

Lesions Produced by Radiofrequency Ablation of the Cavotricuspid Isthmus in an Experimental Model

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Introduction and objectives. Experimental studies have shown that deeper and wider lesions (up to 10 mm long or deep) can be safely created using an 8 mm or irrigated tip catheter for ablation to treat atrial flutter. However, potential damage to the tricuspid valve or inferior cava vein has not been systematically evaluated.

Patients and method. The cavotricuspid isthmus was ablated in 26 pigs (body weight 26-52 kg), with a total of 187 radiofrequency pulses. Standard 4 mm, 8 mm and irrigated tip catheters were used at random. For each ablation, energy, impedance and temperature were recorded continuously.

Results. The lesions were larger with irrigated tip and 8-mm catheters than with standard ones. In 7 animals (1 with an irrigated tip, 4 with an 8-mm, and 2 with a standard tip) the tricuspid valve was damaged. The tricuspid valve was severely damaged in 3 pigs and lesions were moderate in 4. In animals with tricuspid valve lesions, maximal energy was higher (59 ± 27 vs. 51 ± 24 W; $p = 0,03$) and higher temperatures were reached (63 ± 4 vs. 55 ± 11 °C; $p < 0,001$). Low energy pulses measured before ablation were also more intense in animals in which damage was produced ($0,55 \pm 0,24$ vs. $0,35 \pm 0,29$; $p = 0,001$), indicating greater contact pressure.

Conclusions. The tricuspid valve may be severely damaged during the ablation of the cavotricuspid isthmus for atrial flutter: damage was seen most often with high energy pulses and with 8-mm catheters, but can also occur with usual energy levels and standard catheters. To minimize damage this technique should not be used from the inside of the right ventricle just above the tricuspid valve.

Key words: Radiofrequency. Ablation. Atrial flutter.

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Lesiones producidas por la ablación con radiofrecuencia del istmo cavotricuspídeo en un modelo experimental

Introducción y objetivos. El empleo de catéteres con punta de 8 mm o irrigados para la ablación del aleteo auricular produce lesiones más anchas y profundas que los estándares, hasta de 10 mm de longitud y profundidad. El daño potencial sobre la válvula tricúspide o la vena cava inferior no se ha evaluado de forma reglada.

Pacientes y método. Se hizo ablación del istmo cavotricuspídeo en 26 animales (cerdos, con un peso de 26-52 kg) con un total de 187 aplicaciones, empleando aleatoriamente catéteres estándar de 4 y 8 mm, y catéteres irrigados, con control de la potencia, la impedancia y la temperatura.

Resultados. Los catéteres irrigados y de 8 mm produjeron lesiones de mayor tamaño. En 7 animales (uno con catéter irrigado, 4 con catéter de 8 mm y 2 con catéter estándar) se dañó la válvula tricúspide, la lesión fue severa en 3 casos y moderada, en 4. Los casos con lesión valvular habían recibido mayor potencia (59 ± 27 frente a 51 ± 24 W; $p = 0,03$) y alcanzado temperaturas más altas (63 ± 4 frente a 55 ± 11 °C; $p < 0,001$). La medición del pulso de baja energía preablación fue también mayor cuando se produjeron lesiones ($0,55 \pm 0,24$ frente a $0,35 \pm 0,29$; $p = 0,001$), lo que indicó una mayor presión de contacto del catéter.

Conclusiones. El daño valvular durante la ablación del istmo cavotricuspídeo puede ser más frecuente con el uso de alta energía y con catéteres de 8 mm e irrigados, pero también se puede producir con catéteres estándares y energías habituales. Para evitarlo, no se deben hacer aplicaciones en el interior del ventrículo derecho, justo encima de la válvula tricúspide.

Palabras clave: Radiofrecuencia. Ablación. Aleteo auricular.

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ABBREVIATIONS

CTI: cavotricuspid isthmus.
TV: tricuspid valve.
RF: radiofrequency.
AVB: atrioventricular block.
IVC: inferior vena cava.

INTRODUCTION

Radiofrequency ablation (RF) has become a common treatment for atrial flutter in most electrophysiology laboratories.¹ Large numbers of patients with this type of arrhythmia have been treated with the technique, and few complications have been reported. The length of the cavotricuspid isthmus (CTI) ranges from 19 to 40 mm,²⁻⁶ with an atrial muscle thickness of 9 to 10 mm. Treatment requires complete lines of ablation with no gaps to reduce relapse,⁵ but this might damage the tricuspid valve (TV) and adjacent structures. New irrigated-tip catheters or those with an 8 mm tip, used to achieve larger, deeper lesions in the CTI, may accentuate this damage.^{4,5,7-13,14-22}

In this randomized prospective experimental study, we performed radiofrequency ablation of the CTI in an animal model to investigate whether this caused TV lesions and to compare the damage from different types of catheter.

PATIENTS AND METHODS

Experimental preparation

Standard recommendations for the care and use of laboratory animals were followed. We anesthetized 26 pigs weighing between 26 and 52 kg with 25 mg/kg intravenous sodium pentobarbital, orotracheal intubation and mechanical ventilation with oxygen. General anesthesia was maintained with 2%-3% isofluorane. Hemostatic sheaths were used with venous access via the right jugular vein (to place the coronary sinus catheter) and the right femoral vein (for the ablation catheter). The surface electrocardiogram and intracardiac electrograms were recorded with a multichannel apparatus (Cardiac Pathways Corp, Sunnyvale, CA, USA). Changes in clinical status, the ST segment, and the appearance of arrhythmias were also recorded during and after the ablation procedure.

Electrophysiological study

Activation of the tricuspid annulus was analyzed

during atrial stimulation with a 20 pole halo catheter (Cordis Webster; Baldwin Park, CA, USA). Correct location was checked in 45° anterior oblique view. After ablation, bidirectional CTI conduction block was confirmed by measuring the atrial activation sequence after stimulation of the low right atrium and coronary sinus.

Ablation catheters

For standard RF ablation, a Marin® 7 Fr 4-mm deflectable tip catheter was used (Medtronic Inc., Minneapolis, MN, USA), with an Atak® II RF generator (Medtronic). The operation was performed in temperature control mode, with a target temperature of 70 °C and a power limit of 50 W. The irrigated tip catheter used was the Chilli Cooled Ablation Catheter (Cardiac Pathways Corp.), a 7 Fr quadripolar catheter with a 4 mm tip. The central conduit of this catheter contains 2 fluid channels to allow circulation of a saline solution. An infusion pump (model 8004, Cardiac Pathways Corporation) was used during RF ablation to irrigate the electrode with saline solution (0.9% heparinized saline serum at room temperature) at a flow of 15 mL/min. Powers of either 25 or 50 W were selected at random in temperature control mode with a target temperature of 50 °C. For 8 mm tip catheters, we used the Conduct® model (Medtronic Inc., Minneapolis, MN, USA), with a power limit of 100 W and a target temperature of 60 °C.

Protocol for RF ablation

The type of catheter ablation tip (standard 4 mm tip, irrigated tip or 8 mm tip) was randomly assigned for each procedure. The catheter was introduced through the sheaths until the right heart chambers were reached. Contact between the catheter and tissue was verified with radioscopic imaging. A single linear lesion was made starting from the tricuspid annulus, with progressive withdrawal of the catheter towards the inferior vena cava (IVC). The ablation lesion was made point by point to create a block line. To determine the starting point for RF applications on the ventricular side of the CTI, the catheter, in bipolar mode, was progressively withdrawn from the right ventricle until the ratio between atrial and ventricular amplitudes was 1:5. This procedure was used with all types of electrode. The objective of each procedure was to make a single ablation line, regardless of the acute result, with as many RF applications as necessary to form a line from the TV to the IVC. The RF current was applied between the distal electrode of the ablation catheter and an adhesive patch as an external electrode. For standard catheters, the temperature target for RF application was set to 70 °C and the power limit to 50

W, with each application lasting 60 s. For irrigated tip catheters, the powers used were 25 W in five animals and 50 W in five animals, with a preset temperature target of 50 °C (irrigation at 15 mL/min). For the 8 mm tip catheters, a power limit of 100 W was used with the temperature target of 60 °C. During each RF application the power, temperature and impedance were monitored and recorded. Immediately after ablation, heart rate and electrogram at the ablation site were repeatedly recorded. The electrocardiograms were analyzed during and after each application of energy and at the end of the procedure to monitor changes in the ST segment.

Primary objective of the procedure

The primary objective was to ablate a single line of the CTI and evaluate conduction along the CTI before and after the procedure. The ablation was defined as successful if it achieved bidirectional conduction block between the tricuspid annulus and the IVC. This procedure was chosen to provide a better analysis of the pathological changes associated with the creation of a single ablation line of with a given catheter at a given power. Another electrophysiological evaluation was performed for all animals within 30 minutes of ablation.

Pathological anatomy after ablation

The animals were killed a week after the procedure. The pathologist who assessed the lesions of the isthmus and the valve apparatus did not participate in the ablation procedure and did not know which catheter and what power had been used. After initial external macroscopic inspection, the hearts were fixed in a 10% formol solution for subsequent examination. After examination of the epicardial surface to assess possible transmural lesions, the right atrium was carefully opened and the CTI examined. Lesion size, extent of ablation damage, closeness of the lesions, transmural and evidence of pericardial or vascular damage were all assessed. Particular attention was paid to the presence of IVC and TV lesions, assessing damage to the annular insertion of the valve, leaflet or papillary muscle lesions, as well as prolapses or perforations of the valve (Figure 1). After examining the epicardial surface for transmural lesions, transverse sections were made in order to look for macroscopic lesions. Tricuspid valve lesions were defined as serious if there was loss of macroscopic anatomical continuity of the endothelium anywhere in the valve apparatus. Anatomical sections of the CTI and TV were then cut and fixed in paraffin. Strips 3.5

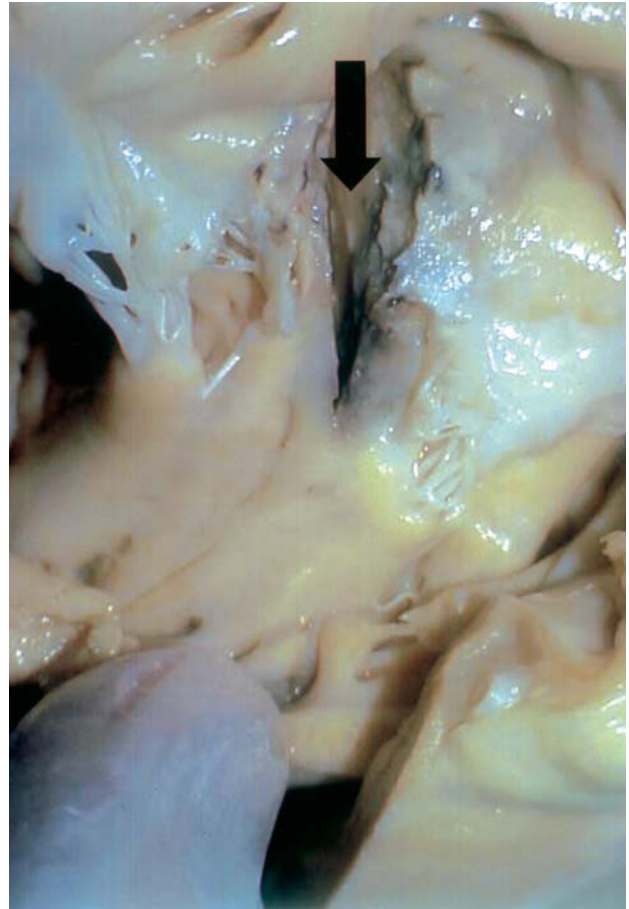


Fig. 1. Macroscopic appearance of the lesions produced after radiofrequency application. A large transmural lesion can be seen with complete destruction of the valve leaflet and chordae retraction. A fragment was removed for microscopic examination.

µm thick were cut for staining with hematoxylin-eosin prior to microscopic analysis.

Statistical analysis

Continuous variables were expressed as mean±standard deviation. The ANOVA test was used to compare quantitative variables in the three groups. A result was considered statistically significant if $P < .05$.

RESULTS

No significant differences were observed in weight of the animals across groups (33±4 kg in the group treated with the 8 mm tip catheter, 32±2 kg in the group treated with the standard catheter and 34±3 kg in the group treated with the irrigated tip catheter). Heart weight was also similar (205±33 g in the group treated with the 8 mm tip catheter, 199±25 g in the group treated with the standard catheter and 215±38 g

in the group treated with the irrigated tip catheter). Likewise, there were no differences in the total procedure time, fluoroscopy time or the number of applications in the different groups. A total of 187 RF applications were made for 26 animals (eight with a 4 mm tip Marin® catheter, ten with an irrigated tip catheter and eight with an 8 mm tip Conduct® catheter). After line ablation, electrophysiological block of the cavotricuspid isthmus was achieved in 20 animals; seven with the 8 mm catheter, eight with the irrigated catheter and five with the standard catheter. The procedural information is summarized in Table 1.

Larger lesions were obtained with irrigated tip catheters and 8 mm tip catheters. An anatomically complete line of ablation was made in 14 animals with no valve damage. In 7 animals (four treated with the 8 mm tip catheter, 2 with the standard catheter and one with the irrigated tip catheter) we observed a line of ablation that affected the TV and also the right ventricle. This lesion was mild in 4 animals (15%) and serious in 3 (11%). The types of valve damage were valve insertion lesion (3 animals), leaflet damage (7 animals), papillary muscle lesion (4

animals), leaflet retraction (4 animals) and leaflet perforation (3 animals). Valve damage was associated with use of a greater maximum power (59 ± 27 W for animals with valve damage vs 51 ± 24 W for those without; $P<.03$), and a higher mean temperature at the tip (63 ± 4 °C for animals with valve damage vs 55 ± 11 °C for animals without; $P<.001$). Damage was also associated with a larger value for LEM (low energy pulse measurement of temperature change) (0.55 ± 0.24 for animals with valve damage vs 0.35 ± 0.29 for animals without; $P=.001$), indicating a higher catheter contact pressure. There were no significant differences in mean impedances reached in the 2 groups (99 ± 24 Ohms for animals with valve damage vs 109 ± 32 Ohms for animals without). Table 2 presents the most relevant results.

There were no significant complications during or after the procedure, evaluated either clinically or with 12-lead electrocardiography. We saw no evidence of acute myocardial ischemia or arrhythmias. When the heart was removed for examination, we found that no animal had evidence of pericardial effusion.

TABLE 1. Summary of the ablation procedure

Nº.	Lesión ^a	Catheter	Applications (n)	Energía ^b	Power reached Duration (s)	Impedance (W)	Mean temperature (Ohm)	reached (°C)
1 ^c	Yes	8 mm	5	100	54±4	38±12	74±4	66±2
2 ^c	Yes	8 mm	8	100	55±8	52±15	94±5	60±1
3 ^c	Yes	8 mm	12	100	48±13	46±19	103±15	63±3
4 ^c	Yes	8 mm	6	100	60	43±3	96±4	64±1
5	No	8 mm	10	100	34±16	88±7	95±9	55±9
6	No	8 mm	6	100	51±8	72±13	162±50	58±4
7	No	8 mm	11	100	66±8	33±14	114±23	64±2
8	No	8 mm	6	100	69±12	66±8	92±10	58±6
9	No	Irrigated	7	50	42±19	47±0.3	99±10	43±4
10	No	Irrigated	7	50	48±15	47±0.7	102±4	45±3
11	No	Irrigated	13	25	60	25	87±4	32±3
12	No	Irrigated	10	25		25		
13	No	Irrigated	6	50	28±17	49±0.4	140±36	
14	No	Irrigated	4	25	60	25	111±1.2	31±2
15 ^c	Yes	Standard	5	50	60	34±10	113±9	58±6
16	No	Irrigated	2	25	101±40	25	111±1	31±2
17	No	Irrigated	6	50	46±19	49±0.3	136±46	40±6
18	No	Standard	5	50	60	34±3	129±7	50±1
19	No	Standard	10	50	60	27±13	84±9	65±4
20	No	Standard	10	50	60	18±11	87±9	64±3
21 ^c	Yes	Irrigated	5	25	89±32	25	131±58	49±13
22	No	Standard	5	50	60	34±8	107±5	59±4
23	No	Standard	9	50	104±28	23±17	98±11	60±8
24	No	Irrigated	13	50	19±9	49±0.4	1323±48	63±3
25 ^c	Yes	Standard	12	50	46±22	16±8	90±9	65±3
26	No	Standard	5	50	90±30	21±9	115±9	63±3

^aDamage to tricuspid structures. ^bMaximum power limit in Watts. ^cData for animals in which tricuspid damage occurred during treatment for atrial flutter. When the preset power was 25 W, mean power is not shown.

TABLE 2. Summary of the ablation data for animals with tricuspid lesion

Catheter	Application	Maximum	Power	Impedance	Temperature	INS lesion	VAL lesion	PAP lesion	VAL retraction	Perforation
	time	power	Mean							
	(s)	applied (W)	applied (W)	(Ohm)	(°C)	(n)	(n)	(n)	(n)	structures (n)
8 mm 100 W	59±10	76±24	46±16	94±14	63±3	3	4	3	3	2
Standard 50 W	50±22	40±10	21±8	97±9	63±3	0	2	1	1	1
Irrigated 25 W	89±32	25	25	131±58		0	1	0	0	0

INS indicates insertion of the leaflet in the annulus; PAP, papillary muscle; VAL, valve leaflet; n, number.

Macroscopic pathological analysis

Transmural lesions in the epicardium appeared as white-red areas of varying sizes with an irregular outline. The right atrium was opened at the posterior wall to examine the lesions and record the anatomical size of the CTI. Mean length was 22 ± 7 mm and maximum thickness at the lesion site was 4.25 ± 0.91 mm. An anatomically complete line was found in 17 animals (7 after ablation with an 8 mm tip catheter, 6 after ablation with an irrigated tip catheter and 4 after ablation with a standard catheter). We found completely transmural lesions (observed macroscopically from the epicardium, regardless of whether or not the line in the cavotricuspid isthmus was complete) in 23 animals. Subacute lesions appeared as a shallow reddish depression in the surrounding healthy endocardium with a clearly defined irregular outline. The area of lesions with the irrigated tip catheter and 8 mm tip catheter was greater than the area with standard catheter lesions (7 ± 3 mm for irrigated tip catheters and 8 mm tip catheters versus 4 ± 2 mm for standard catheters). No animal presented mural thrombus or myocardial perforation.

Microscopic analysis

The results of the histological examination were similar for all animals. We saw extensive coagulation necrosis of atrial striated muscle, with inflammatory infiltrate surrounding the necrotic areas consisting of lymphocytes, plasma cells, monocytes and macrophages with neutrophils and some eosinophils. We also found granulomatous reactions involving giant cells. In 3 animals repair was more «fibroblastic.» Around the area of ablation, the cytoplasm was condensed. Hematoxylin-eosin staining revealed hypereosinophilia, with nuclear condensation and signs of apoptosis. We found homogenization of cytoplasm and loss of transverse myocyte striation with pyknosis or loss of nuclei, and foci of cellular disintegration. The necrosis observed in our experiment differs from contraction band necrosis, which shows striations in the cytoplasm because of contracture of the sarcolemma. Monocyte- and macrophage-like inflammatory cells were present to

remove debris of myocardial fibers by phagocytosis. We observed edema among the necrotic fibers. Occasionally, small vessel vasculitis was observed in the most inflamed areas with fibrinoid necrosis of the wall, and in 3 animals, recent thrombi were found in the pericardial arteries. The most severe lesions were observed in fig 3 (Figure 1 and compare with Figure 3), with partial destruction of the valve.

DISCUSSION

Since the introduction of catheter ablation to treat cardiac arrhythmias in 1982,²³ advances in technology and the excellent results obtained have extended the indications for the technique. Coyeso et al²⁴ proposed sequential application of RF energy in CTI for the treatment of typical atrial flutter. Anatomical variations and the complex structure of CTI can make some cases more complicated. For example, some parts of the circuit of atrial flutter may be near the epicardium, lying too deep for standard RF lesions to reach. Local topography is also important because the anatomy of the CTI may be complex, with large recesses where good convective cooling may not occur, thus limiting energy delivery.

Some experimental studies have shown that irrigated tip catheters and 8 mm tip catheters can induce deeper and broader lesions.^{13-20,25-27} Irrigation of the tip with saline solution maintains a small electrode-tissue interface that allows greater RF energy delivery and deeper lesions. Ablation is also quicker, fluoroscopy time is shorter, the success rate is greater, and there may be fewer recurrences in such conditions.^{28,29} Despite these advantages, we think that possible damage to structures close to the CVI as a result of these larger lesions has yet to be adequately studied. Structures susceptible to damage include the TV and the IVC. The functional consequences of larger lesions have also not been fully studied. We found that despite carefully performing the ablation procedure with radioscopic and continuous electrophysiological control at each point along the ablation line, damage occurred in the valvular and subvalvular tricuspid structure in 26% of the animals. The lesion, however, was classified as serious in only 3 animals (11%). The potential to damage tricuspid structures increased with

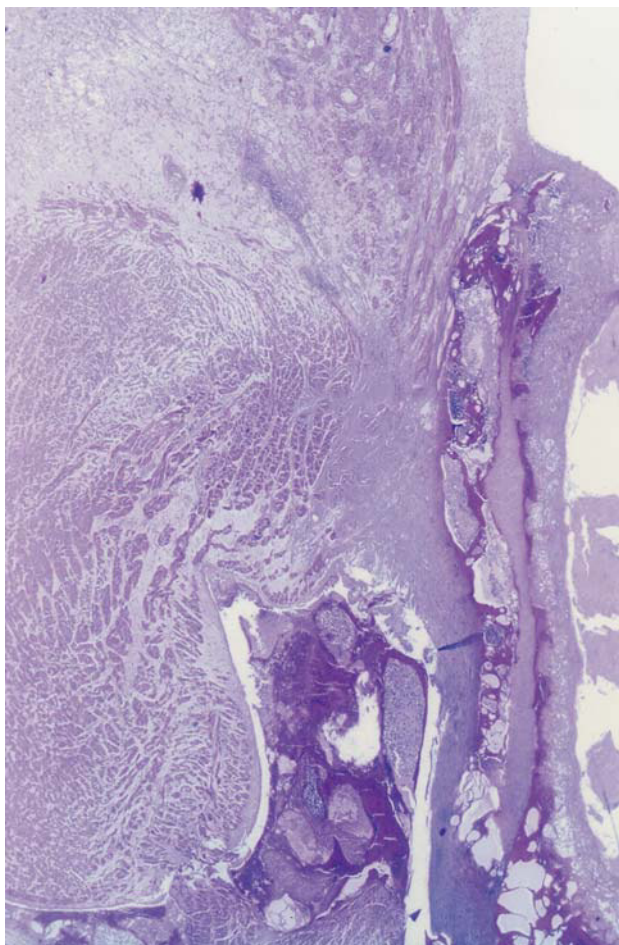


Fig. 2. Microscopic appearance of the lesions found in animal 3. Necrotic, hemorrhagic and inflammatory processes affect the pericardium, myocardium and endocardium, including valve tissue. Necrosis is of the acute coagulative type in heart muscle tissue, accompanied by an inflammatory reaction of lymphocytes and plasma cells that affect the entire heart wall. A hemorrhagic lesion is observed with accumulation of material of the consistency of fibrin, mainly in the valve wall itself.

the use of catheters at higher powers. No animal had damage to the IVC.

Complications of radiofrequency ablation in earlier reports

Different complications have been described after RF ablation. These are mostly related to the vascular catheterization technique itself, and to a lesser extent, to the RF energy applied,³⁰⁻³² although of course the number of complications is much lower if the electrophysiological team and the operator are experienced. Calkins et al³¹ published one of the most recent studies on complications after RF ablation, but this study did not include treatment of atrial flutter. These researchers observed important complications

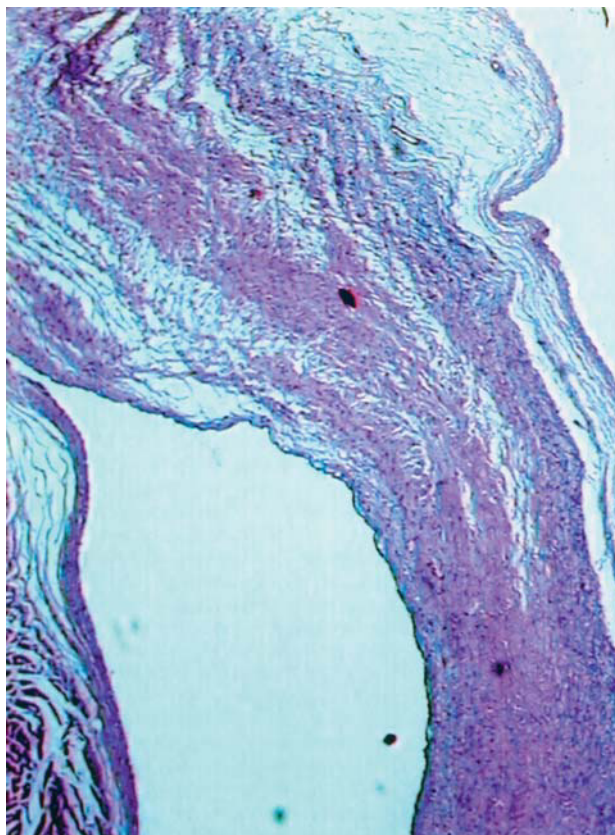


Fig. 3. Microscopic appearance of a healthy tricuspid valve.

in 32 out of 1050 patients. In other populations treated for typical atrial flutter, few complications have been described after ablation,^{1,28,29} except for interventions at the base of the septum close to the coronary sinus ostium, with a greater risk of atrioventricular block (AVB).³³ The MERF³⁰ study included 141 ablation interventions for atrial tachycardia and fluttering. The rate of complications was 5%, of which 0.7% corresponded to an ischemic event and the remainder to pericardial effusion, perforations, AVB, venous thrombosis and embolism. Acute ischemic events have not been described in recent studies with standard or irrigated tip catheters.^{1,28} Likewise, our group has recently shown that the application of RF to the CTI does not cause damage to the right coronary artery.³⁴

Limitations of the study

The objective of the procedure was to produce a single line of ablation in the CVI. Of course, the probability of damage to tricuspid structures increases if more lines are required to ablate the isthmus. Subacute changes emerging one week after ablation were analyzed in this study. If we had removed the heart in the acute phase after ablation, we could have

checked for arterial thrombosis, though there were no clinical or electrocardiographic alterations pointing to this condition. Furthermore, our experiment did not allow us to study chronic changes that might start to appear 2 months after ablation. Although we tried to produce the line of ablation in the lateral isthmus, the anatomy of the pig heart forced us to make the line in the septal region, where damage to the TV might be greater. Ablation may inadvertently occur inside the ventricle, though this can also happen in theory in humans. Thus, many factors may influence the damage produced in addition to the type of catheter, the power used or positioning of the catheter. Our conclusions should therefore be applied only to this specific experimental model and to this form of applying energy.

CONCLUSIONS

The tricuspid valve may be damaged by the application of radiofrequency to ablate the cavotricuspid isthmus, using high powers (100 W) with 8 mm tip catheters (57% cases), but also with lower powers using standard catheters (28% cases) and irrigated tip catheters. Therefore, the starting point for radiofrequency ablation should be carefully chosen to avoid unnecessary application to the valve apparatus.

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