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CLINICAL RESEARCH

Remote-controlled magnetic pulmonary vein isolation combined with superior vena cava isolation for paroxysmal atrial fibrillation: A prospective randomized study

Étude prospective randomisée évaluant l'intérêt de l'isolation des veines pulmonaires couplée à l'isolation de la veine cave supérieure à l'aide d'un robot magnétique

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KEYWORDS
Paroxysmal atrial fibrillation;
Pulmonary vein;
Remote magnetic navigation;
Superior vena cava;
Randomized study

Summary
Background. — Radiofrequency ablation (RFA) of paroxysmal atrial fibrillation (PAF) has focused on pulmonary vein isolation (PVI). However, despite initial positive results, significant recurrences have occurred, partly because of pulmonary vein (PV) reconnection or non-PV ectopic foci, including the superior vena cava (SVC).
Objectives. — This prospective, randomized study sought to investigate the efficacy of additional SVCI combined with PVI in symptomatic PAF patients referred for ablation.
Methods. — From November 2011 to May 2013, RFA was performed remotely using a CARTO® 3 System in patients randomized to undergo PVI for symptomatic drug-refractory PAF, with (PVI + SVCI group) or without (PVI alone group) SVCI. PVI and SVCI were confirmed by spiral catheter recording during ablation. Procedural data, complications and freedom from atrial tachycardia (AT) and atrial fibrillation (AF) were assessed.

Abbreviations: 3D, three-dimensional; AF, atrial fibrillation; AT, atrial tachycardia; LA, left atrium/atrial; PAF, paroxysmal atrial fibrillation; PV, pulmonary vein; PVI, pulmonary vein isolation; RA, right atrium; RFA, radiofrequency ablation; RMNS, remote magnetic navigation system; SVC, superior vena cava; SVCI, superior vena cava isolation; VKA, vitamin K antagonists.

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Results. — Over an 18-month period, 100 consecutive patients (56 ± 9 years; 17 women) with symptomatic PAF were included in the study (PVI + SVCI, $n = 51$; PVI, $n = 49$); the CHA_2DS_2-VASc score was 0.9 ± 1. Median duration of procedure (± interquartile), 2.5 ± 1 hours; total X-ray exposure, 13.3 ± 8 minutes; transseptal puncture and catheter positioning, 8 ± 5 minutes; left atrium electroanatomical reconstruction, 3 ± 2 minutes; and catheter ablation, 3.7 ± 3 minutes. After a median follow-up of 15 ± 8 months, and having undergone a single procedure, 84% of patients were symptom free, while 86% remained asymptomatic after undergoing two procedures. The cumulative risks of atrial arrhythmias (AT or AF) were interpreted using Kaplan-Meier curves and compared using the log-rank test. Long-term follow-up revealed no significant difference between groups, with atrial arrhythmias occurring in six (12%) patients in the PVI + SVCI group and nine (18%) patients in the PVI alone group ($P = 0.6$). One transient phrenic nerve palsy and one phrenic nerve injury with partial recovery occurred in the PVI + SVCI group.
Conclusions. — SVCI combined with PVI did not reduce the risk of subsequent AF recurrence, and was responsible for two phrenic nerve injuries. Accordingly, the benefit-to-risk ratio argues against systematic SVCI.

MOTS CLÉS
Fibrillation atriale paroxystique ;
Veine pulmonaire ;
Technique du robot magnétique ;
Veine cave supérieure ;
Étude randomisée

Résumé
Contexte. — L'ablation par radiofréquence (RFA) de la fibrillation atriale paroxystique (FAP) repose sur l'isolement des veines pulmonaires (VPs). Malgré les bons résultats de la technique, il existe un taux d'échec et de récidives non négligeables qui peuvent être dus soit à des reconnections de VPs, soit à d'autre sources dont l'origine peut-être la veine cave supérieure (VCS). Les données de la littérature sont controversées sur l'intérêt de l'isolement systématique de la VCS en combinaison avec l'isolement des VPs dans le traitement de la FAP.
Objectifs. — Cette étude randomisée a cherché à évaluer l'efficacité de l'isolement systématique de la VCS en complément de l'isolement des VPs chez les patients avec FA paroxystique symptomatique par la technique de robot magnétique.
Méthodes. — De novembre 2011 à mai 2013, les patients devant bénéficier d'un traitement par RFA pour FAP étaient randomisés soit dans un groupe avec isolement des VPs couplé à un isolement de la VCS soit dans un groupe sans isolement de la VCS. Le critère principal de jugement était basé sur les récidives de FA ou d'autres arythmies atriales.
Résultats. — Sur une période de 18 mois, 100 patients consécutifs avec FAP (56 ± 9 ans ; 17 femmes) ont été inclus, 51 pts dans le groupe 1 et 49 pts dans le groupe 2. Au cours d'un suivi de 15 ± 8 mois après une seule procédure, 84 % étaient asymptomatiques avec absence de récidives, alors que 86 % étaient asymptomatiques après 2 procédures. Les récidives d'arythmies étaient les suivantes : 1 tachycardie atriale (1 %), 8 FAP (14 %), 1 FA persistante (1 %). Le suivi à long-terme n'a pas montré de différence significative entre les 2 groupes, avec 6/51 récidives (12 %) dans le VCS + VP groupe (FAP, $n = 5$; TA, $n = 1$) contre 9/49 patients (18 %) dans le VCS groupe (FAP, $n = 9$; $p = 0,6$). Deux paralysies phréniques ont été observées dans le groupe 1 avec récupération totale dans un cas.
Conclusions. — Cette étude randomisée avec la technique du robot magnétique montre que l'isolation systématique de la VCS en combinaison avec l'isolement des VPs ne réduit pas le risque d'arythmies atriales mais au contraire expose les patients à d'autres complications comme la paralysie phrénique.

Background

For several years now, radiofrequency ablation (RFA) therapy has played a decisive role in the treatment of complex arrhythmias and, particularly, atrial fibrillation (AF) [1—3]. To date, RFA of paroxysmal atrial fibrillation (PAF) has focused on pulmonary vein isolation (PVI), regardless of whether the PVI approach was segmental or circumferential [1,4,5]. However, despite initial positive results, significant recurrences occurred after the first procedure, partly because of pulmonary vein (PV) reconnection, although non-PV ectopic foci, including the superior vena cava (SVC), might also be implicated [6—10]. Applying a strategy of SVC isolation (SVCI) in addition to PVI appears to improve the outcome of AF ablation solely in patients exhibiting PAF [11,12], although this is still subject to debate. There are, in fact, only two randomized studies available, which are hampered by several limitations and contradictory results [12,13]. We therefore need further investigation into whether SVCI combined with PVI

provides additional clinical benefits in a PAF population [12,13].

The only beneficial randomized study available, by Corrado et al., involved procedures performed with non-irrigated catheters, and clinical evaluation seems to have been obtained retrospectively [12]. Conversely, Wang et al. did not find any additional benefits, but their study follow-up was short term, and patients were randomized before evaluation of SVC arrhythmogenicity [13]. Moreover, no data exist concerning the feasibility of SVCI using the remote magnetic navigation system (RMNS), which was developed with the aim of improving the benefit-to-risk ratio for both patient and operator [14—19].

This study had two objectives: first, to prospectively compare the effect of PVI plus SVCI versus PVI alone on PAF patient outcome; second, to determine SVCI feasibility using the RMNS.

Methods

Catheter ablation was performed remotely via the Niobe® II RMNS (Stereotaxis, St. Louis, MO, USA), combined with a new three-dimensional (3D) non-fluoroscopic navigation system (CARTO® 3 System; Biosense Webster, Diamond Bar, CA, USA), in 100 consecutive patients who underwent PV disconnection for symptomatic drug-refractory paroxysmal AF. Randomization was only carried out at the time of the procedure if the circular-mapping catheter placed above the right atrium (RA)-SVC junction revealed active electrical potentials in the SVC (detected in sinus rhythm or under stimulation). Patients with persistent and permanent AF were excluded from participation, as were those with an electrically silent RA-SVC junction. All patients provided written informed consent before the procedure, but were only included if their SVC was electrically active, with all patients blinded to their group assignment.

Electrophysiological procedures

All patients received anticoagulation therapy with vitamin K antagonists (VKA) over a minimum period of at least 2 months before the procedure (target international normalized ratio, 2 to 3), and therapeutic anticoagulation was maintained with intravenous or low-molecular-weight heparin, with treatment commencing after VKA discontinuation and 3 days before the intervention. Transoesophageal echocardiography was performed within the 48 hours before the procedure, to exclude left atrial (LA) thrombus. VKA administration was resumed on the day after the procedure, and effective anticoagulation was maintained with heparin until the international normalized ratio was > 2.0. Surface electrocardiograms and bipolar endocardial electrograms (filtered from 30 to 500 Hz) were monitored continuously and recorded on a computer-based digital amplifier-recorder system. A deflectable quadripolar catheter (5 mm interelectrode spacing; Xtrem; ELA Medical, Montrouge, France) was positioned in the coronary sinus to carry out pacing and recording. The left atrium (LA) was accessed either via a patent foramen ovale, when present, or by transseptal puncture. A guidewire was inserted into the LA using an 8F sheath. Over the course of the procedure, the sheath was perfused with heparinized solution (3000 U of heparin in 500 mL of sodium chloride 0.9% at a rate of 150 mL/h). A multipolar deflectable catheter (LASSO®; Biosense Webster, Diamond Bar, CA, USA) was inserted through the long sheath to enable the mapping of the PV ostia required for the ablation procedures. RFA was performed using a 3.5 mm open irrigated-tip magnetic ablation catheter (NAVISTAR® RMT ThermoCool®; Biosense Webster, Diamond Bar, CA, USA). The catheter was introduced into the LA through a second transseptal puncture; the venous sheath was then withdrawn into the RA and continuously perfused. After the transseptal puncture, intravenous unfractionated heparin was administered as a bolus (7500 U); additional boluses were given throughout the procedure to ensure an activated clotting time of at least 300 seconds. The activated clotting time was determined 30 minutes after the transseptal puncture and every 30 minutes thereafter. When the activated clotting time was < 300 seconds, an additional bolus of 2500 U was administered. Deep sedation was achieved using intravenous nalbuphine and midalzolam.

Radiofrequency catheter ablation procedures

For both study groups, the endpoint of ablation was the isolation of the PVs, defined by complete elimination or dissociation of pulmonary potentials, confirmed in all cases with a circumferential mapping catheter. Radiofrequency was applied using an open irrigated-tip catheter, with a power output not exceeding 35 W when positioned close to the PV ostia, and not exceeding 25 W when in the posterior part of the PV ostia or the SVC ostia. Tip irrigation was achieved by using sodium chloride 0.9% at a rate of 20—35 mL/min to maintain a tip temperature of < 43 °C. SVCI was performed by segmental ablation in all cases.

CARTO® 3 System features

This study used the CARTO® 3 System, which allows for real-time advanced catheter location and visualization of both ablation and circular-mapping catheters (NAVISTAR and LASSO). The catheter location display was identical to that of the fluoroscopic view. The CARTO® 3 System combines electromagnetic technology (as in the CARTO XP System) with new Advanced Catheter Location™ technology that enables visualization of multiple catheters without requiring fluoroscopy. Briefly, Advanced Catheter Location is an impedance-based catheter localization system that enables precise cardiac mapping and navigation with multiple electrodes. Six electrode patches were attached to the body surface, constantly monitoring the current, which was emitted at a frequency unique to each individual catheter electrode. In addition, each electrode patch was equipped with a magnetic sensor, enabling 3D localization. The currents detected at the patches were associated with the 3D positioning of the electrode inside the human body. The ability of the CARTO® 3 System to visualize the manipulation and placement of circular-mapping catheters in each vein could further reduce the duration of fluoroscopy procedures. This system also improved catheter stability during ablation and facilitated the identification of each catheter electrode pair position. The visualization of catheters and electrode pairs was provided via a real-time

on-screen display of a geometrically-reliable icon representing the distal part of the LASSO catheter along with the electrode positions. LA reconstruction was obtained using a fast anatomical map algorithm. This method produced a continuous (non-gated) record of the movements of the magnetic NAVISTAR catheter. Based on this volume sampling, surface reconstruction was built in accordance with the set resolution level. On completion of the map, a 3D computed tomography scan was performed to optimize LA reconstruction.

Remote magnetic navigation system

The Niobe II RMNS is a technological platform that employs a steerable magnetic field to remotely guide a supple catheter inside the heart [14—19]. The steerable magnetic field contains two giant computer-controlled 1.8 tonne magnets positioned on opposite sides of the fluoroscopy table. A magnetic field of 0.08 to 0.1 Tesla was generated (according to the initial choice) so that the three small magnets incorporated in parallel into the tip of the radiofrequency catheter could enable 3D navigation. The magnetic field was applied to a theoretical cardiac volume of 20 cm × 20 cm. By means of a vector-based computer system (Navigant 2.1; Stereotaxis Inc., St. Louis, MO, USA), precision guiding of the catheter tip was possible. This system operated by aligning the catheter to the generated magnetic field, making the movements of the catheter dependent on the changes in direction of the two magnets, each in relation to the other. A computerized motor drive system (Cardiodrive®; Stereotaxis Inc., St. Louis, MO, USA) advanced or retracted the catheters, whereas the computerized work station (Navigant 2.1) was required to guide their orientation in space. Using a keypad (arrows) or joystick, the catheter could be continuously advanced, retracted or even adjusted (from 1 mm to 9 mm). Use of the second-generation Niobe II enabled us to tilt the magnets at angles ranging from 40° left anterior oblique to 30° right anterior oblique. The magnetic field was constantly generated during the ablation procedure, thus keeping the catheter tip in permanent contact with the endocardial tissue throughout the cardiac cycle, and therefore improving the delivery of the radiofrequency currents. Given that the magnetic field exerted a weak force (15—20 gm) and the catheter was very flexible, navigation inside the heart was highly reliable, with nearly zero risk of perforation [14—19]. The system was able to store certain data, such as the position of veins, and these vectors could then be reapplied during examination to facilitate catheter navigation or reduce procedure time.

Measurements: procedural and fluoroscopy variables

The following variables were recorded for all patients and were compared between study groups: total duration time (skin to skin); total X-ray procedure time, from needle insertion to ultimate catheter removal; skin to catheter positioning X-ray time, from femoral access to the final catheter positioning in the LA, including transseptal access; LA electroanatomical mapping X-ray time, from catheter positioning in the LA to satisfactory electroanatomical reconstruction compared with LA computed tomography scan; ablation X-ray time from first to last radiofrequency delivery.

Endpoints

The procedure endpoint was PVI, confirmed in all patients by spiral catheter recording during ablation. PVI was defined as abolition or dissociation of activities in all PVs. PV potentials and far-field potentials were distinguished by means of a pacing technique from the LA, LA appendage or coronary sinus, using the ablation or quadripolar catheter. Segmental ablation was defined as targeting the earliest RA-SVC conduction in cases where the RA-SVC conduction sequence could be detected in the sinus rhythm or by RA or proximal coronary sinus pacing. SVCI was characterized as the disappearance of SVC potentials or dissociation of SVC potentials with RA activity. Phrenic nerve injury prevention was achieved by avoiding the posterolateral wall or by high-output pacing stimulation (30 mA). Procedural data was collected, including X-ray exposure and complications.

Follow-up

Patients were hospitalized for 3 days post-procedure, as standard, with a 2-month blanking period. The blanking period was defined as the interval during which early recurrences were considered a transient phenomenon rather than a procedure failure. Antiarrhythmic medication was continued for at least 3 months and then stopped. VKA administration was continued, taking into account the CHA_2DS_2-VASc score. Success was defined as the absence of any documented arrhythmia or symptoms suggestive of arrhythmia recurrences (atrial tachycardia [AT], atrial flutter and AF). We performed 24-hour Holter monitoring each time a patient experienced palpitations. Patients were followed-up clinically every 6 months, and a redo procedure was permitted > 6 months after the index procedure, at the request of the patient. We systematically performed 24-hour Holter monitoring at the end of follow-up, and assessed long-term complications. The patient and the medical practitioner who carried out the follow-up were blinded to the patient's group assignment.

Statistical analysis

The baseline characteristics of the patients were examined using Fisher's exact test for categorical variables or a *t*-test. The differences between groups were analysed by analysis of variance. Summary values are expressed as means ± standard deviations. All reported levels of significance were two-sided. A probability value of $P < 0.05$ was considered statistically significant. We estimated that the enrolment of 100 patients with symptomatic paroxysmal AF would be necessary to detect a 20% reduction in AF recurrence in the PVI plus SVCI group versus in the PVI alone group, with 80% power and a two-sided α level of 0.05. The primary endpoint was time to symptomatic AF recurrence, confirmed by electrocardiogram or Holter monitoring. The secondary endpoint was symptom evaluation and occurrence of other atrial arrhythmias. The primary analysis was an intention-to-treat comparison of time to AF recurrence. For all time-to-event analyses, rates were estimated

Table 1 Patient characteristics ($n = 100$).

Age (years)	56 ± 9
Women	17
Arterial hypertension	32
Diabetes mellitus	4
Tobacco use	2
Hypercholesterolaemia	18
CHA_2DS_2-VASc score	0.9 ± 1
Duration of atrial fibrillation[a] (months)	49 ± 37
Structural heart disease	18
History of atrial flutter	34
Left ventricular ejection fraction (%)	63 ± 7
Transversal left atrial diameter (mm)	42 ± 2
Left atrial surface (cm^2)	19 ± 5
Number of antiarrhythmic agents tested[a]	2 ± 1

CHA_2DS_2-VASc: cardiac failure or dysfunction, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female).
Data are mean $\pm$ standard deviation or %, unless otherwise stated.
[a] Median $\pm$ interquartile.

by means of the Kaplan-Meier method and were compared using the log-rank test. Patient data were censored at time of last contact, withdrawal from the study or death. Symptomatic and asymptomatic episodes of AF were recorded. The authors had full access to the data and assume complete responsibility for its integrity. All authors have read and agreed to the manuscript as written. All analyses were performed using StatView® 5.0 (StatView IV; Abacus Concept, Berkeley, CA, USA).

Results

Baseline population characteristics

Baseline clinical data are summarized in Table 1. In total, 100 patients were prospectively included, with the following patient characteristics: mean age was 56 ± 9 years; 17% were female; mean LA diameter was 41 ± 7 mm; 18% presented with structural heart disease. The percentage of complete circumferential isolation, as confirmed by spiral catheter recording during ablation, was 97% for the PVs and 100% for the SVC. No significant difference in variables was revealed on comparison of SVCI plus PVI with PVI alone (Table 2).

Total fluoroscopy (median $\pm$ interquartile)

The median duration of the procedure ($\pm$ interquartile) was 2.5 ± 1 hours; total X-ray exposure time was 13.3 ± 8 minutes; transseptal puncture and catheter positioning time was 8 ± 5 minutes; LA electroanatomical reconstruction time was 3 ± 2 minutes; and catheter ablation time was 3.7 ± 3 minutes.

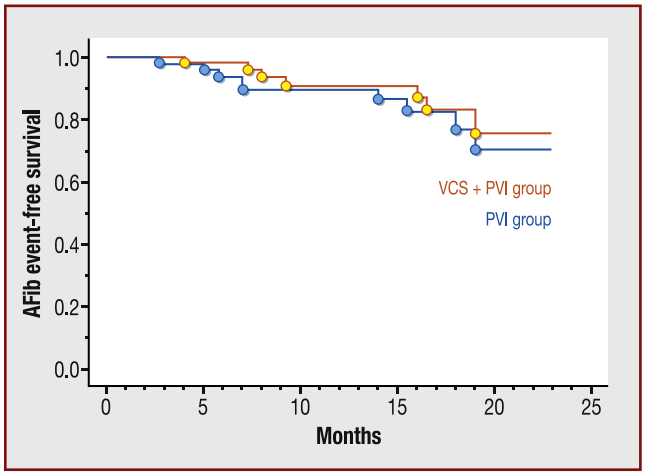

Figure 1. Kaplan-Meier estimates of the percentage of patients remaining free of recurrence of atrial arrhythmias in the pulmonary vein isolation (PVI) + superior vena cava isolation (SVCI) group (orange line) versus PVI alone (blue line). AF: atrial fibrillation.

Clinical outcome

After a median follow-up of 15 ± 8 months, and having undergone a single procedure, 84% of patients were symptom free, while 86% remained asymptomatic after undergoing two procedures. We observed the following recurrences: AT in one (1%) patient, paroxysmal AF in eight (14%) patients and persistent AF in one (1%) patient. Redo ablation was performed in six (6%) patients, because of AT in one (1%) patient and paroxysmal AF in five (5%) patients. The cumulative risks of atrial arrhythmias, such as AT or AF, were assessed using Kaplan-Meier curves and compared using the log-rank test. Long-term follow-up revealed no significant difference between the groups, with atrial arrhythmias occurring in six (12%) of 51 patients in the PVI + SVCI group (AF, $n = 5$; AT, $n = 1$) and nine (18%) of 49 patients in the PVI alone group (AF, $n = 9$; $P = 0.6$) (Fig. 1). No tamponade was noted, and no char formation was found on the catheter tip upon its removal.

Functional status was assessed, and we found no significant difference between the PVI + SVCI and PVI alone groups, as shown by these respective figures: 44 of 51 (86%) vs. 39 of 49 (80%) asymptomatic; and 7 of 51 (14%) vs. 10 of 49 (20%) ($P = 0.2$) partially ameliorated or not ameliorated.

Complications

No sinus node injury or tamponade was observed in our series of ablation procedures. Four serious complications occurred: one severe symptomatic pulmonary stenosis requiring stenting in the PVI alone group; one transient ischaemic attack with complete recovery in the PVI alone group; one transient phrenic nerve palsy in the PVI + SVCI group; and one phrenic nerve injury with partial recovery in the PVI + SVCI group.

Table 2 Comparison of superior vena cava isolation plus pulmonary vein isolation and pulmonary vein isolation alone.

Characteristic	PVI + SVCI($n = 51$)	PVI alone($n = 49$)	P
Age (years)	55 ± 10	58 ± 9	0.3
Female	11 (21.6)	10 (20.4)	0.5
Structural heart disease	8 (15.7)	33 (67.3)	0.7
Hypertension	16 (31.3)	16 (32.7)	0.9
Diabetes mellitus	1 (2.0)	3 (6.1)	0.3
Cholesterol	10 (19.6)	8 (16.3)	0.7
Tobacco use	11 (21.6)	11 (22.4)	0.9
Duration of atrial fibrillation[a] (months)	47.5 ± 30	50 ± 44	0.7
CHA_2DS_2-VASc score	0.8 ± 0.9	1 ± 1	0.5
Left atrial systolic diameter (mm)	42 ± 7	39 ± 6	0.3
Left ventricular ejection fraction (%)	63 ± 7	64 ± 7	0.6
Procedure duration (hours)	2.4 ± 0.6	2.5 ± 0.8	0.6
Total X-ray exposure time (minutes)	14 ± 5	15 ± 6	0.4
X-ray time dedicated to radiofrequency (minutes)	3.6 ± 2.7	3.8 ± 3.3	0.7
Long-term follow-up			
Atrial arrhythmias	6 (11.8)	9 (18.4)	0.6
Atrial fibrillation	5 (9.8)	9 (18.4)	
Atrial tachycardia	1 (2.0)	—	

PVI: pulmonary vein isolation; SVCI: superior vena cava isolation; CHA_2DS_2-VASc: cardiac failure or dysfunction, hypertension, age ≥ 75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65—74 and sex category (female).
Data are mean ± standard deviation or number (%), unless otherwise stated.
[a] Median ± interquartile.

Discussion

Major findings

This randomized, single-centre, prospective study has established that a strategy combining SVCI with PVI yields similar long-term clinical results to PVI alone in symptomatic PAF patients; this approach must not, therefore, be used as standard in clinical practice. Moreover, although the risk of phrenic nerve damage is low, this side-effect could be extremely detrimental, particularly in a young population. The study has also established that segmental RFA isolation via RMNS is feasible, without causing additional risk, and that the procedure is not time consuming. Accordingly, RMNS represents the optimal tool for performing effective AF ablation, with the ultimate aim of reducing patient and operator X-ray exposure and limiting operator fatigue. Finally, the use of a flexible magnetic catheter considerably increases the safety of complex procedures like AF RFA.

Superior vena cava and atrial fibrillation

Several studies have clearly established PVs as the principal origin of ectopies that initiate PAF [1,20], despite the occurrence of PVI recurrences, caused by PV reconnection or ectopies originating from other sources, such as the coronary sinus or the ligament of Marshall [8]. Ectopies originating in the SVC or RA can also provoke AF, as reported in several publications [6,8,10,20—22]. SVC arrhythmogenicity could be caused by anatomical muscle input from the RA provoking anisotropy because of cardiomyocyte size and assembly [8,23]. Anatomical studies have reported that the RA-SVC junction is formed by discontinued myocardial sleeves protruding by 13 mm (mean thickness 1.2 mm) into the SVC, as has been observed in PV sleeves [24]. A recent study focusing on SVC arrhythmogenicity factors suggested that a long SVC sleeve (> 30 mm) and a large SVC potential (> 1 mV) strongly predict SVC AF foci [25]. Working on the basis of these conclusions, several authors have investigated the role of SVC arrhythmogenicity in the clinical setting [6,9,22]. For example, Goya et al. assessed 16 PAF patients after PVI, and discovered a sharp potential existing inside the SVC, with a similar breakthrough to that in the PV [6]. SVC potentials were detected over a large circumference, suggesting widespread muscle coverage of the SVC [6]. The same authors also proved the feasibility of SVCI [6]. In a series of 293 patients with clinically documented drug-refractory PAF, Lee et al. sought to determine predictors of non-PV ectopic beats initiating PAF [22]. Of 94 patients with non-PV ectopic beats initiating PAF, 38 (40%) had SVC ectopic beats, representing 13% of the overall PAF population [22]. Lin et al. reported similar results with SVC-originated PAF in 27 (37%) of 68 cases with non-PV-originated AF [9], although this prevalence was difficult to substantiate, as other

studies had reported prevalence rates ranging from 3.7% to 12% [11,13]. Given the unknown role of SVC in AF genesis or perpetuation, such as that observed in clinical practice with PVs, systematic SVCI from the RA could, therefore, impact PAF RFA results, as has been reported [11,12].

Superior vena cava isolation and clinical studies

The debate surrounding the need to perform SVCI routinely in every AF patient has yet to be resolved [26]. Despite the efficacy of PVI, and in order to improve success rates and reduce recurrence rates, some authors have investigated the clinical role of SVCI [8,9,11—13,26]. Lin et al. showed that 20% of recurrences were initiated by SVC triggers, especially the late recurrences (> 12 months) [8]. In order to increase AF RFA success rates, targeting SVC RA triggers could be a reasonable adjunctive strategy, as SVCI appears both feasible and safe, especially if the procedure is guided by a 3D non-contact or contact system and includes a detailed geometry of the SVC, sinus node location and phrenic nerve route [6,11,26]. Thus, Arruda et al. assessed the feasibility of empirical SVC electrical isolation combined with PVI in symptomatic AF patients [11], performing the procedure in 208 out of 217 patients exhibiting SVC potentials, with SVCI obtained in only 127 (59%) patients [11]. This study was limited by the lack of randomization, and by the authors only confirming the feasibility and clinical efficacy of SVCI in the subset of patients showing SVC triggers initiating AF during the procedure ($n = 24$), who were symptom free at long-term follow-up [11]. Because of the various limitations of the published studies, SVCI needed further investigation [11,26]. There are only two randomized studies available; each had several limitations and they produced contradictory results [12,13]. Corrado et al. were the only investigators to report beneficial results in a randomized study of empirical electrical SVC plus PV isolation, but some limitations may have influenced their study results [12]: the RFA procedures were performed with non-irrigated catheters (an 8 mm tip catheter); and the only positive result was obtained in the PAF group, which was an analysis subgroup [12]. Using an 8 mm tip allowed SVCI in 84% of cases, and in the overall population-based intention-to-treat analysis, no difference was revealed between SVCI plus PVI (81%) versus PVI alone (74%) after 12 months ($P = 0.16$) [12]. Conversely, Wang et al. did not find any additional benefits, but their study follow-up was short term, and patients were randomized before evaluation of SVC arrhythmogenicity; both of these limitations could have affected the results [13]. Our study used a prospective, randomized design, and both patients and medical practitioners carrying out the follow-up were blinded to patient group assignment. Our study results revealed no additional clinical effects of SVCI on long-term follow-up (15 months). Moreover, the presence of SVC connection and the absence of RFA impact on AF recurrence do not support the role of RA arrhythmogenicity in patients with paroxysmal symptomatic AF. In combination with the literature analysis, our results therefore confirmed that SVCI may be useful in only a subset of AF patients with demonstrated SVC triggers initiating AF. Empirical electrical isolation combined with pulmonary isolation does not appear to be required in a symptomatic PAF population.

Potential complications related to superior vena cava isolation [27—29]

With SVCI, there is the potential for transient or permanent diaphragmatic paralysis as a result of phrenic nerve thermal injury. Two patients (2%) in our population exhibited a phrenic palsy: transient in one case; and with partial recovery in the other. This lesion can be avoided by pacing at the posterolateral part of the SVC with high-output (30 mA) [29]. Sinus node injury can occur if the ablation sites are located closer to the sinus node. This complication did not arise in our study, probably because of our use of segmental isolation, the 3D geometry of the atrium and SVC with the CARTO® 3 System, and RMNS facilitating very stable catheter positioning. Lastly, SVC stenosis could occur, although prevention is possible through a signal segmental approach and 3D CARTO geometry, in order to stay in close proximity to the SVC ostium [11—13,26]. If necessary, therefore, SVCI should be performed below the level of both the SVC triggers and the phrenic nerve capture site, and above the level of the sinus node origin [27—29].

Clinical implications

This randomized, prospective study sought to investigate the role of SVC arrhythmogenicity on subsequent atrial arrhythmia risk after PVI. Our study established that empirical SVCI offered no benefits to patients with symptomatic paroxysmal AF. To the best of our knowledge, no study has yet tested the feasibility, safety and efficacy of RMNS when attempting to isolate the SVC. Furthermore, the vicinity of structures such as the phrenic nerve and the sinus node could represent a potential risk with SVC ablation. The occurrence of two phrenic nerve injuries in the SVCI group, together with the non-significant reduction in subsequent AF recurrence, argue against systematic SVCI because of the poor benefit-to-risk ratio. SVCI should therefore be reserved for patients presenting with recurrent AF, with no PV recovery conduction, and exhibiting SVC triggers initiating AF episodes.

Study limitations

The major limitations of this study were its single-centre study design and its small sample size. However, it should be noted that we were able to provide longer-term follow-up results than those published so far. Furthermore, this study only involved patients with electrical SVC connection. Nevertheless, multicentre, randomized studies are difficult to perform, particularly when using the same technology (RMNS) throughout. Although our follow-up does not preclude that asymptomatic AF occurred, it is of note that we enrolled only symptomatic PAF patients, and in this context, freedom from symptoms appears to be a clinically relevant criterion.

Conclusions

This randomized study has established that SVCI in combination with PVI does not reduce the risk of subsequent AF recurrence, and was responsible for two phrenic nerve injuries. Accordingly, systematic SVCI does not appear to be required routinely in AF ablation, given the poor benefit-to-risk ratio.

Disclosure of interest

Professor A. Da Costa is a consultant for St. Jude Medical, Medtronic, Biotronik, Boston Scientific and Sterotaxis Inc.; he has received financial support from St. Jude Medical, Medtronic, Biotronik, Boston Scientific, Sterotaxis Inc. and the Sorin Group.

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