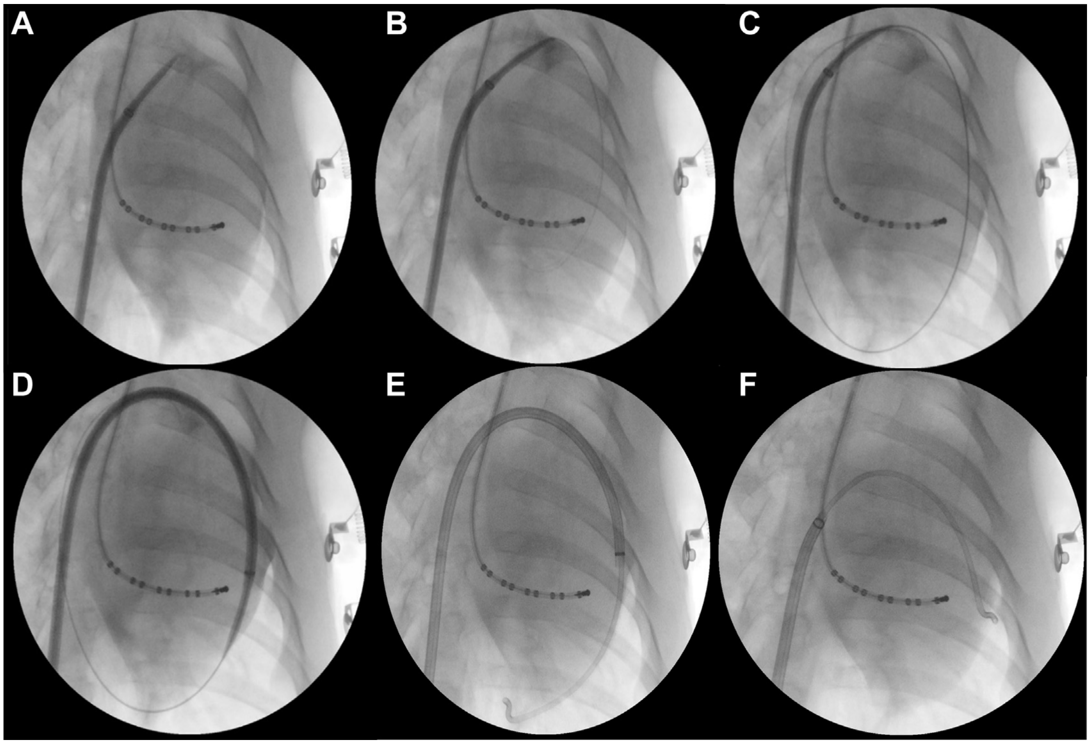
TABLE 1 Group A: Clinical and Procedural Characteristics

Animal	Weight (kg)	Sex	MAP (mm Hg) Initial	MAP (mm Hg) Final	Heart Rate (beats/min) Initial	Heart Rate (beats/min) Final	Hemodynamic Instability	Duration (min)	X-ray Time (min)	Bleeding (mL) After the Puncture	Bleeding (mL) After Mapping	Bleeding (mL) After Withdrawal of the Introducer Into the RA
1	23	M	72	76	84	98	No	170	25	8	0	40
2	25	M	86	79	90	106	No	150	19	5	10	50
3	26	F	76	85	120	110	No	160	22	0	20	80
4	30	M	62	72	110	100	No	140	24	0	8	60
5	33	M	74	65	88	126	No	150	20	10	0	120
6	18	F	65	0	97	Death	Yes	60	12	300	N/A	N/A
7	22	F	68	70	80	120	No	130	21	10	10	20
8	21	F	91	94	90	92	No	150	24	15	0	0
9	19	M	84	70	120	100	No	160	18	0	10	70
10	24	M	60	55	100	115	No	140	16	8	10	40

MAP = mean arterial pressure; N/A = not applicable; RA = right atrium.

FIGURE 1 Transatrial Access Technique



(A) Contrast injection through the long sheath to confirm the placement of the dilator within the right atrial appendage. (B) Slight pressure of the dilator against the left atrial appendage wall, advancing the guidewire simultaneously with the contrast injection through the bifurcator to perforate the left atrial appendage and reach the pericardial space. (C) Guidewire contouring the cardiac silhouette and confirming its positioning in the pericardial space. (D) Sheath and dilator advanced into the epicardial space over the guidewire; then, the guide was withdrawn/removed. (E,F) Removal of the sheath from the pericardial space to the right atrium, maintaining the Judkins right 6-F catheter and negative pressure for 30 minutes.

massive right pneumothorax. Thoracotomy demonstrated collapse and atelectasis of the left lung. A likely reason for the pneumothorax identified was the jugular puncture to position the catheter in the coronary sinus. Macroscopic analysis of the heart showed a well-positioned prosthesis in the RAA, without evidence of pericardial bleeding (Figure 5A).

Animal 7 showed displacement of the prosthesis into the pericardial space a few minutes after its release, with a reduction in the cardiac border movement, associated with hypotension and tachycardia. The animal was observed for 30 minutes after displacement and ending the procedure by awakening the animal was chosen following the protocol. In this case, a contrast injection into the appendix was not performed to avoid a possible increase in bleeding.

The 9 surviving animals were sent to the farm. All of them gained weight during the study period, except animal 7 (initial weight: 20.7 ± 2.1 kg; final weight: 21.9 ± 1.4 kg). Except for animal 7 (which developed cyanosis in the extremities and had a documented fever episode within 2 days of the evaluation; 37.3 °C), the other animals maintained their behavior unchanged.

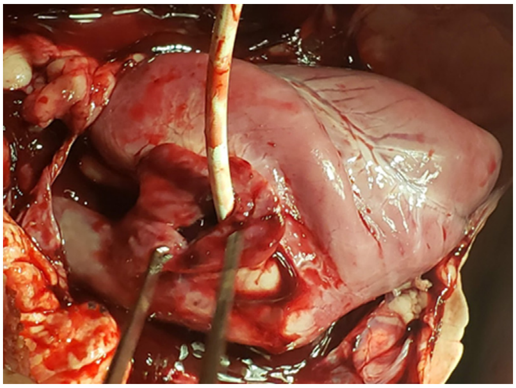
One week later (see Table 3), the animals returned for evaluation of cardiac contractility by radioscopy, and it was maintained similar to the previous evaluation during the procedure, except in animal 7, in which it was reduced. On evaluation, the mean heart rate was 101 ± 19 beats/min.

In the animals 3, 5, 9, and 10, transesophageal echocardiography was performed shortly after the prosthesis was released, being repeated after the 7 days of observation (Figure 5B). The echocardiogram did not indicate the presence of pericardial effusion and showed the prosthesis properly positioned in the RAA without a sign of displacement.

Postmortem, macroscopic analysis showed the absence or a minimum amount of blood in 8 animals, with a usual-appearing pericardial space and without adherence (Figure 5C). In all animals, the prosthesis was properly positioned in the RAA release sites; in the roof in 5 animals, and its tip in 3 animals. In the animal with prosthesis displacement, an intense pericardial inflammatory reaction was identified, with a pattern of fibrinohemorrhagic pericarditis (Figures 6A and 6B).

In 3 animals, it was observed that the external disk of the prosthesis projected toward the aortic root (Figures 7A and 7B). However, macroscopic analysis, including sagittal sections and histological analysis, showed no damage to the aortic wall (Figure 7C).

FIGURE 2 Laceration of the RAA (Animal 6)



Animal 6: Postmortem analysis revealed a laceration of the right atrial appendage (RAA) as the cause of death. In this case, thoracotomy was performed without removing the sheath to elucidate the mechanism of death.

All animals (except animal 7) gained weight relative to the observation period on the farm. The group without pericarditis showed weight gain relative to the animal with fibrinohemorrhagic pericarditis (+2.1 ± 1.1 kg and −1.0 kg, respectively; $P = 0.035$).

After 1 week of observation, the mean heart rate of the animal with pericarditis remained elevated relative to the other animals (140 and 96 ± 13 beats/min, respectively; $P = 0.016$).

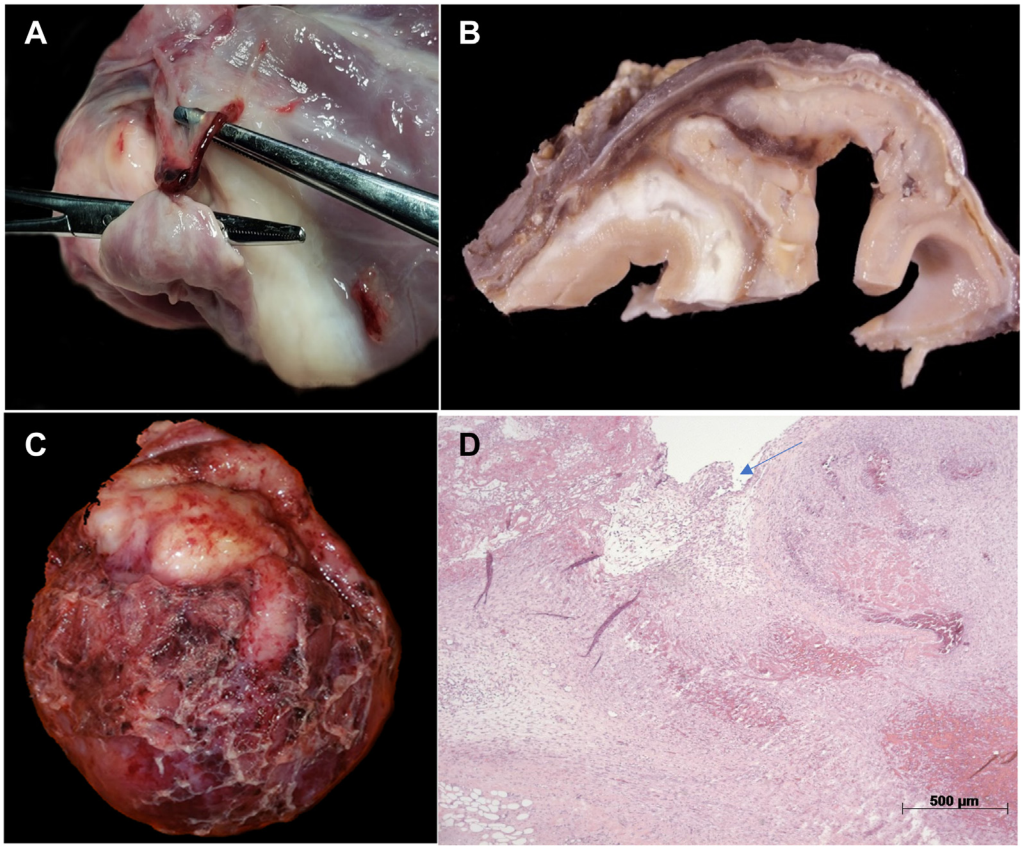
In group B, death occurred in 1 animal secondary to pneumothorax. We did not observe a direct relationship with transatrial access or even with device release. Although the analyzed specimens presented the usual appearance, the histological analysis revealed that a focal pericarditis is a frequent finding after transatrial pericardial access, similar to what was observed in the group without occlusion device, occurring locally in all analyzed animals. The specific immunohistochemical reaction against actin-myosin demonstrated the existence of positive cells (brown color) in the walls of newly formed vessels, as well as infiltration within inflammatory vessels (Figures 8A and 8B).

However, in the animal in which prosthesis displacement occurred, which resulted in fibrinohemorrhagic pericarditis (Figures 6A and 6B), micro abscesses were identified on histological evaluation.

DISCUSSION

The main contribution of this study was to show that performing epicardial mapping and ablation by

FIGURE 3 Postmortem Analysis of Group A Animals



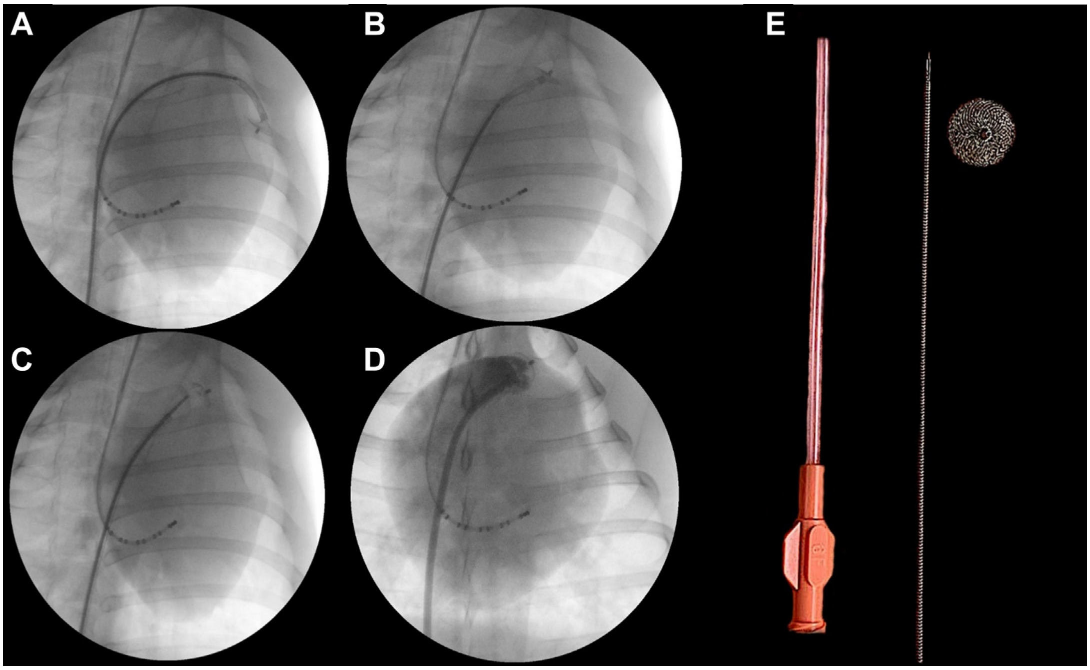
(A) Animal 4: Epicardium of usual aspect; localized adhesion of the parietal pericardium to the perforation hole occurred in the left atrial appendage, associated with the formation of clot and thrombus near the puncture site. (B) Animal 2: After fixation in formalin solution, the cut in the left atrial appendage demonstrates a course with a thrombus, associated with the presence of localized pericarditis at the perforation site. (C) Animal 5: Fibrinohemorrhagic pericarditis throughout the epicardial surface associated with the adhesion areas. In the photo, the parietal pericardium has been reflected, showing diffuse epicarditis (visceral pericardium). (D) Animal 8: Photomicrograph of the path of the atrial perforation obtained 7 days after the procedure, showing the formation of thrombosis along this path, from the endocardium to the epicardium, in addition to deposits of fibrin next to the perforation orifice (blue arrow). There is also necrosis and calcification close to the path of thrombosis. Hematoxylin-eosin staining.

TABLE 2 Group B: Clinical and Procedural Characteristics

			MAP (mm Hg)		Heart Rate (beats/min)					Bleeding (mL)		
Animals	Weight (kg)	Sex	MBP Initial	MBP Final	Heart Rate Initial	Heart Rate Final	Hemodynamic Instability	Total Procedure Time (min)	X-ray Time (min)	After the Puncture	After Mapping 60 min	Proper Positioning of Prosthesis
1	20	M	65	69	90	102	No	160	30	0	0	Yes
2	22	M	60	55	130	110	No	140	23	10	0	Yes
3	20	F	60	90	120	110	No	150	18	0	10	Yes
4	19	F	75	67	130	100	No	170	26	0	5	Yes
5	20	M	79	69	88	94	No	140	24	10	0	Yes
6	26	F	59	74	120	100	No	150	22	0	10	Yes
7	21	F	84	59	120	150	No	140	25	10	0	No
8	20	F	72	70	93	104	No	170	20	5	0	Yes
9	18	M	55	50	100	92	No	150	24	0	20	Yes
10	21	F	64	68	106	98	No	120	23	10	10	Yes

MBP = mean blood pressure; other abbreviations as in Table 1

FIGURE 4 **Positioning of the Occlusion Device**



(A) Exteriorization of the external disk by the sheath within the pericardial space. (B) After releasing the first disk in the pericardial space, the set was withdrawn toward the wall of the right atrium, promoting the coupling of the external disk to the epicardial surface of the atrial wall. (C) Then, the sheath was withdrawn into the right atrium, releasing the internal disk inside the appendix. The set was then advanced against the endocardial face toward the external disk, and then adjustment and fixation of the prosthesis were performed, thus occluding the access hole. (D) Prosthesis properly positioned at the puncture site for transatrial access. A contrast was injected to assess a possible occurrence of extravasation into the pericardial space. (E) Konar-MF VSD Occluder (Lifetech Scientific) occlusion device, assist introducer, and release cable.

transatrial access in swine by direct puncture of the RAA is possible, in the presence of heparinization, with the survival of the animals over a week of observation. Negative pressure contributes to achieving acute bleeding control after removal of the pericardial sheath; however, it does not prevent some degree of bleeding in the following days or hours, because hemorrhagic pericarditis was observed in 30% of the animals. Furthermore, the use of the occlusion device prevents bleeding after the pericardial space sheath is removed, provided the device is properly positioned, avoiding the occurrence of hemorrhagic pericarditis after 1 week of observation.

Pericardial access with mapping and ablation was safely achieved in 19 of 20 animals. Interestingly, major bleeding was not observed throughout the procedure even though mapping and ablation lasted for 1 hour.

Considering future perspectives, such as the use of the technique in humans, it is important to understand the aspects of the swine anatomy—the hearts of these animal species are rotated counterclockwise compared to the human heart. As a result, the left ventricle and atrium are oriented caudally, whereas the right atrium and ventricle are located cranially. Specifically regarding the atrial appendages, the right auricle has a narrow tubular appearance compared to the triangular shape of the human heart. It is proportionally larger in relation to the rest of the right atrium compared to humans and has similar thickness.[11]

Despite these anatomical differences, we did not encounter significant difficulties regarding the movement of the catheter during mapping. Once the epicardial surface is reached, it is possible to access all regions of both atria and ventricles. Clockwise and counterclockwise rotation movements of the sheath

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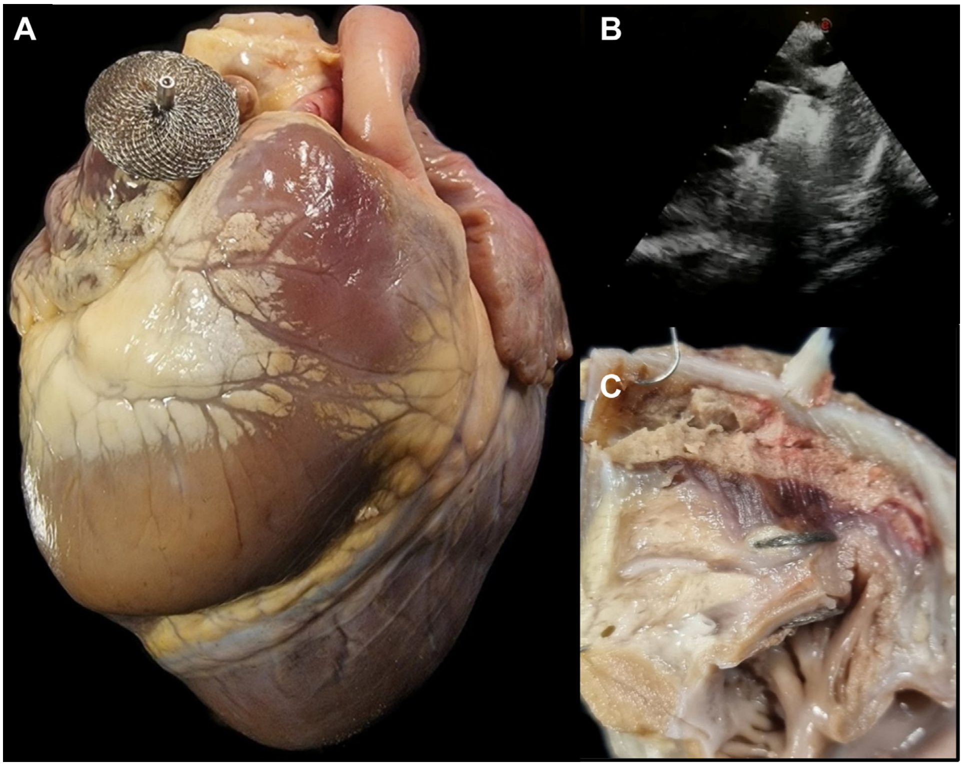
FIGURE 5 Macroscopic Analysis of a Well-Positioned Prosthesis



(A) Animal 6: Macroscopic analysis of the heart in anterior view showed a well-positioned prosthesis in RAA (without evidence of pericardial bleeding). Image obtained 7 days after fixation in formalin solution. (B) Animal 5: Transesophageal echocardiogram indicating the absence of pericardial effusion and appropriately positioned prosthesis at the apex of the left atrial appendage, without sign of displacement 1 week after implantation. (C) Animal 8: Prosthesis well positioned; external disk on the pericardial face and internal disk on the endocardial face of the roof of the left atrial appendage. Small and localized blood collection was observed near the external disk. RAA = right atrial appendage.

facilitate the catheter's movement. If necessary, the sheath can be retracted or advanced distally to the transatrial puncture site, taking care not to allow its return to the inside of the atrial appendage (Supplemental Figure 1). The use of intracavitary electrograms assisted in locating the catheter over the atria or ventricles.

In group A, animal 6 died a few minutes after the transatrial puncture, because of atrial laceration after the puncture; it is noteworthy that this animal had the lowest weight in the sample. The low weight of the animal and its heart may be related to the greater fragility of the tissue as well as its consequent rupture. At the time of the accident, the prosthesis was not available; however, some lacerations could be treated by releasing the occlusion device to seal the hole.

In group A, in which the maintenance of negative pressure was performed, fibrinohemorrhagic pericarditis was related to the volume of blood aspirated, occurring in 30% of the animals. Several studies have related the presence of blood in the pericardial space as the main factor for the development of constrictive pericarditis in the clinical course of the patient,[12] and this high prevalence would be unacceptable in humans. Thus, in the strategy of transatrial access to the pericardial space, preventing the bleeding that occurs after the sheath retraction to the interior of the right atrium is a fundamental step. On the other hand, continuous negative pressure (Judkins right catheter; 30 minutes) prevented major bleeding into the pericardial space in 6 of 9 animals. After 1 week, the macroscopic appearance of the pieces did not indicate a major abnormality. These findings are consistent

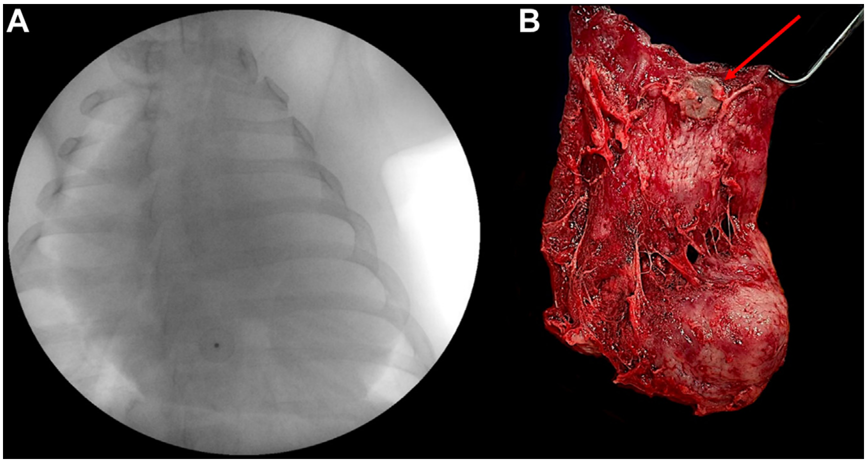
TABLE 3 Groups A and B: Characteristics After 1 Week

Animal	Weight (kg)	MAP (mm Hg)	Heart Rate (beats/min)	Heart Weight (g)	Hemopericardium in Pathology (g)	Hemorrhagic Pericarditis
Group A						
1	27	72	90	154	10	No
2	30	80	88	190	No	No
3	27	80	122	205	30	Yes
4	35	62	90	220	No	No
5	34	70	108	180	20	Yes
6[a]	Acute death			120	250	No
7	24	68	76	145	No	No
8	25	91	94	160	No	No
9	19	70	118	140	20	Yes
10	26	60	98	150	No	No
Group B						
1	23	72	93	140	No	No
2	24	60	100	166	No	No
3	20	80	126	130	20	No
4	22	70	88	138	No	No
5	23	60	90	150	No	No
6[b]	Death 12 h after intervention			170	No	No
7[c]	20	65	140	135	150	Yes
8	22	64	98	128	No	No
9	21	75	92	140	No	No
10	22	74	84	150	No	No

[a]Laceration of the right atrial appendage with cardiac tamponade. [b]Massive right pneumothorax 12 hours after procedure. [c]Displacement of the prosthesis into the pericardial space.

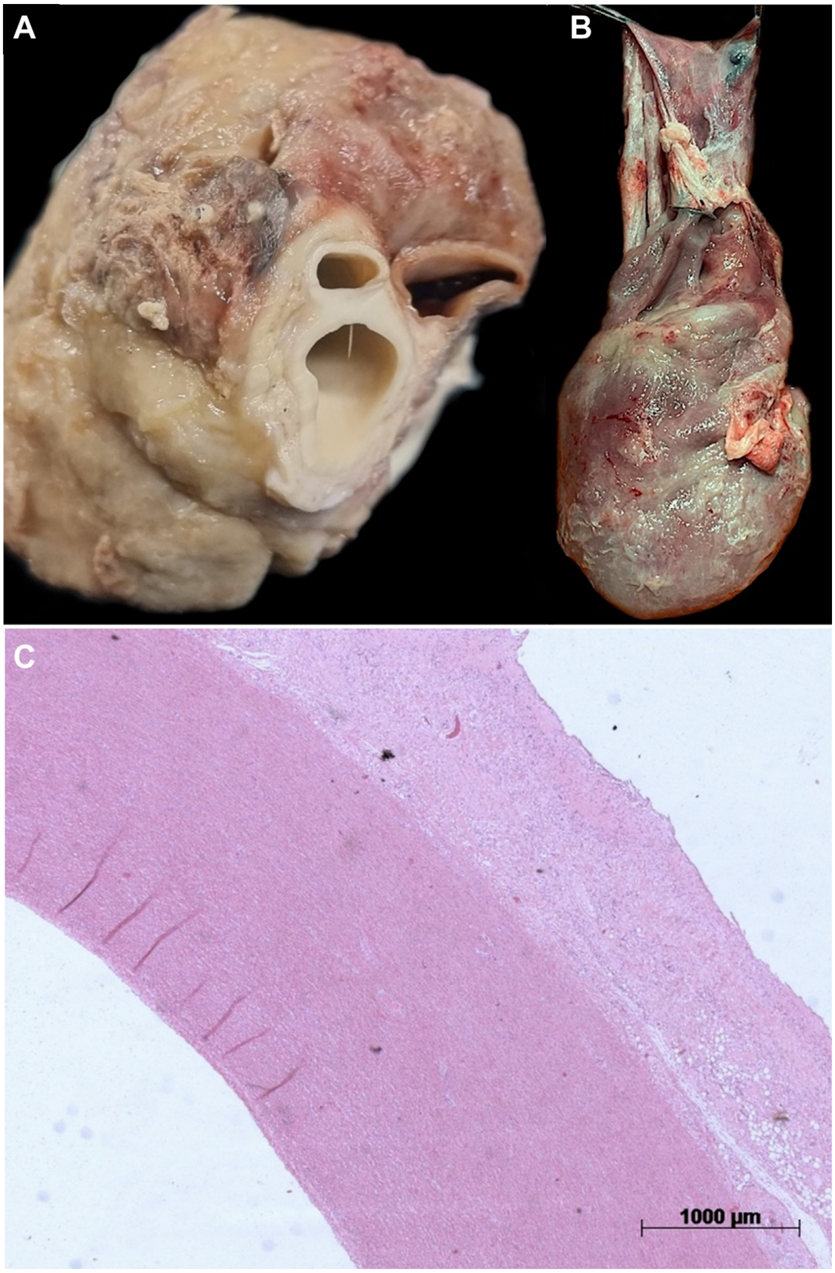
MAP = mean arterial pressure.

FIGURE 6 Displacement of the Prosthesis Into the Pericardial Space With Fibrinohemorrhagic Pericarditis



(A) Animal 7 presented displacement of the prosthesis into the pericardial space, a few minutes after its release. (B) Animal 7: Macroscopic view of the heart from where the parietal pericardium (pericardial sac) was partially retracted with a pattern of fibrinohemorrhagic pericarditis; prosthesis adhered to the parietal pericardium was observed, which embolized 1 week after implantation (red arrow).

FIGURE 7 Prosthesis Projected Toward the Aortic Root

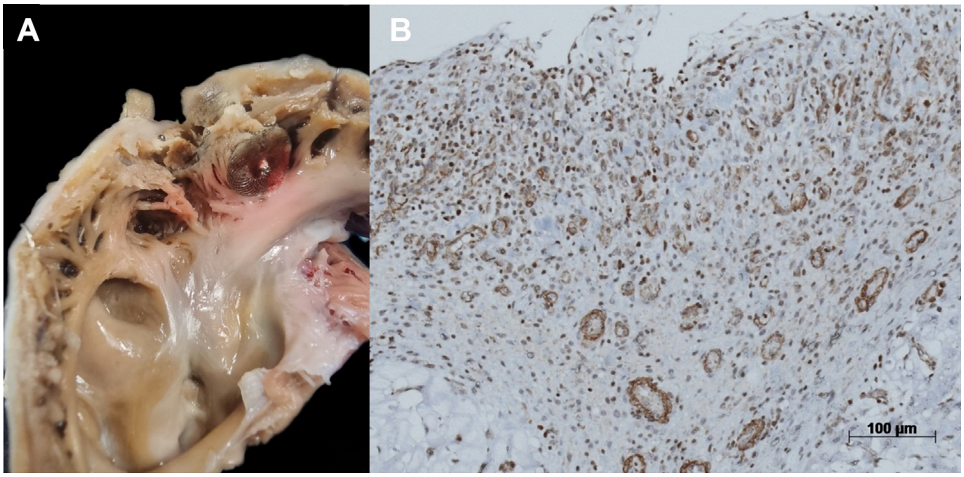


(A,B) Animals 2 and 9, respectively: It was observed that the external disk of the prosthesis projects into the aortic root. However, macroscopic, and histological evaluations ruled out a lesion in its wall. (C) Photomicrograph of the intrapericardial segment in the ascending aorta (animal 2). Fibrous thickening of the adventitia layer can be seen. Hematoxylin-eosin staining (original objective magnification: 2.5×).

with the observations of Macias et al[13] and of our group, Chokr et al,[14,15] and showed that negative pressure can be useful in the management of massive hemopericardium in the electrophysiology laboratory, allowing hemodynamic control of the patient and delaying or even avoiding the need for surgery.

In group B, the release of the prosthesis occurred satisfactorily in 9 of 10 animals. In animal 7, displacement of the prosthesis into the pericardial space occurred a few minutes after its release. One week after release, this animal presented extensive fibrinohemorrhagic pericarditis, and the prosthesis

FIGURE 8 Focal Pericarditis After Transatrial Pericardial Access



(A) Animal 4: Macroscopic view of the endocardial surface in the right auricle showing prosthesis (internal disk) well positioned next to the trabeculated musculature. (B) Animal 4: Photomicrograph of the parietal pericardium next to the prosthesis (animal P2). The section was subjected to an immunohistochemical reaction with smooth-muscle-specific actin. Positive cells (brown color) can be observed on the walls of neoformed vessels, as well as infiltrated inside the vessels. Immunohistochemical reaction counterstained with Harris hematoxylin (original objective magnification: 20×).

was found to be adhered to the parietal pericardium. A recent review described that displacement and embolization of occlusion devices of the left atrial appendage may occur in up to 4% of patients; the main mechanism being an inadequately sized (oversized or undersized) prosthesis.[16] Thus, a possible hypothesis is that the larger size of the prosthesis, concerning the size of the porcine atrial appendage, may have favored its displacement into the pericardial space a few minutes after its release.

Animal 6 died (approximately 12 hours after prosthesis release) secondary to pneumothorax. The postmortem evaluation confirmed the absence of bleeding in the pericardial space, with a well-positioned prosthesis in the RAA and complete atelectasis of the left lung. A jugular puncture to position the coronary sinus at the beginning of the procedure could be a possible cause of pneumothorax, the mechanism of death being unrelated to the release of the prosthesis.

In group B, the only animal in which bleeding into the pericardial space occurred, with the development of fibrinohemorrhagic pericarditis, was the one in which prosthesis displacement occurred. These observations suggest that the occlusion device can prevent bleeding and thus the development of fibrinohemorrhagic pericarditis, provided the device is well positioned.

The transesophageal echocardiogram was used to confirm the positioning of the prosthesis and to assess the formation of pericardial effusion in groups A (2 animals) and B (4 animals). In our experience, its use to release the prosthesis was limited because the transducer was positioned in front of the area of interest. Thus, we chose to release the prosthesis using radioscopy and positioning assessment afterward. In this sense, the use of intracardiac echocardiography may facilitate its use to release the prosthesis.

Regarding the bleeding that occurred in 4 animals (3 in group A; 1 in group B), the observation over a week allowed us to indicate a possible relationship with the lower weight gain in these animals, suggesting the possible occurrence of a more intense inflammatory response that resulted in more pronounced systemic involvement in these animals.

The study by Verrier et al,[8] who described the transatrial approach, acutely evaluated the strategy with small-diameter introducers (4-F) in the drug infusion inside the pericardial space in 19 pigs without observing signs of hemopericardium in the anatomopathological evaluation. Two years later, the same group evaluated the safety of this strategy over 2 weeks, using a catheter of the same diameter. A localized inflammatory reaction was observed close to the puncture site, but it was suggested that such a finding was not of clinical relevance in the observation period. It is interesting to note that 2 animals (10% of the sample) developed a diffuse inflammatory reaction with the formation of adhesions identified at necropsy. Mickelsen et al[17] evaluated the positioning of epicardial electrodes using larger diameter sheaths for transatrial access (8- and 9-F); they observed bleeding with hemodynamic instability in 4 of 8 animals in which the strategy was used. In 2 of these animals, which had major bleeding during the procedure, a moderate inflammatory reaction was observed at necropsy, again raising concerns regarding the evolution to severe forms of pericarditis when larger caliber sheaths are used.

Scanavacca et al[10] showed for the first time the possibility of using transatrial access to the pericardial space for mapping and ablation in 17 pigs. However, this study only acutely evaluated heparin-free animals. In 2 animals, in which punctures in the tricuspid ring and right ventricular outflow tract occurred inadvertently, significant bleeding followed by death occurred, showing the importance of the puncture site in the inside of the atrial appendage in this population. Regarding the previous publication, the main uncertainty is related to bleeding, which could occur in a longer observation period or even be increased in heparinized animals. In the present study, increased bleeding was observed after sheath retraction to the right atrium in group A animals (compared to Scanavacca et al[10]). However, the animals were heparinized.

Regarding the mechanism of orifice occlusion, similar to the observations by Scanavacca et al,[10] in group A, after 1 week of observation, thrombus formation along the course, with deposition of fibrin in the exit orifice, seems to be the mechanism associated with the interruption of bleeding. In group B, the stopping of bleeding was caused by the mechanical occlusion of the prosthesis. However, the immunohistochemical reaction against actin-specific smooth muscle shows that the processes of cell repair and localized inflammation are present 1 week after the intervention (**Figure 4**).

In group B, systematic use of the occlusion device appears to prevent bleeding into the pericardial space and thus the development of severe forms of pericarditis despite heparin infusion. Recently, Da-Wariboko et al[18] published a series using 6 animals submitted to transatrial access through the left atrial appendage, releasing the occlusion device (Amplatzer, Abbott) to close the access. One hour after the release of the prosthesis, the animals were sacrificed and blood was not identified in the pericardial space. Da-Wariboko et al[18] used this strategy to clinically validate the use of an occlusion device (Amplatzer) to treat a perforation in the left atrial appendage (which resulted in persistent bleeding), thus avoiding the need for heart surgery. Furthermore, an imaging study confirmed prosthesis maintenance at the implant site 94 days after the accident, with the patient showing a satisfactory clinical course.

From the point of view of the strategy of access to the pericardial space, the transatrial approach allows the guide to pass tangentially to the heart as soon as it is externalized to the epicardium. This approach minimizes the risk of injury to venous or arterial branches, making cardiac laceration or perforation unlikely. Because this procedure involves programmed drilling in the RAA, this may cause eventual discomfort for the operator to perform the same procedure in humans. Thus, the present study indicates the possibility of effectively sealing the orifice at the end of the procedure. The development of dedicated perforation occlusion prostheses can also minimize the risk of dislocation, making the procedure reproducible by different operators. Unfamiliarity with the subxiphoid puncture may facilitate the learning of the vascular route for epicardial access for electrophysiologists who do not feel safe with the conventional strategy. However, the need for a specific prosthesis can increase the cost of the procedure, being more interesting in specific conditions (eg, megacolon).

Prosthesis proximity to the aortic base was observed in 3 animals in group B. After this observation, an attempt was made to perform the puncture in a more lateral orientation. However, this did not result in significant separation of the outer surface of the prosthesis from the aorta. This may be because the prosthesis is of a single size and not adapted to the size of the animal. Although the macroscopic and histological evaluations rule out the possibility of injury to the aortic wall, prolonged friction of the occluder device against the aortic root may result in erosion into the aorta and fistula formation with significant hemodynamic consequences. Therefore, a long-term survival study lasting 3-6 months may be necessary to address this important question. In this sense, bioabsorbable prostheses could minimize the risk of any injury over time, as well as facilitate access if further transatrial interventions are needed.

STUDY LIMITATIONS. Although some studies show that negative pressure can control bleeding in humans, the experimental results obtained so far show that hemorrhagic pericarditis can occur in up to 30% of animals; thus, extrapolating the results to humans is not possible. In this study, ventricular ablation was not performed, which could lead to a more intense inflammatory response.

Another noteworthy aspect is that a longer observation period may reveal some degree of involvement of the aortic wall by the prosthesis. Furthermore, the prostheses used in this study had a unique size and were not fitted to the size of the animal's heart.

CONCLUSIONS

The transatrial access by direct puncture of the RAA, in the presence of heparinization, allows mapping and ablation of the epicardial surface, with the survival of the animals over a week of observation.

Negative pressure contributes to achieving acute bleeding control after removal of the pericardial sheath, but it does not prevent the occurrence of hemorrhagic pericarditis, which can occur in up to 30% of animals in which the technique is used. The use of the occlusion device prevents bleeding after the pericardial space sheath is removed if it is properly positioned, thus preventing the occurrence of hemorrhagic pericarditis after a week of observation.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Within 1 week of observation, transatrial epicardial access seems to be safe in swine, even in heparinized subjects, if strategies to reduce major bleeding are used. Negative pressure contributes to achieving acute bleeding control after removal of the pericardial sheath, but it does not prevent the occurrence of hemorrhagic pericarditis, which can occur in up to 30% of animals in which the technique is used. The use of the occlusion device, if it is properly positioned, prevents the occurrence of bleeding and hemorrhagic pericarditis.

TRANSLATIONAL OUTLOOK: Transatrial epicardial access was demonstrated experimentally in previous, small series and may be an alternative to subxiphoid access to map and ablate arrhythmias, especially in scenarios where classical epicardial access is technically limited (eg, epicardial adhesions, chagasic megacolon). Further studies are necessary to ensure these strategy safety and future applicability in humans.

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APPENDIX For supplemental Methods and a figure, please see the online version of this paper.