Curing atrial fibrillation (AF) by catheter ablation has significantly improved patient morbidity and mortality. The circumferential pulmonary vein isolation technique is established as the principal procedure, with a high cure rate and acceptable safety, for paroxysmal AF, but new adjunctive ablation strategies targeting the AF substrates and sources for long-standing persistent/chronic AF have been developed. These new techniques include linear ablation, complex fractionated atrial electrogram guided ablation, dominant frequency map-guided ablation, ganglionated plexi ablation and disconnection of the coronary sinus and superior vena cava to ablate the AF substrates and sources. The long-term usefulness of the established technique and these innovative adjunctive approaches for the treatment of AF remains to be investigated. (Circ J 2007; Suppl A: A-82–A-89)

Key Words: Adjunctive ablation technique; Atrial fibrillation; Atrial tissue ablation; Catheter ablation; Pulmonary vein isolation

Ablation Strategies Targeting the PV and Its Junction to the LA and Their Outcomes

The new PVI strategies were developed, and have become established as principal and standardized techniques, to avoid PV ostial narrowing or obstruction11–14 and residual PV peri-ostial or antral foci are recognized as potential risks and limitations of segmental PV ostial isolation10. These techniques are CPVA10,15–19 PV antrum isolation (PVAI)20–23 and extensive encircling ipsilateral PVI (EEPVI)24–26 which target either the atrial tissue surrounding the PVs or the border between the LA and PV antrum. The technique of circumferential PVI is guided by 3D electroanatomical mapping or a new navigation system10,15–19,25,26 by angiography and fluoroscopy24–26 or by intracardiac echocardiography (ICE)20–23. The endpoint for this procedure is electrical disconnection of all the PVs, except for the CPVA techniques of Pappone et al10,15–17 and Oral et al18,19 the latter demonstrating that CPVA is significantly more effective than segmental PV ostial isolation (AF-free rate at 6 months: 88% vs 67%, respectively, p=0.02). Pappone et al also reported a series of 589 patients, including 115 (20%) with AAD, in which the AF-free rate at 1, 2 and 3 years after CPVA was 84%, 79% and 78%, respectively15. A recent study demonstrated that complete electrical PVI was significantly more effective for curing AF. In 2004 the Cleveland Clinic group described a success rate of ICE-guided PVAI as 85% for PAF and 75% for persistent AF; their updated success rate amounted to 95% for PAF and 93% for persistent AF20–23.

Ouyang et al showed a 95% success rate without AAD for both PAF and persistent AF at a mean follow-up of 6 and 8...
months, respectively, after continuous circular PVI around ipsilateral PVs guided by 2 Lasso catheters and 3D electroanatomical mapping.\textsuperscript{25,26}

Data for the outcomes of catheter ablation of AF derived from large prospective randomized multicenter trials are not available at present. According to 3 recent randomized clinical trials\textsuperscript{19,27,28} comparing the outcomes of catheter ablation and AAD, the success rate of ablation at 1-year follow-up was 87%, 74% and 86%, with approximately 1% major complications. A world-wide survey in 1995–2002\textsuperscript{29}
of 8,745 patients in 90 centers reported 52% success rate without AAD and 79% success rate with AAD at 1-year follow-up, with 6% major complications. These data indicate that the efficacy and risk of catheter ablation of AF might depend on the experience, technique and skill of the operator and the institution.

In EEPVI performed at Tsuchiura Kyodo Hospital, both the ipsilateral superior and inferior PVs are isolated by an encircling continuous ablation line located on the border between the PV antrum and LA wall at the posterior junction and on the border between the anterior PV edges and surrounding tissue at the anterior junction (Fig 1). The ablation site and intra-PV electrograms are monitored and evaluated by the ablation catheter and 2 Lasso catheters positioned in both the ipsilateral PVs (Figs 2,3). Point-by-point ablation is performed in a linear fashion using a 4-mm tip standard electrode at a target temperature of 50°C with radiofrequency (RF) energy of 30–35 W delivered for 25–35 s (Figs 1–3). By this method, the ipsilateral PVs are usually disconnected simultaneously (Fig 2). EEPVI has been performed in 450 AF patients (paroxysmal: 320, persistent: 130). In 74 patients (16%), multiple procedures were performed for recurrence of AF, atrial tachycardia or symptomatic and frequent atrial premature beats. In the mean follow-up period of 26±15 months, neither recurrence of symptomatic AF nor ECG documentation of AF occurred in 86% of patients (382/450) without AAD and in 94% (423/450) with AAD (unpubl data).

**Electrophysiologic Basis for Extensive Encircling or Circumferential PVI**

AF initiation and perpetuation require both AF triggers and susceptible substrates. Although the PVI technique was originally invented to eliminate AF triggers, it is now well accepted for the following reasons that circumferential ablation with or without PVI can modify and also isolate the susceptible substrates for AF initiation and perpetuation.

1. Persistent AF can be terminated by line ablation at the junction between the arrhythmogenic PV and LA before achievement of complete electrical disconnection.
2. Inducibility of sustained AF by programmed electrical stimulation is significantly decreased after successful EEPVI.
3. Sustained intra-PV tachycardia can be induced by programmed electrical stimulation inside the PVs and surrounding LA tissue disconnected from the LA.
4. After successful EEPVI, intra-PV tachycardia, which is similar to that functioning as AF driver before isolation, can occur spontaneously or be induced (Fig 4).
Fig 4. Electrophysiological evidence of atrial fibrillation (AF) trigger and substrate isolation by extensive encircling pulmonary vein isolation (EEPVI). (A) Pre EEPVI of the right pulmonary veins (PVs): spontaneous PV tachycardia triggered by its firing initiated and drove the sustained AF. (B) Post EEPVI: similar PV tachycardia confined in the disconnected PV and its junction to LA started and perpetuated without initiation of AF. RSPV, right superior PV; CS, coronary sinus; PVI, PV isolation.

Fig 5. Electrophysiological evidence of atrial fibrillation rotor and substrate isolation by extensive encircling pulmonary vein isolation (EEPVI). In the extensively isolated left common pulmonary vein trunk (LCPV) area, as shown in the CARTO map after achievement of EEPVI and restoration of sinus rhythm, sustained regular rapid tachycardia inside the LCPV and fibrillatory activity in the antral area are simultaneously recorded. HRA, intracardiac electrogram at high right atrium; Map, intracardiac electrogram recorded by mapping electrode; PV, pulmonary vein; RSPV, right superior PV; RIPV, right inferior PV.
Ablation Strategies Targeting Non-PV Foci, LA Substrates and Rotors

The search for and ablation of non-PV triggers is commonly done after PVI. The incidence of non-PV foci triggering AF is reported to be 10–30%.

Provocative maneuvers, such as administration of high dose of isoproterenol up to 200μg/min and cardioversion of induced AF can facilitate identification of non-PV foci.

The prevalent sites of non-PV foci are the superior vena cava (SVC), Ligament of Marshall, crista terminalis, limbus of the fossa ovalis and the posterior LA wall. The SVC is the most common site (~40%) and foci existing more than 20mm from the SVC and RA junction can be isolated with low RF energy application to the junction.

As an adjunctive ablation strategy for substrate modification, linear lesion formation was first introduced to improve the ablation outcome for persistent AF. The linear lesions are commonly made at the roof between the superior left and right PVs (roof line) and at the isthmus between the mitral valve and left inferior PV (mitral isthmus line).

Haïssaguerre et al initially reported that the additional mitral isthmus line increased the AF cure-rate remarkably from 68% to 87%, but they later reported only 64% of paroxysmal and persistent AF patients with line of block on the roof and anterior LA and PVI completed remained AF-free without AAD at a mean follow-up of 28 months, from which they concluded that the beneficial effect of linear lesions is modest and the procedure for making a complete block-line is technically challenging, with a potential risk of serious complications and iatrogenic macroreentry AT (MAT).

New substrate-modification modalities have currently been developed. Nademanee et al developed a new ablation modality targeting the areas with complex fractionated atrial electrograms (CFAEs), based on the hypothesis that these might represent AF substrates such as slow conduction, functional conduction-block and pivot points of macroreentrant wavelets.

While the highest DF sites were prevalent during ongoing AF in paroxysmal and permanent AF, according to their data, the highest DF site was prevalent within the PV and its junction to LA in paroxysmal AF, whereas it was located in the LA and coronary sinus (CS) in permanent AF. Ablation at high-DF sites resulted in prolongation of the AF CL and AF termination in 87% of PAF patients (17/19), but in none of 13 cases of long-standing persistent AF, which may reflect a difference in the underlying mechanism between paroxysmal and long-standing persistent AF.

A potential role of ablation of atrial autonomic ganglionated plexi (GP) in AF cure was indicated by reports that CPVA brings beneficial AF-cure effects by vagal denervation in humans, and electrical stimulation of atrial autonomic GP facilitates AF initiation in dogs.

Four major GPs of superior left, inferior left, anterior right and inferior right GPs were shown to be located around the each PV-LA junction in the CFAE sites during AF. At present GP ablation is actually not performed solely, because the sites can be included in the area to be isolated by antrum and circumferential ablation and are targeted by CFAE-guided ablation.

Lemery et al reported that the AF-free rate after GP ablation plus circumferential ablation in 7 cases each of paroxysmal and persistent AF was only 50% during a mean follow-up of 8 months.

Stepwise Ablation Strategy for Curing Long-Standing AF

Haïssaguerre et al studied the relative contributions of various atrial and thoracic venous sites to maintain AF in 60 cases of long-standing AF with a mean AF interval of 17 months. They evaluated the effects of ablation at different sites on prolongation of the AF CL and conversion of AF to atrial tachycardia or SR by randomized sequence of stepwise ablation. Their stepwise approach comprises electrical isolation of all PVs (Step 1), disconnection of the CS and SVC (Step 2), LA ablation guided by local electrograms with fractionation, continuous activity, short CL, activation gradient and centrifugal activation (Step 3), and linear ablation on the roof and mitral isthmus (Step 4).

They showed that ablation at the base of the LA appendage, CS and PV–LA junction has the highest efficacy for converting atrial tachycardia to SR, and termination of long-standing AF was finally achieved in 87% of patients. In their ablation series, 95% of cases of long-standing AF were AF-free without AAD after a mean of 1.6 procedures and a mean follow-up of 11 months.

The stepwise ablation approach helped elucidate the potential mechanism underlying the maintenance of persistent and CAF. Haïssaguerre et al attempted to identify the AF sources by conventional endocardial mapping using a 20-electrode catheter with 5 radiating spines (PentaRay, Biosense-Webster) in 50 patients with AF organized by prior stepwise ablation. They reported that discrete AF sources were identified in 28% of patients and they concluded that AF associated with consistent atrial activation sequences after prior PVI and linear ablation might be maintained by local AF sources preferentially located at the CS, the base of the LA appendage and the interatrial septum, all of which can be identified and ablated.

Complications

Major complications from AF ablation include vascular access accidents, cardiac perforation/tamponade, thrombo-
embolic events, PV stenosis, injury of extracardiac tissues such as the esophagus and nerves, and LA reentry tachycardia. According to a worldwide survey by Cappato et al of 8,745 treated patients, the overall incidence of major complications amounted to 6%, which included peri-procedural death (0.05%), cardiac tamponade (1.2%), stroke and thromboembolism (0.9%), ≥50% PV stenosis (1.9%) and LA tachycardia (LAT) (3.7%). Compiled data from 6 major studies between 2003 and 2004 of AF ablation in 1,039 patients showed that major complications amounted to 3%: 0.3% vascular access accident, 0.5% cardiac tamponade, 0.5% thromboembolism, 1.3% moderate (≥240/s)/asymptomatic PV stenosis and 0.6% severe (>70%)/symptomatic PV stenosis.14,18,21,25,34,54

The thromboembolic complications can be minimized by careful screening of intra-LA thrombi formation prior to the ablation procedure, intensive anticoagulation with an activated coagulation time >300–400 s, and careful flushing of the transseptal sheaths during procedure.55–59

The incidence of significant PV stenosis after PVI is reported to be approximately 5% in an initial series and 1% or less in recent series, which is the result of a better understanding of the causes and mechanisms of PV stenosis, increased operating experience, shifting the ablation site from inside the PV to the outside and a reduction of target temperature and amount of energy delivered during ablation. The clinical presentation of patients with severe PV stenosis varies from asymptomatic to highly symptomatic with recurrent pneumonia, hemoptysis, cough, dyspnea and chest pain. Because the relief of acquired PV stenosis is difficult to achieve with balloon angioplasty and stenting,12,13,16,61,62 preventive strategies are mandatory, including the placing of isolation lines outside the PV orifice, reduction of the target temperature and applied energy, and the introduction of ICE or special navigation systems for catheter positioning.

Atrio-esophageal fistula is not common (0.05%), but its outcome is serious (mortality rate of 50%63–65). A recent anatomical study revealed that the esophageal artery and vagus nerve plexus on the anterior surface of the esophagus is susceptible to heat damage by RF energy and might play a role in producing LA–esophageal fistula. Although no optimal means have been established to avoid thermal injury of the esophagus at present, careful titration of RF optimal means have been established to avoid thermal injury of the esophagus at present, careful titration of RF energy and LA reentry tachycardia (FAT). The mechanism of LAT post circumferential PVI and LA circumferential ablation with adjunctive linear ablation, with the incidence ranging 2.5% to 27%.68 There are 2 mechanisms: MAT and focal reentry (FAT). The mechanism of LAT post circumferential ablation with linear ablation is mostly MAT, with slow conduction in the gap of the ablation line in the LA posterior or wall or mitral isthmus. At Tsuchiura Kyodo Hospital, 4 cases of FAT caused by reentry with slow conduction in the gap of the peri-ostial PV line and 1 case of MAT occurred after extensive circumferential PV in 450 patients (unpubl. data). Ouyang et al reported peri-ostial PV reentry AT in 24% of patients after circumferential PV, similar to our method, and all these cases of LAT were eliminated by closing the gaps in the isolation line.

Conclusions

Many ablation strategies and techniques have been proposed since PV ostial isolation for eliminating AF triggers was introduced in 2000. Circumferential PVI/CPVA, PVAI or EEPVI have been performed widely as principal procedures, because they have attained high AF cure rates with acceptable safety. Various adjunctive ablation strategies have been also developed to modify the AF substrate and autonomic nerve tone, and to ablate AF source in the PV–LA junction area in cases of CAF. These new techniques include linear ablation, CFAE-guided area ablation, DF map-guided ablation, GP ablation and disconnection of the CS and SVC. The utility of circumferential PV with or without these innovative adjunctive approaches for various types of AF remains to be investigated by large prospective randomized multicenter trials.

References


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IESAKA Y et al.


