J Appl Biomed
DOI: 10.32725/jab.2023.007
journal homepage: http://jab.zsf.jcu.cz

Journal of Applied Biomedicine

Original research article

Sequential hybrid ablation versus surgical CryoMaze alone for treatment of atrial fibrillation (SurHyb Trial): a protocol of the multicentre randomized controlled trial

Alan Bulava [1] *, Aleš Mokráček [1], Dan Wichterle [2], Petr Budera [2], Pavel Osmančík [3], Petr Kačer [3], Linda Vetešková [4], Petr Němec [4], Tomáš Skála [5], Petr Šantavý [5], Jan Chovančík [6], Piotr Branny [6], Vitalii Rizov [7], Miroslav Kolesár [7], Marian Rybář [8]

[1] *University of South Bohemia in České Budějovice, Faculty of Health and Social Sciences; Cardiac Centre, České Budějovice Hospital, České Budějovice, Czech Republic*
[2] *Institute for Clinical and Experimental Medicine, Praha, Czech Republic*
[3] *Charles University and University Hospital Královské Vinohrady, 3rd Faculty of Medicine, Praha, Czech Republic*
[4] *Centre of Cardiovascular Surgery and Transplantation, Brno, Czech Republic*
[5] *Palacký University, Faculty of Medicine and Dentistry; University Hospital Olomouc, Olomouc, Czech Republic*
[6] *Hospital Agel Třinec-Podlesí, Třinec, Czech Republic*
[7] *Masaryk Hospital, Ústí nad Labem, Czech Republic*
[8] *Czech Technical University in Prague, Faculty of Biomedical Engineering, Department of Biomedical Technology, Kladno, Czech Republic*

Abstract
Background: Atrial fibrillation is common in patients with structural heart disease who are undergoing cardiac surgery. Surgical CryoMaze has been shown to be an effective treatment in several trials, but success rates have varied considerably, between 47–95%. The sequential hybrid approach, combining surgical CryoMaze followed by radiofrequency catheter ablation, can achieve high freedom from atrial arrhythmias. However, in patients with concomitant surgical atrial fibrillation treatment, data comparing the hybrid approach to CryoMaze alone are lacking.
Methods: The SurHyb study was designed as a prospective, open-label, multicentre randomized trial. Patients with non-paroxysmal atrial fibrillation who were scheduled for coronary artery bypass grafting or valve repair/replacement were randomized to either surgical CryoMaze alone or surgical CryoMaze followed by radiofrequency catheter ablation 3 months post-surgery. The primary outcome measure was arrhythmia-free survival without class I or III antiarrhythmic drugs, which has been evaluated using implantable cardiac monitors.
Conclusions: This is the first randomized study that compares concomitant surgical CryoMaze alone with the staged hybrid surgical CryoMaze followed by catheter ablation, in patients with non-paroxysmal atrial fibrillation using rigorous rhythm monitoring. The results may contribute to the optimization of the treatment in patients undergoing concomitant CryoMaze for atrial fibrillation.

Keywords: Atrial fibrillation; Catheter ablation; Cryomaze; Hybrid treatment

Highlights:
The publication of a detailed study protocol of the first randomized study comparing concomitant surgical CryoMaze alone with the staged hybrid surgical CryoMaze followed by catheter ablation, in patients with non-paroxysmal atrial fibrillation using rigorous rhythm monitoring. The results may contribute to the optimization of the treatment in patients undergoing concomitant CryoMaze for atrial fibrillation and may affect further guidelines.

Introduction

Atrial fibrillation (AF), the most common cardiac arrhythmia, is associated with increased mortality and morbidity (Kannel et al., 1998). In patients indicated for cardiac surgery, the prevalence of AF is higher compared to the general population (Banach et al., 2008), and it can be as high as 50% in individuals with mitral valve disease (Grigioni et al., 2002). Both surgical and catheter ablations have become recognized treatments for AF. Surgical ablation consists of a pre-defined set of lesions in both atria. The Cox MAZE IV procedure was developed as an alternative to the cut-and-sew procedure (Cox MAZE I) to decrease invasiveness. Currently, the procedure is performed

* **Corresponding author:** Alan Bulava, University of South Bohemia in České Budějovice, Faculty of Health and Social Sciences; Cardiac Centre, České Budějovice Hospital, České Budějovice, Czech Republic; e-mail: alanbulava@seznam.cz
http://doi.org/10.32725/jab.2023.007
Submitted: 2023-02-06 • Accepted: 2023-05-05 • Prepublished online: 2023-05-11
J Appl Biomed 21/x: xxx–xxx • EISSN 1214-0287 • ISSN 1214-021X

using cryothermal tissue destruction (CryoMaze) (Gammie et al., 2005). The CryoMaze procedure is usually done in conjunction (*i.e.*, concomitant ablation) with a coronary artery bypass grafting (CABG) or valve surgery.

The efficacy of the concomitant CryoMaze procedure as treatment for persistent AF has been shown in several studies, but the results were somewhat marginalized by small numbers of patients and far from optimum follow-up assessments of heart rhythm (often just telephone interviews with only occasional use of continuous electrocardiographic (ECG) recordings (Grigioni et al., 2002; Hanke et al., 2010). Inconsistency of ECG monitoring methods has led to discordant rates of "freedom from AF" that were reported between 47–95% (Gammie et al., 2009; Watkins et al., 2014). So far, no study assessing the effect of the CryoMaze procedure has used continuous ECG monitoring using an implantable cardiac monitor. Moreover, in contrast to endocardial catheter ablation using 3D mapping, the conduction block across the ablation lines after cryoenergy delivery during the surgical procedure is difficult to assess. Incomplete lines after CryoMaze have been proven as common and could be pro-arrhythmic (McElderry et al., 2008; Wazni et al., 2006). The lines can be mapped and completed using subsequent transvenous radiofrequency catheter ablation (RFCA). However, the effect of RFCA performed routinely on top of previous surgical procedures is unknown. In a non-randomized study in patients with non-paroxysmal AF, sequential surgical CryoMaze procedures followed by RFCA (*i.e.*, "hybrid" approach) led to excellent rhythm outcomes using stringent ECG monitoring (Eisenberger et al., 2015). However, randomized clinical trials comparing the hybrid approach to the CryoMaze procedure alone are lacking. Therefore, recommendations regarding the best treatment strategy for post-CryoMaze patients are not available.

We proposed a multicentre, prospective, open-label, parallel-group, randomized controlled trial, entitled "Sequential Hybrid Ablation versus Surgical CryoMaze Alone for the Treatment of Atrial Fibrillation" (*SURHYB*), aimed at comparing a staged hybrid approach consisting of surgical CryoMaze followed by RFCA, to surgical CryoMaze alone. The purpose of this article is to provide a comprehensive review of the study protocol.

Materials and methods

The main study hypothesis was that routinely performed RFCA, which maximizes completeness of the previous CryoMaze lesion set, will be associated with better sinus rhythm control and favourable clinical outcomes.

A flowchart of the SURHYB trial is shown in Fig. 1. Patients were recruited from seven major cardiovascular centres in the Czech Republic. Patients were approached during the clinical review before the surgery and were offered an opportunity to participate in the study.

The study protocol was reviewed and approved by the institutional ethics committees. The study has been conducted in accordance with the Helsinki Declaration of 1964 and its later amendments, and the Good Clinical Practice Guidelines. Written informed consent was obtained from all patients before the study. Participants could withdraw their consent to the trial at any time for any reason without their medical care being affected. The reason for withdrawal was documented whenever possible.

The study was investigator-initiated and supported by the research grant of the Agency for Medical Research of the Czech Republic (registration No NV19-02-00046). The regulations regarding medical confidentiality and data protection were fulfilled. The trial was registered in the Czech Clinical Trials Registry, cz-020420181253 (accessible at www.ablace.cz).

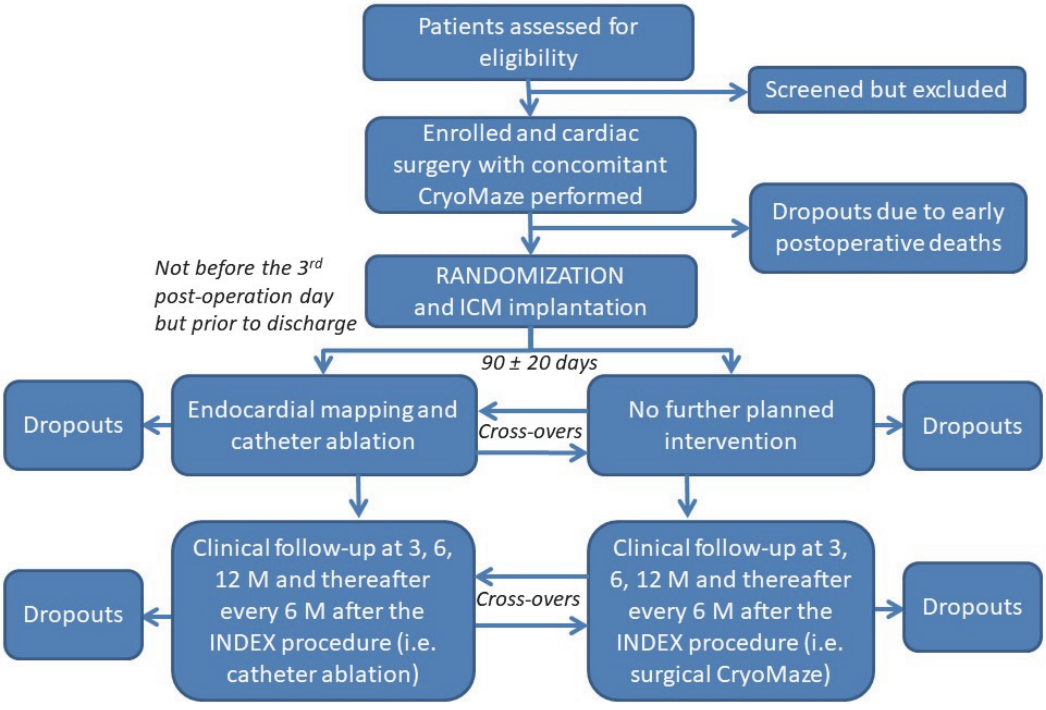

Fig. 1. SurHyb study flow chart. Randomization in a 1 : 1 ratio. *ICM – implantable cardiac monitor*

Enrolment criteria

Inclusion criteria

Patients with non-paroxysmal AF need to meet all criteria as follows:

- planned cardiac surgery (CABG or valve surgery, or a combination of both) with concomitant CryoMaze as a treatment for non-paroxysmal AF based on the 2018 definition (Calkins et al., 2018);
- documented AF using repetitive 12 lead ECGs or continuous long-term monitoring devices;
- age ≥18 years;
- ability to comply mentally/physically with all pre-, post-operative, and follow-up testing and requirements;
- willingness to sign the informed consent form.

Exclusion criteria were as follows:

- paroxysmal AF;
- previous surgical or catheter ablation for AF or atrial tachycardia (AT);
- AF secondary to a reversible or non-cardiac cause;
- left atrial (LA) diameter (in parasternal long axis view) >55 mm;
- chronic kidney disease (CKD Stage ≥4);
- estimated life expectancy <1 year;
- pregnancy or the possibility of pregnancy, or breastfeeding potential;
- contraindication to systemic anticoagulation;
- enrolment in a clinical study evaluating another device or drug.

Randomization

The screening was done before the surgery. However, the suitability of patients for the study was reassessed after cardiac surgery, and patients with unfavourable short-term prognosis were not ultimately offered participation. Dropout reasons (*e.g.*, significant change in health status, consent withdrawal, etc.) were recorded. Thus, the study was offered to patients with favourable prognosis, *i.e.*, surviving ≥3 days after the surgery. After providing informed consent, patients were randomly assigned to one of two groups, (i) *the hybrid group* or (ii) *the surgery group*, in a 1 : 1 ratio. Covariate-adaptive randomization was used to ensure the balance between treatment groups. The covariates included binary factor of the type of surgery (open/closed-heart) and the CHA_2DS_2-VASc score in three categories (i) 0–2, (ii) 3–5, and (iii) 6–9. The randomization was done using a web-based electronic system. Post-operative randomization ensured that the surgeons performing CryoMaze were unaware of treatment group allocation at the time of surgery.

Interventions

In the hybrid group (treatment group), patients received surgical CryoMaze followed by RFCA after 90 ± 20 days. In the surgical group (control group), participants received surgical CryoMaze only. RFCA in the hybrid group and CryoMaze in the surgery group were considered *index procedures*. During a 3-month blanking period following the index procedure, any treatment was allowed to maintain normal SR (*i.e.*, electrical or pharmacological cardioversion, antiarrhythmic drugs (AADs) initiation, or dose escalation), except repeated RFCA, unless an urgent clinical need arose. All Class I and III AADs were discontinued at the end of the blanking period (*i.e.*, 3 months after the index procedure).

Surgical ablation

The CryoMaze was performed as an adjunct to CABG, valve surgery, or a combination of both. It was done using the standard sternotomy approach, and each lesion was created using an application of cryoenergy at a fixed temperature depending on the system (argon-based or nitrous-oxide-based). The target temperature, duration of application, and location of each lesion were recorded. The freezing period for each lesion was at least 2 minutes.

The minimum CryoMaze procedure protocol consisted of circular lesions around the ipsilateral right and left pulmonary veins with linear lesions between the superior and inferior pulmonary veins to create a "box lesion", *i.e.*, isolation of the LA posterior wall. Pulmonary vein isolation and box lesion were carried out either endocardially or epicardially, depending on the type of concomitant surgery (*e.g.*, with or without opening of the left atrium) and the operator's preference. A mitral isthmus ablation line was created in all patients from the inferior connecting lesion towards the mitral annulus. In addition, the ligament of Marshall was cut off in all patients. The LA appendage was excluded in patients with a CHA_2DS_2-VASc score ≥2, preferably using the AtriClip® Left Atrial Appendage Exclusion System (AtriCure, USA). However, other techniques may have been also used. No other lines were allowed in the LA. In the right atrium (RA), additional cryolesions may have been created at the surgeon's discretion. Such lesions may have included but were not limited to superior vena cava isolation, intercaval lesion, and cavotricuspid isthmus lesion.

All patients who remained in AF after the surgical procedure underwent cardioversion before chest closure, and later, if the arrhythmia persisted, before implantable cardiac monitor (ICM) insertion. An ICM with telemonitoring capabilities and everyday ECG transmission (Biomonitor 2-AF and later Biomonitor III, Biotronik, Germany) was implanted before hospital discharge, but not earlier than the 3rd post-operative day. Telemonitoring function of the device was enabled, and the patient unit (Cardiomessenger) was distributed to all patients. If the patient refused ICM implantation, he/she was not excluded from the study, but 7-day Holters were serially performed at each clinical follow-up visit.

Catheter ablation

Patients randomized to the hybrid group were admitted for a staged RFCA 90 ± 20 days after the surgical procedure. The procedure was performed in conscious sedation and target activation clotting time of 300–350 seconds. Double transseptal puncture was done with the guidance of intracardiac echocardiography. Dense electroanatomical mapping of the left and right atria was performed using a CARTO3 navigation system and a Thermocool SmartTouch® ablation catheter (Biosense Webster, Inc., USA) to provide information about the location of the cryolesions (usually regions with low voltages, *i.e.*, <0.1 mV in sinus rhythm).

In patients coming in normal sinus rhythm, RFCA of the cavotricuspid isthmus in the RA was the first step. If the superior vena cava was isolated during surgery, electrical isolation was verified using a multi-electrode circular mapping catheter, and eventual gaps were eliminated. Then, pulmonary vein isolation was confirmed after a demonstration of both entry and exit blocks using a multi-electrode circular mapping catheter. If found incomplete, electrical isolation was finalized at the original surgical circular lesions. Completeness of all remaining linear lesions in the LA was confirmed by proving a bidirectional conduction block. Any identified gaps were ablated.

If the patient presented with AT (focal or re-entry) at the beginning of the catheter procedure, the arrhythmia was mapped and ablated as the first step. The same applied to all mappable ATs observed or subsequently induced during the procedure. In patients who present with AF, electrical cardioversion was performed at the beginning of the procedure to restore sinus rhythm. Then, the ablation protocol was performed as described above.

The inducibility of AF or AT was assessed at the end of the procedure. Burst atrial pacing, preferably from the coronary sinus, starting at 200 bpm with increments of 10 bpm up to 300 bpm or loss of 1 : 1 capture, was mandatory. Neither isoproterenol challenge nor adenosine testing was performed.

Follow-up

Patients were seen at outpatient clinics at 3, 6, 12, and thereafter every 6 months after the index procedure (CryoMaze in the surgical group and RFCA in the hybrid group). An extended (up to 5 years) follow-up is planned for the final assessment of clinical endpoints.

Clinical status, medication, blood pressure, 12-lead ECG, and any adverse events were documented during every visit. Unless necessary, all Class I and III AADs were discontinued at the 3-month visit, at the end of the blanking period. Medical records were reviewed at each visit to record the history of all changes in antiarrhythmic medication.

A transthoracic echocardiography was performed at baseline and at the 12-month follow-up visit. LA size was determined using the long-axis parasternal view and the apical 4-chamber view. Changes in quality of life (QoL) were also assessed using both the generic instrument – EuroQOL/EQ-5D, the last-updated questionnaire version of the EuroQOL working group, and the disease-specific instrument – the Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) comparing the patients' status between baseline and the 12-month visit.

The absence or presence of atrial tachyarrhythmias on ICM recordings was assessed at regular intervals in a central core lab for all enrolled patients. Cardiologists who were experienced in Holter tracings reading were blinded to the randomized assignment of the study participants. Total AF burden, longest AF/AT episode, and maximal and average heart rate during episodes of arrhythmias were also recorded.

The trial was initiated in May 2019 and the recruitment was completed on March 31, 2022, with a final enrolment of 236 subjects. It is anticipated that the trial's primary results will be available in December 2023.

Study objectives

Primary endpoints

(1) Time to the first recurrence of AF/AT lasting >6 minutes during the post-blanking follow-up period starting 3 months after the index procedure, or failure to discontinue Class I or III AADs at the beginning of the post-blanking period. Death from any cause will be considered a competing event.
(2) The composite of two competing events: cardiovascular death or hospitalization for any of the following events: arrhythmia recurrence, worsening of heart failure, cardioembolic event, or significant bleeding, as the clinical study endpoint.

Secondary endpoints

(1) The first recurrence of on-AADs AF/AT lasting >6 minutes during the post-blanking follow-up period (*i.e.*, disregarding all off-AAD episodes).
(2) Arrhythmia burden irrespective of AADs (i) within the first year following the index procedure and (ii) throughout the entire duration of the study.
(3) Number of hospitalizations and/or emergency out-patient visits related to AF/AT recurrence, worsening of heart failure or to other cardiovascular diseases.
(4) Number of electrical cardioversions.
(5) Proportion of patients on AADs at the end of follow-up.
(6) RFCA-related complications.

Other endpoints

(1) Description of predilection sites of electrical reconnections (gaps) of surgical circumferential or linear lesions.
(2) Comparison of efficacy (continuity) of endocardial vs. epicardial surgical cryolesions.
(3) Comparison of efficacy (continuity) of argon-based vs. nitrous-oxide-based cryolesions.
(4) Change in LA dimensions and left ventricular function between baseline and the 12-month visit.
(5) Change in N-terminal of the pro-brain natriuretic peptide levels between baseline and the 12-month visit.
(6) Change in quality of life between baseline and the 12-month visit.

Statistical methods and sample size consideration

The primary hypothesis was that the hybrid approach will be superior to surgical ablation only. In our previous non-randomized study on concomitant CryoMaze complemented by an electrophysiological study and RFCA, we found the AF/AT recurrence rate to be 14% after one year, based on 7 consecutive days of ECG Holter monitoring (Eisenberger et al., 2015). Before catheter ablation (2–3 months after the CryoMaze procedure), any AT/AF (paroxysmal or persistent) was documented in 54% of patients. Therefore, using the more rigorous ICM-based follow-up, we hypothesised that the actual arrhythmia recurrence rate might be as high as 30% in the hybrid arm (worst-case scenario), and is very likely to be at least 50% in the surgical arm (optimistic scenario). Hence, for statistical power analysis, we set the off-AAD arrhythmia recurrence rate (primary endpoint) after the hybrid vs. surgical ablation procedure to be 30% vs. 50%, respectively. To ensure 90% power of the study to detect the difference between both arms at the 5% significance level (one-sided Z-test), a total of 101 patients had to be analysed in each arm of the trial. With a predicted dropout rate of 10%, the trial was designed with an enrolment target of 222 patients.

Outcome measures will be compared between the randomized groups according to the principle of "intention-to-treat". Additionally, per protocol analysis will also be performed. Cause-specific cumulative incidence functions as a function of follow-up time for the primary (AF/AT recurrence) as well as for the composite clinical endpoint in the presence of competing risk (all-cause death, or non-cardiovascular death, as appropriate) will be shown for the two trial groups (Putter et al., 2007). Additionally, hazard ratios (HR) with associated 95% confidence intervals and Wald tests of the treatment group effect, all derived from the Fine-Gray subdistribution hazard model (Austin and Fine, 2017; Fine and Gray, 1999) will be calculated. Further, a multivariable Fine-Gray model will be fitted for each outcome measure while including the treatment group among the covariates and adjusting for the effect of gender, age, surgery type, and LA size. Interactions between treatment allocations and those additional patient baseline characteristics will be assessed. P-values < 0.05 will be considered statistically significant. Analyses will be performed using the R software (R Core Team, 2022).

Data management and safety monitoring

A dedicated electronic web-based case report form was used to collect all relevant data during the screening, enrolment/randomization, treatment, and follow-up periods. A core lab for ECG tracing evaluation consisting of cardiologists experienced in Holter readings was established. A central adjudication committee was also established to ascertain the cardiovascular nature of recorded deaths.

A Data and Safety Monitoring Board (DSMB) was constituted. The interim efficacy and safety analysis was performed at least once per year. Serious adverse events (SAE) were defined as life-threatening events, or events resulting in death or hospitalization. All SAE linked with the study were reported within 24 hours of investigators becoming aware of the event. SAE forms were completed with detailed information, such as event description, date of onset and resolution, severity, and action taken. DSMB was empowered to suggest termination of the trial at any time based on the appearance of SAEs, or if one of the study groups appeared to have superior outcomes in terms of clinical endpoints.

Significance of the trial

Recommendations regarding the best treatment strategy for patients undergoing CryoMaze are currently unavailable. This randomized controlled trial is the first of its kind in which hybrid ablations are compared with surgical CryoMaze alone concerning (1) freedom from atrial tachyarrhythmias and (2) overall clinical outcomes. Hybrid ablations can potentially overcome the limitations associated with both surgical and transvenous endocardial ablations alone. However, neither of the approaches alone can guarantee transmurality of the created lesions, which is crucial in controlling arrhythmia – particularly in the setting of non-paroxysmal AF. It is also possible to ablate all ATs after surgical ablation, which would otherwise be left untreated. By using rigorous ICM follow-up and composite clinical endpoints, our study may have the power to influence future guidelines on AF management, specifically addressing the adjunctive effect of RFCA after concomitant CryoMaze procedures.

Success rates for CryoMaze procedures have been reported to be as high as 95% at 12 months. However, follow-ups were "lenient", and in some studies were only conducted through telephone interviews (Gammie et al., 2005). When more accurate methods were used to determine heart rhythm, success rates fell to 76% or even 47% (Gammie et al., 2009; Watkins et al., 2014). Thus, our SURHYB study using ICM will, for the first time, allow specific insight into the success of standardized CryoMaze procedures alone (*i.e.*, the surgery group), and may also allow a comparison of the efficacy of epicardial and endocardial cryolesions in a human setting (*i.e.*, the hybrid group).

Numerous studies on simultaneous or sequential hybrid procedures have reported success rates from 83–94%, but the experience has only been with bipolar or monopolar radiofrequency energy (Bulava et al., 2015; Gehi et al., 2013; Osmancik et al., 2016; Pison et al., 2012). On the contrary, the only two so far published reports on hybrid ablations used cryoenergy during the surgical part of the procedure, and revealed overall freedom from atrial tachyarrhythmias to be 86% at 12 months (Eisenberger et al., 2015) or 73% after 10-year follow-up (Gaita et al., 2013). Both studies were small and observational (35 and 33 patients, respectively) and both studies revealed a considerable proportion of incomplete lesion scheme after CryoMaze. In the study of Gaita et al. (2013), the accomplishment of the planned lesion scheme led to significantly higher preservation of normal sinus rhythm when compared to patients in whom RFCA was unable to complete the lesion set (81% vs. 43%, $P = 0.048$). As far as we know, there are no other ongoing randomized trials using cryoenergy for the surgical part of the hybrid procedure.

Conclusions

This is the first randomized study that compares concomitant surgical CryoMaze alone with the staged hybrid surgical CryoMaze followed by catheter ablation in patients with non-paroxysmal atrial fibrillation using rigorous rhythm monitoring. The results may contribute to the optimization of the treatment in patients undergoing concomitant CryoMaze for atrial fibrillation.

Trial registration

Czech Clinical Trials Registry, cz-020420181253. Registered on 2nd April 2018.

Funding

The study was supported by the Ministry of Health of the Czech Republic, grant nr. NV19-02-00046.

Ethical aspects and conflict of interests

The authors have no conflict of interests to declare.

References

Austin PC, Fine JP (2017). Practical recommendations for reporting Fine-Gray model analyses for competing risk data. Stat Med 36(27): 4391–4400. DOI: 10.1002/sim.7501.

Banach M, Mariscalco G, Ugurlucan M, Mikhailidis DP, Barylski M, Rysz J (2008). The significance of preoperative atrial fibrillation in patients undergoing cardiac surgery: preoperative atrial fibrillation – still underestimated opponent. Europace 10(11): 1266–1270. DOI: 10.1093/europace/eun273.

Bulava A, Mokracek A, Hanis J, Kurfirst V, Eisenberger M, Pesl L (2015). Sequential Hybrid Procedure for Persistent Atrial Fibrillation. J Am Heart Assoc 4(3): e001754. DOI: 10.1161/jaha.114.001754.

Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al. (2018). 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation. EP Europace 20(1): e1–e160. DOI: 10.1093/europace/eux274.

Eisenberger M, Bulava A, Mokracek A, Hanis J, Kurfirst V, Dusek L (2015). Sequential Hybrid Surgical CryoMaze and Transvenous Catheter Ablation of Atrial Fibrillation. Pacing Clin Electrophysiol 38(12): 1379–1385. DOI: 10.1111/pace.12686.

Fine JP, Gray RJ (1999). A Proportional Hazards Model for the Subdistribution of a Competing Risk. J Am Stat Assoc 94(446): 496–509. DOI: 10.1080/01621459.1999.10474144.

Gaita F, Ebrille E, Scaglione M, Caponi D, Garberoglio L, Vivalda L, et al. (2013). Very Long-Term Results of Surgical and Transcatheter Ablation of Long-Standing Persistent Atrial Fibrillation. Ann Thorac Surg 96(4): 1273–1278. DOI: 10.1016/j.athoracsur.2013.05.054.

Gammie JS, Didolkar P, Krowsoski LS, Santos MJ, Toran AJ, Young CA, et al. (2009). Intermediate-term Outcomes of Surgical Atrial Fibrillation Correction with the CryoMaze Procedure. Ann Thorac Surg 87(5): 1452–1459. DOI: 10.1016/j.athoracsur.2009.02.008.

Gammie JS, Laschinger JC, Brown JM, Poston RS, Pierson RN, Romar LG, et al. (2005). A Multi-Institutional Experience With

the CryoMaze Procedure. Ann Thorac Surg 80(3): 876–880. DOI: 10.1016/j.athoracsur.2005.03.075.

Gehi AK, Mounsey JP, Pursell I, Landers M, Boyce K, Chung EH, et al. (2013). Hybrid epicardial-endocardial ablation using a pericardioscopic technique for the treatment of atrial fibrillation. Heart Rhythm 10(1): 22–28. DOI: 10.1016/j.hrthm.2012.08.044.

Grigioni F, Avierinos J-F, Ling LH, Scott CG, Bailey KR, Tajik AJ, et al. (2002). Atrial fibrillation complicating the course of degenerative mitral regurgitation Determinants and long-term outcome. J Am Coll Cardiol 40(1): 84–92. DOI: 10.1016/s0735-1097(02)01922-8.

Hanke T, Charitos EI, Stierle U, Sievers H-H, Misfeld M (2010). Intermediate Outcome of Surgical Atrial Fibrillation Correction With the CryoMaze Procedure. Ann Thorac Surg 89(1): 340–341. DOI: 10.1016/j.athoracsur.2009.08.023.

Kannel WB, Wolf PA, Benjamin EJ, Levy D (1998). Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol 82(8A): 2N–9N. DOI: 10.1016/s0002-9149(98)00583-9.

McElderry HT, Mcgiffin DC, Plumb VJ, Nanthakumar K, Epstein AE, Yamada T, Kay GN (2008). Proarrhythmic Aspects of Atrial Fibrillation Surgery. Circulation 117(2): 155–162. DOI: 10.1161/circulationaha.107.688358.

Osmancik P, Budera P, Zdarska J, Herman D, Petr R, Straka Z (2016). Electrophysiological findings after surgical thoracoscopic atrial fibrillation ablation. Heart Rhythm 13(6): 1246–1252. DOI: 10.1016/j.hrthm.2016.02.007.

Pison L, La Meir M, van Opstal J, Blaauw Y, Maessen J, Crijns HJ (2012). Hybrid Thoracoscopic Surgical and Transvenous Catheter Ablation of Atrial Fibrillation. J Am Coll Cardiol 60(1): 54–61. DOI: 10.1016/j.jacc.2011.12.055.

Putter H, Fiocco M, Geskus RB (2007). Tutorial in biostatistics: competing risks and multi-state models. Stat Med 26: 2389–2430. DOI: 10.1002/sim.2712.

R Core Team (2022). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. [online] [cit. 2023-01-22]. Available from: https://www.R-project.org

Watkins AC, Young CA, Ghoreishi M, Shorofsky SR, Gabre J, Dawood MY, et al. (2014). Prospective Assessment of the CryoMaze Procedure With Continuous Outpatient Telemetry in 136 Patients. Ann Thorac Surg 97(4): 1191–1198. DOI: 10.1016/j.athoracsur.2013.10.041.

Wazni OM, Saliba W, Fahmy T, Lakkireddy D, Thal S, Kanj M, et al. (2006). Atrial Arrhythmias After Surgical Maze Findings During Catheter Ablation. J Am Coll Cardiol 48(7): 1405–1409. DOI: 10.1016/j.jacc.2006.05.061.