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Pulmonary vein isolation – still the cornerstone in atrial fibirillation ablation?

Izolacja żył płucnych – nadal podstawa ablacji podłoża migotania przedsionków?

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atrial fibrillation, catheter ablation, pulmonary vein isolation

Słowa kluczowe
migotanie przedsionków, ablacja przezskórna, izolacja żył płucnych

Summary

Catheter ablation of atrial fibrillation (AF) has become an important treatment option for patients with symptomatic, drug refractory AF. Both European Sociaty of Cardiology (ESC) and Heart Rhythm Society (HRS) guidelines consider complete electrical pulmonary vein isolation (PVI) as the cornerstone of the AF ablation procedure, which can be supported with additional substrate modification targeting extrapulmonary triggers, like additional left atrial lines, complex fractionated atrial electrograms (CFAE) and ganglionated plexi of autonomic nervous system ablation. There is a body of evidence suggesting that targeting the extrapulmonary triggers may have similar or better results, compared to PVI alone. On the contrary, we have strong data proving that PVI alone is superior to the supplementary substrate modification. Furthermore, there are several techniques developed to achieve durable PVI in a straightforward manner with circumferential multipolar or balloon ablation catheters. We review the literature and discuss the optimal strategy for non-farmacological treatment of atrial fibrillation.

Streszczenie

Ablacja podłoża migotania przedsionków jest uznaną formą terapii w przypadku pacjentów z nawracającymi, lekoopornymi epizodami arytmii. Aktualne wytyczne Europejskiego Towarzystwa Kardiologicznego (ESC) przyjmują uzyskanie pełnej elektrycznej izolacji żył płucnych jako podstawę zabiegu ablacji migotania przedsionków, którą można uzupełnić o dodatkową modyfikację substratu arytmii, jak dodatkowe linie aplikacji w lewym przedsionku, ablacja stref rozfragmentowanych potencjałów przedsionkowych (CFAE) lub zwojów układu współczulnego położonych w lewym przedsionku. Niektóre opublikowane prace sugerują, że wykonanie wyłącznie ablacji pozażylnych ognisk arytmii może mieć podobną skuteczność w zapobieganiu nawrotom arytmii. Z drugiej strony, przedstawione ostatnio wyniki randomizowanych badań klinicznych wykazują, że wykonanie dodatkowej modyfikacji substratu lub ablacji ognisk pozażylnych istotnie wydłuża czas trwania zabiegu bez uzyskania dodatkowych korzyści klinicznych. Ponadto coraz szerzej w praktyce klinicznej stosowane są cewniki dedykowane do zabiegu izolacji żył płucnych, skracające czas procedury przy porównywalej skuteczności. W przedstawionej pracy dokonano przeglądu aktualnego piśmiennictwa poruszającego ten temat oraz omówiono optymalną strategię inwazyjnego leczenia migotania przedsionków.

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INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia with significant morbidity and mortality. It increases the risk of stroke 5-fold and doubles the risk of all-cause mortality (1, 2). Recent data suggest that AF hospitalizations have increased to overtake myocardial infarction and heart failure as the most common cause of cardiovascular admissions globally (3, 4). This common arrhythmia also significantly reduces the quality of life in affected patients (5). Considering the limited efficacy and possible side-effects of antiarrhythmic drugs (AAD), radiofrequency (RF) catheter ablation become a standard procedure as a second-line therapy after failure of at least one AAD, or alone as a first-line therapy in selected patients. The latter strategy is supported by numerous trials demonstrating superiority of catheter ablation over AAD therapy in maintaining sinus rhythm. For instance, multiple clinical trials report

AF free survival of 50-75% at 1-year post ablation, opposing to 10-30% with AADs only (6-11). In most of the multi-center, randomized clinical trials the ablation arm strategy was to achieve complete electrical pulmonary vein isolation, confirmed by the presence of exit and entrance block to the left atrium. In consequence, current ESC and HRS guidelines recognize PVI as "the cornerstone" in atrial fibrillation ablation. On top of pulmonary vein isolation, additional ablation targets can be considered, especially in patient with non-paroxysmal atrial fibrillation. Of these strategies, the most often applied are complex fractionated atrial electrograms (CFAE), ganglionated plexi ablation, additional linear ablation, and focal impulse or rotor modulation (FIRM).

PULMONARY VEIN ISOLATION

The initial concept of electrical isolation of pulmonary veins as treatment modality for paroxysmal AF was first proposed by Haïssaguerre et al. in 1998 (12). They demonstrated than ectopic beats originating from pulmonary veins can trigger AF, and electrical isolation of ectopic foci by means of catheter ablation may prevent the recurrence of arrhythmia. Out of 45 patients they studied a single point of origin of atrial ectopic beats was found in 29 patients, two points were identified in 9 patients, and three or four ectopic sites were identified in 7 patients. The important fact was that for a total of 69 ectopic foci, 65 were localized in the pulmonary veins (94%). In this initial study, RF catheter ablation of the ectopic foci resulted in freedom from AF recurrences in 62% patients in the follow up of 8 ± 6 months. This pioneer study by Haïssaguerre and colleagues launched the era of non-farmacological treatment of atrial fibrillation, based on pulmonary vein isolation by means of catheter ablation. Numerous radnomized clinical trials comparing PVI to antiarrhythmic therapy proved PVI to be far better effective in maintaining sinus rhythm than AADs alone (6-11).

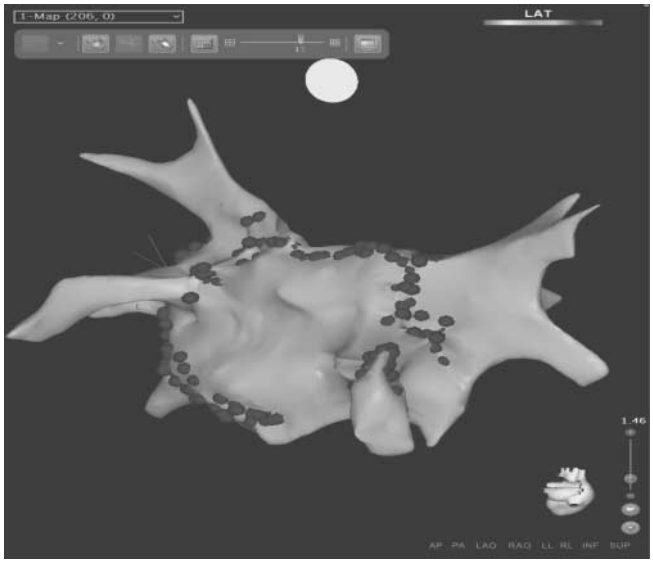

Fig. 1. Linear point-by-point isolation of pulmonary veins with 3D electroanatomical system.

The "gold standart" to achieve complete electrical pulmonary vein isolation is to perform point-by-point ablation with irrigated-tip catheter with the support a tree-dimensional (3D) electroanatomical system (fig. 1) and usually multipolar diagnostic catheter for pulmonary vein potentials assessment (fig. 2).

However, performed in this manner, it is still a time-consuming procedure with rather long learning curve. Additionally, creating steady contiguous transmural lesions with a single-point catheter is a challenge and may be problematic in some patients, especially with difficult pulmonary veins ostia anatomy. This emerged the search for specialized ablation catheters specifically designed for AF ablation. There are several so called "single-shot" PV isolation systems, based on the idea of achieving complete electrical PVI with a single application with a dedicated tool, which can be generally divided into techniques employing multipolar or balloon catheters. Non-irrigated Pulmonary

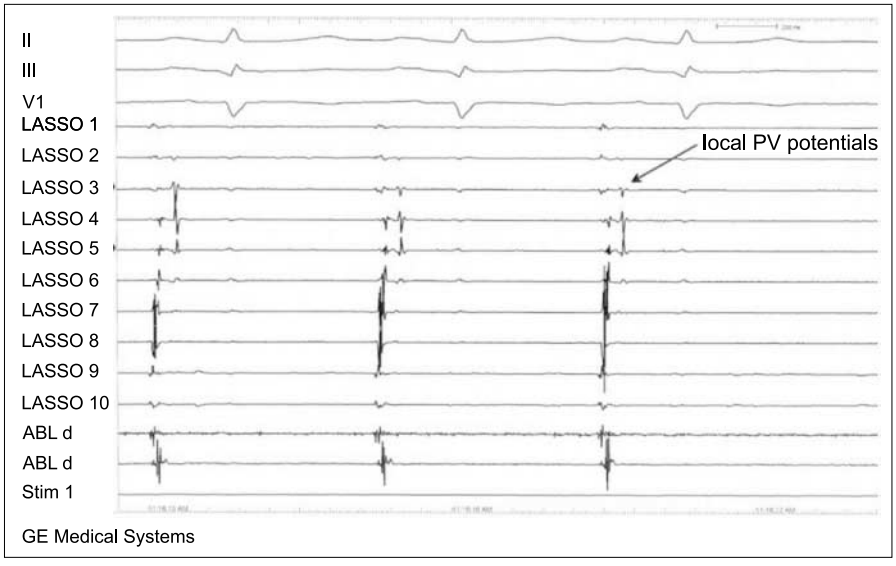

Fig. 2. Pulmonary vein potentials recorded by circumferential diagnostic catheter.

Vein Ablation Catheter (PVAC) and irrigated nMarq are the two multipolar ablation catheters applied in clinical practice for pulmonary vein isolation. Non-irrigated PVAC is an over-the-wire multipolar catheter, both diagnostic and delivering duty-cycled bipolar and unipolar radiofraquency energy at relatively low power of 8-10 W (13, 14) (fig. 3). This technique requires only single transseptal puncture, and in most cases 2-3 applications per vein are sufficient to obtain complete electrical pulmonary vein isolation, confirmed by PV entrance and exit block assessed by the same catheter. Following randomized trials as well as published single-center data comparing duty-cycled multipolar ablation with classical point-by-point PVI proved the non-inferiority of this straightforward technique (15-19). Recently we demonstrated significant shortening of procedure and fluoroscopy times with multipolar phased RF ablation (fig. 4) (20). In 129 consecutive cases we compared procedural parameters and acute success in the first 30 (group 1) and over 30 (group 2) procedures. All PVs were successfully isolated in 29 (96.6%), and 95 (95.9%) patients in group 1 and 2, respectively. Procedure time was significantly reduced with experience (180 vs 121 min, $p < 0.001$) in group 1 and 2, respectively. The reduction of fluoroscopy time was also significant (33 vs 19 min, $p < 0.001$) and most of the last 10 cases were completed with fluoroscopy times less than 10 minutes. There were no significant procedural complications. A learning curve effect was demonstrated with significant reduction of procedure and fluoroscopy times, but not in the acute success of pulmonary vein isolation, which was above 95% and did not change with growing experience.

The other multipolar catheter applied in clinical practice for pulmonary vein isolation is the irrigated nMarq, which combines both multipolar RF ablation through open-irrigation design with 3-D electroanatomic mapping capability. Preliminary reports on pulmonary vein isolation with this novel tool demonstrate a good acute success (21, 22).

Fig. 3. Phased RF multipolar catheter.

Other techniques dedicated for simplified pulmonary vein isolation are laser-baloon (23) and cryobaloon (fig. 5). The latter, widely used in clinical practice was demonstrated safe and effective in several randomized trials comparing cryobaloon ablation with classical point-by-point PVI (24-26). Moreover, cryoablation was proved to be effective as the first-line ablation strategy in patients with persistent atrial fibrillation (27).

TARGETING EXTRAPULMONARY TRIGGERS

There are several approaches to target the additional AF triggers beyond the pulmonary veins. The most widely used in clinical practice are additional linear lesions, usually created in mitral isthmus and the roof of LA (28) and sometimes in the right atrium: cavo-tricuspid isthmus and circumferential line isolating superior vena cava. They are considered to improve the outcome in persistent AF ablation.

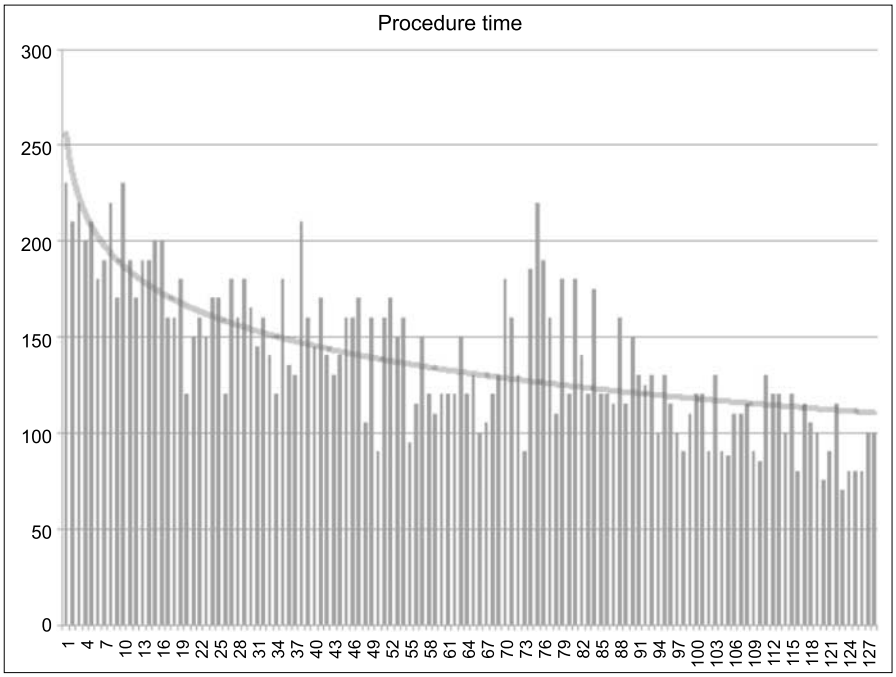

Fig. 4. Learning curve for PVI with multipolar phased RF catheters.

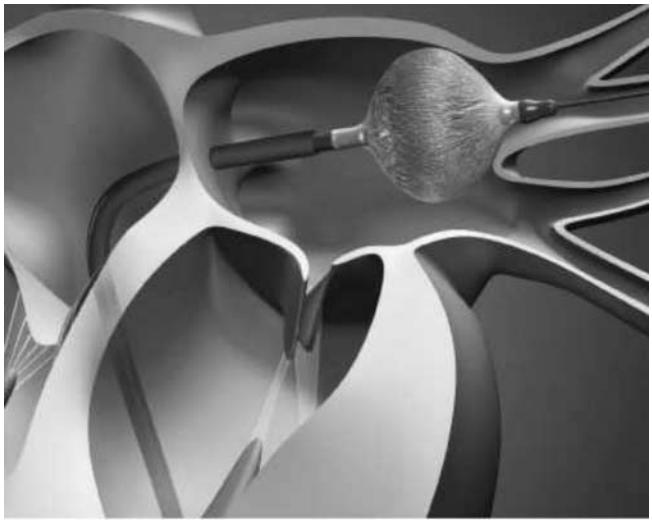

Fig. 5. Cryobaloon for pulmonary vein isolation.

Another strategy is to target the sites where complex fractionated atrial electrograms (CFAE) are recorded, introduced by Nademanee et al (29). It become popular and usually employs dedicated software for analysis of electrograms. Ganglionated plexi (GPs) ablation (30, 31) is another technique, usually targeting the same areas in the left atrium where fractionated electrograms are present. Another approach is focal impulse or rotor modulation (FIRM) introduced by Narayan et al. (32). This technique requires dedicated diagnostic basket catheters introduced to both atria for simultaneous recording of electrical activity of ongoing atrial fibrillation to create the rotor map, identifying the potential ablation targets.

COMPARISON OF PVI ALONE VERSUS PVI WITH ADDITIONAL EXTRAPULMONARY SUBSTRATE MODIFICATION

In persistent AF, both current ESC and HRS guidelines consider additional substrate modification on top of the pulmonary vein isolation (PVI) as the preferred ablation strategy. The multi-center, randomized STAR AF II study was designed to assess which of the two most commonly applied extrapulmonary substrate modification should be targeted: additional linear lesions or complex fractionated electrogram (CFAE) in the population of patients with persistent AF, however there was a third arm assessing PVI alone strategy (33). In this very important study conducted in 48 experienced ablation centers from 12 countries, a total of 589 patients with persistent AF were randomized in 1:4:4 manner to receive either pulmonary vein ablation alone (PVA; n = 67); PVA plus ablation complex fractionated electrograms (PVA + electrograms; n = 263); or PVA plus linear lesions in the left atrium (PVA + lines; n = 259). Most patients (76%) had been experiencing continuous atrial fibrillation for at least 6 months before the index procedure (median duration 2.2 years). Effective pulmonary vein isolation was accomplished in 97% of all patients with no differences between groups, although procedural time was significantly shorter for the PVA alone group (167 min) compared to the PVA+electrograms and PVA + lines groups (229 and 223 min, respectively; $p < 0.001$). Surprisingly, at 18 months follow up, patients from PVI alone group had the lowest rate of AF recurrence, however it was not statistically significant (freedom from AF recurrence either with or without anti-arrhythmic medication was observed in 59% of patients in PVA alone group, 48% in PVA + electrograms, and 44% in PVA + lines). Moreover, there was no difference between groups for the number of patients who were free from AF recurrence without anti-arrhythmic medication (PVA alone 48%; PVI + electrograms 37%; and PVI + lines 33%; $p = 0.11$). STAR AF II study, performed by experienced operators on a largest so far cohort of patients with persistent AF, demonstrated that additional substrate modification prolongs the procedure time without additional benefit to the patients; in fact the PVI alone group had the lowest AF recurrence rate. Although the overall rate of serious adverse events in this trial was very low, it is meaningful that one atrio-esophageal fistula leading to death occurred in a patient who underwent additional CFAE ablation Thus, considering extensive ablation in persistent AF, 'less may be more'.

In another randomized study, coming from an experienced center, the additional linear block at the LA roof was not associated with an improved clinical outcome compared with PV isolation alone in a group of 120 pts with paroxysmal AF (34). What is important, the study protocol required confirmation of linear block by pacing maneuvers, so the lack of additional benefit may not be explained by the incomplete LA roof isolation. Also in the recently published multicenter, randomized Minimax study (35) comparing minimal (i.e. PVI only) and maximal (additional lines on both intravenous ridges) authors demonstrated no statistical difference between the two approaches in ablation success during mean follow-up of 17 months.

CONCLUSIONS

Despite the growing experience, supported by the results of numerous trials, we still do not possess enough information to tailor the ablation strategy in each individual, which could result in more efficient and probably less extensive ablations in some patients. We should keep in mind, that additional and perhaps unnecessary ablation in consequence increases the risk of complications.

For now, a 'minimalist' strategy based on effective PV isolation appears sensible in most patients, reserving more extensive ablations for individual patients with broad fibrosis, very enlarged atria, or long-standing persistent AF, respecting the fact that even in the best hands, the anticipated outcome in such patients will be limited.

We are probably facing the advent of minimalistic era in the field of AF ablation, recalling the idea of 'less is more' – an expression from a poem by Robert Browning, that was promoted by minimalist architect Mies van der Rohe.

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