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Kateterska ablacija fibrilacije atrijske Catheter ablation for atrial fibrillation

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SAŽETAK: Kateterska ablacija predstavlja suvremenu i učinkovitu metodu liječenja simptomatske fibrilacije atrijske (FA). Prema zadnjim smjernicama iz 2006. godine ova je metoda liječenja indicirana u pacijenata sa simptomatskom FA usprkos terapiji antiaritmikima klase Ic (propafenon, flekainid) ili klase III (amiodaron).

Nedavno objavljena meta-analiza učinkovitosti ablacije u usporedbi s antiaritmikima koja se temeljila na nekoliko randomiziranih kliničkih studija zaključuje da je radiofrekventna ablacija (RFA) apsolutno preferabilni oblik liječenja za održavanje sinusnog ritma u pacijenata s FA. Za vjerovati je kako će dosad objavljeni podaci, uz nadolazeće velike studije učinkovitosti RFA FA kao prvog izbora u terapiji (CABANA studija), rezultirati preporukama za ranije odlučivanje o primjeni kateterske ablacije FA u određenih kategorija pacijenata.

KLJUČNE RIJEČI: ablacija fibrilacije atrijske, izolacija plućnih vena, elektroanatomski mapping

ABSTRACT: Catheter ablation represents a modern and efficient therapeutic method for symptomatic atrial fibrillation (AF). According to the latest guidelines from 2006, this treatment method is indicated in patients with symptomatic AF despite the treatment with class Ic of antiarrhythmic drugs (propafenone, flecainide) or class III (amiodarone).

The recently published meta-analysis on efficiency of ablation in comparison to antiarrhythmics that was based on a few randomised clinical studies resulted in a conclusion that radiofrequency ablation (RFA) is absolutely a preferred method of maintaining sinus rhythm in patients with AF. It is to be expected that the results published so far, together with another large prospective study on the efficiency of RFA for AF as the first line therapy (the CABANA study), will result in guidelines for earlier application of catheter ablation for AF in certain categories of patients.

KEYWORDS: ablation for atrial fibrillation, pulmonary vein isolation, electroanatomic mapping

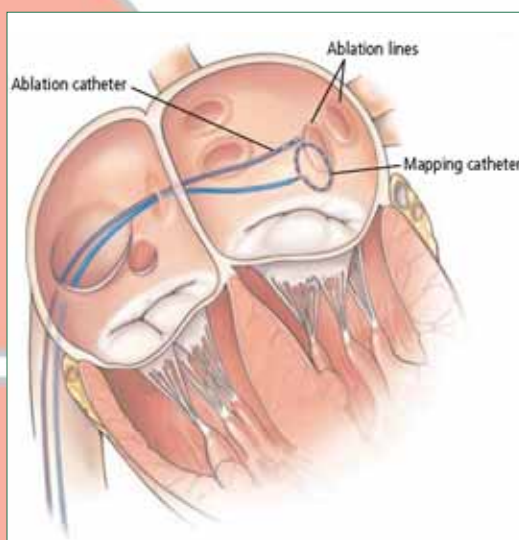


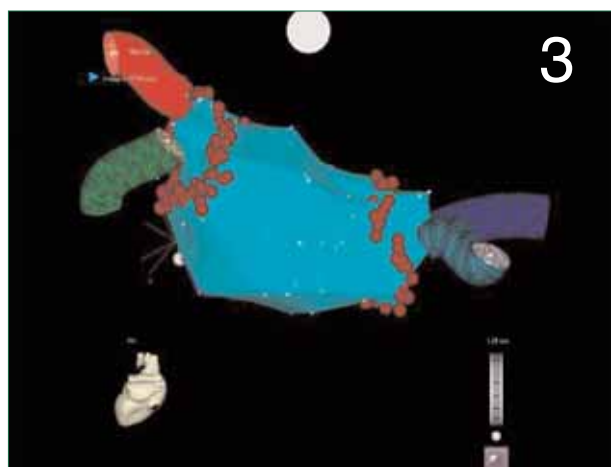
Figure 1. Ablation and Lasso catheter are transeptally introduced in the left atrium where circular ablation lesions around the confluence of every pulmonary vein are being made guided by the Lasso catheter and the recorded potentials on it (point by point ablation is applied).

Chowdhury P, Lewis WR, Schweikert RA, Cummings JE. Ablation of atrial fibrillation: What can we tell our patients? *Cleve Clin J Med.* 2009;76: 543-550. Reprinted with permission. Copyright © 2009 Cleveland Clinic. All rights reserved.



Usporedno s ubrzanim razvojem invazivne elektrofiziologije, devedesetih godina prošlog stoljeća dolazi do rasvjetljavanja patofizioloških mehanizama odgovornih za fibrilaciju atrijsa (FA). Tada postaje jasno da je ektopična električna aktivnost iz fokusa u plućnim venama (PV) ili iz fokusa na spoju PV i lijevog atrijsa (LA) odgovorna za većinu (90-95%) paroksizama FA. Do održavanja FA dolazi nastupom prvo električnog, a potom i strukturnog "remodelinga" atrijskog miokarda.

Kako je u to vrijeme metoda kateterske radiofrekventne ablacije (RFA) bila široko primjenjivana za cijeli niz drugih supraventrikularnih i ventrikularnih aritmija, nije prošlo puno vremena od objašnjenja mehanizma do primjene RFA FA u praksi. Skupina elektrofiziologa iz Bordeauxa 1998. godine objavljuje početna iskustva¹. Od tada metoda doživljava neslutivu evoluciju, a sve je veći broj dokaza o učinkovitosti²⁻⁶.



Ablacija paroksizmalne fibrilacije atrijsa

Prve ablacije FA sastojale su se od pozicioniranja ablacijskog katetera uvedenog transeptalnim pristupom unutar PV te fokalne-segmentalne RFA u veni odgovornoj za ektopičnu aktivnost (najčešće lijeva gornja ili desna gornja). Usprkos obećavajućim rezultatima metoda je brzo evoluirala zbog spoznaje da se ektopična električna aktivnost mogla s vremenom javiti i u drugim venama, ali i zbog nedopustive stope stenoza PV na mjestu primjene RFA.

Simultaneously, with the rapid progress of invasive electrophysiology, the pathophysiological mechanisms responsible for atrial fibrillation (AF) were discovered in 1990s. At that point, it became clear that ectopic electrical activity from a focus in the pulmonary veins (PV) or from the focus on the connection of PV and left atrium (LA) is responsible for the majority (90-95%) of paroxysms of AF. The persistence of AF is at first caused by electrical but then joined by structural remodelling of the atrial myocardium.

As the method of radiofrequency ablation (RFA) was widely used at that time to treat a number of other supraventricular and ventricular arrhythmias, it didn't take long from the explanation of the mechanism to the use of RFA for AF in practice. A group of electrophysiologists from Bordeaux reported their first experiences in 1998¹. Since then, the method has evolved dramatically with an increasing number of evidence of its efficiency²⁻⁶.

Figure 2. Posterior-anterior view on the 3D map of left atrium (LA) created by CARTO system. Pulmonary veins (PVs) are being reconstructed by using so called tubular models — in this case all 4 PVs annex separately to the posterior wall of LA (to be compared to reconstruction obtained by MSCT angiography done prior to the procedure in the same patient shown in Figure 4).

Figure 3. Previously described map of circular ablation lesions (red dots) surrounding ipsilateral pulmonary veins.

Figure 4. MSCT angiographic reconstruction of the left atrium and pulmonary veins; posterior-anterior projection.



Ablation for paroxysmal atrial fibrillation

The first ablations for AF were composed of positioning the transeptally inserted ablation catheter within PV and focal-segmental RFA in the vein responsible for ectopic activity (mostly left superior or right superior). Despite promising results, the method evolved fast due to understanding that the ectopic electrical activity could, in time, appear in other veins, but also due to unacceptably high rate of PV stenosis on the RFA application site.



Kako je dakle trebalo izbjegavati primjenu RFA unutar PV orijentalno se na stvaranje cirkularnih lezija na ušćima PV, tj. na spoju s LA, u smislu stvaranja fibrozne barijere koja bi onemogućila provođenje ektopične električne aktivnosti iz PV pa stoga i indukcije FA. Ova tehnika, sada nazvana izolacija plućnih vena (*pulmonary vein isolation* — PVI) je zahtijevala uvođenje i drugog katetera transseptalnim pristupom. Naime, kreiran je cirkularni mapping kateter, tzv. *laso kateter*, kojeg je bilo moguće zbog svojeg oblika pozicionirati na samom ušću PV u LA te se njim služiti kao orijentir kod stvaranja lezija. Težilo se pojedinačnoj izolaciji svake PV tako stvorenom cirkularnom RF lezijom oko njezina ušća (**slika 1**). Ova modifikacija pridonijela je većoj učinkovitosti postupka, no zahtijevala je iznimnu vještinu operatera uz vrlo visoke doze Rtg zračenja zbog fluoroskopskog navođenja tijekom ablacije.

Konačno, razvoj vrlo sofisticirane opreme za tzv. elektroanatomski mapping omogućio je sljedeću fazu razvoja ove procedure. Korištenjem posebnih sustava (npr. CARTO sustav) i s njima kompatibilnih ablacijskih katetera stvori se virtualna 3D mapa srčane šupljine od interesa, u ovom slučaju LA s pripadajućim PV (najčešće su to 4 vene, 2 lijeve i 2 desne koje se svaka sa zasebnim ušćem pripaja na stražnji zid LA — **slika 2**). Na tako dobivenoj mapi ne analizira se samo anatomija, već i podaci o propagaciji električnih impulsa te je moguće razaznati regije fibroze-ožiljka. Jednom stvorena CARTO mapa služi za orijentaciju i planiranje ablacijskih lezija te smanjuje vrijeme potrebne fluoroskopije. Korištenjem ovakvih sustava moguće je stvaranje cirkularnih lezija koje obuhvaćaju obje ipsilateralne PV uz izbjegavanje primjene RFA unutar istih te obuhvaćanje sve veće regije LA koja sada ostaje unutar linije električne izolacije tzv. antruma PV (*wide antral circumferential ablation*) — **slika 3**.

Kombiniranje i spajanje rekonstrukcija LA i PV dobivenih primjenom MSCT angiografije prije samog postupka (**slika 4**) s elektroanatomskom mapom pomoću 3D mapping sustava tijekom samog postupka daljnji je korak u nastojanju što preciznijeg planiranja i izvođenja ablacijskih linija koji doprinosi dodatno uspjehu procedure te smanjenju ekspozicije pacijenta i operatera ionizacijskom zračenju.

Usporedno s evolucijom tehnike došlo je i do velikog zaokreta u tehnologiji ablacijskih katetera te su irigacijski (fiziološkom otopinom hlađeni) kateteri postali standard. Pomoću njih se postižu konzistentnije transmuralne lezije što se odrazilo u većoj učinkovitosti, uz smanjenje učestalosti tromboembolijskih incidenata⁷.

Ablacija perzistentne fibrilacije atrija

Gore opisana eliminacija "triggera" FA primjenom PVI se pokazala nešto manje učinkovita u pacijenata s trajnijim oblikom FA. Postalo je jasno da će za bolji uspjeh u ovoj grupi pacijenata biti potrebna i određena modifikacija substrata u atrijskom miokardu. Zbog navedenog se za ablaciju perzistentne FA osim PVI koriste i dodatne lezije u smislu linearnih lezija (najčešće preko krova ili dna LA te preko tzv. mitralnog istmusa — spoj mitralne valvule s lijevom donjom PV) ili ablacija regija s kompleksnim, fragmentiranim potencijalima za koje se pokazalo da mogu

As the use of RFA inside PV should be avoided, creating circular lesions on the confluence of PV, i.e. on the connection of PV and LA, has become the centre of attention. This meant creating a fibrous barrier that would prevent the conduction of the ectopic electrical activity from PV and thus the induction of AF. This technique, now called *pulmonary vein isolation* (PVI) required introducing another catheter transseptally. Namely, circular mapping catheter was created, the so called *Lasso catheter* that, due to its shape, could be located on the confluence of PV into LA itself and thus serve as a landmark when creating the lesions. The aim was to isolate every PV with such RF lesion around its confluence (**Figure 1**). This modification has contributed to higher efficiency of the procedure, but it demanded exceptional ability of the operator together with high doses of X-ray radiation due to fluoroscopic navigation during the ablation.

Finally, the development of very sophisticated equipment for the electroanatomical mapping has made the next developmental phase of the procedure possible. A virtual 3D map of the relevant heart chambers, in this case the LA with belonging PVs (usually 4 veins, 2 left and 2 right every with its own opening annexed to the posterior wall of the LA — **Figure 2**), is created with the use of special systems (e. g. CARTO System) and compatible ablation catheters. On such a map not only anatomy is analysed but also the electrical impulse propagation data which make it possible to distinguish fibrous-scar regions. Once created, the CARTO map is used for orientation and planning of the ablation lesions which decreases the time needed for fluoroscopy. Using this kind of systems enables making circular lesions that involve both ipsilateral PVs thereby avoiding the use of RFA within PVs as well as containing a bigger proportion of the LA, that is now inside the electrical isolation line, of the so called PV antrum (*wide antral circumferential ablation*) — **Figure 3**.

Combining and merging LA and PV reconstructions obtained by MSCT angiography prior to the procedure (**Figure 4**) with electroanatomical map by using 3D mapping system during the procedure is the next step in the effort of accomplishing as precise ablation line planning and application as possible. This additionally contributes to the success of the procedure and decreases the exposure of the patient and the surgeon to the ionizing radiation.

A turning point in the technology of ablation catheters came along with the evolution of the technique making irrigated (cooled by saline solution) catheters a standard. More consistent transmural lesions are achieved with such catheters resulting in higher efficiency with a decrease in thromboembolic events⁷.

Ablation for persistent atrial fibrillation

The above described elimination of AF trigger by using PVI proved to be less effective in patients suffering from permanent AF. It has become obvious that in this group of patients, in addition to previously mentioned procedures, a certain modification of substrate in the atrial myocardium will be necessary to achieve better results. This is the reason as to why in addition to PVI further lesions in the sense of linear lesions (mostly over the LA top or bottom as well as so called mitral isthmus — the connection between mitral valve and left inferior PV) or ablation of regions with



podržavati FA (najčešće na stražnjem zidu LA). Korištenje 3D mapping sustava je ključno kod ovakve vrste ablacije.

Uspjeh i komplikacije radiofrekventne ablacije fibrilacije atrijske

Nakon prva dva do tri mjeseca u kojima dolazi do organizacije i definitivne fibroze lezija u LA, oko 80-85% pacijenata s paroksizmalnom FA te oko 60-65% s perzistentnom FA ostaje slobodno od rekurencije FA do godinu dana nakon ablacije. Kako se metoda izolacije plućnih vena koristi tek nekoliko zadnjih godina, nema puno studija s višegodišnjim praćenjem pacijenata nakon ablacije, no početna iskustva sugeriraju da se učinak u velikoj mjeri održava nakon 2 i 3 godine⁸. Potreba za drugim postupkom je u oko 25-30% pacijenata s paroksizmalnom FA te u oko 40-45% s perzistentnom FA kako bi se održao učinak kroz duže vrijeme praćenja nakon početne ablacije.

Od komplikacija treba spomenuti tamponadu i tromboembolijske incidente, incidencija kojih se razvojem i evolucijom tehnike smanjila na manje od 1%. Pojava manjih hematoma na mjestu umetanja uvodnica u preponama je uobičajena. Vrlo rijetke, ali ozbiljne komplikacije, predstavljaju paraliza n. phrenicus te atrijsko-ezofagealna fistula⁹.

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Literature

1. Haissaguerre M, Jais P, Shah DC, Takahashi T, Hocini M, Quiniou G, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med.* 1998;339:659-66.
2. Fuster V, Ryden LE, Cannom DS, Curtis AB, Ellenbogen KA, Le Heuzey J, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Europace.* 2006;8:651-745.
3. Terasawa T, Balk EM, Chung M, Garlitski AC, Alsheikh-Ali AA, Lau J, et al. Systematic review: comparative effectiveness of radiofrequency catheter ablation for atrial fibrillation. *Ann Intern Med.* 2009;151:191-202.
4. Wazni OM, Marrouche NF, Martin DO, Verma A, Bhargava M, Saliba W, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation: a randomized trial. *JAMA.* 2005;293:2634-40.
5. Pappone C, Augello G, Sala S, Gugliotta F, Vicedomini G, Paglino G, et al. A randomized trial of circumferential pulmonary vein ablation versus antiarrhythmic drug therapy in paroxysmal atrial fibrillation: the APAF Study. *J Am Coll Cardiol.* 2006;48:2340-7.
6. Jais P, Cauchemez B, Macle L, Daoud E, Khairy P, Subbiah R, et al. Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study. *Circulation.* 2008;118:2498-505.
7. Kanj MH, Wazni O, Fahmy T, Thai S, Patel D, Elay C, et al. Pulmonary vein antral isolation using an open irrigation ablation catheter for the treatment of atrial fibrillation: a randomized pilot study. *J Am Coll Cardiol.* 2007;49:1634-41.
8. Bertaglia E, Tondo C, De Simone A, Zoppo F, Mantica M, Turko P, Iltiano A, et al. Does catheter ablation cure atrial fibrillation? Single procedure outcome of drug-refractory atrial fibrillation ablation: a 6 year multicentre experience. *Europace*, doi:10.1093/europace/eup349 (19. 12. 2009)
9. Cappato R, Calkins H, Chen SA, Davies W, Lesaka Y, Kalman J, et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation.* 2005;111:1100-5.

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