



The Year in Hungarian Cardiology 2023: Arrhythmias

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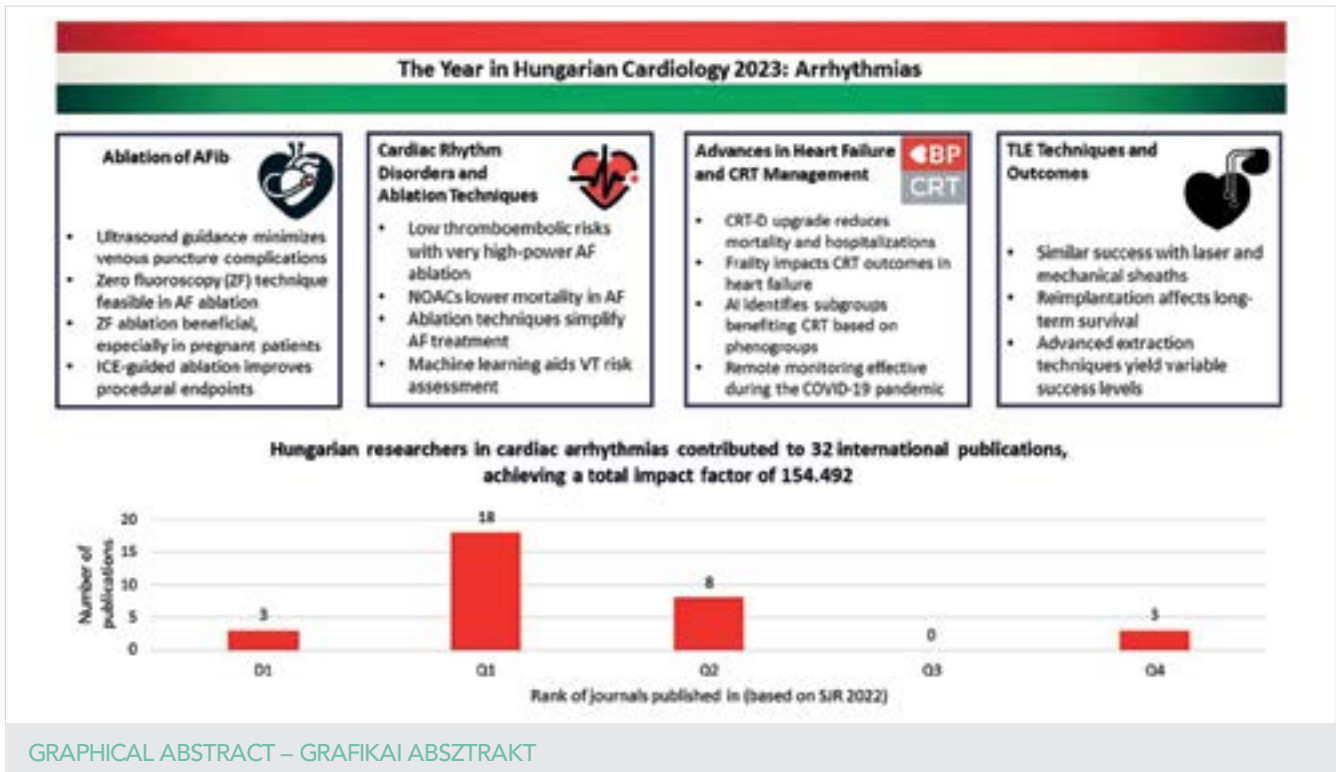
In 2023, Hungary produced notable scientific publications focused on cardiac arrhythmias. This review highlights the most impactful papers, authored at least in part by Hungarians, featuring work conducted at Hungarian research sites and published in international peer-reviewed journals. We give a short overview regarding papers dealing with the role of imaging (different types of ultrasound, cardiac magnetic resonance imaging and electroanatomical mapping) in treating cardiac arrhythmias. We summarize the novelties of ischemic complications of atrial fibrillation (AF), cerebral safety of AF ablation, and current AF ablation techniques. Optimizing risk stratification of ventricular tachycardia (VT) ablation was a landmark paper of our “machine learning” research. Further studies have made significant strides in cardiac device therapy, notably through the groundbreaking BUDAPEST-CRT Upgrade Trial for heart failure, which demonstrated marked reductions in deaths and hospitalizations following Cardiac Resynchronization Therapy (CRT) upgrade procedures. Research on the impact of frailty on CRT outcomes has underscored the importance of tailored treatments. Artificial intelligence, particularly topological data analysis, has been crucial in personalizing CRT therapy. Additionally, advancements in remote monitoring and lead extraction techniques have mirrored the rapid evolution of cardiac technology and care.

Keywords: intracardiac echocardiography, zero fluoroscopy, ablation of ventricular tachycardia, cardiac resynchronisation therapy upgrade, machine learning

A magyar kardiológia eredményei 2023-ban: szívritmuszavarok

2023-ban Magyarország számos jelentős tudományos publikációt közölt a szívritmuszavarokra összpontosítva. Ez az összefoglaló kiemeli a legjelentősebb publikációkat, amelyek legalább részben magyar szerzők által íródtak, magyar kutatási helyszíneken végeztek munkát, és nemzetközi, szakértők által felülvizsgált folyóiratokban jelentek meg. Rövid áttekintést adunk azokról a publikációkról, amelyek az ultrahang különböző típusait, a mágneses rezonanciás képalkotást a szívről és az elektroanatómiai térképezést vizsgálják a szívritmuszavarok kezelésében. Összefoglaljuk a pitvarfibrilláció (PF) iszkémiás szövődeményeinek újdonságait, a PF-abláció cerebrális biztonságát és az aktuális PF-ablációs technikákat. A kamrai tachycardia ablációja rizikóstratifikációjának optimalizálása a „machine learning” kutatásunk kiemelkedő jelentőségű publikációja volt. További tanulmányok jelentős előrelépéseket tettek a szívritmuszavarok kezelésében, különösen a BUDAPEST-CRT Upgrade-vizsgálat a szívelégtelenség esetében, amely jelentős csökkenést mutatott a halálozás és a szívelégtelenség események miatti kórházi beutalások tekintetében a Kardiális Reszinkronizációs Terápia (CRT) Upgrade eljárások után. A krónikus betegségek hatását vizsgáló kutatások hangsúlyozták a személyre szabott kezelés fontosságát. A mesterséges intelligencia, különösen a topológiai adatelemzés, kulcsfontosságú volt a CRT terápia személyre szabásában. Ezenkívül a távmonitorozás és az elektródaeltávolítási technika fejlődése tükrözte a kardiális technológia és az ellátás gyors fejlődését.

Kulcsszavak: intrakardiális echokardiográfia, nulla fluoroszkópos abláció, a kamrai tachycardia ablációja, kardiális reszinkronizációs terápia upgrade, gépi tanulás



Electrophysiology – ablation

Imaging in ablation

Ensuring safety during ablation procedures has become crucial. *Kupó et al.* from the University of Szeged emphasized the importance of ultrasound guiding femoral venous access in patients undergoing pulmonary vein isolation (PVI) for AF (1). They have shown that ultrasound-guided puncture minimizes the complications of femoral venous puncture.

Over the years, with the evolving ablation techniques, the avoidance of ionizing radiation has become achievable; even AF ablation is feasible and effective with the zero fluoroscopy (ZF) technique, according to another publication from *Debreceni et al.* from the University of Pécs (2). They also showed in two studies that ZF cavo-tricuspid isthmus ablation guided solely by intracardiac echocardiography (ICE) for atrial flutter is feasible, safe; furthermore, it is associated with improved procedural endpoints, such as procedure time, fluoroscopy exposure compared to fluoroscopy-guided approach (3, 4). They also published that leveraging ICE guidance for anatomical slow pathway ablation in AVNRT patients can offer significant advantages compared to procedures guided by electroanatomical mapping systems (EAMS). Therefore in cases where EAMS-guided ablation proves unsuccessful, transitioning to ICE-guided ablation is a recommended alternative (5). The zero fluoroscopy ablation is important in all patient groups. The technique's benefits are more pronounced in fertile-aged and especially in pregnant patients. *Mla-*

doniczky et al. published a case series of 13 pregnant women successfully ablated with the completely fluoroscopy-less method (6).

Piros et al. demonstrated in a study involving 186 patients that the ZF ablation approach is as safe and effective as the conventional fluoroscopic approach in treating AVNRT and typical atrial flutter. Their study represents the first investigation encompassing all three widely utilized EAMS with similar results and procedure characteristics for total ZF supraventricular tachycardia (SVT) ablations (7). The electrophysiology working group of Semmelweis University was also involved in one big multicenter international collaboration – the design paper of which has already been published (8).

The anatomical properties that could potentially influence the effectiveness of ablation procedures have been the subject of investigation for an extended period. *László Nagy et al.* studied 67 patients with 3D transesophageal echocardiography before pulmonary vein cryoablation, and found that parameters related to the right superior pulmonary vein (RSPV) can be evaluated with an acceptable accuracy (9). Furthermore, in alignment with a prior Hungarian report (10), they also found that RSPV parameters can predict the recurrence of AF after catheter ablation (11). *Márton Kiss et al.* also investigated the role of pulmonary vein anatomy and found no significant difference in the procedural parameters and clinical outcome between patients with left common pulmonary vein and those with normal left atrial anatomy (12).

Semmelweis University's working groups have widely investigated the potential roles of preprocedural imaging techniques. According to them, a new non-contrast-enhanced BOOST cardiac MR sequence is suitable for visualizing the PVs in patients with AF, and it may also be suitable for detecting larger LAA thrombi (13, 14).

AF – thromboembolic complications

AF might lead to thromboembolic complications. Most often, it causes stroke, but embolism can happen at any location, even in coronary arteries, as researchers at the University of Debrecen have pointed out (15). Anticoagulation decreases mortality in these patients. The same working group also searched the Hungarian National Health Insurance Fund (NHIF) database and showed that NOACs yielded significantly lower mortality than VKA treatment in patients with nonvalvular AF (16).

In certain circumstances, embolic events may arise during the invasive treatment of AF. Initial inquiries have sparked concerns regarding the potential association of very high-power, short-duration (vHPSD; 90 W/4 s) PVI with an increased incidence of silent cerebral embolism (SCE) when compared to low-power, long-duration ablation. In a prospective trial involving 328 patients, out of which 61 underwent diffusion-weighted brain magnetic resonance imaging (MRI) imaging after ablation procedures, they showed that vHPSD PVI has excellent cerebral safety profile. The incidence of silent cerebral embolism was below the previously reported range, and no clinically overt cerebral complications were observed (17).

AF – ablation techniques

The global prevalence of AF has increased over the years. Therefore, ablation of AF is one of the hottest research topics nowadays. In an international trial including the working group of Semmelweis University, investigated the minimal distance between individual application points during PVI to simplify the AF ablation workflow (18). In another multicentric trial, *Földesi et al.* showed cryoballoon ablation is a safe and effective treatment for AF in octogenarians, with efficacy and adverse events rates akin to ablations performed in younger patients (19).

Ventricular tachycardia

The ablation of ventricular tachycardia (VT) continues to present challenges, with post-catheter ablation recurrence remaining a significant concern. This underscores the importance of accurate risk assessment. *Komlósi et al.* addressed this by employing machine learning techniques to develop a risk stratification system that proficiently predicts mortality outcomes for patients with structural heart disease who have undergone ablation for ventricular tachycardia (VT) (20).

Pacemaker, Implantable Cardioverter Defibrillator and CRT

The first Randomized Clinical Trial on Right Ventricular Pacing Upgrade

The first multicenter, prospective, investigator-initiated trial on the field of CRT upgrade was published in 2023. This trial evaluated the efficacy and safety of with a defibrillator (CRT-D) upgrade in heart failure patients with a priorly implanted pacemaker (PM) or implantable cardioverter defibrillator (ICD) with intermittent or permanent right ventricular pacing (RVP) and reduced ejection fraction (HFrEF) as compared to ICD alone. Altogether 360 patients had been enrolled across 7 countries from 17 centres, and they were randomly assigned to have a CRT-D upgrade or an ICD therapy. Their milestone trial revealed, that CRT-D upgrades substantially lowered the risk of all-cause mortality, heart failure hospitalizations, and lack of reverse remodeling, without increasing the incidence of procedure- or device-related complications as compared to ICD alone during the 12.4 month mean follow-up time. Moreover, patients upgraded to CRT-D exhibited remarkable improvements in echocardiographic parameters, which was associated with a significantly lower incidence of major arrhythmias (21).

Frailty Among Heart Failure Patients Eligible for CRT

Frailty is a complex clinical syndrome associated with aging and comorbidities. *Kuthi et al.* focused on the prevalence of frailty in heart failure patients eligible for CRT and its impact on long-term outcome. Utilizing a 30-item frailty index the study classified patients into different frailty groups and examined the relationship between frailty and mortality rates, as well as response to CRT over a median follow-up time of 4.8 years. These findings highlighted the significant association between frailty and adverse outcomes, emphasizing the critical role of frailty assessment in the management of heart failure patients undergoing CRT (22). Another paper by *Behon et al.* highlighted the prevalence of frailty and the importance of CRT in elderly HFrEF patients, considering that the benefit in these individuals did not attenuate over time, they can respond as well as the younger ones. Moreover, those with a higher age did not have a higher rate of complications (23).

Efficacy of CRT-D vs. CRT-P devices

A systematic review and meta-analysis examined the impact of CRT, with or without a defibrillator (CRT-D vs. CRT-P), on mortality rates. Analyzing data from 26 observational studies encompassing 128,030 patients, the meta-analysis sought to determine how these therapies affect all-cause mortality and to identify patient subgroups that might benefit from CRT-D over CRT-P. The analysis found that CRT-D significantly reduced all-cause mortality compared to CRT-P, particularly in

certain patient subgroups such as ischemic etiology, and younger age. Moreover, it highlighted the changes of CRT eligible patients' characteristics and treatment effects over time (24). Similar associations were described by *Merkel et al.* when using the Goldenberg Risk Score (GRS) to determine the survival benefit of CRT-D versus CRT-P in non-ischemic HFrefEF patients. They found that low GRS patients showed significant long-term mortality benefit with CRT-D, whereas high-risk patients did not. These findings highlighted the importance of individual risk assessments (25).

Artificial-Intelligence-based tools (Topological Data Analysis) to identify phenogroups undergoing CRT procedures

A study by *Veres et al.* employed topological data analysis (TDA) to categorize patients within a cohort of 2603 undergoing CRT into phenogroups based on clinical features. This innovative approach aimed to discern which patients would derive greater benefit from CRT-D versus CRT-P. The study identified distinct phenogroups with varying survival benefits, showing TDA's potential to refine personalized treatment strategies for heart failure patients (26). Another paper investigated the TDA phenotyping of 326 patients undergoing CRT upgrade. The research identified phenogroups showing more favorable clinical outcome with CRTD treatment compared to CRT-P and developed a deep learning classifier able to characterize patients to predetermined phenogroups (27).

Use of Remote monitoring during COVID-19 pandemic

Nagy et al. discussed the management of patients with cardiac implantable electronic devices (CIEDs) through remote monitoring system during the COVID-19 pandemic. It highlights the effectiveness of telecardiology as a safe alternative to in-person visits, without significant changes in heart failure parameters. The study indicated no deterioration in patients' quality of life, although increased levels of anxiety and depression were reported. The research underscores the potential of remote monitoring in maintaining patient care and reducing infection risks during the pandemic (28).

Historical overview of ICD therapy

Rostás et al. provides a historical overview of the development and application of electrical defibrillation and cardioversion, detailing the evolution from early experiments on animals to the modern use of these life-saving techniques in clinical settings (29).

Transvenous Lead Extraction

Zsigmond et al. in their study compared the efficacy and safety of laser versus powered mechanical sheaths in transvenous lead extraction (TLE) procedures. They found that both types of sheaths have similar outcomes

in terms of procedural success and safety. However, in cases where a crossover from one type to the other was necessary, powered mechanical sheaths showed better performance in achieving clinical success. This suggests the importance of having a variety of tools available for complicated cases to improve outcomes (30). Moreover, they investigated long-term mortality following TLE in patients with CIEDs, focusing on a high-risk cohort. It highlighted the procedural success rates, complications, and the impact of reimplantation on patient survival. The findings described a favorable short- and long-term mortality rate post-TLE, emphasizing the importance of reassessing the need for CIED reimplantation to potentially avoid unnecessary procedures (31). *Sághy et al.* also published new investigations on TLE, which provided comprehensive insights into the procedures, patient demographics, indications for lead extraction, outcomes, and comparisons with international data. The study emphasizes the importance of advanced extraction techniques, the high success rate of TLE, and the critical role of experience and equipment availability in managing complex cases and achieving optimal outcomes (32).

Conclusion

As highlighted in the ongoing review, Hungarian researchers in 2023 collaborated on numerous significant scientific papers within the realms of clinical and invasive electrophysiology as well as arrhythmology. The review encapsulated a total of 32 international publications, accumulating a cumulative impact factor of 154,492, published across three D1, eighteen Q1, eight Q2, and three Q4 journals, as per the Scimago Journal Rank (refer to the Graphical abstract). Various contemporary topics such as AF and SVTs ablation, CRT, ICD, and transvenous lead extraction were addressed. These publications underscore the active, current, and globally esteemed scientific contributions of Hungarian researchers in the field of cardiac arrhythmias.

Declaration of interest

The authors has reported that they has no relationships relevant to the contents of this paper to disclose.

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