

Raziskovalni prispevek/Research article

## FOLLOW-UP AFTER LASSO-GUIDED IRRIGATED TIP RADIOFREQUENCY CATHETER ABLATION IN PAROXYSMAL AND PERSISTENT ATRIAL FIBRILLATION

KLINIČNI IZIDI PO RADIOFREKVENČNI ABLACIJI PAROKSIZMALNE IN PERZISTENTNE ATRIJSKE FIBRILACIJE S POMOČJO LASOKATETRA IN ABLACIJSKEGA KATETRA S HLAJENO KONICO

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### Izvleček

- Izhodišča** *V tej raziskavi ocenjujemo klinične izide nove metode zdravljenja atrijske fibrilacije, tj. radiofrekvenčna kateterska segmentna/krožna izolacija pljučnih ven (PV) in linearna defragmentacija. V naši prvi skupini bolnikov s paroksizmalno ali perzistentno obliko atrijske fibrilacije (PAF/PEAF). Primarni cilj posega je bil odpraviti simptomatične napade AF/undulacije/tahikardije brez uporabe antiaritmičnih zdravil (AAZ).*
- Metode** *V obdobju od septembra 2003 do junija 2007 smo uvrstili na prospektivni način vse zaporedne bolnike z močno simptomatičnimi napadi PAF/PEAF, ki smo jih neuspešno zdravili z AAZ. Vsi so bili mlajši od 70 let, z iztisnim deležem levega prekata > 40 % in premerom levega preddvora < 50mm. Med prvim posegom smo ablirali območja okoli ustij 2–4 PV, žariščno aktivnost zunaj območja PV in pri tistih z dokumentirano ali izzično tipično atrijsko undulacijo še kavotrikuspidalno ožino (KTO). Naslednji poseg smo napravili, če se je aritmija ponovila po več kot 3 mesecih. Najprej smo ablirali prevodne vrzeli okoli PV in na KTO. Pri bolnikih s PEAFA še hitre fragmentirane/kompleksne elektrograme vzdolž linij, ki povezujejo zgornji ustji PV in/ali ustje PV z bližnjo anatomsko strukturo. Dvosmerno blokado prevoda smo preverili samo na KTO. Za poseg smo uporabili ablacijski kateter s hlajeno konico, diagnostični kateter v obliki zanke, t. i. lasokateter (Biosense-Webster), in diagnostični kateter v koronarnem sinusu. Za prehod med preddvoroma in za vodenje katetrov smo uporabili rentgensko fluoroskopijo. Bolnike smo sledili 3 in 12 mesecev po posegu, nato enkrat letno. Ob sumu na ponovitev aritmije smo naročili posnetke EKG med palpitacijami ali več posnetkov Holterjeve monitorizacije.*
- Rezultati** *Vključili smo 58 bolnikov, 43 moških, starih 50 let, rang 19–69 let. Štiriintrideset (59 %) jih je imelo PAF, 24 (41 %) PEAFA. Napravili smo 113 posegov: en poseg pri 20 bolnikih, 2 posega pri 24, 3 pri 11 bolnikih in 4 posege pri 3 bolnikih. KTO smo ablirali pri 30 (52 %) bolnikih. Zaplete je imelo 5 bolnikov (8,6 %). Tamponada je nastala pri 2 bolnikih (1,7 %), akutni izliv brez tamponade pri 1, zaradi punkcije v perikardialni prostor smo prekinili poseg pri 2 bolnikih. Nihče ni imel kliničnih znakov stenoze PV, poškodbe požiralnika ali možganske kapi v 16-mesečnem obdobju (4–47 mesecev) spremljanja. Primarni cilj smo dosegli pri 42 bolnikih (72 %); delni cilj s pomembnim zmanjšanjem epizod PAF ob zdravljenju z AAZ smo dosegli pri 5 bolnikih (9 %); pri 11 bolnikih (19 %) poseg ni bil uspešen. S posegom smo torej dosegli ugoden klinični rezultat pri 81 % bolnikov – pri 93 % bolnikov s PAF in pri 63 % s PEAFA.*
- Zaključki** *Radiofrekvenčna segmentna/krožna izolacija PV in linearna defragmentacija s pomočjo lasokatetra in ablacijskega katetra s hlajeno konico je za večino bolnikov srednjih let varna in dolgoročno uspešna metoda zdravljenja PAF in PEAFA.*

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**Ključne besede** *atrijska fibrilacija; radiofrekvenčna kateterska ablacija; ablacija s hlajeno konico; klinični izid*

## Abstract

- Aims** *We evaluated clinical outcome of segmental/circumferential pulmonary vein (PV) isolation and linear defragmentation procedure in our first series of patients with paroxysmal or persistent atrial fibrillation (PAF/PEAF). The freedom from symptomatic AF/flutter/tachycardia recurrences with patients off antiarrhythmic treatment (AAD) was primary endpoint of the procedure.*
- Methods** *Consecutive patients with highly symptomatic PAF/PEAF and AAD failure were prospectively recruited from September 2003 to June 2007. Patients < 70 years with left ventricular ejection fraction > 40 % and left atrial diameter < 50mm were included. During the first procedure 2–4 PVs, non-PV foci, and/or flutter isthmus (FI) were targeted. If arrhythmia recurred, conducting gaps to PVs and FI are ablated after blanking period of > 3 months. In patients with PEAf, fast fragmented/complex electrograms were ablated in a linear fashion, connecting upper PV ostia and/or PV ostia with proximal anatomical structures. Only FI line was tested for completeness of block. The irrigated-tip radiofrequency ablation catheter and Lasso catheter (Biosense-Webster) were used after standard transseptal approach with X-ray/fluoroscopy guidance. The suspected arrhythmia recurrences were evaluated by series of ECG/Holter recordings.*
- Results.** *Fifty-eight patients, 43 men, average age 50 years, range 19–69, including 24(41 %) with PEAf, were enrolled. In these patients, 113 procedures were performed: single study in 20, 2 in 24, 3 in 11, and 4 in 3 patients, respectively. Complications occurred in 5 patients including tamponade in 2, acute effusion in 1, and inadvertent pericardial puncture in 2. No PV stenosis, esophageal injury, or stroke were detected clinically during 16-month (4–47) follow-up. We achieved primary endpoint in 42 patients (72 %); partial endpoint in 5 patients (9 %) with significant reduction of AF/flutter/tachycardia recurrences on AAD; and in 11 patients (19 %) procedure was not successful. Overall, 81 % of our patients (93 % with PAF, 63 % with PEAf) benefited from the procedure.*
- Conclusions** *Lasso-guided irrigated-tip RF PV isolation and linear defragmentation is safe and long-term successful treatment of PAF/PEAF in majority of middle-aged patients.*
- Key words** *atrial fibrillation; radiofrequency catheter ablation; irrigated-tip ablation; long-term follow-up*

## Condensed abstract

We evaluated 16-month clinical outcome of lasso-guided irrigated-tip radiofrequency segmental/circumferential pulmonary vein isolation and linear defragmentation in 58 middle-aged patients with paroxysmal or persistent atrial fibrillation. No significant complications occurred except tamponade in 2 patients. Forty-two patients (72 %) were free of symptomatic recurrences, 5 patients (9 %) had rare AF/flutter/tachycardia recurrences on antiarrhythmics, and 11 patients (19 %) were not successful. Overall, 81 % of our patients benefited from the procedure.

## Introduction

Since the recognition that focal activity (triggered, localized reentrant, or even enhanced automaticity) is able to initiate and perpetuate atrial fibrillation (AF),<sup>1–8</sup> radiofrequency catheter ablation (RFA) of AF has evolved rapidly to a commonly performed ablation procedure in many hospitals throughout the world. In

our institution, the procedure was introduced in 2003. We based our approach on circumferential catheter-guided segmental ostial pulmonary vein (PV) isolation,<sup>9</sup> and linear left atrial (LA) ablation.<sup>10</sup> In addition, we were influenced by the work of Pappone<sup>11</sup> with his anatomical circumferential/antral PV ablation approach, and Nademanee's<sup>12</sup> co-called electrophysiologic substrate modification approach, targeting areas with fast fragmented electrograms.

This study was designed to evaluate the clinical outcome of segmental/circumferential PV isolation and linear defragmentation approach in our first series of patients with paroxysmal (PAF) or persistent AF (PEAF). Freedom from symptomatic AF/flutter/tachycardia recurrences with patients off antiarrhythmic treatment (AAD) was primary endpoint of the procedure.

## Methods

Consecutive patients with highly symptomatic PAF/PEAF were prospectively recruited from September 2003 to June 2007. Patients younger than 70, with

left ventricular ejection fraction > 40 %, LA diameter < 50 mm, and failed AAD were included. At least one episode of AF lasting more than 7 days was defined as PFAF. In all, magnetic resonance (MR) imaging of LA and PVs was routinely obtained before the procedure because of the PV anatomy presentation. Transoesophageal echocardiogram was performed within 24 hours before the procedure, searching for atrial thrombi. The study had been approved by state's appointed ethics committee and an informed consent was obtained from all patients.

Our primary ablation goal was a complete PV isolation - segmental or circumferential - with no high frequency PV or peri-PV electrograms (ECs) and no focal ectopic activity. Normal atrial ECs and low amplitude-low frequency ECs (suspected as far-field potentials) were not ablated. The focal ectopic activity or ectopic focus was defined as a site with spontaneous electrical activity or with activity induced and removed by RF application. The flutter isthmus (FI) was ablated and tested for bi-directional block in patients with previously documented or induced FI dependent flutter and in patients with PFAF. If arrhythmia recurred, conducting gaps to PVs, FI, and focal activity are checked and ablated after a blanking period of at least 3 months. In patients with PFAF and in those with macroreentrant atrial tachycardia (MAT), fast fragmented/complex EGs were planned for ablation in a linear fashion, connecting upper PV ostia and/or PV ostia with proximal anatomical structures - mitral annulus, fossa ovalis, or inferior vena cava. Targeted regions were mitral isthmus with vein-ligament of Marshall, LA roof and bottom, left and right interatrial septum, coronary sinus (CS), left and right appendage base, superior vena cava ostium, and terminal crest. The aim was complete removal of fast fragmented/complex ECs, defined as: cycle length of less than 140 ms, at least 3-phase morphology, and amplitude less than 0,5 mV. Finally, electroconversion and/or intravenous ibutilide or propafenone were given to achieve sinus rhythm. PV isolation and FI ablation were completed in sinus rhythm.

The irrigated-tip RFA catheter (25-35 W, 39-43 °C, 17 ml/min, impedance < 110 Ω; Osypka generator), 10- or 20-polar circumferential Lasso catheters (Biosense-Webster), and 10-polar CS catheter were used after standard transseptal approach. X-ray fluoroscopy was used for guiding the procedure. A single long sheath was used in majority of cases and was irrigated with heparinized saline - 2 ml/min. PV ostia were identified from MR image, by fluoroscopy, typical PV/atrial ECs, and by impedance measurements of less than 110 Ω. The oesophagus was located by barium paste swallow. All patients were treated with conscious sedation (fentanyl and midazolam) and intravenous unfractionated heparin (ACT > 300 s) after successful transseptal passage.

The follow-up visits were planned at 3-4 months and yearly or at symptom or arrhythmia recurrences. The suspected arrhythmia recurrences were evaluated by series of standard ECGs or Holter recordings. Simple descriptive statistics and Fisher's exact test were used for data analysis.

## Results

Fifty-eight patients, including 43 men (74 %), with average age of  $50 \pm 12$  years ( $x \pm SD$ ), range 19-69 years, were enrolled. Thirty-four patients had PAF (59 %) and 24 had PFAF (41 %). The mean AF history was  $6 \pm 5$  years (range 1-22). Altogether, we performed 113 procedures: single study in 20 patients, 2 in 24, 3 in 11, and 4 in 3 patients, respectively. Patients were in sinus rhythm before RFA in 60 % of procedures and afterwards in 90 %. In 48 patients (83 %) all PVs were successfully isolated. PVs only were targeted in 39 patients (28 PAF, and 11 PFAF) and PVs combined with linear defragmentations in 19 (33 %), including 6 patients with PAF and 13 patients with PFAF. In 30 patients (52 %), FI RFA was also performed: single study in 22 patients, and 2 in 8 patients, respectively. The number of patients ablated at different anatomical atrial sites according to repeated procedure is shown in Figure 1. In 41 patients (70 %) focal activity as defined could have been demonstrated. From 86 foci, 73 (85 %) were located at PV sites (31 in left superior PV or antrum, 20 in right superior PV, 14 in left inferior PV, and 8 in right inferior PV, respectively). Other sites with focal activity were left or right appendage base - 5 foci, terminal crest - 3, and superior vena cava ostium - 2 foci. Single foci were found at tricuspidal annulus, coronary sinus ostium, and mitral isthmus, respectively. Fluoroscopy procedure time was  $44 \pm 18$  min (range 15-97) and ablation time was  $107 \pm 47$  min (range 14-269 min). Serious complications occurred in 5 patients (8.6 %). Two patients (1.7 %) had acute tamponade necessitating pericardiocentesis, 1 patient had acute effusion, and in 2 patients inadvertent pericardial puncture occurred during transseptal attempt. Persistent chest pain at the end of the procedure was reported in 9 patients, and

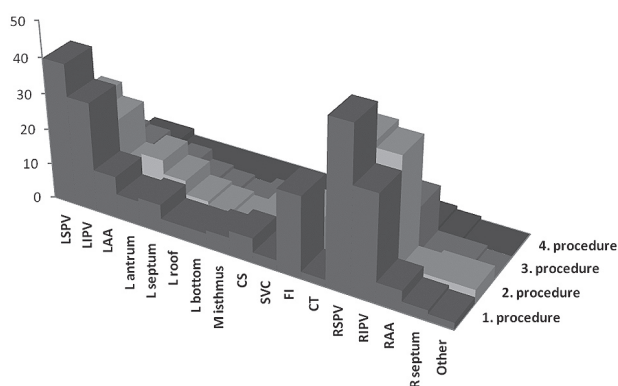


Figure 1. The number of patients ablated at defined sites according to the repeated procedure. Pulmonary vein ostia were the main ablation target regardless of the procedure number.

LSPV(RSPV) - left(right) superior pulmonary vein, LIPV(RIPV) - left(right) inferior pulmonary vein, LAA(RAA) - left(right) atrial appendage, L - left, R - right, M - mitral, CS - coronary sinus, SVC - superior vena cava, FI - flutter (cavo-tricuspidal) isthmus, CT - terminal crest

Sl 1. Število bolnikov glede na ablacijsko mesto in ponovni poseg. Najpogostejše ablacijsko mesto je bilo na ustjih pljučnih ven.



small (< 10 mm) pericardial effusion was documented before discharge in additional 9 patients. Pericardial effusion was not related to the amount of RF energy delivered or to the procedure success. No PV stenosis, oesophageal injury or thromboembolic event were detected clinically after a mean follow-up of  $16 \pm 12$  months, range 4–47 months. From 28 patients with recurrences, MAT was documented in 14 (50 %) and ablated with wide circumferential PV ablation and linear defragmentation in areas with good concealed entrainment. In 42 patients (72 %), we achieved clinical success (no documented AF/flutter/tachycardia and no AAD). Five patients (9 %) had documented AF/flutter recurrences on AAD but were rare, less than once a month, and in 11 patients (19 %) the procedure was not successful (however, 3 patients are on the list for another procedure). The chance of attaining clinical benefit was 93 % in patients with PAF compared to 63 % in patients with PEAf ( $p = 0.005$ ). The success rate in the group with PV ablation and linear defragmentation was equal to the success rate of the group with PV ablation only (N.S.). However, linear defragmentations were performed more frequently in patients with PEAf than in PAF (54 % vs. 19 %). Overall, 81 % of our patients benefited from the procedure.

## Discussion

The long-term clinical success of our RFA approach for PAF/PEAF is in the upper part of the reported 30–81 % success range of non-randomized clinical trials.<sup>13</sup> As expected, the chance of attaining beneficial result was significantly better in patients with PAF (93 %) as compared to those with PEAf (63 %). A complete PV isolation was prerequisite for the procedure success in majority of our patients. Placement of additional linear defragmentation RFAs possibly improved the procedure success in our patients with PEAf. In patients with PAF, linear lesions were probably not necessary or even harmful. These issues have to be elucidated in the future. Recently published data have shown that PEAf could have been terminated by catheter ablation without linear lesions, but the majority required LA roof and mitral isthmus linear ablation lines for MAT prevention.<sup>14</sup> In majority of our patients with MAT recurrences, we successfully performed wider circumferential PV ablation and linear defragmentation in areas with good entrainment. Three-dimensional preacquired MR/computed tomographic images may be needed for better guidance of ablation procedure and for reduction of X-ray exposure in patients with PEAf.<sup>15</sup> Our procedure has to be implemented with this technology in the future.

We achieved very good procedure success, but at the cost of higher number of repeated procedures. With experience and skill, more successful single study procedures with lower cost/efficacy ratio are expected. Anyhow, recurrences of AF/flutter/tachycardia needed reablation procedure were reported in 20–40 % of patients<sup>16</sup> and represent a potential limitation of the procedure.

In our patients, the complication rate was acceptably low. Most severe complication was tamponade,

occurring in about 2 % of our procedures. It is again in the reported 1–6 % range of comparable series of patients.<sup>15</sup> We did not demonstrate any other serious complication like: PV stenosis, atrio-esophageal fistula, phrenic nerve injury, or thromboembolism.

There are some other potential limitations of AF catheter ablation procedure: a) a prolonged learning curve due to transseptal approach, demanding catheter navigation through complex LA/PV anatomy, and difficult ECG interpretation, b) repeated procedures due to AF/flutter/tachycardia recurrences, particularly for PEAf, c) radiation exposure, d) non-defined amount and extent of applied RF energy for the best safety/efficacy profile, and e) non-defined optimal RFA protocol for longstanding PEAf. In addition, the estimated procedure success may be biased by asymptomatic AF recurrences. Whereas only 5 % of patients consistently had AF episodes without symptoms prior to RFA, 37 % of patients had asymptomatic episodes afterwards.<sup>17</sup> Nevertheless, this treatment is currently available at our institution for selected highly symptomatic younger patients.

In conclusion, circumferential catheter-guided irrigated-tip RF PV isolation and linear defragmentation is safe and long-term successful treatment. We would recommend this therapeutic option for highly symptomatic young patients with PAF/PEAF.

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