

Attila Benak ORCID iD: 0000-0002-6143-8933

Péter Kupó ORCID iD: 0000-0002-9422-4245

Róbert Pap ORCID iD: 0000-0002-7009-5063

## Is prophylactic ablation of the cavotricuspid and peri-incisional isthmus justified in patients with postoperative atrial flutter after right atriotomy?

Attila BENAK MD<sup>1</sup>, Peter KUPO MD, PhD<sup>1</sup>, Gabor BENCSIK MD, PhD<sup>1</sup>, Attila MAKAI MD, PhD<sup>1</sup>, Laszlo Saghy MD, PhD<sup>1</sup>, Robert PAP MD, PhD<sup>1</sup>

<sup>1</sup> 2nd Department of Internal Medicine and Cardiology Centre, University of Szeged, Szeged, Hungary

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Address for correspondence:

Robert PAP, MD, PhD

2nd Department of Internal Medicine and Cardiology Centre, University of Szeged

H-6725, Szeged, Semmelweis u. 8.

Tel.: +36-62-341-559, Fax: +36-62-342-538

Email: pap.paprobert@gmail.com

### Abstract

**Background:** The two most common postoperative atrial flutter (AFL) circuits after right atriotomy are the cavotricuspid isthmus (CTI) dependent and the lateral, peri-incisional. We

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investigated whether radiofrequency ablation (RFA) of both circuits results in more favorable long-term outcomes.

**Methods:** Single-center retrospective cohort study of consecutive patients who underwent RFA of AFL after open-heart surgery. The effect of surgery type and RFA strategy on AFL recurrence was evaluated.

**Results:** One hundred and forty-two patients (mean age  $64.5 \pm 12.7$  years, 65% male) were enrolled. Patients with right atrial (RA) flutter (n=124) were divided into two groups based on the index RFA procedure: only one RA circuit was ablated (**Group 1**, n= 84, 67.7%) or both the CTI and the peri-incisional circuit ablated (**Group 2**, n= 40, 32.3%). The previous open-heart surgery was categorized based on the extension of the RA incision: limited (**Type A**) or extended (**Type B**) atriotomy. After a mean follow-up of  $36 \pm 28$  months, flutter recurrence was not different among patients with limited RA atriotomy (25% vs. 22% in Group 1A and 2A, respectively,  $p=1.0$ ). However, after type B surgery, ablation of both AFL circuits was associated with a reduced recurrence rate (63% vs. 26% in Group 1B and 2B, respectively,  $p=0.002$ ).

**Conclusions:** In patients with postoperative RA flutter after extended right atriotomy, ablation of both the CTI and the peri-incisional isthmus significantly reduces the AFL recurrence rate. Prophylactic ablation of both isthmi, even if not proven to support reentry, is reasonable in this population.

**Keywords:** atrial flutter, radiofrequency ablation, open-heart surgery, atriotomy

## Introduction

Open heart surgery frequently involves incising the right atrial (RA) free wall. The atriotomy scar creates the substrate for both cavotricuspid isthmus (CTI) dependent and peri-incisional atrial flutter (AFL). When these patients undergo catheter ablation, AFLs ongoing at the commencement or inducible during the course of the electrophysiologic (EP) study are targeted. However, recurrences are common with this strategy, due to the development of a previously unmapped AFL circuit in up to 25-50% of patients during follow-up<sup>[1, 2]</sup>. Commonly occurring AFL circuits related to RA atriotomy are limited to two types: CTI dependent and RA peri-incisional AFL<sup>[3]</sup>. Recurrent flutter after targeting one of the two circuits likely utilizes the other unablated circuit. The aim of this study was to test if addressing both circuits by ablation, compared to only one of them, leads to fewer recurrences and to thereby estimate the possible impact of prophylactic ablation in those cases when only one or neither AFL is encountered during the index procedure.

## Methods

### Study population

Between January 2010 and December 2018, 142 patients were included in the analysis, which was designed as a single-center retrospective cohort study. Patients with documented, clinical AFL after previous open-heart surgery involving a RA incision, who underwent their first electrophysiology study and catheter ablation during this period were included. Recent heart surgery (less than 3 months) and complex congenital heart disease requiring more than a single atriotomy (eg. atrial switch operation) were exclusion criteria. Patients who underwent at least one RA flutter ablation during the study were divided into two groups: either a CTI dependent *or* a peri-incisional RA flutter was ablated in **Group 1**, while both CTI dependent *and* peri-incisional flutter ablations were performed in **Group 2**. The two groups were compared in clinical characteristics and arrhythmia-free survival. *Figure 1* demonstrates the flowchart of the study population. The study was approved by the institutional review board and it was conducted in accordance with the Declaration of Helsinki.

### Previous heart surgery

Patients were also grouped according to the specific RA incision applied during open heart surgery (Supplemental figure). In 56 patients (39.4 %), limited right atriotomy (**Type A** procedure) was created for cardiopulmonary bypass during coronary artery bypass graft surgery (CABG; n=37, 26%), aortic valve replacement (AVR; n=13, 9.1%), CABG plus AVR (n=2, 1.4%) or Bentall procedure (n=4, 2.8%). Eighty-six patients had extended RA incision (**Type B** procedure) in case of mitral valve repair/replacement through a transeptal approach (n=59, 40.6%), tricuspid valve repair/replacement (n=2, 1.4 %), atrial or ventricular septal defect surgery (n=14, 9.6%), a combination of the aforementioned (n=4, 2.8%) or other types of surgery, such as excision of atrial myxoma (n=2, 1.4%), correction of Fallot tetralogy (n=1, 0.7%), cor triatriatum (n=1, 0.7%), pulmonary vein transposition (n=1, 0.7%), pulmonary valvuloplasty (n=1, 0.7%) and Glenn procedure (n=1, 0.7%).

### Electrophysiology procedure

The electrophysiology procedures were done under conscious sedation using midazolam and/or fentanyl. Diagnostic catheters were introduced via the right and/or left femoral veins in the majority of the cases. In some patients, internal jugular or subclavian veins were also used for catheter entrance. Catheters were positioned into the coronary sinus, right ventricle, and right atrium with fluoroscopy and (if available) intracardiac echocardiography (ICE) guidance. ICE was used in most of the cases for continuous monitoring of complications and catheter locations.

If the patient presented in sinus rhythm, programmed atrial stimulation (with up to 3 extrastimuli and two drive cycle lengths, without isoproterenol) was performed for arrhythmia induction. Alternatively, if the ECG documentation of the clinical arrhythmia was characteristic for typical flutter (counterclockwise CTI dependent AFL) empirical ablation of the CTI was performed in sinus rhythm. This latter approach is based on the high specificity of the typical ECG for CTI dependent flutter and congruent with guideline recommendation to consider CTI ablation after an episode of typical AFL.<sup>[4-6]</sup> Noninducible patients with atypical AFL ECG documentation were not ablated and not included in this study. No empirical ablation was performed outside the CTI.

All RA flutters - whether spontaneous or induced - were mapped and targeted by the previously described approach<sup>[3]</sup>. Briefly, entrainment pacing was performed first at the CTI. If CTI dependent flutter was diagnosed, linear radiofrequency (RF) ablation was created between the tricuspid annulus and the inferior vena cava (IVC) using an irrigated catheter in power controlled (30-40W) mode. When the AFL terminated and bidirectional CTI block was achieved induction was attempted by programmed stimulation to reveal further atrial arrhythmias. For non-CTI dependent flutter activation mapping with an electroanatomic (EA) mapping system (CARTO 3, Biosense Webster, Diamond Bar, CA, USA) and/or entrainment mapping was used to delineate the arrhythmia circuit. In case of peri-incisional RA flutter, linear RF ablation was performed between the atriotomy scar and an anatomic barrier such as the IVC, superior vena cava (SVC), or tricuspid annulus (TA). Sites of reconnection along the atriotomy line were also targeted by RF ablation. **Figure 2** illustrates the 3D EA image of the RA and the ablation lesion sets after CTId and peri-incisional flutter ablation. The end point of the procedure included arrhythmia termination and non-inducibility, combined with conduction block along linear lesions demonstrated by pacing close to the line and observing an activation detour by mapping on the opposite side. Bidirectional conduction block across the linear CTI lesion was checked by pacing from both sides of the line.

### Follow-up

After the electrophysiology procedure, patients had follow-up at 3 months and 12 months in our institution. Thereafter, follow-up was continued in our outpatient clinic or in the referring hospital depending on the patients' preferences. 12-lead ECG was performed during every follow-up and hospitalization. Event recorder, 24 hours, 72 hours, or 1-week Holter monitoring was used based on the patients' complaints. Patients with implantable electronic devices and an atrial lead had continuous monitoring of atrial high rate episodes. If a flutter recurrence was documented, a redo procedure was recommended based on the clinical scenario. Repeated procedures were performed in the same manner as the index procedures. For the survival analysis, if the previously ablated flutter recurred, follow-up time

was counted from the redo procedure. In case of atrial fibrillation during the follow-up, a rhythm or rate control strategy was implemented, considering the symptoms, demographic and echocardiographic data. Patients who had not completed the 3 months follow-up were excluded from the survival analysis.

### Statistical analysis

IBM SPSS Statistics 26 was used for statistical analysis. Continuous variables are indicated as mean  $\pm$  SD, and categorical variables are expressed in percentage form. The difference between the two groups was tested by the chi-square test in case of categorical variables and Student's t-test was used for the continuous variables. We used the Cox proportional hazards regression model to estimate hazard ratios (HR) and 95% confidence intervals (CI) for new RA flutter recurrence in the two groups. The time to recurrence during the follow-up period was tested by the Kaplan-Meier curve with the log-rank analysis. Logistic regression was utilized to determine the predictor factors of peri-incisional flutter occurrence after CTId flutter ablation.  $p < 0.05$  was considered statistically significant.

## Results

### Baseline characteristics

There was no difference between the two groups in terms of age, gender, LA diameter, and prevalence of comorbidities except diabetes mellitus, which was significantly more frequent in Group 1. Time between the surgery and the flutter occurrence, prior cardioversion attempt, and antiarrhythmic drug usage were comparable between the groups. Clinical characteristics in detail are summarized in *Table 1*.

### Index procedure

In the study period 142 patients with previous open-heart surgery involving RA atriotomy underwent their first catheter ablation for AFL. During the index procedure, 124 (87.3%) patients had at least one RA flutter ablated, 18 (12.7%) had only LA flutter. Of the 124 patients with RA ablation, 79 (63.7%) had only the CTI ablated and 5 (4%) had only the RA peri-incisional flutter ablated during the index procedure (Group 1). Forty patients (32.2%) had both RA circuits ablated (Group 2). In 14 patients with documented typical atrial flutter CTI RF ablation was performed in SR and arrhythmia induction was implemented afterwards. Of those patients who had both RA AFLs during the index procedure, the majority (75%) presented with CTId AFL, and the peri-incisional AFL occurred after CTI ablation. Thirty out of 110 (27.3%) patients who underwent an initial CTI ablation had spontaneous or induced peri-incisional flutter afterward. On the other hand, 10 out of 14 (71%) patients had subsequent CTId flutter after ablation of the initial peri-incisional circuit. In patients with

peri-incisional AFL the ablation line was created mostly between the atriotomy scar and the IVC (31/45, 69%), while in some cases the SVC (4/45, 9%) or the tricuspid annulus (1/45, 2.2%) was utilized as an electrical barrier. Sites of reconnection were ablated focally within the atriotomy scar in 4 patients (9%) and extended ablation (IVC+SVC) was needed in 5 cases (11%). The ablation end point was achieved in all RA flutter cases except one, where creating complete bidirectional CTI block was not possible despite extensive ablation.

### Follow-up and redo procedures

Six patients (3 patients each from Group 1 and 2) were lost to follow-up, the remaining 118 were followed for  $36\pm 28$  months. During follow-up, 47/118 (39.8 %) experienced flutter recurrence, 37 of them underwent a redo procedure. During redo 29 patients had RA flutter, 7 had LA flutter and one had both. Out of the 30 patients with RA flutter at redo: 5 had CTId, 24 peri-incisional AFL and 1 patient both. In 22 of 30 (73%) patients recurrence of a previously not treated RA flutter (2 CTId, 20 peri-incisional) was documented during redo, while the rest had reconduction in a circuit ablated during the index procedure.

### Outcome according to flutter circuits ablated at the index procedure

Of the 118 patients with follow-up 81 (68.6%) had only one RA flutter ablated during the index procedure (Group 1), 37 (31.4%) had both CTId and peri-incisional flutter ablated (Group 2). During follow up 37/81 (46%) in Group 1 and 10/37 (27%) in Group 2 had flutter recurrence ( $p=0.049$ ).

### Effect of surgery type

Overall, the frequency of CTId flutter at the index or repeat procedures was not different according to atriotomy type, but a peri-incisional flutter was more common after Type B surgery (**Table 2**). Furthermore, in patients with initial CTId flutter ( $n=113$ ), only the surgery type was a significant predictor (OR: 3.4, CI: 1.3-8.7) for subsequent peri-incisional flutter occurrence in a multivariate regression analysis (including age, gender, ejection fraction and surgery type).

In patients with type A surgery, the rate of flutter recurrence was not different between those that had only one flutter circuit vs. both CTI and peri-incisional circuits ablated during the index procedure (25% vs. 22% in Group 1A and 2A, respectively,  $p=1.0$ ). However, in patients with type B surgery the recurrence rate was 63% in Group 1B (one circuit ablated), compared to 26% in Group 2B (both circuits ablated) ( $p=0.002$ ). **Figure 3**. The number needed to treat (NNT) by ablation of both circuits to prevent one flutter recurrence after type B surgery was 2.7. Therefore, both RA circuits being ablated at the index procedure had a

substantial impact on recurrence in surgical group B and accounted for all of the differences observed in the total population of postoperative flutter patients.

### Atrial flutter after type B surgery

In **Group 1B** 39/42 patients had CTId and 3/42 had only peri-incisional flutter ablated at the index procedure. After CTI RF ablation, the majority of flutter recurrences (15/24, 62.5 %) were peri-incisional, while peri-mitral and other LA (unmapped) flutter occurred in 20.8% and 16.6%, respectively. One CTId, 1 peri-mitral, and 1 unmapped LA flutter was observed in 2 patients after initial peri-incisional flutter ablation.

In contrast in **Group 2B**, no new RA flutter was diagnosed during redo. Five patients suffered a recurrence of a previously ablated flutter (3 incisional, 1 CTId, 1 both), and 2 patients had LA flutter (1 peri-mitral, 1 unmapped).

### Emergence of a new RA flutter during follow-up in Group B

To quantify the relative importance of inadequate ablation technique versus novel arrhythmogenesis in determining flutter recurrence, we also analyzed the occurrence of a new RA flutter separately from that due to reinduction in a previously targeted circuit. Accordingly, we performed a survival analysis in surgical group B (**Figure 4**), where survival time was counted from the redo procedure in those that had only a previously ablated RA circuit reablated at redo. After  $1.3 \pm 0.5$  procedures targeting one (Group 1B) or both (Group 2B) RA circuits, survival free of new RA or unmapped flutter (LA flutters excluded, patient censored if permanent AF developed or end of follow up,) was  $59.7 \pm 6.5$  vs.  $108.5 \pm 6.5$  months, respectively ( $p < 0.001$ ).

## Discussion

The following can be concluded from the results of this study:

1. Patients with postoperative RA flutter after right atriotomy who have both the CTI and the peri-incisional circuit ablated during the index procedure experience less recurrence compared to those who have only one of the circuits ablated (27% vs. 46%).
2. This difference however only presents in those postoperative patients who had an extended RA free wall incision (Type B procedure).
3. In patients with RA flutter after Type B atriotomy, based on a NNT of 2.7, prophylactic ablation of both RA circuits (CTI and peri-incisional) is reasonable

When only spontaneously occurring and induced AFLs are targeted during catheter ablation of postoperative atrial flutter recurrence rate remains high despite modern technology, related to multiple possible AFL circuits<sup>[1, 2]</sup>. Common wisdom and previous experience with scar-related AFLs suggest that the more flutter circuits are encountered during the index procedure, the more likely recurrence would occur<sup>[7]</sup>. However we found the opposite situation in patients after extended RA atriotomy: when both CTI dependent and peri-incisional AFL presented during the index procedure and were targeted by ablation, better outcome ensued, compared to when only one of them was encountered. The surgical incision on the RA free wall not only acts as a central obstacle during peri-incisional reentry, but also promotes the development of CTI dependent AFL<sup>[8]</sup>. This explains why both flutter circuits are prevalent after extended RA atriotomy. The CTI dependent AFL is the most common macroreentrant arrhythmia after open heart surgery, followed by peri-incisional reentry in patients after RA atriotomy. Other types of RA tachycardias are uncommon in this population<sup>[3]</sup>. We have shown previously that the distribution of different AFL circuits depends upon the surgical technique, with a longer RA incision associated with a higher percentage of peri-incisional reentry<sup>[3]</sup>. In line with these results, we have observed a higher risk for the development of a new RA flutter after ablation of one circuit in patients with extended (Type B) vs. limited (Type A) RA atriotomy (63% vs. 25%, respectively). The patients after a Type B procedure who underwent ablation of both the CTI and the peri-incisional isthmus during the index procedure experienced a markedly increased success rate compared to those who only had one circuit targeted (74% vs. 47%, respectively). Therefore, in patients presenting with RA flutter with such an arrhythmogenic, long RA incision (Type B procedure) ablation of both AFL circuits (CTI dependent and peri-incisional) prophylactically will likely decrease the otherwise high recurrence rate.

Similar results have been published in a special type of post-surgical AFL population who had cannulation of the coronary sinus for retrograde cardioplegia<sup>[9]</sup>. After coronary artery bypass grafting using this technique the rate of postoperative AFL was reported to be increased, likely associated with both the incision and crush injury from clamping on the RA free wall<sup>[10]</sup>. The use of this technique is relatively limited<sup>[11]</sup> and was not represented in our population of patients.

### Limitation

This was a single center, observational study. Only future prospective, randomized trials can definitively establish the strategy of prophylactic ablation of both RA circuits in postoperative flutter patients.



## Conclusion

In patients with postoperative RA flutter after extended right atriotomy (Type B procedure) linear ablation of both the CTI and the isthmus between the RA incisional scar and the IVC is justified regardless of whether macroreentry is documented in these circuits, after considering individual patient characteristics. Prophylactic ablation of both RA circuits will likely decrease recurrences in this population.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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**Table 1.** Clinical characteristics

	<b>Group 1</b> (n=84)	<b>Group2</b> (n=40)	p value
Age	64.9 ± 13	61.2 ± 11.7	0.122
Sex (% , male)	67.9	65	0.750

Hypertension (%)	90.5	80	0.104
<b>Diabetes mellitus (%)</b>	<b>32.1</b>	<b>12.5</b>	<b>0.019</b>
Ischaemic heart disease (%)	46.4	35	0.229
COPD (%)	10.7	5	0.295
CKD (%)	3.6	0	0.226
LA diameter (mm)	50.5 ± 6.4	49.9 ± 6.2	0.776
Time since surgery (years, median)	9	8	0.713
AAD use (%)*	10.3	17.5	0.259
Prior cardioversion (%)	16.1	20	0.589

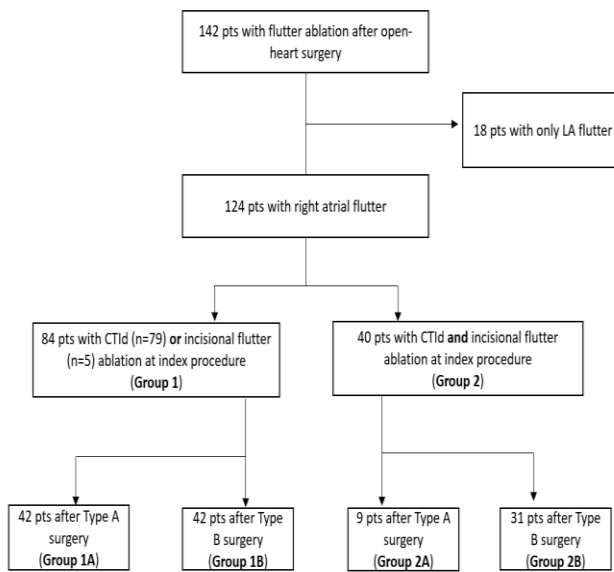
AAD= antiarrhythmic drug, CKD= chronic kidney disease, COPD= chronic obstructive pulmonary disease, LA = left atrium

\*at the time of the index procedure

**Table 2.** Cumulative incidence of cavotricusid isthmus dependent (CTId) and peri-incisional flutter in the study population at the index and the redo procedure(s).

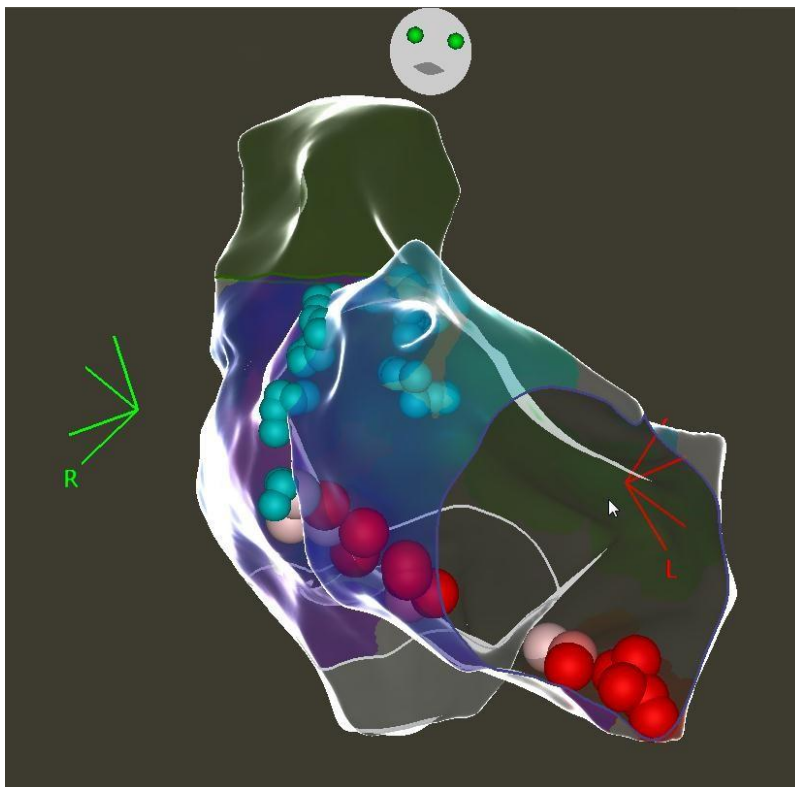
	<b>Type A (n=51)</b>	<b>Type B (n=73)</b>	<b>p value</b>
<b>Index procedure</b>			
<i>CTId</i>	49 (96.1%)	70 (95.9%)	0.96
<i>Peri-incisional</i>	11 (21.6%)	34 (46.6%)	0.04
<b>Redo procedure(s)</b>			
<i>CTId</i>	50 (98%)	71 (97.3%)	0.077
<i>Peri-incisional</i>	16 (31.4%)	49 (67.1%)	< 0.001

**Figure 1.** Flowchart of the patient population

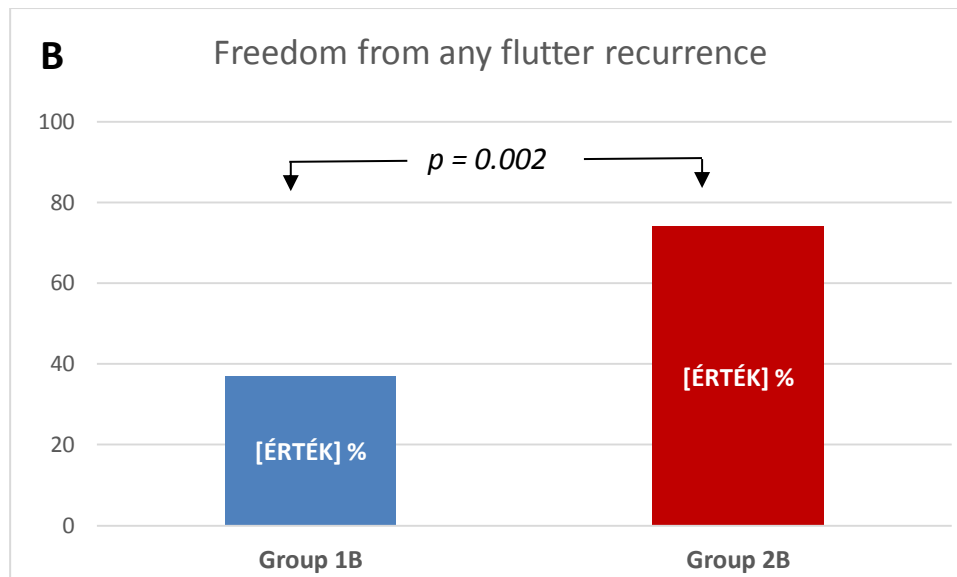
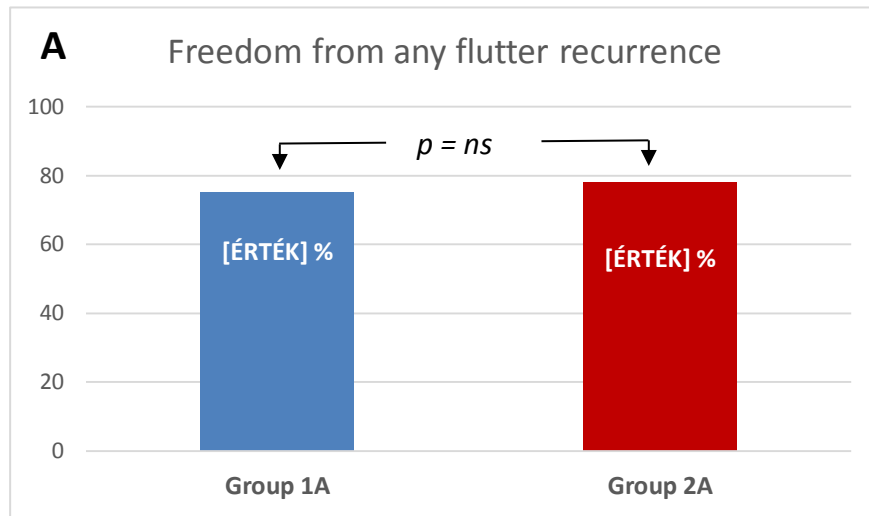


**Figure 2.** Three-dimensional electroanatomic map of the right atrium in a patient with previous MVR through a transeptal surgical approach. Blue dots mark sites where double potentials were recorded along the atriotomy line extending from the lateral wall anteriorly and onto the septum. After the RF ablation (red dots) of the ongoing CTId flutter, peri-incisional flutter was induced and successfully terminated with a lesion set between the atriotomy scar and the IVC.

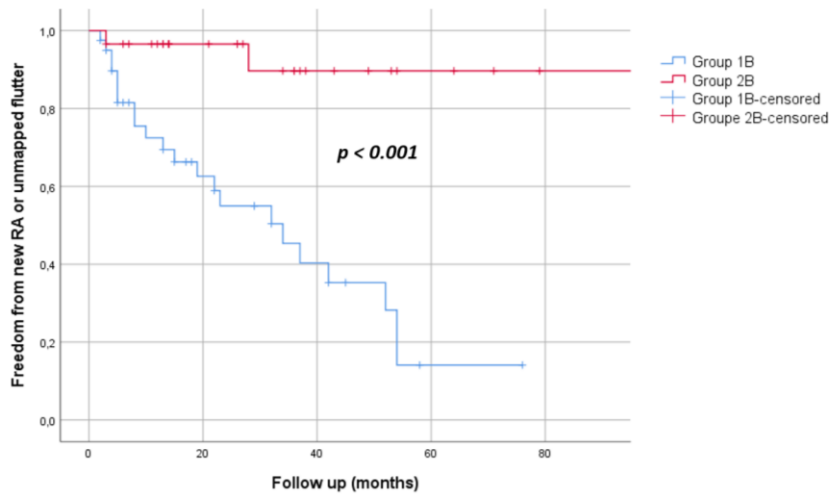
CTId= cavotricuspid isthmus dependent, IVC=inferior vena cava, MVR=mitral valve replacement



**Figure 3.** Freedom from any flutter recurrence in patents after Type A and Type B surgery after the index procedure



**Figure 4.** Kaplan-Meier curve for new RA or unknown flutter in patients after type B surgery.



**Patients at risk**

Group 1B	40	17	8	1	0
Group 2B	29	18	8	4	1