

# One-year clinical outcome after pulmonary vein isolation using the novel endoscopic ablation system in patients with paroxysmal atrial fibrillation

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**BACKGROUND** Pulmonary vein isolation (PVI) is an established treatment option for atrial fibrillation (AF). Recently the novel endoscopic ablation system (EAS) was introduced and proved potential for successful acute PVI.

**OBJECTIVE** This study sought to investigate the 1-year follow-up results after EAS-based PVI.

**METHODS** A total of 40 patients (20 female, age  $57 \pm 9$  years) with a long history ( $5 \pm 4$  years) of drug-refractory ( $2 \pm 1$  antiarrhythmic drugs) paroxysmal AF were included into our analysis. PVI was performed using exclusively the novel EAS. Follow-up included regular telephonic interviews, Holter electrocardiographic (ECG) and transtelephonic ECG recordings. A symptomatic or documented AF episode  $>60$  seconds after a blanking period of 3 months was defined as recurrence.

**RESULTS** A total of 155 PVs were targeted; 153 of 155 (99%) PVs were isolated successfully using exclusively the novel EAS. During a median follow-up of 402 (331 to 478; quartile 1 to quartile 3) days, 24 of 40 patients (60%) remained free of any symptomatic or documented AF episode without antiarrhythmic drugs after a single procedure. Seven patients suffering from AF recurrence underwent radiofrequency current-based Re-PVI  $203 \pm 102$  days after the index EAS-based procedure. Left atrium to pulmonary vein reconduction was found in 17 of 25 initially isolated PVs. No

PV stenosis was detected based on magnetic resonance imaging 3 months postablation.

**CONCLUSION** Patients after EAS-based PVI due to paroxysmal AF demonstrate 1-year single-procedure success rates similar to those of other ablation techniques and ablation energies. The major determinant for AF recurrence after EAS treatment seems to be reconnection of previously isolated PVs. More patients and longer follow-up periods are mandatory before final conclusions can be drawn regarding the efficacy and safety of the EAS.

**KEYWORDS** Atrial fibrillation; Pulmonary vein isolation; Endoscopic ablation system; Long-term follow-up

**ABBREVIATIONS** AF = atrial fibrillation; EAS = endoscopic ablation system; ECG = electrocardiographic; HIFU = high-intensity focused ultrasound; LA = left atrium; LC = left common; LI = left inferior; LS = left superior; MRI = magnetic resonance imaging; PAF = paroxysmal atrial fibrillation; PV = pulmonary vein; PVI = pulmonary vein isolation; RFC = radiofrequency current; RI = right inferior; RS = right superior; TP = transseptal puncture; TS = transseptal sheath

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## Introduction

Electrical isolation of the pulmonary veins (PV) is the cornerstone for catheter ablation of atrial fibrillation (AF) and is implemented in the latest guidelines for AF treatment.<sup>1,2</sup> Using radiofrequency current (RFC), complete circumferential linear lesions are deployed in a point-by-point

fashion to achieve complete electrical pulmonary vein isolation (PVI).<sup>3,4</sup> Long-term success rates after RFC-based PVI for patients suffering from paroxysmal atrial fibrillation (PAF) lie in the range of 29% to 89%.<sup>5–8</sup> PV to left atrial (LA) reconduction is the major determinant of clinical AF recurrence, and it is still a challenge to achieve permanent continuous transmural lesions using RFC.<sup>9</sup> Limitations of RFC kindled the interest to develop and investigate new energy sources as well as new catheter designs. Recently, novel balloon-based ablation systems have been introduced using either cryothermal energy,<sup>10–13</sup> high-intensity focused ultrasound (HIFU)<sup>14,15</sup> or laser energy.<sup>16–18</sup> The cryothermal and HIFU balloons have shown the potential to achieve complete PVI with a single application. However, because

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both systems consist of a noncompliant balloon and because their energy delivery is binary (on/off), they do not allow for individual lesion or power settings. Due to severe complications (atrial-to-esophageal fistula), the HIFU system is not longer in clinical use.<sup>19</sup>

The novel endoscopic ablation system (EAS) (Cardio Focus, Inc., Marlborough, Massachusetts) allows for deployment of point-by-point lesion sets in respect to individual PV anatomy and for individual power settings.<sup>16-18</sup> Recently, promising acute success rates using the novel EAS have been described.<sup>16-18</sup> However, long-term success rates are still unknown.

## Methods

### Inclusion and exclusion criteria

Between August 2009 and August 2010, consecutive patients suffering from highly symptomatic, drug-refractory PAF were admitted and eligible for PVI. Exclusion criteria were persistent AF, previous PVI, LA diameter >50 mm, severe valvular heart disease, and contraindications to postinterventional oral anticoagulation. Because the EAS has a maximal diameter of 35 mm, an average PV diameter >35 mm was an additional exclusion criterion.

Prior to PVI, transesophageal echocardiography was performed in each patient to assess LA diameter and to rule out intracardiac thrombi. Additional cardiac magnetic resonance imaging (MRI) was performed to assess PV diameter and PV and LA geometry before the ablation procedure. Each patient gave written informed consent for PVI.

### The novel endoscopic ablation system

The novel EAS consists of a nonsteerable, compliant balloon allowing treatment of PVs from minimal 9 mm to maximal 35 mm in diameter (Fig. 1). The balloon, being continuously filled and flushed with D<sub>2</sub>O, is introduced into the LA via a 12-F steerable transseptal sheath (TS) (CardioFocus, Inc.). The catheter shaft contains a 2-F fiberoptic endoscope enabling visualization of the targeted PV antrum. In addition, the shaft houses a second fiber connected to a 980-nm laser diode source, which delivers laser energy. An aiming beam is directed to the desired ablation spot.

Laser energy is applied for 20 to 30 seconds depending on the preselected ablation power (range from 5.5 to 14 W). The laser projection can be steered independently from the balloon itself, allowing for individualized ablation line design. Lesions are deployed in a point-by-point fashion, whereas a single ablation lesion covers 30° of a circle. Because transmural lesions are intended and mandatory, lesions are overlapped by 30% to 50%. To detect potential gaps within the ablation line and to confirm sufficient overlap of individual lesions, all endoscopic images are stored and reviewed on a second screen using customized software. Rotating and/or advancing and retracting the aiming beam and consequently the laser beam, facilitates individual lesion application and individual line design. In addition, the diameter of the balloon is adjustable according to the



**Figure 1** The novel endoscopic ablation system consists of a nonsteerable, compliant balloon being continuously filled and flushed with D<sub>2</sub>O. The catheter shaft contains a 2-F fiberoptic endoscope and a second fiber connected to a 980-nm laser diode source, which delivers laser energy. An aiming beam is directed to the desired ablation spot. (Image courtesy of CardioFocus, Inc.)

individual PV size. This guarantees optimal sealing and maximizes tissue exposure to the laser arc.

To correlate the position and orientation of the endoscopic view with fluoroscopic orientation, the catheter shaft is equipped with a radiopaque L-shaped marker.

### Ablation procedure

PVI was performed under conscious sedation using boluses of midazolam, fentanyl, and a continuous infusion of propofol (1%). Venous access was achieved through the right and left femoral veins and the left subclavian vein. Prior to transseptal puncture (TP), 2 diagnostic catheters were placed in the coronary sinus (7-F, Webster TM, Biosense Webster, Inc., Diamond Bar, California) and at the His bundle region (6-F, Webster TM, Biosense Webster, Inc.). Double TP was performed under fluoroscopic guidance using a modified Brockenbrough technique and two 8.5-F transseptal sheaths (SL1, St. Jude Medical, Inc., St. Paul, Minnesota). After TP, heparin boluses were administered targeting an activated clotting time between 300 and 350 seconds. Selective PV angiographies were performed to identify the PV ostia. A spiral catheter (Biosense Webster,

Inc., Diamond Bar, California) was positioned near the PV ostium, and initial PV potentials were recorded using a computerized EP system (EP workmate, St. Jude Medical, Inc.; LabSystem Pro, C.R. Bard, Inc., Lowell, Massachusetts).

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 as well as the balloon pressure was adjusted to expose a circumferential ring of myocardium atrial to the respective PV. The appropriate position of the balloon was identified using selective pulmonary vein angiography. No intracardiac echocardiography was used. The catheter shaft obstructs a portion of the total PV circumference, requiring rotation of the balloon to complete ablation of the respective PV.

Because a wide circumferential ipsilateral ablation line design as a figure of 8 was attempted, 2 incomplete circles were created, connecting at the PV carina. The EAS balloon was initially positioned along the superior PV, creating a circle that excluded the carina. This was followed by placement of the balloon at the ostium of the ipsilateral inferior PV, deploying a second circular lesion set that connected the superior circle at the level of the carina. During ablation of the inferior PV, a spiral catheter was positioned within the superior PV to record PV electrical activity and document PV isolation. Electrical isolation of the inferior PV was assessed thereafter. For an ipsilateral ablation line design as a figure of 8, partial or complete visualization of the inferior PV during balloon position along the superior PV or vice versa was mandatory. If simultaneous visualization of the superior and inferior PV was not feasible, individual isolation of the ipsilateral veins was performed. Applied energy power was up to 10 W along the anterior portion and was limited to a maximal power of 8.5 W along the posterior, superior, and inferior portion of the respective PV. After completion of the circumferential ablation line, LA to PV conduction was assessed using a multipolar spiral mapping catheter.

Gap mapping was performed if electrical PVI was not achieved after completion of the ablation line. 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 proven with the spiral catheter after a 30-minute waiting period after the last energy application.

During ablation along the right superior PV, phrenic nerve pacing was continuously performed (20 mA, 5 ms) via a diagnostic catheter placed in the superior caval vein. If loss of capture occurred, energy delivery was terminated instantaneously.

## Repeat procedures

In patients admitted for a repeat procedure due to AF recurrence, venous access and TP were performed as previously described. The presence or absence of electrical activity inside the PVs was assessed using a spiral catheter. An electroanatomical LA map (Carto, Biosense Webster) was generated, and the PV ostia were tagged. Identified gaps within the previously performed ablation lines were closed by irrigated RFC ablation using a 3.5-mm irrigated-tip catheter (Biosense Webster, Navi-Star, Thermo-Cool). RFC was delivered at a target temperature of 43°C using a power limit of 30 W and an infusion rate of 17 ml/min along the superior, posterior, and inferior portions of the PVs and a power limit of 40 W and an infusion rate of 25 ml/min along the anterior part. Ablation was performed until complete electrical PVI.

## Postprocedural care

All patients underwent transthoracic echocardiography and thoracic fluoroscopy the day after ablation to rule out pericardial effusion and/or pneumothorax, respectively. After ablation, all patients were treated with pantoprazole 40 mg twice daily for 6 weeks. Low-molecular-weight heparin was administered until a therapeutic international normalized ratio of 2 to 3 was achieved. Previously ineffective antiarrhythmic drug therapy was continued for 30 days.

## Follow-up

A blanking period of 3 months after PVI was defined. Outpatient clinic visits at 1, 3, 6, and 12 months including 24-hour Holter ECGs were performed. After 3 months postablation, all patients were equipped with an event recorder allowing for transtelephonic ECG transmission. ECGs were transmitted once weekly for a period of 9 months. Additionally, outpatient clinic visits, Holter ECG, and event monitoring were immediately initiated in the case of symptoms suggestive for a recurrent arrhythmia. After 3 months, a cardiac MRI was repeated to check for PV stenosis.

## End points

The primary end point was defined as recurrence of any symptomatic episode suggestive of AF or documented episode of AF >60 seconds after a blanking period of 3 months. Secondary end points were defined as procedure-related symptoms and complications such as cerebral or cardiac embolism, phrenic nerve palsy, PV stenosis, or atrial-to-esophageal fistula.

## Statistical analysis

All continuous variables are expressed as means and standard deviation or median and quartiles where appropriate. The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed to the article as written.

**Table 1** Baseline characteristics

Patients (n)	40
Age (yrs)	56 ± 10
Female gender, n (%)	20 (50)
LA size (mm)	42 ± 3
Mean duration of PAF (yrs)	5 ± 4
Hypertension, n (%)	22 (55)
Coronary artery disease, n (%)	4 (10)
Antiarrhythmic drugs, mean ± SD	2 ± 1

LA = left atrial; PAF = paroxysmal atrial fibrillation.

## Results

### Patient characteristics

Forty consecutive patients (20 female, mean age 57 ± 9 years) with a long history (5 ± 4 years) of drug-refractory (2 ± 1 antiarrhythmic drugs), symptomatic PAF were exclusively treated with the novel EAS and included in the analysis. Mean LA diameter was 42 ± 4 mm (Table 1); all patients had a normal left ventricular function. Twenty-two patients, 4 patients, and 2 patients had a known history of arterial hypertension, stable coronary artery disease, and diabetes mellitus, respectively. None of the patients had a previous PVI attempt or other left atrial ablations.

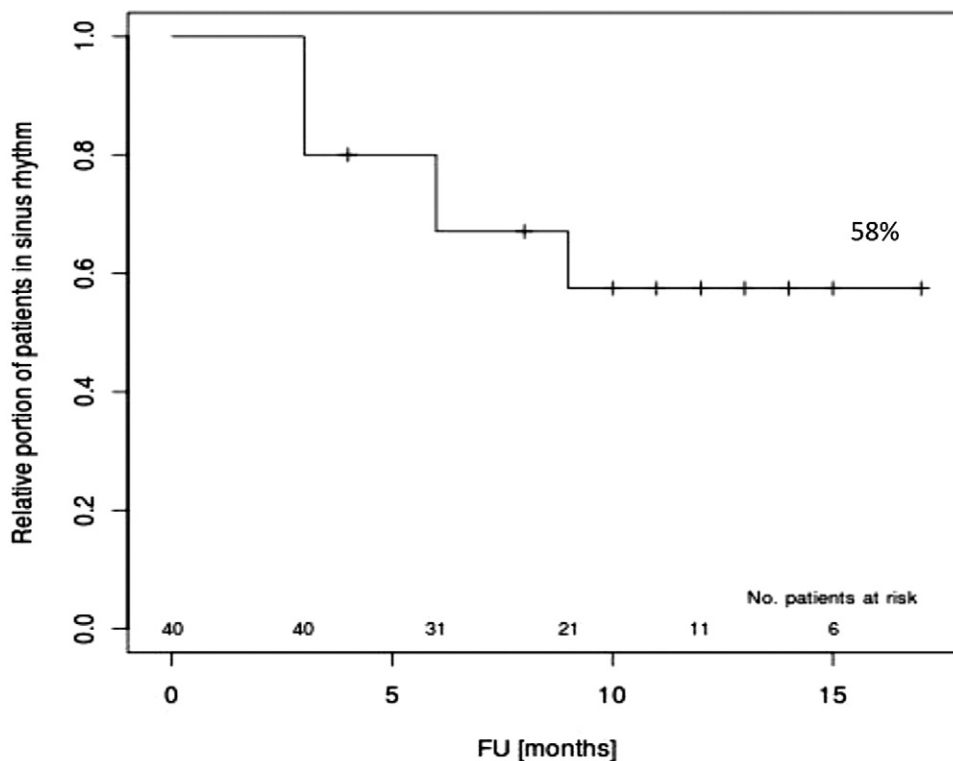
PV diameters for the right superior (RS) PV, right inferior (RI) PV, left superior (LS) PV, and left inferior (LI) PV were 16 ± 3 mm, 15 ± 3 mm, 16 ± 2 mm, and 15 ± 2 mm, respectively. Five patients had a left common (LC) PV with a diameter of 23 ± 4 mm.

### PVI using the EAS

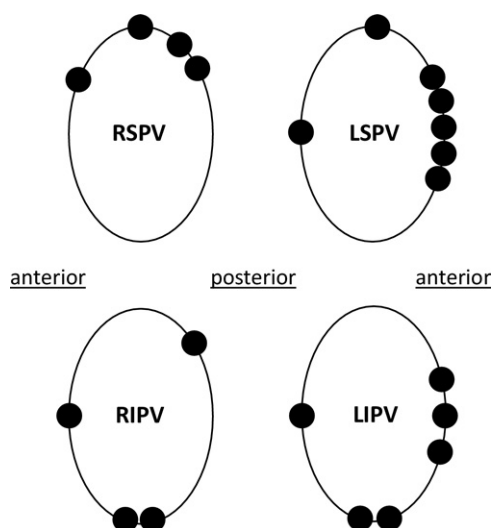
A total of 155 PVs were targeted; 153 of 155 (99%) PVs were isolated successfully using exclusively the EAS, including all LCPV. In 1 patient, ablation of the RIPV was stopped due to an endoscope failure, and in another patient ablation of the RSPV was not completed because of a phrenic nerve palsy. No additional ablation lines were performed. Mean procedure and fluoroscopy time was 240 ± 62 minutes and 30 ± 17 minutes, respectively.

### Follow-up

During a median follow-up of 402 (331 to 478; quartile 1 to quartile 3) days, 24 of 40 patients (60%) remained free of any symptomatic and/or documented AF episode without antiarrhythmic drug after a single EAS-based PVI procedure with a blanking period of 3 months (Fig. 2). A symptomatic and/or documented tachyarrhythmia recurrence was observed in 16 of 40 patients (40%), including both patients in whom 1 PV each was not isolated during the initial procedure. There were no patients being symptomatic without documentation of tachyarrhythmia. Thirteen of 16 patients having tachyarrhythmia recurrence were symptomatic and had a documentation in their event recordings. An additional 3 patients were asymptomatic, but AF was documented in the event recordings. Fourteen of 16 patients (88%) having tachyarrhythmia recurrence presented with PAF, 1 of 16 patients (6%) with PAF and documented typical atrial flutter and 1 of 16 patients (6%) with PAF and atrial tachycardia, respectively.



**Figure 2** Kaplan-Meier curve demonstrating the relative portion of patients in stable sinus rhythm during a median follow-up period of 402 (331 to 478; quartile 1 to quartile 3) days from a single procedure. FU = follow-up.



**Figure 3** Gap localization in initially isolated pulmonary veins assessed during repeat radiofrequency current-based pulmonary vein isolation. Gaps were assigned to superior, inferior, anterior, or posterior localization. LIPV = left inferior pulmonary vein; LSPV = left superior pulmonary vein; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

### Repeat procedures

Seven of 16 patients (44%) suffering from recurrence of AF underwent RFC-based repeat PVI  $203 \pm 102$  days after the index EAS-based PVI. LA-to-PV reconduction was found in 17 of 25 initially isolated PVs (2 of 6 RSPVs, 4 of 6 RIPVs, 5 of 6 LSPVs, 5 of 6 LIPVs, 1 of 1 LCPV) that were successfully re-isolated using RFC.

The location of the conduction gaps at the respective PVs was randomly distributed (Fig. 3). In 1 patient with documented PAF and typical atrial flutter, the cavotricuspid isthmus was ablated and blocked bidirectionally, too. Mean repeat procedure time was  $135 \pm 34$  minutes, with a mean fluoroscopy time of  $18 \pm 8$  minutes. In 1 patient, a second repeat PVI is scheduled due to recurrence of symptomatic and documented PAF.

### Complications

In 1 patient, phrenic nerve palsy occurred while ablating the RSPV due to a dislocation of the pacing catheter that was not recognized immediately. Although the patient was completely asymptomatic, the palsy was still present during repeat fluoroscopy 3 months postablation. However, at another fluoroscopy 9 months postablation, the phrenic nerve has completely recovered.

In 1 patient, LA perforation occurred. Because the TS was under tension, it did not keep its curve when retracting the EAS from the LIPV. As soon as the EAS lost contact with the roof of the LIPV while retracting into the TS, the TS dislodged into the LA roof. The patient required immediate surgical intervention and fully recovered. In a second patient, a pericardial tamponade occurred, most likely due to trauma to the left atrial appendage while trying to insert the balloon catheter into the LSPV. That patient did not require surgical intervention and was treated conservatively.

In none of our patients was a PV stenosis detected at cardiac MRI performed 3 months postablation. In addition, no cardioembolic events or atrial-to-esophageal fistula occurred.

### Discussion

The current study is the first reporting the 1-year follow-up after PVI using the novel EAS. This study found that (1) longer-term follow-up results after EAS-based PVI are comparable with established ablation systems, (2) the major determinant of clinical recurrence of AF seems to be electrical reconduction of previously isolated PVs, and (3) no PV stenosis occurred by correlating the initial cardiac MRI to repeat MRI 3 months postablation.

Balloon-based ablation devices using different energy sources (e.g., cryothermal energy, hot balloon, HIFU) for the treatment of PAF have been introduced. Due to severe complications in the form of atrial-to-esophageal fistula, the HIFU balloon is no longer in clinical use.<sup>19</sup> The cryoballoon has proven feasibility, safety, and efficacy in the treatment of PAF.<sup>10-13</sup> But due to its noncompliant balloon and its binary energy delivery, it does not allow for individual lesion sets respecting individual PV size and PV anatomy.

The first-generation EAS catheter was also designed as a noncompliant balloon device equipped with a fixed laser arc of  $90^\circ$ .<sup>17</sup> In an initial first-in-human multicenter clinical feasibility phase in 30 patients suffering from PAF, the 12-month drug-free rate of freedom from AF was 60%.<sup>17</sup>

However, the novel EAS consists of a compliant balloon, and therefore allows for adaption on individual PV size and anatomy. In addition, the laser arc of  $30^\circ$  allows for very discrete lesions. The laser energy is titratable and is applied under direct visualization of the respective PV ostium to guide catheter ablation of the left atrium-PV junction.

The short-term success rate of 80% after EAS-based PVI, defined as freedom of AF, was promising.<sup>18</sup> In the current analysis, we focused on midterm follow-up in a cohort of 40 patients, including 30 patients previously assessed for feasibility, safety, and acute efficacy of PVI utilizing the EAS.<sup>18</sup> We found that 24 of 40 (60%) patients treated with the novel EAS were free of symptomatic and/or documented recurrence suggestive of AF after a median follow-up period of 402 days, including a blanking period of 3 months. That success rate is comparable to published follow-up data after cryoballoon-based PVI in patients with PAF.<sup>22,23</sup> It might be speculated that growing numbers of EAS-based PVIs and consequently a growing experience in the use of the system might even improve the results.

Most of AF recurrences (13 of 16) after EAS-based PVI occurred during the first 6 months of follow-up. Regarding repeat PVI procedures, the major determinant of clinical recurrences seems to be electrical reconduction of previously isolated PVs. That correlates to the experience with circumferential RFC-based PVI and might indicate the failure to achieve permanent transmural ablation lesions.<sup>9,20</sup>

Defining the appropriate laser energy setting will require further investigation. The use of higher power settings may

herald the benefits and increase the risk of peripheral damage to adjacent anatomical structures such as the esophagus or the phrenic nerve. The incidence of esophageal thermal lesions after EAS-based PVI was previously described at 18% (43% minimal thermal lesions, 57% thermal ulcerations).<sup>21</sup> That correlates to published data about the incidence of thermal esophageal trauma after RFC-based<sup>24,25</sup> or cryothermal-based PVI.<sup>26,27</sup> No atrial-to-esophageal fistula occurred.

One ablation-related clinically asymptomatic phrenic nerve palsy occurred and has completely recovered in a repeat fluoroscopy performed 9 months after ablation. The incidence of phrenic nerve palsies after EAS treatment seems to be moderate compared with other balloon-based ablation systems but needs further investigation.<sup>10,15,23</sup>

Because the EAS is not designed as an over-the-wire system, it is sometimes challenging to direct and stabilize the balloon catheter within the LA or the respective PV. That fact may have contributed to the occurrence of 2 periprocedural tamponades in our study due to perforation of the LA roof and the LA appendage.

Considering other possible ablation-related complications using the novel EAS, we could rule out significant PV stenosis by correlating a preinterventional cardiac MRI with a repeat MRI 3 months postablation.

Procedure times are comparable with those of established balloon-based ablation systems.<sup>10</sup> Fluoroscopy times of  $30 \pm 17$  minutes may be considered rather long, but were reduced significantly between the first 20 and the last 20 procedures ( $37 \pm 19$  minutes vs.  $23 \pm 11$  minutes;  $P < .05$ ). However, studies providing higher patient numbers and longer follow-up periods are mandatory for further investigation of the novel EAS.

## Study limitations

Patients treated with the novel EAS were limited to patients with PAF. Its effectiveness in patients with persistent AF remains debatable. Results from RFC-based trials for ablation of persistent AF suggested that PVI alone may not be sufficient to obtain a favorable long-term outcome.<sup>5,7</sup> This is underlined by follow-up results after cryothermal balloon-based PVI that is associated with rather poor results in patients with persistent AF.<sup>23</sup> Moreover, our study is limited to 40 patients and a median follow-up period of 402 days. Consequently, higher patient numbers and longer follow-up periods are mandatory.

## Conclusion

After PVI due to PAF using the novel EAS, patients demonstrate 1-year success rates similar to other ablation techniques and other ablation energies. The major determinant for AF recurrences after EAS treatment seems to be reconnection of previously isolated PVs. However, higher patient numbers and longer follow-up periods are mandatory to investigate the long-term efficacy and safety of the EAS.

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