The influence of varying energy settings on efficacy and safety of endoscopic pulmonary vein isolation

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BACKGROUND The optimal energy setting for endoscopic pulmonary vein (PV) isolation (PVI) has not yet been determined.

OBJECTIVE To assess the influence of varying energy settings on the efficacy and safety of endoscopic PVI.

METHODS In the current prospective study, 30 patients with paroxysmal atrial fibrillation were consented for PVI using the endoscopic ablation system. Ablation was performed by using 5.5 and 7.0 W (group A), 7.0 and 8.5 W (group B), and 8.5 and 10.0 W (group C) along the posterior and anterior portion of each PV, respectively. Intraluminal esophageal temperature was measured via a temperature probe with a cutoff of 38.5°C. Endoscopy was performed 2 days postablation.

RESULTS After the completion of the initial circular lesion set, acute PVI was achieved in 25 of the 36 (69%) PVs in group A, in 29 of the 40 (73%) PVs in group B, and in 36 of the 40 (90%) PVs in group C, respectively. The rate of acute PVI was significantly higher in group C than in group A ($P = .025$) and group B ($P = .045$); there was no difference when comparing group A and group B ($P = .77$). Esophageal thermal lesions were detected in 0 of the 10 patients in group A, in 1 of the 10 (10%) patients in

group B, and in 1 of the 10 (10%) patients in group C. Mean procedure and fluoroscopy times were 219 ±42 and 30 ± 10, 239 ± 61 and 38 ± 14, and 207 ± 31 and 28 ± 8 minutes for group A, B, and C, respectively.

CONCLUSIONS The use of higher energy settings increases the efficacy of acute endoscopic ablation system–based PVI without comprising safety. Further investigation is mandatory before final conclusions can be drawn.

KEYWORDS Ablation; Atrial fibrillation; Laser; Pulmonary vein isolation

ABBREVIATIONS EAS = endoscopic ablation system; **EGD** = esophagogastroduodenoscopy; **HIFU** = high-intensity focused ultrasound; **LA** = left atrial; **LIPV** = left inferior pulmonary vein; **LSPV** = left superior pulmonary vein; **PAF** = paroxysmal atrial fibrillation; **PV** = pulmonary vein; **PVI** = pulmonary vein isolation; **RF** = radio frequency; **RIPV** = right inferior pulmonary vein; **RSPV** = right superior pulmonary vein; **TP** = transseptal puncture; **TS** = transseptal sheath

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Introduction

As implemented in the latest guidelines on the interventional treatment of atrial fibrillation, electrical isolation of the pulmonary veins (PVs) is the cornerstone of catheter ablation.[1,2] Complete circumferential linear lesions are deployed in a point-by-point fashion by using radio frequency (RF) current to achieve complete electrical pulmonary vein isolation (PVI).[3,4] Permanent transmural lesions are the prerequisite for long-term clinical success because PV to left atrial (LA) reconduction is the major determinant of clinical atrial fibrillation recurrence.[5] The inherent limitations of RF current kindled the interest to develop and investigate new

energy sources as well as new catheter designs. Novel balloon-based ablation systems that have been introduced are using cryothermal energy,[6–9] high-intensity focused ultrasound (HIFU),[10,11] or laser energy.[12–14] The cryothermal energy system and the HIFU system implement a noncompliant balloon capable of PVI with a single application. However, because the energy delivery for both systems is binary (on/off), neither allows individualized lesion or power settings. After fatal complications (atrio-to-esophageal fistula) following PVI, HIFU is no longer in clinical use.[15]

The novel endoscopic ablation system (EAS; CardioFocus, Inc, Marlborough, MA) adapts to varying PV sizes and PV shapes, permits the deployment of individual point-by-point lesion sets, and allows adjustable power settings.[12–14,16] Favorable acute and mid-term success rates have been published.[17] Importantly, EAS-based PVI demonstrates an acceptable risk profile.[14,18] However, the impact of varying energy settings on the rate of acute PVI, the short-term success rate, or the incidence of ablation-related complica-

tions such as phrenic nerve palsy or thermal esophageal lesions is unknown.

Methods

Inclusion and exclusion criteria

Between February and December 2011, consecutive patients suffering from highly symptomatic, drug-refractory paroxysmal atrial fibrillation (PAF) were admitted and eligible for EAS-based PVI. Exclusion criteria were a previous LA ablation procedure, an LA diameter of >55 mm, an average diameter of >35 mm of all PVs, severe valvular heart disease, and contraindications to postinterventional oral anticoagulation.

Prior to PVI, transesophageal echocardiography was performed in each patient to assess the LA diameter and to rule out intracardiac thrombus. No additional preinterventional imaging was performed.

Each patient gave written informed consent for EAS-based PVI.

The EAS

As previously described, the EAS consists of a nonsteerable, compliant balloon adjustable in size from a minimal of 9 mm to a maximum of 35 mm in diameter. The balloon diameter is adjustable to individual PV size in 9 steps, allowing optimal sealing and maximizing tissue exposure to the laser arc.

The balloon is continuously filled and flushed with heavy water (deuterium, D_2O) and is introduced into the left atrium via a 12-F (outer diameter 15-F) steerable transseptal sheath (TS; CardioFocus, Inc). The catheter shaft embeds a 2-F fiber-optic endoscope for the visualization of the target PV antrum. In addition, a second fiber connected to a 980-nm laser diode source delivers laser energy. An aiming beam is directed at the desired ablation spot.

Laser energy is applied for 20–30 seconds depending on the preselected ablation power (range from 5.5 to 12 W). The laser arc can be steered independently from the balloon itself, permitting an individualized lesion line design. Lesions are deployed in a point-by-point fashion, while a single ablation lesion covers 30° of a circle. Laser applications need to overlap by 30%–50% to create transmural lesions. To confirm sufficient overlap and to detect potential gaps within the ablation line, all endoscopic images and lesions are stored for review on a second screen by using customized software. Rotating and/or advancing and retracting the aiming beam and consequently the laser beam facilitate individual lesion application and individual line design.

A radiopaque Z-shaped marker on the distal catheter shaft allows for the correlation of the position and of the orientation of the endoscopic view with the fluoroscopic orientation.

Ablation procedure

PVI was performed in deep sedation by using boluses of midazolam and fentanyl and a continuous infusion of propo-

fol (1%). Venous access was achieved through the right and left femoral veins and the left subclavian vein. Prior to transseptal puncture, 2 diagnostic catheters were placed within the coronary sinus (7F, Webster TM, Biosense Webster, Inc, Diamond Bar, CA) and at the His-bundle region (6F, Webster TM, Biosense Webster, Inc). Double transseptal puncture was performed under fluoroscopic guidance in right anterior oblique (RAO) 30° and left anterior oblique (LAO) 40° projections by using a modified Brockenbrough technique and two 8.5-F TSs (SL1, St Jude Medical, Inc, St Paul, MN). After transseptal puncture, heparin boluses were administered targeting an activated clotting time of 300 seconds. Selective PV angiographies were performed in RAO 30° and LAO 40° projections to identify the individual PV ostia. A spiral catheter (Biosense Webster, Inc) was positioned at the PV ostium, and initial PV potentials were recorded (Axiom Sensis, Siemens AG, Munich, Germany).

One of the 8.5-F TS was exchanged over the wire for a 12-F steerable TS (CardioFocus, Inc). The EAS balloon was inserted and placed at the respective PV ostium. The balloon position and balloon pressure were adjusted to expose a circumferential ring of myocardium antral to the respective PV. The target position of the balloon was identified by using the previously performed selective PV angiographies.

Because the catheter shaft obstructs a portion of the total PV circumference, rotation of the balloon is typically required to complete ablation of the respective PV. In the current study, the right PVs were targeted first, followed by ablation of the left superior pulmonary vein (LSPV) and the left inferior pulmonary vein (LIPV) or the left common pulmonary vein, respectively.

Each PV was isolated individually. Electrical isolation of the respective PV was assessed thereafter.

In patients in group A, ablation was performed by using 5.5 W along the posterior, superior, and inferior portions and 7.0 W along the anterior portion of the respective PV. Accordingly, 7.0 W was used along the posterior, superior, and inferior portions and 8.5 W along the anterior portion in patients in group B. In group C, 8.5 W was applied when ablating the posterior, superior, and inferior portions and 10.0 W when ablating the anterior portion. If 5.5 and 7.0 W was used, energy was applied for 30 seconds. If >7.0 W was used, a single energy application lasted 20 seconds. PVI was assessed after the completion of the ablation line.

In the case of nonisolation, gap mapping was performed. A multipolar spiral mapping catheter was positioned distal to the inflated balloon to demonstrate PVI during laser energy application. To avoid incomplete PV sealing at the targeted ablation site, the shaft of the spiral catheter was positioned opposite to the presumed electrical gap.

The end point of ablation was achieved if all PVs demonstrated persistent isolation 30 minutes after the last energy application verified by spiral-catheter recordings. During ablation along the right superior pulmonary vein (RSPV), continuous phrenic nerve pacing was performed (10 mA, 2.9 ms) via a diagnostic catheter placed in the

Table 1 Baseline data

	Group A	Group B	Group C
Patients (n)	10	10	10
Age (y)	62 ± 9	59 ± 16	66 ± 10
Sex: Woman, n (%)	3 (30)	4 (40)	6 (60)
LA size (mm)	44 ± 4	42 ± 5	44 ± 7
Mean duration of PAF (y)	9 ± 7	3 ± 2	7 ± 6
Hypertension, n (%)	6 (60)	4 (40)	7 (70)
Use of AAD (mean)	2 ± 1	2 ± 1	2 ± 1

AAD = antiarrhythmic drug; LA = left atrium; PAF = paroxysmal atrial fibrillation.

superior vena cava. If loss of capture occurred, energy delivery was aborted instantaneously.

Temperature monitoring

In all patients, a standard temperature probe equipped with 3 thermistors (SensiThermTM, St Jude Medical) was inserted into the esophagus transorally under fluoroscopic guidance; its position was adjusted depending on the anatomic level of ablation. Esophageal temperature was continuously measured. Energy application was stopped once the preselected temperature cutoff of 38.5°C was exceeded. Maximum temperature and the corresponding anatomical location of ablation were noted. Once the temperature cutoff was reached, the position of the EAS balloon was adjusted and/or energy was reduced.

Postprocedural care

All patients underwent transthoracic echocardiography and thoracic fluoroscopy the day after ablation to rule out pericardial effusion and/or pneumothorax, respectively. Following ablation, all patients were treated with pantoprazol 40 mg twice daily for 6 weeks. Low-molecular-weight heparin was administered until a therapeutic international normalized ratio of 2–3 was achieved. Previously ineffective antiarrhythmic drug therapy was continued for 90 days.

Esophagogastroduodenoscopy

Two days postablation, an esophagogastroduodenoscopy (EGD) was performed in all patients to assess for the presence and severity of possible thermal injury and signs of gastric hypomotility. EGD findings were classified as no lesion, superficial thermal lesion (erythema with intact mucosa), ulceration, or perforation.[19] In the presence of thermal injury, EGD was repeated after 5 days.

End points

The primary end point in our study was defined as acute PVI after a single, complete circumferential ablation line using the predefined energy settings for the respective groups. Secondary end points included short-term success rate and ablation-related complications such as thermal esophageal lesions, gastric hypomotility, phrenic nerve palsy, or pericardial effusion.

Statistical analysis

All continuous variables are expressed as means and standard deviation or median and quartiles where appropriate. Between-group comparisons were performed by using the chi-square test. A P value of $<.05$ was considered statistically significant. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed to the manuscript as written.

Results

Patient characteristics

Thirty patients with a history of symptomatic, drug-refractory PAF were included in the study. Each group consisted of 10 patients (group A: 3 women, mean age 62 ± 9 years, mean LA diameter 44 ± 4 mm, mean PAF duration 9 ± 7 years; group B: 4 women, mean age 59 ± 16 years, mean LA diameter 42 ± 5 mm, mean PAF duration 3 ± 2 years; group C: 6 women, mean age 66 ± 10 years, mean LA diameter 44 ± 7 mm, PAF duration 7 ± 6 years; Table 1).

None of the patients in either group had a previous PVI or left atrial ablation attempt.

Acute ablation results

Following completion of the initial circumferential ablation line around each PV, acute PVI was achieved in 25 of the 36 (69%) PVs (8 of 10 [80%] RSPV, 8 of 10 [80%] right inferior pulmonary vein [RIPV], 1 of 6 [17%] LSPV, 5 of 6 LIPV [83%], and 3 of 4 [75%] left common pulmonary vein) in group A, in 29 of the 40 (73%) PVs (9 of 10 [90%] RSPV, 7 of 10 [70%] RIPV, 5 of 10 [50%] LSPV, and 8 of 10 LIPV [80%]) in group B, and in 36 of the 40 (90%) PVs (10 of 10 [100%] RSPV, 10 of 10 [100%] RIPV, 6 of 10 [60%] LSPV, and 10 of 10 [100%] LIPV) in group C, respectively (Table 2).

In the case of incomplete PVI, spiral mapping catheter recordings from the respective PV facilitated the identification and localization of conduction gaps. Gaps were targeted by using the EAS at higher energy levels. By using this strategy, successful PVI was achieved in 10 of 11 (91%)

Table 2 Rate of acute pulmonary vein isolation

	RSPV	RIPV	LSPV	LIPV	LCPV
Group A (n = 10)	7 of 10 (70%)	8 of 10 (80%)	2 of 6 (33%)	5 of 6 (83%)	3 of 4 (75%)
Group B (n = 10)	9 of 10 (90%)	9 of 10 (90%)	5 of 10 (50%)	8 of 10 (80%)	
Group C (n = 10)	10 of 10 (100%)	10 of 10 (100%)	6 of 10 (60%)	10 of 10 (100%)	

LCPV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

Table 3   Endoluminal esophageal temperature rise during ablation

	n (%)		
	Group A (n = 10)	Group B (n = 10)	Group C (n = 10)
Esophageal temperature >38.5°C	5 (50)	6 (60)	4 (40)
RSPV	0	0	0
RIPV	1 (10)	1 (10)	0
LSPV	0	0	0
LIPV	4 (40)	5 (50)	4 (40)
LCPV	0	0	0

LCPV = left common pulmonary vein; LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

initially not isolated PVs in group A, in 10 of 11 (91%) PVs in group B, and in 4 of 4 (100%) PVs in group C. In 1 of 11 (9%) PVs in group A, RF touch-up ablation was required because of EAS balloon failure. In group B, 1 of 11 (9%) PVs could not be isolated by using the EAS, requiring RF touch-up ablation.

No additional ablation lines were performed in either group. The rate of acute PVI after a single circular lesion set was significantly higher in group C than in group A (P = .025) and in group B (P = .045). However, there was no statistically significant difference between group A and group B (P = .77).

Importantly, loss of phrenic nerve (PN) capture was not observed in any patient during ablation along the right PVs.

Mean procedure and fluoroscopy times were 219 ± 42 and 30 ± 10, 239 ± 61 and 38 ± 14, and 207 ± 31 and 28 ± 8 minutes for group A, B, and C, respectively.

Esophageal temperature

In group A, energy application was stopped in 5 of the 10 (50%) patients because of temperature rise ≥38.5°C. The median maximum measured endoluminal temperature in these patients was 40.2°C (range 39.1–42.0°C). In 3 of the 5 (60%) patients, the predefined energy cutoff was exceeded during ablation along the posterior portion of the LIPV and in 2 of the 5 (40%) patients during ablation along the posterior portion of the RIPV (Table 3).

In group B, energy application had to be stopped in 6 of the 10 (60%) patients with a median maximum endoluminal temperature of 41.3°C (range 40.0–42.3°C). In 4 of the 6 (67%) patients, the peak temperature was measured along the posterior portion of the LIPV and in 2 of the 6 (33%) patients along the posterior portion of the respective RIPV.

In group C, the predefined temperature cutoff was exceeded in 4 of the 10 (40%) patients along the posterior portion of the LIPV. The median maximum endoluminal temperature in these patients was 41.0°C (range 40.1–42.8°C).

Endoscopic results

In all patients, EGD was performed 2 days postablation. Superficial thermal lesions and thermal ulcerations were found in 0 of 10 and in 0 of 10 patients in group A, in 0 of 10 and 1 of 10 (10%) patients in group B, and in 1 of 10 (10%) and 0 of 10 patients in group C, respectively. No atrio-to-esophageal fistula occurred. In the patients with an esophageal lesion, repeat EGD was performed 5 days following the index EGD and demonstrated healed lesions. A single case of gastric hypomotility was detected in the patient in group C who also demonstrated an esophageal thermal lesion. Both patients with esophageal thermal lesions exceeded the preselected temperature cutoff of 38.5° during PVI (group B, patient 7: 42.1°C during ablation at the posterior portion of the LIPV; group C, patient 3: 42.8°C during ablation at the posteroinferior portion of the LIPV). However, in every group, there were patients without thermal esophageal lesions despite exceeding the preselected temperature cutoff of 38.5°C.

Complications

In 1 of the 30 (3%) patients (group B), a severe groin hematoma was successfully treated conventionally without the need for blood transfusion. There was no phrenic nerve palsy, pericardial effusion, cardioembolic event, or pneumothorax noted in any of the groups (Table 4).

Clinical follow-up

After a median follow-up period of 186 days (range 93–391 days), 8 of the 10 (80%) patients in group A, 6 of the 10 (60%) patients in group B, and 7 of the 10 (70%) of patients in group C were in stable sinus rhythm. Five of the 10 (50%) patients in group A, 5 of the 10 (50%) patients in group B, and 6 of the 10 (60%) patients in group C were still on antiarrhythmic medication. Three patients in group B (patients 5, 6, and 10) with symptomatic, documented atrial fibrillation recurrence underwent RF-based repeat PVI 30, 92, and 142 days after the index procedure. In patient 5, reconduction gaps were detected along the superior portion of the RSPV, at the inferior aspect of the RIPV, and at the posteroinferior aspect of the LIPV. In patients 6 and 10, electrical reconduction of all previously isolated PVs was detected, while the exact location of individual reconduction gaps was not assessed. During the index EAS-based procedure in patient 5, an increase in applied energy to 10 W was necessary along the anterior portion of the LSPV to achieve electrical isolation. The remaining PVs were iso-

Table 4   Complications

|	Group A (n = 10)	Group B (n = 10)	Group C (n = 10)
Superficial thermal lesion	0 of 10	0 of 10	1 of 10
Thermal ulceration	0 of 10	1 of 10	0 of 10
Phrenic nerve palsy	0 of 10	0 of 10	0 of 10
Cardioembolic events	0 of 10	0 of 10	0 of 10
Pericardial effusion	0 of 10	0 of 10	0 of 10

lated according to the previously described energy setup. In patients 6 and 10, all PVs were isolated by using the previously described energy setup.

Discussion

The current prospective study is the first to systematically investigate the impact of varying energy levels used during EAS-based ablation on the acute and midterm outcome of PVI and potential injury to adjacent anatomical structures. This study found (1) that the use of greater energy levels is more effective with a statistically significant higher success rate for a single circular lesion set to result in acute PVI and (2) that greater energy levels do not correlate with a higher rate of injury to adjacent structures. Importantly, 2 esophageal thermal lesions detected during postprocedural EGD resolved without residue following treatment with proton-pump inhibitors.

EAS-based PVI has demonstrated encouraging acute and midterm success rates.[14,17] Nearly all PVs can be targeted and successfully isolated, irrespective of PV or LA anatomy as assessed by preprocedural cardiac magnetic resonance imaging.[16] Other balloon-based ablation systems operating with cryoenergy or HIFU utilize a noncompliant balloon, while energy delivery is binary (on/off). The HIFU system is no longer in clinical use because of its deleterious effect on the esophagus, resulting in the formation of an atri-oesophageal fistula.[15] The EAS, on the other hand, utilizes a compliant balloon that adapts to the individual PV in 9 steps ranging between 9 and 35 mm in diameter. In addition, the operator can titrate the energy level between 5.5 and 12 W. Hence, the EAS offers a tailored approach to ablation, allowing for customized lesion design and individualized energy delivery that takes into account the proximity of the PVs to adjacent anatomical structures such as the esophagus or phrenic nerve. A high rate of durable PVI of 86% at 3 months postablation was reported.[20] The superiority of higher energy levels regarding chronic PVI has been suggested on the basis of a porcine model.[21]

However, previous studies did not assess the impact of varying energy levels on the acute success rate of PVI or potential collateral damage to adjacent structures. Hence, the preferred energy setting guaranteeing safe and effective use of the EAS for PVI was unknown. The current study reports a success rate for acute PVI following a single circumferential lesion set of 69% and 73% in group A and group B, respectively. The success rate increased to 90% in group C. Notably, in the latter group after a single circular lesion set and using the highest energy level, all RSPVs, RIPVs, and LIPVs were isolated, while 4 of the 10 (40%) LSPVs demonstrated continued PV-to-LA conduction. All gaps within the initial ablation line were located along the anteroinferior portion of the LSPV at the continuation to the carina (Figure 1), which is typically characterized by thick muscular tissue. Applying a higher energy level (12 W, 20 seconds) along this specific portion of the LSPV may further improve acute success.
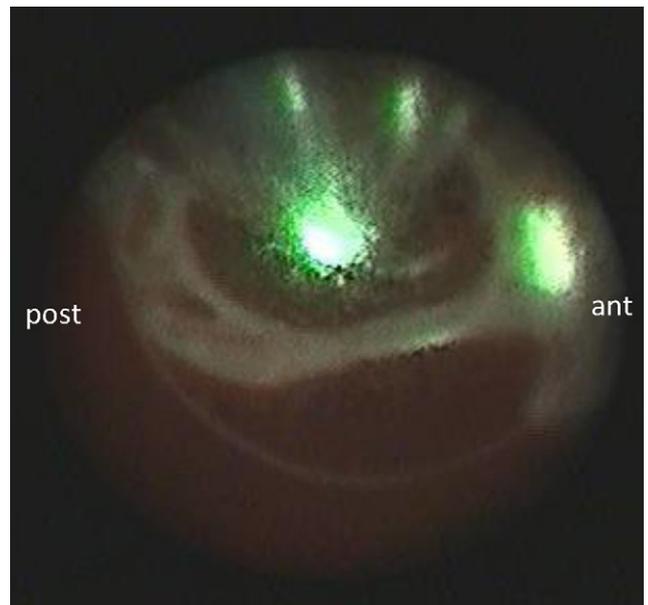
Figure 1 Endoscopic view of the ipsilateral left-sided pulmonary veins (PVs). The endoscopic ablation system is positioned within the left superior PV. The shaft obstructs direct view of roof. The green light is the aiming beam of the laser. Electrical gaps within the ablation line around the left superior PV are commonly located at the continuation between the anterior part of the left superior PV and the carina (site of aiming beam). ant = anterior; post = posterior.

Esophageal thermal lesions were not detected in patients treated with the lowest energy level (group A). However, in group B and group C, only 1 of 10 (10%) patients each was diagnosed with a postprocedural esophageal thermal lesion. Following treatment with a proton-pump inhibitor, both patients demonstrated complete resolution of thermal injury on repeat EGD.

However, the use of higher energy levels does not necessarily correlate with greater intraluminal esophageal temperatures or with the incidence of esophageal thermal injury. The position and course of the esophagus in relationship to the PVs is highly variable in each individual. Consequently, the measurement of endoluminal esophageal temperature may contribute to a better safety profile during PVI but will not necessarily prevent esophageal injury.

In the current study, the incidence of esophageal injury was too small to detect a significant difference between groups. Nevertheless, postprocedural use of a proton-pump inhibitor should strongly be considered in any patient undergoing EAS-based PVI.

Reported mean procedure times between 207 ± 31 minutes (group C) and 239 ± 61 minutes (group B) may be considered long; however, procedure times included the time spent on the preparation of the EAS and a 30-minute waiting period following the isolation of the last PV.

Similarly, mean fluoroscopy times ranging from 28 ± 8 minutes in group C to 38 ± 14 minutes in group B were influenced by several factors. First, the exchange of the 8.5-F TS for the 12-F sheath was performed under fluoroscopic guidance. Second, the EAS is not an over-the-wire

system. Consequently, it may be challenging to insert the balloon catheter into the respective PV. Repositioning or size readjustment of the EAS balloon may be necessary until complete circumferential sealing is obtained.[22] Because the catheter shaft does not permit a complete circumferential view, the completion of PVI commonly necessitates repositioning of the EAS.

The reported success rates ranging from 60% (group B) to 80% (group A) will need to be substantiated during an extended follow-up period.

Limitations

The current study enrolled a small number of patients with a short clinical follow-up. Larger studies and longer follow-up periods are needed to assess the long-term benefit of higher energy levels on the rate of recurrence and clinical improvement. Furthermore, the risk of collateral damage to adjacent structures such as the esophagus needs to be explored.

Conclusions

The current prospective study demonstrates that the use of higher energy settings increases the efficacy of acute EAS-based PVI without compromising safety. Further investigation is mandatory before final conclusions can be drawn.

References

1. Kirchhof P, Auricchio A, Bax J, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Eur Heart J 2007;28:2803–2817.
2. Calkins H, Brugada J, Packer DL, et al. HRS/EHRA/ECAS expert Consensus Statement on catheter and surgical ablation of atrial fibrillation: recommendations for personnel, policy, procedures and follow-up. A report of the Heart Rhythm Society (HRS) Task Force on catheter and surgical ablation of atrial fibrillation. Heart Rhythm 2007;4:816–861.
3. Ouyang F, Bänsch D, Ernst S, et al. Complete isolation of the left atrium surrounding the pulmonary veins: new insights from the double-Lasso technique in paroxysmal atrial fibrillation. Circulation 2004;110:2090–2096.
4. Arentz T, Weber R, Bürkle G, et al. Small or large isolation areas around the pulmonary veins for the treatment of atrial fibrillation? Results from a prospective randomized study. Circulation 2007;115:3057–3063.
5. Ouyang F, Antz M, Ernst S, et al. Recovered pulmonary vein conduction as a dominant factor for recurrent atrial tachyarrhythmias after complete circular isolation of the pulmonary veins: lessons from double Lasso technique. Circulation 2005;111:127–135.
6. Chun KR, Schmidt B, Metzner A, et al. The "single big cryoballoon" technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. Eur Heart J 2009;30:699–709.
7. Garan A, Al-Ahmad A, Mihalik T, et al. Cryoablation of the pulmonary veins using a novel balloon catheter. J Interv Card Electrophysiol 2006;15:79–81.
8. Van Belle Y, Janse P, Rivero-Ayerza MJ, et al. Pulmonary vein isolation using an occluding cryoballoon for circumferential ablation: feasibility, complications, and short-term outcome. Eur Heart J 2007;28:2231–2237.
9. Klein G, Oswald H, Gardiwal A, et al. Efficacy of pulmonary vein isolation by cryoballoon ablation in patients with paroxysmal atrial fibrillation. Heart Rhythm 2008;5:802–806.
10. Schmidt B, Chun KR, Kuck KH, Antz M. Pulmonary vein isolation by high intensity focused ultrasound. Ind Pacing Electrophysiol J 2007;7:126–133.
11. Schmidt B, Antz M, Ernst S, et al. Pulmonary vein isolation by high-intensity focused ultrasound: first-in-man study with a steerable balloon catheter. Heart Rhythm 2007;4:575–584.
12. Dukkipati SR, Neuzil P, Skoda J, et al. Visual balloon-guided point-by-point ablation: reliable, reproducible, and persistent pulmonary vein isolation. Circ Arrhythm Electrophysiol 2010;3:266–273.
13. Reddy VY, Neuzil P, Themistoclakis S, et al. Visually-guided balloon catheter ablation of atrial fibrillation: experimental feasibility and first-in-human multicenter clinical outcome. Circulation 2009;120:12–20.
14. Schmidt B, Metzner A, Chun KR, et al. Feasibility of circumferential pulmonary vein isolation using a novel endoscopic ablation system. Circ Arrhythm Electrophysiol 2010;3:481–488.
15. Neven K, Schmidt B, Metzner A, et al. Fatal end of a safety algorithm for pulmonary vein isolation with use of high-intensity focused ultrasound. Circ Arrhythm Electrophysiol 2010;3:260–265.
16. Metzner A, Kivelitz D, Schmidt B, et al. Impact of pulmonary vein anatomy assessed by cardiac magnetic resonance imaging on endoscopic pulmonary vein isolation in consecutive patients. Europace. 2012;14:474–480.
17. Metzner A, Schmidt B, Fuernkranz A, et al. One-year clinical outcome after pulmonary vein isolation using the novel endoscopic ablation system in patients with paroxysmal atrial fibrillation. Heart Rhythm 2011;8:988–993.
18. Metzner A, Schmidt B, Fuernkranz A, et al. Esophageal temperature change and esophageal thermal lesions after pulmonary vein isolation using the novel endoscopic ablation system. Heart Rhythm 2011;8:815–820.
19. Tilz RR, Chun KR, Metzner A, et al. Unexpected high incidence of esophageal injury following pulmonary vein isolation using robotic navigation. J Cardiovasc Electrophysiol 2010;21:853–858.
20. Dukkipati SR, Neuzil P, Kautzner J, et al. The durability of pulmonary vein isolation using the visually guided laser balloon catheter: multicenter results of pulmonary vein remapping studies. Heart Rhythm 2012;9:919–925.
21. Dukkipati SR, D'Avila A, Neuzil P, Reddy VY. Comparison of radiofrequency ablation vs. visually-guided laser balloon ablation in achieving chronic pulmonary vein isolation in a porcine model. Circulation 2009;120:S706.
22. Schmidt B, Gunawardene M, Urban V, et al. Visually guided sequential pulmonary vein isolation: insights into techniques and predictors of acute success. J Cardiovasc Electrophysiol. January 9, 2012. [Epub ahead of print.]