Journal of Interventional Cardiac Electrophysiology (2024) 67:1981–1991
https://doi.org/10.1007/s10840-024-01841-8

ORIGINAL RESEARCH

Comparison between cryotherapy and radiofrequency energy sources for parahisian accessory pathway percutaneous ablation

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Received: 29 February 2024 / Accepted: 28 May 2024 / Published online: 4 June 2024

Abstract

Background Catheter ablation of parahisian accessory pathways (PHAP) are challenging due to their proximity to the normal conduction system. Retrospective studies suggest that cryoablation has a better safety profile but a higher recurrence rate when compared to radiofrequency ablation (RFCA). The objective of this study was to compare the results of parahisian AP ablation performed by electrophysiologists with experience in both technologies.

Methods Prospective single-center, non-blinded and 1:1 model was used. Patients included had parahisian AP confirmed by an electrophysiological study and referred for radiofrequency or cryotherapy ablation according to current guidelines, under fluoroscopic guidance. No electroanatomic mapping was used.

Results A total of 30 patients (mean age of 25±9.4 years; 90% male) were enrolled between Oct/2018 to Feb/2020. Acute success rate between RFCA and CRYO were similar (93% *vs.* 87%, $p = 0.54$). A nonsignificant reduction in short-term recurrence rate for RFCA (14% vs. 30%, $p = 0.3$) and mechanical trauma (6% vs. 20%; $p = 0.28$) was observed. Long-term recurrence rate and event-free survival time were similar in both groups after 1-year follow-up ($p = 0.286$). No persistent complete AV block or conduction disturbance was also observed.

Conclusion Considering the limitation of a small sample size and the lack of use of electroanatomic mapping for RFCA, the efficacy and safety profile of parahisian AP ablation with RFCA was not different from CRYO, when performed by experienced electrophysiologists. No cases of permanent complete AV block were reported with either energy modalities.

Keywords Electrophysiology · Wolff-Parkinson-White · Accessory pathway · Parahisian accessory pathway · Cryoablation · Radiofrequency

1 Introduction

The term accessory pathway (AP) of atrioventricular conduction refers to the presence of a bundle of anomalous electrical conduction able to connect atria and ventricles outside the normal conduction system [1]. The main consequences associated with anomalous electrical conduction are the formation of a substrate for re-entrant tachyarrhythmias and rapid ventricular conduction of supraventricular rhythms, which can degenerate into malignant arrhythmias or sudden death [2, 3].

Percutaneous ablation of the accessory pathway (AP) by radiofrequency (RF) is considered the treatment modality of choice; however, it can become complex depending on its location in the atrioventricular ring [4]. Parahisian accessory pathways (PHAP) are situated near the native conduction system [5]. Here, the risk of a permanent third-degree atrioventricular block (TAVB) during percutaneous ablation is the most important concern [6–10].

Cryotherapy has been studied as a safer alternative for the ablation of parahisian accessory pathways compared to RF due to the inherent advantages of the injury mechanism [11–14]. On the other hand, more recent scientific evidence in the field of RF also shows a high safety profile, either through energy titration protocols or the development of alternative routes such as the non-coronary sinus retroaortic approach [15–18]. Until now, publications on

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randomized studies directly comparing both percutaneous treatment modalities in this specific setting have yet to be found.

The objective of this study was to assess the safety profile and efficacy of PHAP ablation, comparing two energy sources: cryotherapy and radiofrequency.

2 Methods

2.1 Study design

This was a 1:1 prospective, interventional, unblinded, single-center study in which patients with PHAP aged ≥12 years were selected; indication for percutaneous treatment is in accordance with current guidelines: a) symptomatic patients despite antiarrhythmic therapy and b) asymptomatic patients with non-invasive or invasive findings at high risk of sudden cardiac death. Patients with a previous history of cryoablation or RF ablation using retroaortic method, pregnant women or those with severe hemostasis disorders were excluded.

All eligible patients have given informed consent in accordance with the Declaration of Helsinki. The study design was approved by the Ethics Committee of the Scientific Committee of InCor, HC-FMUSP, and registered on the *clinicaltrials.gov* website (ID NCT04361006).

The long-term success rate after a minimum of one year of follow-up after the procedure was the primary efficacy endpoint. The incidence of permanent procedure-induced TAVB was the primary safety outcome. Secondary analyzes of patient groups submitted to each of the energy modalities were also performed to identify possible factors associated with success rate.

2.2 Electrophysiology study

All antiarrhythmic drugs were discontinued for at least five half-lives before ablation (amiodarone for one month). Patients were referred to standard electrophysiological study (EPS), performed under general anesthesia. Decapolar deflectable catheters (Inquiry 2-5-2 mm, Abbott/ USA) were positioned in the coronary sinus and right ventricle through femoral venipuncture for electrophysiological characterization of the AP. The diagnosis of PHAP was defined by the presence of an His bundle electric potential with amplitude ≥0.1 mV at the site of earliest ventricular activation (viewed through a block in AP conduction during programmed atrial stimulation) or in which ablation was successful (such in cases of exclusive retrograde conduction).

After electrophysiological confirmation, patients were selected to RF (Group 1) or cryotherapy (Group 2) PHAP ablation.

2.3 Group 1 - radiofrequency ablation (RF)

A third deflectable catheter was positioned in the non-coronary sinus via retroaortic access by femoral arterial puncture to capture simultaneous signals on both sides of the His bundle.

The initial treatment route (femoral vein or retroaortic) was decided at the operator's discretion based on local AV signal (Fig. 1A-D). A therapeutic 4-mm quadripolar RF catheter (Abbott/ USA) was used. For right-sided approach, maximum power was limited to 50w, and maximum temperature was limited to 60°C. On the other hand, the power was limited to 40w on aortic cusps.

Applications were carried out with increasing power and temperature, starting with 10w (10-15 seconds) and increasing 5-10w in following applications. Observation of the first sign of AV block (first blocked P wave) or junctional rhythm during application was the criterion for interruption. Eliminating the accessory pathway was the ultimate goal of the procedure and it was confirmed by either electrophysiological maneuvers or adenosine testing after a 30-min observation period.

In case of unsuccessful ablation using a given route, a new attempt was made through a different access (venous femoral to retroaortic access and vice versa). In all cases, the jugular route was used as a rescue strategy.

2.4 Group 2 - cryotherapy ablation (CRYO)

After electrophysiological evaluation and randomization, a 7F quadripolar deflectable catheter (Freezor Xtra catheter) with a 6-mm tip (Medtronic CryoCath LP/ Canada) was introduced through the femoral venous access using a long Swartz SL0 8F sheath (Fig. 1E). Initially, cryoablation was performed by cooling the system (-80 °C) at probable site. In absence of desired effect or impaired AV conduction, cryotherapy was stopped and restarted at a different location. In case of a sudden loss of pre-excitation or interruption of tachycardia, the energy supply was maintained for two 240-s cycles, interspersed by a brief warming period ("freeze-thaw-freeze" protocol). In cases in which traumatic AP block occurred during mapping maneuvers, at least one cryoablation lesion was performed at the closest site. Repeated electrophysiological study was performed 30 minutes after ablation with adenosine testing to assess both nodal conduction and demonstration of absence of conduction through PHAP.

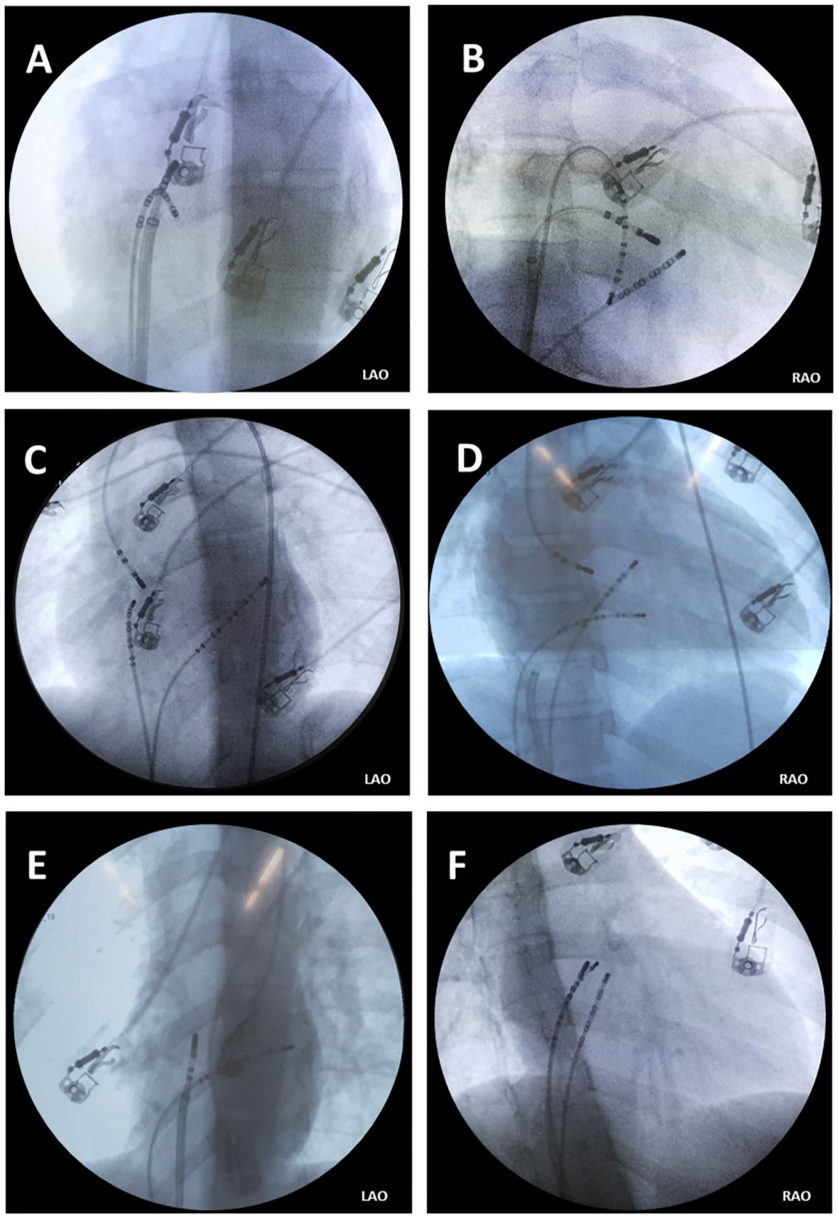


Fig. 1 Fluoroscopy views demonstrating ablation catheter positioning for RF venous femoral (**A-B**), retroaortic approach (**C-D**) and cryoablation (**E-F**) in left anterior oblique (LAO) and right anterior oblique (RAO)

2.5 Follow-up after procedure

Antiarrhythmic medications were discontinued after ablation. First clinical assessment was performed in the next day and after the procedure and the following ones at 30 days, 6 and 12 months after. Ambulatory ECG monitoring exams were performed at last six months later (reported by independent team) to verify long-term success. Patients were followed up to 12 months after the procedure.

Patients who presented recurrence after the successful initial procedure or in whom recurrence was detected in clinical evaluation or ambulatory ECG monitor underwent a new procedure with the same therapeutic modality. Unsuccessful cases or those maintained in conduction by AP after two procedures were kept in clinical treatment.

2.6 Statistical analysis

Categorical data was presented in percentage (%) and compared using Fisher's exact test or χ^2. Quantitative data of normal distribution was presented as mean ± standard deviation and compared using Student's *t*-test. Non-parametric quantitative data was presented as median and tested for statistical significance with Mann-Whitney or Wilcoxon tests. We used the Log-Rank tests and the Kaplan-Meier curve for the analysis of recurrence-free survival at six months. We considered P values <0.05 as statistically significant. We used SPSS (SPSS Inc, IBM) software (v. 25.0) for data analysis and treatment.

3 Results

3.1 Patient baseline characteristics

Thirty consecutive eligible patients were enrolled between Oct/2018 and Feb/2020, from a total of 512 patients screened (Fig. 2) over the period.

Clinical findings are shown in Table 1. The mean age of the sample was 25.3 ± 9.4 years, with a predominance of males (90%) and a previous history of failed attempted right septal RF ablation in 60% of cases. Normal ejection fraction and absence of comorbities were noted. All patients were in sinus rhythm at the beginning of the procedure; 83% (25/30) of them showed evidence of ventricular pre-excitation at rest and for this reason underwent anterograde mapping.

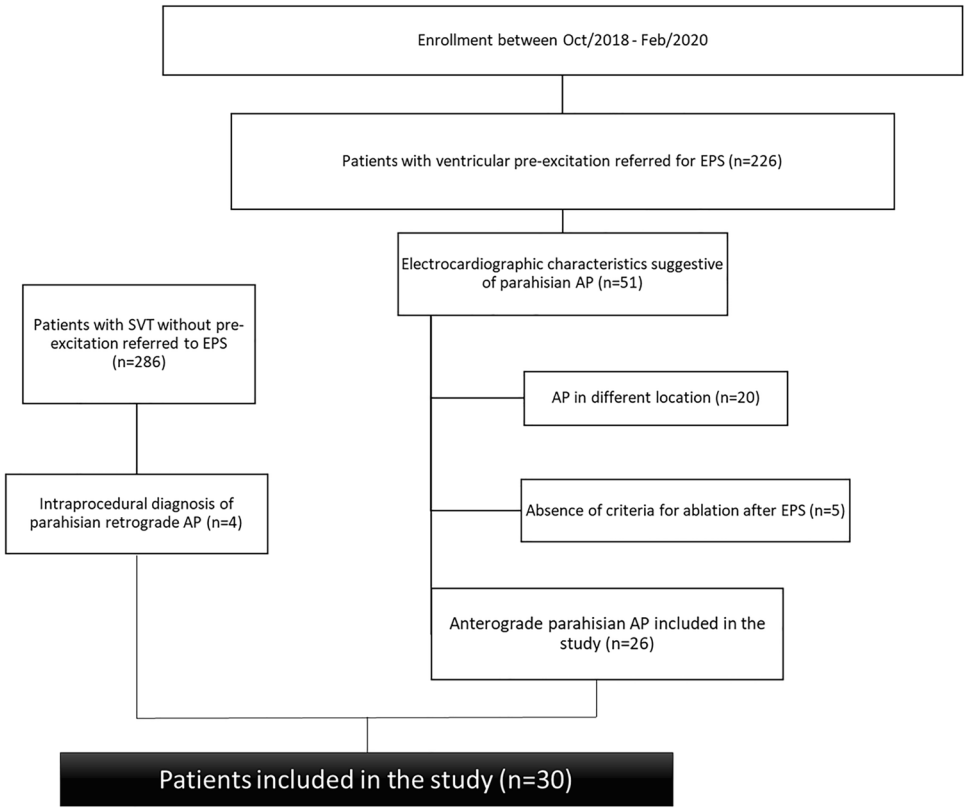


Fig. 2 Diagram of inclusion criteria

Table 1 Baseline patient characteristics

	RF group (*n*=15)	Cryo group (*n*=15)	P*
Age (years)	25.3 ± 7.8	24.5 ± 10.8	0.82
male (%)	93	87	0.54
prior ablation (%)	60%	60%	1.0
LVEF (%)	64% ± 5%	64.1% ± 6%	0.7
Manifest pre-excitation (%)	80	87	1.0
Use of antiarrhythmics			
propafenone (%)	70%	70%	NS
sotalol (%)	10%	10%	NS
amiodarone (%)	0%	10%	NS
none (%)	20%	10%	NS
Indication of the procedure			
Palpitations (%)	40%	40%	NS
Sustained tachyarrhythmia (%)	40%	40%	NS
High-risk findings (%)	20%	20%	NS

LVEF left ventricle ejection fraction, * *NS* nonsignificant

In all pre-excited cases, a positive delta wave was observed in DI, in addition to inferior axis and precordial QRS transition between V2 and V4. Delta wave was negative on V1 and V2 in 20% of patients. A predominant positive polarity in DIII was seen in 84%, with mean R/S ratio of 5.5.

3.2 Ablation approach and immediate outcomes

Electrophysiological findings are shown in Table 2. Overall immediate success rate was 90% (27/30 cases), being similar between groups (RF 93% vs. CRYO 87%, p=0.54). The mean His potential amplitude was 0.3 ± 0.2mV at the application site and the local signal amplitude A/V ratio was similar (0.8-1.0). No electroanatomic mapping system was used.

Compared with the RF group, similar radioactive exposure (6.6 ± 3.0 *vs.* 7.6 ± 4.8min; $p = 0.77$) and procedure times (140.7 ± 38.3 *vs.* 117.7 ± 32.8min; $p = 0.09$) were noticed with cryotherapy.

Complications related to the anesthetic protocol or puncture site were not identified. All patients were discharged the day after the procedure. Three days after hospital discharge, deep venous thrombosis was identified in a patient in the RF group (# 7) which was managed on an outpatient basis with oral anticoagulation without major complications.

Incidence of persistent TAVB was not observed in any patient of the sample (n=30) in the periprocedural period or during outpatient follow-up. Transient TAVB was detected during cryotherapy in two patients in the CRYO group, who had a prompt spontaneous reversal. Persistence of RBBB was documented in three patients (RF=1; CRYO=2), who had a complete reversal in the first follow-up visit.

3.3 Radiofrequency ablation (RF) group analysis

A retrograde approach through non-coronary sinus was the initial strategy in eight patients (53%), whereas applications started from femoral vein in the remaining (47%). Acute success with a single access route was achieved in only one-third of the cases (5/15; aorta=3, femoral=2). In the other cases (10), changing the access route was necessary during the procedure.

Initially, considering those with initial retroaortic attempt, initial success was achieved in only 37.5% of patients (3/8). In the other five patients, switching to femoral vein (2) or jugular (3) was required, mostly due to unsuccess (60%) or repetitive junctional rhythm (40%). Comparatively, initial approach from femoral vein resulted in AP ablation on 28.6% (2/7) of the cases, also requiring switch to another access route due to unsuccess (40%) or repetitive junctional rhythm (60%). Finally, in six cases,

Table 2 Procedural outcomes of parahisian accessory pathway ablation

	RF group (n=15)	Cryo group (n=15)	P*
Immediate success (%)	14/15 (93)	13/15 (87)	0.54
Electrophysiological characteristics			
APERP (ms)	262.5 ± 26.8	248 ± 21	0.16
Tachycardia induction	9/15 (60%)	11/15 (73%)	0.43
Cycle (ms)	306.1 ± 65.8	324.4 ± 58.6	-
Ventricle-atrial interval (ms)	82.5 ± 17.8	82.1 ± 25.8	-
His bundle potential (mV)	0.3 ± 0.2	0.3 ± 0.2	NS
Local A/V ratio	0.8 ± 0.2	1.0 ± 0.5	NS
N° of cryomaps	-	3.8 ± 2.9	-
N° of cryotherapies	-	1.6 ± 1.1	-
N° of RF therapies	12.5 ± 10.5	-	-
Time in RF (min)	6.9 ± 6	-	-
Accessory pathway block time (sec)	4.9 ± 3.9	11 ± 5.3	-
Mechanical trauma of the pathway (%)	1/15 (6)	3/15 (20)	0.28
Fluoroscopy time (min)	7.6 ± 4.8	6.6 ± 3	0.77
Procedure time (min)	117.7 ± 32.8	140.7 ± 38.3	0.09
Recurrence in 30 days (%)	2/14 (14)	4/13 (30)	0.3
Long-term (1 year) success rate (%)	14/15 (93)	12/15 (80)	0.59
N° of procedures performed	17	19	NS
Complications	DVT (1), RBBB (1)	RBBB (2) Transient TAVB (2)	-

APERP accessory pathway anterograde effective refractory period, *DVT* deep vein thrombosis, *RBBB* right bundle brunch block, *TAVB* third-degree atrioventricular block, * *NS* nonsignificant

rescue jugular access was necessary after both two initial strategies have failed, with success rate of 83% (5/6). The only case of unsuccessful jugular attempt occurred in context of ineffective ablation from other routes (Fig. 3).

When comparing ablation success rates from each approach, ablation was more often successful with jugular access in comparison to other routes (83% vs. 37.5%, p. 0.044). However, no statistically significant relationship was observed between baseline electrocardiographic variables or right ventricle endocardial signals and success prediction by any strategy.

In contrast, we noticed a statistically significant relationship between the earliest anterograde signal (in relation to the surface QRS complex) in the non-coronary sinus and success by the retroaortic approach compared to right septal mapping ($p = 0.0004$). The absolute cutoff of local ventricular activation time by the non-coronary sinus $\geq$ 40ms relative to the QRS complex defined success by the retroaortic approach with 100% accuracy. Furthermore, considering all cases submitted to successful non-coronary sinus ablation, we noticed that their ventricular activation time values were always earlier than those on the right septal side (8-18ms).

Junctional rhythm was detected in 36% of patients who underwent RF ablation, unrelated to either HV interval disturbance or incidence of complete AV block during applications. Differences in the incidence of junctional rhythm according to access route (femoral 33,3% *vs.* aorta 41,6% *vs.* jugular 33,3%; p=0.59) were not observed.

Only one case of unsuccessful ablation was registered in the operating room, which was submitted to the three planned mapping strategies, being maintained under clinical treatment.

3.4 Cryotherapy ablation (CRYO) group analysis

Anterograde ablation was performed in 12/15 cases; in the remaining three cases (exclusive RAP), it was indicated during tachycardia. On average, 3.8 ± 2.9 cryomaps were used and 1.6 ± 1.1 cryolesions were applied per procedure. Conduction block through AP occurred after 11 ± 5.4s of cryotherapy.

Considering the cases with anterograde conduction (n=12), the local ventricular activation time preceded surface QRS by at last 20ms (32.5 ± 12.1ms) and no cutoff value was observed to differentiate successful from failed cases. The general outline of the subgroup of patients undergoing cryoablation is shown in Fig. 4.

A non-significant higher incidence of mechanical trauma of the accessory pathway was detected during the procedure (6% *vs.* 20%; $p = 0.28$). In these three cases, cryotherapy was applied where the catheter was located when AP conduction was lost. In all cases, pathway activity did not return at the end of the post-procedure observation period.

Junctional rhythm was not observed during cryotherapy. Transient prolongation of PR interval detected ablation was observed in 27.0% (4/15) of cases. However, progression to transient TAVB (n=2/15; 13% of the total) occurred in half of them, which spontaneously reversed after interruption of therapy. During the cryotherapy sessions that resulted in TAVB, the average amplitude of the bundle of His was statistically higher than that obtained in cases in which

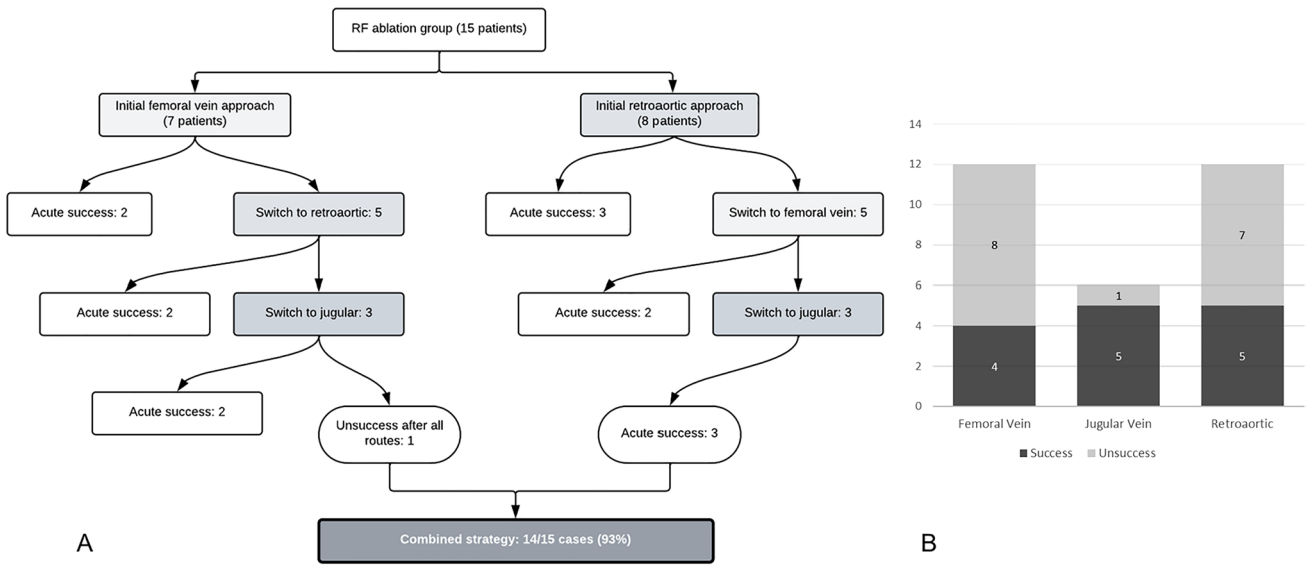


Fig. 3 **A**. Temporal flowchart of treatment plan applied for patients with PHAP referred to RF ablation. **B.** Comparison of successful vs. unsuccessful cases by access route used

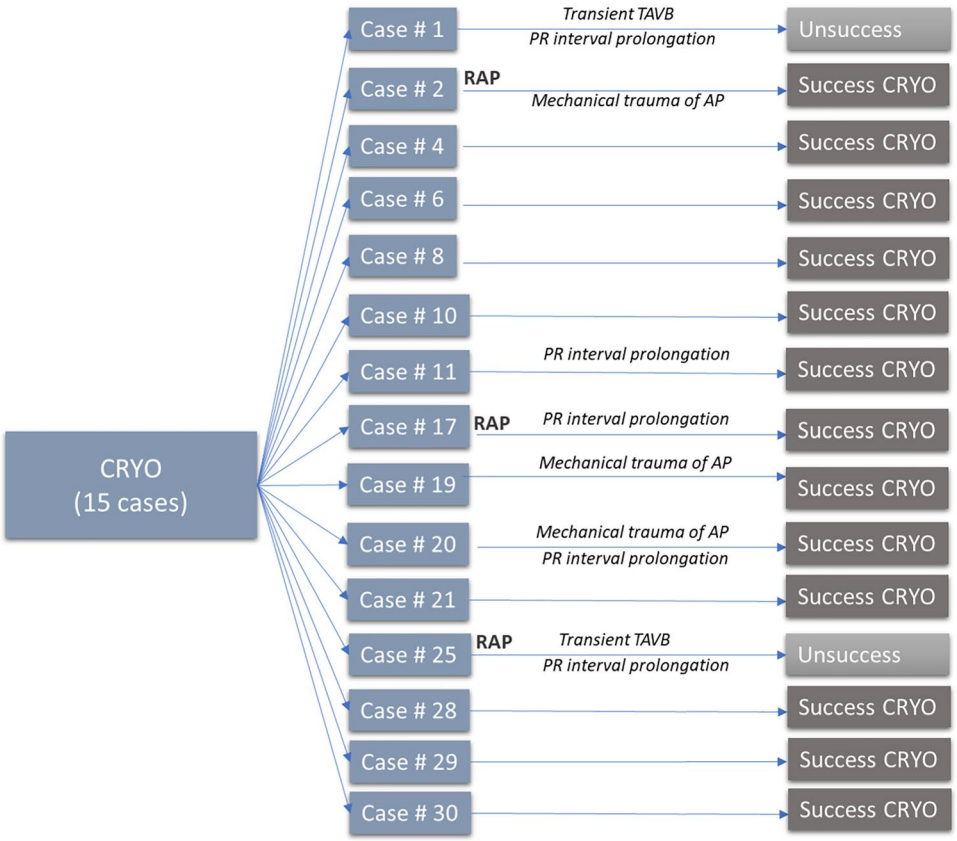


Fig. 4 Therapy outcome for patients submitted to cryoablation as initial strategy. CRYO – cryoablation, TAVB – Third-degree atrioventricular block, AP – accessory pathway, RAP - retrograde accessory pathway

the event was absent (0.8 ± 0.07mV *vs.* 0.35 ± 0.17mV; p=0.004). Voltage differences were not observed between those who had and had not PR interval prolongation (0.52 ± 0.34mV *vs.* 0.37 ± 0.17mV; $p = 0.469$).

A statistical relationship between exclusive retrograde conduction and the emergence of complications was not observed (p=0.45 for RBBB; p=0.52 for trauma; p=0.26 for AVB). After several treatment attempts in both cases in which TAVB occurred (2), it was then decided to end the procedures, which were then classified as unsuccessful. Persistent perturbation of the HV (ms) or PR (ms) intervals were not observed relative to the baseline values of the procedure. The occurrence of persistent TAVB after cryoablation was also not observed.

3.5 Recurrences

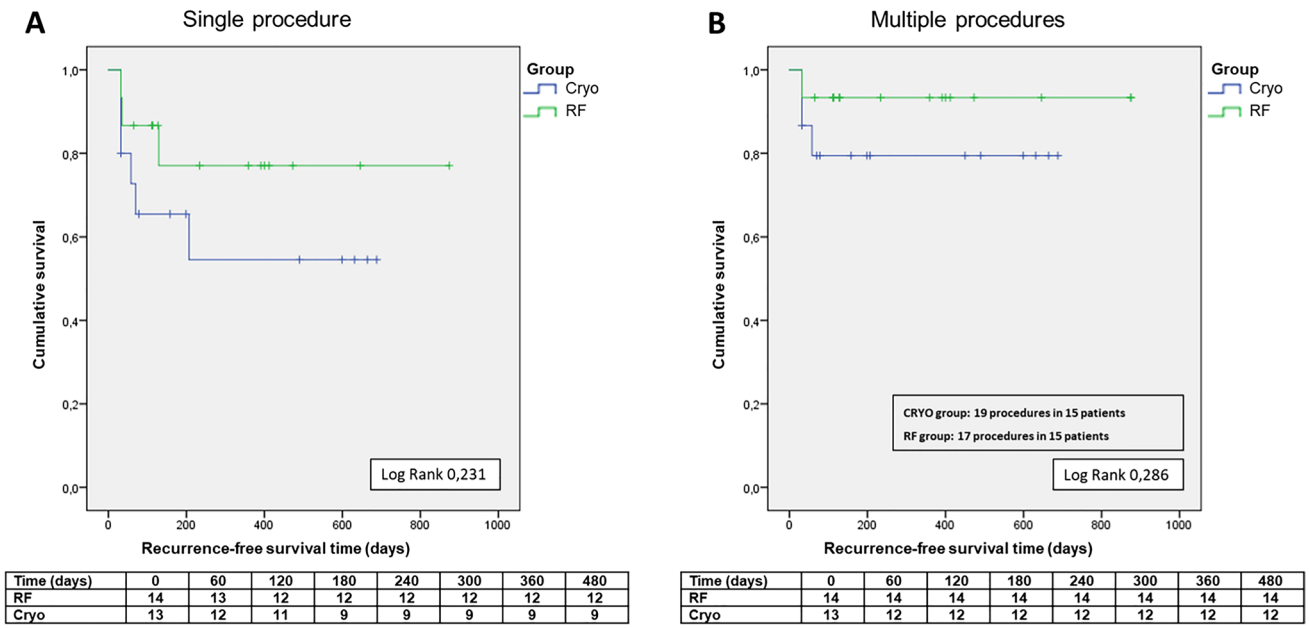
Among the patients initially submitted to successful RF ablation (n=14), early (<30 days) and asymptomatic recurrences were observed in two cases (cases # 5 and 9): they were diagnosed by resting electrocardiogram at first follow-up consultation and treated again with RF ablation though same access site.

Regarding the CRYO group with initial success (n=13), four recurrences (cases # 2, 19, 20, and 29) were detected; in three of them, mechanical trauma of the AP was the reason, although cryotherapy was empirically applied on the site where the loss of conduction by PHAP occurred. In the remaining case, the pathway block occurred late (23s of energy delivery). All cases were adequately treated with a new cryoablation session, except case # 20: several prolongations occurred in the PR interval during the second attempt resulting in interruption of the procedure; the case was classified as unsuccess.

3.6 Long-term follow-up

Mid-term (at 30 days) or late (1 year) recurrences were not detected after follow-up. Prolonged event monitoring did not detect new cases of recurrence compared to clinical assessment with rest electrocardiographic evaluation.

Seventeen procedures were indicated during observation in the RF group, with a final success rate of 93.0% and an average of 1.13 procedures per patient. Regarding the CRYO group, 19 procedures were indicated in the same period, with a final success rate of 80.0% and an average of 1.26 procedures per patient. Statistical difference between groups was not observed regarding the rate of immediate success, recurrence, or delayed success. Kaplan-Meier survival curves for single and multiple procedures are shown in Fig. 5.



Time (days)	0	60	120	180	240	300	360	480
RF	14	13	12	12	12	12	12	12
Cryo	13	12	11	9	9	9	9	9

Time (days)	0	60	120	180	240	300	360	480
RF	14	14	14	14	14	14	14	14
Cryo	13	12	12	12	12	12	12	12

Fig. 5 Kaplan-Meier curve for recurrence-free survival to the type of treatment received, for single (**A**) or multiple procedures (**B**)

4 Discussion

In this study we sought to prospectively compare the use of two energy modalities (cryotherapy and radiofrequency) for percutaneous ablation of PHAP.

The higher mean age we observed in our study (25 years), compared to that found in the literature might be related to either late diagnosis of the disease or even the difficulty of percutaneous ablation in earlier stages of life [4, 10, 11]. We emphasize that 60% of the sample had already been submitted to previous unsuccessful RF ablation attempts; moreover, this is a select sample of more complex cases, which is inherent to the parahisian location.

Owing to strict electrophysiological definition of parahisian location, baseline electrocardiographic characteristics greatly vary between series [19]. Although many non-invasive ECG algorithms have emerged in recent decades, none of them were accurate enough to predict proximity to the His bundle, with rates up to 85% being published [19–21]. In fact, it is believed that distinct ECG patterns may refer to different ventricular insertions of parahisian pathways [22, 23]. It is suggested by some authors that predominantly negative delta waves on V1 and V2 may correlate with endocardial right septal location, but no association between ECG characteristics and success rate by either access route was found in our study [22, 23].

The primary and secondary outcomes were similar in the groups, regarding the rates of immediate success, late success, and major complications; however, these findings may be attributed in part to higher-than-expected RF ablation success rate observed in our study. Although differences were statistically nonsignificant, the recurrence rate in the cryoablation group was twice the rate found in the RF group (30% *vs.* 14%; p=0.3); this data is comparable to meta-analysis results in retrospective studies [24].

Literature data shows that cryoablation generally has a higher recurrence rate when compared to RF ablation regardless of clinical indication [4, 13, 14, 24–27]. This is due to the biophysical properties of the injury mechanism, which is exactly why this energy modality is so advantageous in terms of safety [25]. Cryoablation originates well-demarcated lesions, which cause a smaller volume of tissue injury compared to RF ablation injuries [28]. Furthermore, catheter adhesion to the tissue (cryoadhesion) prevents lesion expansion to adjacent regions, as opposed to RF ablation in which the respiratory oscillation can make the catheter brush the lesion (*brushing effect*) making it even larger[28].

Considering the CRYO subgroup (n=15), success was obtained with a single procedure in nine cases, and recurrences occurred in four cases; three of them occurred due to mechanical trauma of the accessory pathway, which is more related to catheter manipulation and the superficial position of the AP [29]. A non-significant increased rate of mechanical trauma was also observed comparing CRYO *vs.* RF (20.0% *vs.* 6.0%; p=0.28). We believe that the reason for this may be related to the choice of using a long transseptal sheath in the CRYO group, as it was observed that the Freezor Xtra (6mm) catheter had a greater torque and a curvature that made it difficult to map the parahisian region in pre-randomization tests. The use of the sheath in a more structured catheter may have increased the contact force, allowing a higher incidence of trauma.

There was PR interval prolongation during cryotherapy session in four patients, of which two progressed to transient complete AV block. Our protocol involved use of dynamic cryomapping at -80°C, in contrast to classical initial -30°C step to assess for optimal ablation site. Experimental studies showed that tissue function could be completely restored if cryoablation is stopped within 10 seconds of conduction defect appearance, making it a safe and faster method for cryomapping, as long vigilance is maintained [14, 28]. Moreover, AV block might still occur even in a previously adequate cryomap, as adjacent tissues not initially affected could undergo into suppression while the hypothermic wavefront continues to expand during therapy session [14].

As for the RF subgroup, the initial protocol of this study used systematic mapping of the retroaortic region in all cases, even in those in which the initial application occurred through the venous femoral route. This was due to the fact that a sub-analysis was planned to identify factors that could help in the choice for preferred access route; moreover, we believed that a high success rate would occur with the retroaortic route. In contrast to the findings of Xu *et al*., our results were closer to those of Liang *et al*. and Chokr *et al*. that ablation through the non-coronary sinus proved to be more a complementary method than a definitive solution for invasive treatment of PHAP [30, 31]. Also surprisingly, jugular access showed to be a powerful alternative in the therapeutic arsenal of this study. Although this route was not used as an initial strategy, it allowed achieving success in five cases in which the other two methods failed; without it, these cases would have been classified as unsuccess, as highlighted in a previous study [32].

Another interesting point to discuss is the high incidence of junctional rhythm during RF applications through aorta, identified at least once in approximately 41% (5/12) of ablation attempts through this route. Data in the literature show that the retroaortic access is not necessarily the safest, as it is rarely possible to capture near-field signal from the His bundle in non-coronary sinus and there is even a previous report of TAVB during application in this region in a series of cases [33, 34]. This may be due, among others, to the variable anatomical relationship between His bundle and the aortic root. Pang *et al*. used electroanatomical mapping for retroaortic RF ablation and documented that the distance between the target in the non-coronary sinus and the highest near-field signal of the His bundle could be as short as 5 millimeters [35]. Therefore, caution regarding the appearance of inadvertent damage to the conduction system is also necessary during RF applications through aorta.

Therapeutic success through the initial access route chosen by the operator was achieved in only 33.0% (5/15) of the cases. This showed that conventional criteria, such as unipolar signal and AV continuity, did not help to select the correct application site. In our sample, only the anterograde earliest ventricular activation time (V-QRS) from non-coronary sinus correctly selected the best access route. Considering all cases in which the retroaortic approach was effective, the local signal preceded both the surface QRS (>40ms) and the local signal by the right ventricle (8-18ms). This data is in line with the series by Liang *et al*. in which successful cases through the aorta also had a ventricular signal preceding that of the RV (0-14ms) [31]. However, systematic mapping of the aorta is not routinely done in clinical practice, sometimes leaving arterial puncture to be performed after unsuccess via the femoral route. In our study, we did not find any variable obtainable by venous route that could guide an earlier shift to arterial access.

Ultimately, subgroup analysis showed that no superiority among the access routes used for RF ablation was found, but their complementary use may promote a higher success rate. Jugular access proved to be an excellent rescue strategy in complex cases.

4.1 Study limitations

This study had several limitations. This was single-center study with a small sample size. Parahisian accessory pathway is a rare entity, with low incidence and enrollment rate. This negatively impacts the safety outcome, as complications had a low incidence with both techniques and therefore not have been recognized by chance. However, similar studies although being only observational, had a similar number of patients [18, 30, 36, 37].

There was little pediatric representation in the sample, as patients under the age of 12 were excluded. In this age group, the aortic valve apparatus of these patients would be incompletely developed and would not allow mapping in case of randomization to the RF group was our justification for exclusion. Thus, generalizing to this specific population is not possible.

Lastly, no electroanatomical mapping was used in this study, which could have led to different outcomes.

5 Conclusions

Considering the limitation of a small sample size and the lack of use of electroanatomic mapping, no difference was observed on immediate success, recurrence and complication rates in the ablation of parahisian accessory pathways, whether radiofrequency or cryoablation were used. There was no persistent atrioventricular block in the immediate evaluation or during follow-up in any of the patients studied.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Conflicts of interest The authors have no conflict to disclose

Ethical approval The study design was approved by local Ethics Committee and registered on the clinicaltrials.gov website (ID NCT04361006).

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