

# Ablacija fibrilacije atrijske u Republici Hrvatskoj

## Ablation of atrial fibrillation in the Republic of Croatia

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RECEIVED:  
April 9, 2016

UPDATED:  
April 12, 2016

ACCEPTED:  
April 26, 2016



**CITATION:** *Cardiol Croat.* 2016;11(5-6):159–161. | **DOI:** <http://dx.doi.org/10.15836/ccar2016.159>

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Fibrilacija atrijske (FA) najčešća je postojana aritmija u općoj populaciji s prevalencijom oko 1 – 2 % u općoj populaciji. Pretpostavlja se da u Europi oko 5 – 6 milijuna ljudi boluje od FA-a, a kako populacija stari i životni se vijek se produljuje, taj se broj povećava. Iako u Hrvatskoj trenutno nemamo registar ni točne epidemiološke podatke, pod pretpostavkom da je prevalencija ista kao u Europi, dobivamo 40 – 50 000 ljudi koji boluju od FA-a<sup>1</sup>.

Fibrilacija atrijske povezana je s povećanim ukupnim mortalitetom i morbiditetom, rizikom od moždanog udara i srčanog zatajivanja. Osim smrtnosti i pobola koji je prate, FA je veliki socioekonomski problem koji proizlazi iz troškova liječenja, rehabilitacije te bolovanja i prijevremenih mirovina. U Njemačkoj su 2006. godine npr. samo troškovi liječenja bolesnika s FA-om na nacionalnoj razini iznosili gotovo 700 milijuna eura. Zbog svega navedenog izrazito je važno rano otkrivanje i adekvatno liječenje bolesnika s FA-om<sup>2,3</sup>.

Liječenje FA usmjereno je primarno prema smanjenju rizika od moždanog udara i smrtnosti te redukcije simptoma u bolesnika. Danas je samo antikoagulantna terapija kroz redukciju rizika od moždanog udara dokazala i redukciju ukupnog mortaliteta. Smanjenje simptoma, bilo kao kontrola frekvencije bilo kao kontrola ritma, nije do sada nedvosmisleno dokazalo utjecaj na smrtnost<sup>4,5</sup>. Studija AFFIRM, koja je uspoređivala održavanje sinusnog ritma i kontrolu frekvencije, nije pokazala utjecaj održavanja sinusnog ritma na redukciju mortaliteta. Međutim, naknadne su analize pokazale da je sinusni ritam bio prediktor nižeg mortaliteta, a da je povećani mortalitet bio uzrokovan proaritmijom antiaritmika i prerano

Atrial fibrillation (AF) is the most common persistent arrhythmia in the general population, with a prevalence of about 1-2%. It is believed that about 5-6 million people in Europe suffer from AF, and that number is increasing due to the aging of the population and lifespan extension. Although we do not currently have accurate epidemiological data or a registry in Croatia, assuming that the prevalence is the same as in Europe, we can estimate 40-50000 people suffer from AF in Croatia<sup>1</sup>.

Atrial fibrillation is associated with increased total mortality and morbidity and risk of stroke and heart failure. In addition to morbidity and mortality effects, AF represents a large socio-economic issue due to the financial burden of treatment, rehabilitation, sick leave, and early retirement. For example, in Germany in 2006 the treatment costs alone for patients with AF at the national level amounted to almost 700 million euros. Due to the above, early diagnosis and adequate treatment are extremely important in patients with AF<sup>2,3</sup>.

AF treatment focuses primarily on reducing the risk of stroke and mortality as well as symptom reduction in the patient. Currently, only anticoagulation therapy has been proven to reduce total mortality through stroke risk reduction. Symptom reduction in the form of frequency or rhythm control has not yet been unambiguously shown to affect mortality<sup>4,5</sup>. The AFFIRM study that compared maintenance of sinus rhythm and frequency control did not find any effect of sinus rhythm maintenance on mortality reduction. However, consequent analyses showed that sinus rhythm was a predictor of lower mortality, and that increased mortality was caused by the proarrhythmic effects of antiarrhythmic

prekidanom antikoagulantnom terapijom u bolesnika sa sinusnim ritmom<sup>6,7</sup>.

Sa svrhom održavanja sinusnog ritma, bez antiaritmickih lijekova, razvila se izolacija plućnih vena koja je u istraživanjima konzistentno pokazala superiornost u usporedbi s antiaritmickim lijekovima u određene skupine bolesnika. U početku je razvijena „point-by-point“ radiofrekventna ablacija primjenom RTG-a, međutim, tijekom godina unaprijeđena je razvojem 3D *mapping* sustava i novih irigacijskih katetera<sup>8</sup>. Također, unatrag nekoliko godina na tržištu su se pojavile nove tehnologije (krioablacija, kriobalon, multielektrodni ablacijski kateteri, laser, UZV...) koje su pokazale rezultate slične radiofrekventnoj ablaciji. Iako je izolacija plućnih vena pokazala superiornost u održavanju sinusnog ritma u odnosu prema antiaritmickim lijekovima, studije do sada nisu pokazale utjecaj na mortalitet – iako se nadamo da će studije koje su u tijeku u budućnosti dati odgovor na ovo pitanje<sup>9</sup>.

## Stanje u Hrvatskoj

Kako je već navedeno, procjenjuje se da u Hrvatskoj 40 – 50 000 ljudi boluje od FA-a. Navedeno je veliki javnozdravstveni i ekonomski problem. S obzirom na to da točnih podataka nema, Radna skupina za aritmije i elektrostimulaciju Hrvatskoga kardiološkog društva u godini 2016. pokreće Registar fibrilacije atrija koji bi u početku pokrivaio dio populacije (bolnice) s planom da u budućnosti preraste u nacionalni registar FA koji bi dao točne podatke o broju bolesnika, načinu liječenja i socioekonomskom utjecaju.

U području medikamentne terapije, primarno antikoagulantne terapije, u Hrvatskoj su odnedavno na tržištu novi antikoagulantni lijekovi koji su se pokazali, usporedivi ili bolji od dosadašnjeg „zlatnog standarda“ varfarina. Iako su navedeni lijekovi zastupljeni u velikom postotku u Europskoj uniji, s obzirom na cijenu i potrebu plaćanja ili nadoplate, ti su lijekovi za sada dostupni samo malom broju bolesnika u Hrvatskoj. Također, Hrvatska pripada skupini zemalja s velikim brojem bolesnika na varfarinu koji nemaju adekvatno reguliran INR. Ostaje otvoreno pitanje potrebe za standardizacijom edukacije/praćenja bolesnika na antikoagulantnoj terapiji, tj. otvaranja ambulanti/poliklinika za FA i antikoagulantnu terapiju.

Što se intervencijskog liječenja (izolacije plućnih vena) tiče, u Hrvatskoj je unatrag nekoliko godina učinjen veliki napredak. Prve izolacije plućnih vena napravljene su 2009. godine. Danas se izolacija plućnih vena može učiniti u pet centara, od kojih tri centra izvedu više od 100 navedenih ablacija godišnje. U uporabi su gotovo sve tehnologije koje su dostupne i u svijetu, uz napomenom da je RF ablacija najzastupljenija metoda i čini 85 % svih procedura izolacije plućnih vena u 2015. godini. Prošle godine učinjeno je ukupno 446 izolacija plućnih vena (**slika 1**), što je 100 na milijun stanovnika. Prema ovim brojevima hrvatski su centri uz bok centrima u susjedstvu kao što su Mađarska, Austrija i Slovačka (**slika 2**). Radna skupina za aritmije također je ove godine pokrenula Hrvatski i međunarodni registar izolacije plućnih vena u koji je za sada uključeno osam centara iz regije.

U Hrvatskoj je, kao i u svijetu, učinjen veliki napredak u liječenju bolesnika s FA-om. Uspjeh ablacijskog liječenja paroksizmalne i kratko perzistentne fibrilacije atrija (< 1 godine

drugs and premature cessation of anticoagulation therapy in patients with sinus rhythm<sup>6,7</sup>.

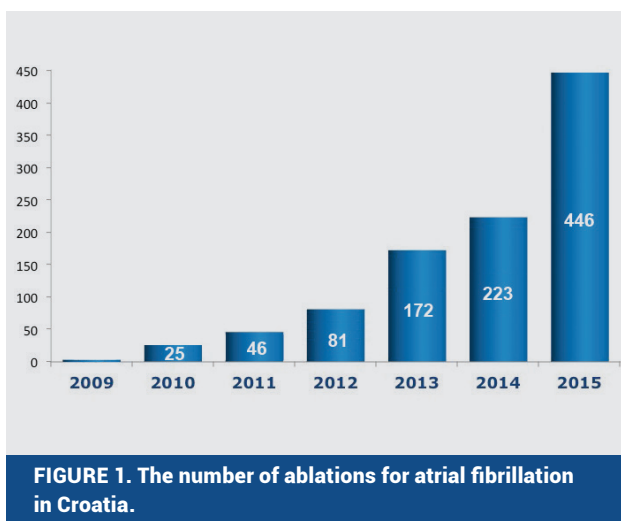
Pulmonary vein isolation for atrial fibrillation was developed as a way to maintain sinus rhythm without using antiarrhythmic drugs, and studies have consistently shown it to be superior in comparison with antiarrhythmic drugs for certain patient groups. Point-by-point radiofrequency ablation using X-ray imaging was developed initially, but it has been improved over the years with the development of 3D mapping systems and new irrigation catheters<sup>8</sup>. Additionally, new technologies have appeared on the market several years ago (cryoablation, cryoballoon ablation, multielectrode catheter ablation, lasers, ultrasound, etc.) that have shown results similar to radiofrequency (RF) ablation. Although pulmonary vein isolation has been shown to be superior in maintaining sinus rhythm in comparison with antiarrhythmic drugs, studies have yet to find any effect on mortality – although we hope that studies will answer this question in the future<sup>9</sup>.

## The situation in Croatia

As stated above, an estimated 40-50000 people suffer from AF in Croatia. This is a serious public health and economic problem. Because there are no accurate data, in 2016 the Working Group on Arrhythmias and Cardiac Pacing of the Croatian Cardiac Society started the Atrial Fibrillation Registry that will initially cover part of the population (hospitals) and is planned to grow into a national AF registry in the future that would provide correct data on patient numbers, treatment, and socioeconomic impacts.

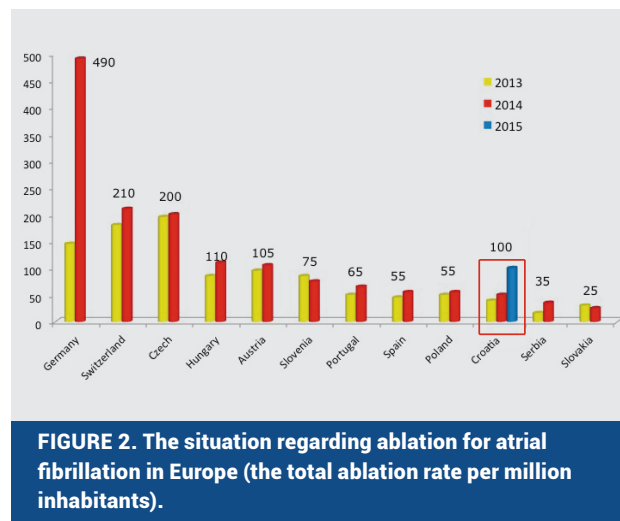
In the domain of medication therapy, primarily anticoagulation therapy, novel oral anticoagulant drugs have recently appeared on the market in Croatia and have demonstrated themselves comparable to or better than the gold standard warfarin therapy. Although use of these drugs is widespread in the European Union, since they are either not covered by insurance or incur additional fees these drugs are currently only available to a small number of patients in Croatia. Croatia also belongs to the group of countries with a large number of patients using warfarin that do not have adequately regulated international normalized ratios (INR). The question remains whether there is a need for standardization in educating/monitoring patients using anticoagulation therapy, i.e. opening clinics/polyclinics for AF and anticoagulation therapy.

As to interventional treatment (pulmonary vein isolation), there has been great progress in Croatia over the past few years. The first pulmonary vein isolation procedures were performed in 2009. Today, pulmonary vein isolation is performed in five centers, of which three perform over 100 such ablations annually. Almost all globally available technologies are in use, with RF ablation being the most common method and amounting to 85% of all pulmonary vein isolation procedures performed in 2015. Last year, a total of 446 pulmonary vein isolation procedures was performed (**Figure 1**), which is 100 per million inhabitants. These numbers mean the performance of Croatian centers is comparable to centers in neighboring countries such as Hungary, Austria, and Slovakia (**Figure 2**). The Working Group for Arrhythmia has also started the Croatian and international pulmonary vein



trajanja) već se penje i do 90 % u periodu praćenja od godine dana u visokovolumnim centrima. Ablacijsko liječenje dugo perzistentne fibrilacije atrijske ni približno ne pokazuje takve rezultate unatoč različitim strategijama takvog liječenja. Osim toga, za točniju verifikaciju rezultata potrebni su dodatni trud i ulaganje u nacionalne registre, kao i u standardizaciju liječenja i praćenja ovakvih bolesnika.

Zaključno, ablacijsko je liječenje u kratkom razdoblju postalo standardni oblik liječenja u Republici Hrvatskoj s brojem postupaka na razini srednjoeuropskih zemalja.



isolation registry this year, which currently includes 8 centers from the region.

Just like in the rest of the world, there has been great progress in the treatment of patients with AF in Croatia. The success rate of ablation therapy for paroxysmal atrial fibrillation and short-term persistent atrial fibrillation (<1 year in duration) is already rising to as much as 90% at one-year follow-up in high-volume centers. Ablation therapy for long-term persistent atrial fibrillation has not been nearly as successful, despite the employment of different strategies of ablation therapy. Additionally, accurate verification of results requires further efforts and investments into national registries, as well as standardization in treatment and follow-up for these patients.

In conclusion, ablation therapy has, over a short period of time, become the standard treatment in the Republic of Croatia, and the number of procedures being performed is now at the level of Central European countries.

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