Evaluation of Factors Correlating with the Outcome of Atrial Tachycardia and Atrial Fibrillation Ablation

Ph.D. thesis

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Introduction

Cardiac arrhythmias encompass a large and heterogeneous group of electrical abnormalities of the heart. Antiarrhythmic drugs were the only therapeutic options until the late 1960s. Nowadays, we are able to manage even the most complex atrial and ventricular arrhythmias with the help of invasive electrophysiology and catheter ablation.

Supraventricular tachycardia (SVT) indicates a tachycardia involving tissue from the His bundle or above; thus, it might originate from the atrial musculature, atrioventricular (AV) node, His bundle, or it can use an accessory pathway as the arrhythmia substrate.

The prevalence of the SVT-s is 2.25 / 1 000 persons. In specialized centers that perform catheter ablations, atrial fibrillation (AF) is the most frequently treated arrhythmia, followed by AV-nodal reentrant tachycardia, atrial flutter, atrioventricular reentrant tachycardia and focal atrial tachycardia (FAT).

With the development of invasive electrophysiology, single-channel evaluation of intracardiac electrograms have given way to simultaneous multichannel mapping, resulting in a more detailed temporal and spatial characterization of specific arrhythmias. It has thereby become more challenging to keep track of an increasing number of channels of electrograms and analyze them within the context of their particular anatomic locations. This limitation has provided the incentive for the development of computer-based electroanatomical mapping systems. The two most commonly used systems are CARTO (Biosense Webster, Inc., Diamond Bar, CA, USA) and EnSite (St. Jude Medical, Inc., MN, USA).

The most effective way of arrhythmia treatment nowadays is catheter ablation; however, the success rate varies widely in case of different arrhythmias. The purpose of ablation is to destroy myocardial tissue by delivery of energy through electrodes on a catheter placed at the area of the arrhythmogenic substrate. Ablation by radiofrequency- (RF) or cryo-energy are important curative treatment modalities for cardiac arrhythmias. Other energy types, such as laser, ultrasound, microwave-based ablation, and stereotactic irradiation approaches, did not become part of the everyday practice.

FAT indicates an organized atrial rhythm ≥100 b.p.m. originating from a discrete ectopic point of the left or right atrium and spreading over both atria in a centrifugal pattern. Antiarrhythmic drugs are usually less effective in FAT; thus, catheter ablation is the recommended treatment choice in symptomatic cases. Catheter ablation is reported to have a variable (75 - 100%) success rate. A significant amount of data is available regarding the outcome of FAT ablation with both conventional mapping and electroanatomical mapping. However, no other working groups compared these two mapping strategies apart from ours so far.

AF is the most common sustained cardiac arrhythmia. It is one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world. Complex management of patients with AF includes treatment of underlying diseases, lifestyle changes, stroke prevention with therapeutic anticoagulation, and rate and/or rhythm control. Catheter ablation is the most effective way for the rhythm control treatment. However, repeated ablation procedures are often necessary to achieve an optimal result. The nature of AF ablation procedures exposes patients to a considerable number of potential complications, which can range between 1% and 8%. The most common adverse events are pericardial effusion and vascular access site complications. However, less frequent adverse events also need attention as they might be life-threatening or may cause severe long-term disability or death, such as stroke or transient ischemic attack (TIA), atrio-esophageal fistula, phrenic nerve palsy or pulmonary vein stenosis. The relatively high number of complications drives a continuous quest for a more effective and safer ablation approach. Recent studies evaluated many potential predictors of complications arising from AF ablation procedures. However, most of these publications are restricted to initial AF ablation procedures, and limited data exist regarding the role of a repeated catheter ablation procedure.

Objectives

Our aim was the examination of factors that may influence the outcome of catheter ablation of complex atrial arrhythmias, namely FAT and AF.

1. Evaluation of the additional value of the CARTO electroanatomical mapping system over conventional fluoroscopy based mapping method in terms of guiding catheter ablation of FAT-s. We sought to evaluate the following procedural parameters: procedure time, fluoroscopy time, acute and 6-month success rate, and complication rate.

2. Evaluation of the predictors that may propose the patient to a higher probability of adverse events related to AF ablation.

Methods

Study protocols were reviewed and approved by the institutional review boards and were in accordance with the declarations of Helsinki.

Patient populations

Our retrospective study of FAT ablation procedures evaluated all consecutive patients who underwent catheter ablation for FAT in two Hungarian cardiology centers: Cardiology Institute of University of Debrecen, Hungary (between 2006 and 2011), and Cardiology Department of Military Hospital, State Health Center, Budapest, Hungary (between 2009 and 2011).

Our prospective registry of AF ablation procedures aimed to describe the incidence and characteristics of all minor and major complications related to AF ablation in the electrophysiology laboratory of the Heart and Vascular Center, Semmelweis University, Budapest, Hungary. All AF ablation procedures between January 2013 and December 2015 were included.

Electrophysiological study and ablation

The protocol of FAT ablation

Antiarrhythmic drugs were ceased for a minimum of five half-lives before the procedure. The electrophysiological study was performed using quadripolar and decapolar catheters positioned in the high right atrium, His bundle region, right ventricular apex, and in the coronary sinus. The arrhythmia was induced by programmed atrial extrastimuli, burst atrial pacing and/or administration of isoprenaline. Mapping of the atrial tachycardia was performed during ongoing atrial tachycardia using the already inserted diagnostic catheters or with the ablation catheter according to the operating physician's preference. The aim of the mapping was to localize the earliest endocardial potential preceding the onset of the surface P-wave. All cases were considered as "conventional" procedures in our analysis, where the electroanatomical mapping system was not used. Additionally or alternatively, an electroanatomical mapping system (CARTO XP V9.6 system and Navistar catheter family, Biosense Webster, Inc., Diamond Bar, CA, USA) was selected by the operating physician based on individual decision. Radiofrequency ablation was performed at the site of the earliest atrial activation with 4 mm tip catheter (temperature-controlled mode, 20-30 Watt).

The protocol of AF ablation

In the case of patients who were anticoagulated with vitamin K antagonists, the ablation procedure was performed if the INR value was between 1.8 and 3.5. Conscious sedation was carried out in all cases with intravenous fentanyl, midazolam, and propofol. The basic vital parameters of the patients were monitored in all cases with non-invasive blood pressure measurements every 10 minutes and continuous pulse oximetry. Pre-procedural left atrial computed tomography (CT), or magnetic resonance (MR) angiography was obtained to evaluate the anatomy of the pulmonary veins. Immediately before the ablation procedure, the presence of a left atrial appendage thrombus was excluded with transesophageal echocardiography or intracardiac echocardiography (ICE).

Femoral venous access was used for all procedures. Transseptal puncture was performed under fluoroscopy guidance and pressure monitoring. Whenever there was difficulty to perform a safe transseptal puncture ICE was used for direct visualization of the interatrial septum. Unfractionated heparin was administered immediately after entering the left atrium (50-120 units per kilogram i.v. bolus depending on pre-procedural anticoagulation strategy), and it was titrated every 20-30 minutes throughout the whole procedure based on activated clotting time (ACT) measurements (target ACT level was > 300 sec). Ablations were performed with the help of an electroanatomical mapping system (either CARTO, Biosense Webster, Inc., Diamond Bar, CA, USA; or EnSite, St. Jude Medical, Inc., MN, USA) to guide ablation (temperature-controlled mode, 43 °C, 25–35 Watt, irrigated 4 mm tip catheter) in the overwhelming majority of cases. In a limited number of cases, we used nMARQ catheter (Biosense Webster, Irwindale, CA, USA) or cryoballoon (Arctic Front Advance, Medtronic, Minneapolis, MN, USA). Pulmonary vein isolation was the goal of each initial procedure. In cases of repeat ablation for persistent AF or ablation for long-standing persistent AF, additional lines might have been drawn on the discretion of the operating physician.

Transthoracic echocardiography was performed right after the procedure and on the next morning to detect pericardial effusion. All patients who developed neurological symptoms were immediately transferred to the hospital's radiology unit to perform brain CT or MR scan. Whenever there was any sign of vascular access complication, an ultrasound was performed to rule out major complications. All patients without complications were discharged the day after the procedure.

Follow-up of the patients

Outpatient clinical follow-up visits were scheduled at six months after FAT ablation and 3, 6, and 12 months and once yearly after that in case of AF ablation. The follow-up visits included clinical assessment of the patient, 24-hour Holter ECG monitoring, and we explored whether patients have had any adverse events since the last visit, and those events were also included in the analysis. In the case of shortness of breath, a chest X-ray was performed to rule out phrenic nerve palsy, and if it was negative, a cardiac CT angiography was performed to detect potential pulmonary vein stenosis.

Definitions

Success definition of FAT ablation

Acute success was defined as the absence and non-inducibility of the arrhythmia 30 minutes after the last radiofrequency application. The ablation procedure was considered unsuccessful if tachycardia remained inducible.

6-month success was defined as no recurrence of FAT episodes without any antiarrhythmic drug. Partial (clinical) success was defined as asymptomatic tachycardia recurrences on 24-hour Holter monitoring or ECG recordings, or cases when symptoms improved but some shorter tachycardia episodes were still present (with or without antiarrhythmic drug therapy), or those cases when the absence of AT episodes was reached with the use of antiarrhythmic drugs (e.g., propafenone, sotalol, amiodarone). Failure was defined as the persistence of symptoms either with or without antiarrhythmic drug therapy.

Definition of minor and major complications of AF ablation

All complications related to AF ablation were analyzed, including cardiac tamponade, pericardial effusion, stroke or TIA, pulmonary vein stenosis, vascular access complications, phrenic nerve palsy, AV-block, atrio-esophageal fistula, and procedure-related death. A major adverse event was defined in our analysis as a complication that required interventional treatment. Therefore, pericardial effusion (> 5 mm was included in the study) and groin hematoma without the need for invasive treatment were considered as a minor complication.

Statistical analysis

Continuous variables showing parametric distribution according to the Shapiro-Wilk normality test are expressed as mean ± standard deviation (SD), while

continuous variables showing non-parametric distribution are reported as median with interquartile ranges. Categorical variables are expressed as event numbers and percentages. Fisher's exact test and Mann–Whitney U test was performed for examining contingency between selected groups. Chi-square for trend test was used for a 6-month success analysis of FAT ablations. To determine predictors of complications related to AF ablation procedure, multivariate analysis, logistic regression was conducted. A two-tailed P-value <0.05 was considered significant. Statistical analysis was performed with GraphPad Prism, version 6.01 (GraphPad Software, Inc., La Jolla, CA, USA) and IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA) software.

Results

Ablation of FAT with and without CARTO electroanatomical mapping system

Our study assessed 60 procedures (6 repeated ablations) of 54 consecutive patients (39 females, age 54 ± 17 years). We registered hypertension in 21 cases, diabetes mellitus in 9 cases, five patients had COPD, ten patients had ischemic heart disease, and five patients underwent heart surgery earlier. Antiarrhythmic drugs were used in 20 and 16 cases for conventional and CARTO-groups, respectively. Baseline parameters did not differ between the two patient populations.

The localization of ectopic foci is shown in Figure 1. The right- or left-sided origin of one septal focus could not be determined. There was no significant difference regarding the localization of ectopic foci between the two compared groups.

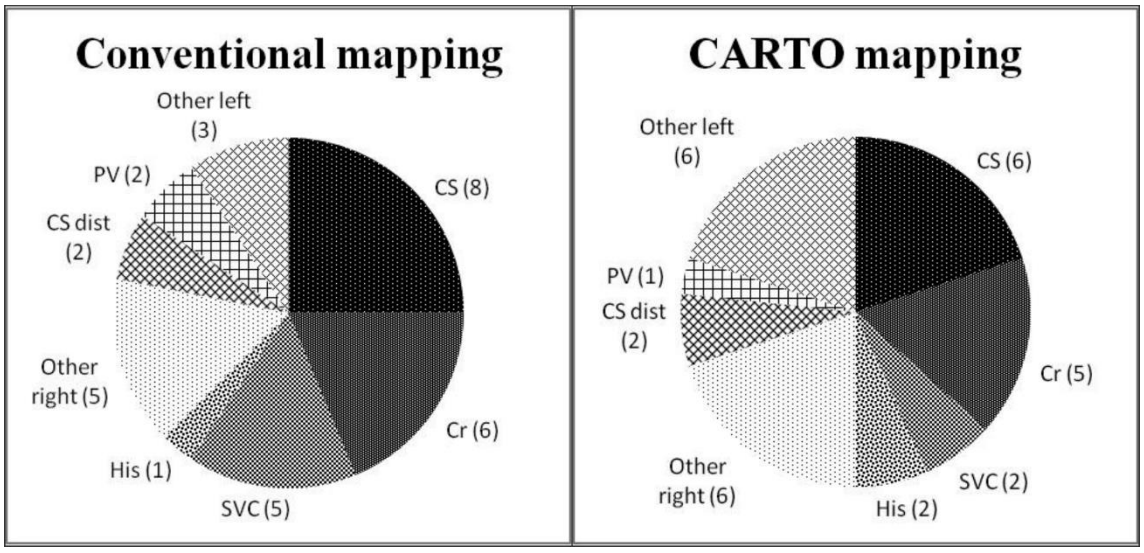

Figure 1. Localization of ectopic foci in case of conventional mapping and CARTO mapping procedures. Absolute numbers of ectopic foci are shown in parenthesis. Abbreviations: CS= coronary sinus, Cr= crista terminalis, SVC= superior vena cava, His= para-Hisian, CS dist= distal coronary sinus, PV= pulmonary vein. Other right and other left categories mean septal, tricuspid annulus, inferior vena cava, mitral annulus, anterosuperior and lateral wall.

<u>The outcome of FAT ablations</u>

Out of the 60 ablation procedures, 30 were mapped with conventional methods only, whereas in another 30 cases CARTO electroanatomical mapping system was used, as well. The acute success rate (Figure 2.) was significantly higher in procedures where CARTO mapping was used (27/30 vs. 18/30, $p < 0.01$). No

statistically significant difference was found between different operating physicians and between irrigated and non-irrigated ablation catheters. There was no significant difference between procedure time (139±59 vs. 96±44 min, p: ns) and fluoroscopy time (18±12 vs. 11±6 min, p: ns). No procedure-related complications occurred.

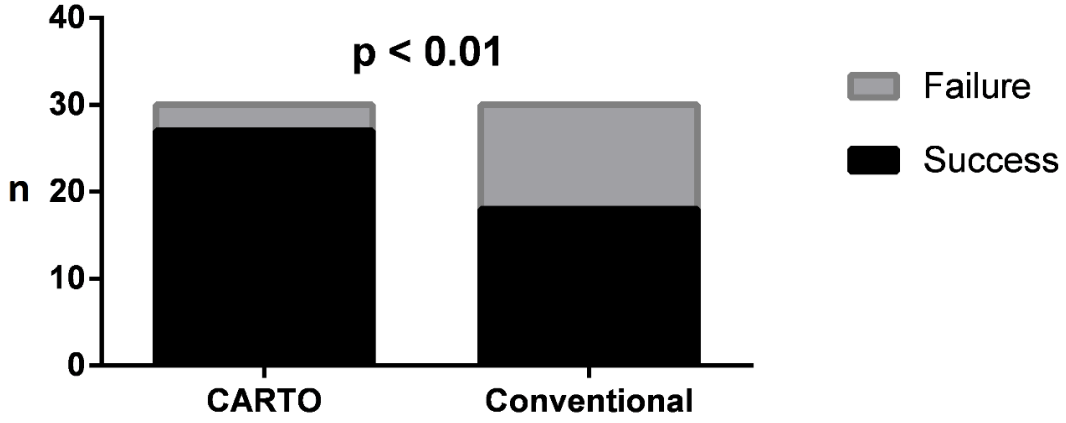

Figure 2. The acute success rate of FAT ablation procedures in the case of CARTO mapping and conventional fluoroscopy-based mapping.
Abbreviation: n= number of cases.

The 6-month follow-up data were available in 56 cases. Success, partial success, and failure occurred in 11 vs. 4, 12 vs. 18, and 4 vs. 7 cases in CARTO enhanced vs. conventionally mapped procedures, respectively (p = 0.045).

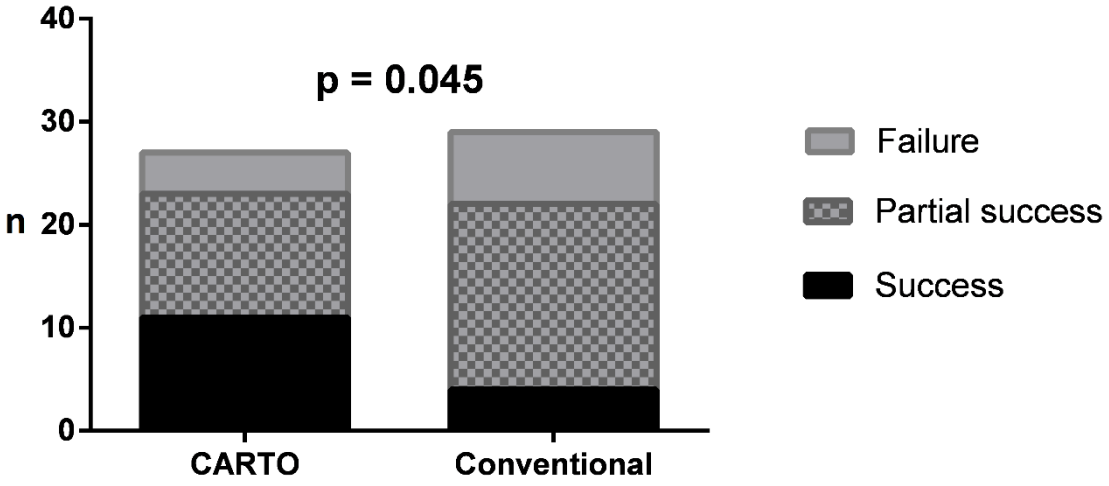

Figure 3. The six-month success rate of FAT ablation procedures in case of CARTO mapping and conventional fluoroscopy-based mapping.
Abbreviation: n= number of cases.

Evaluation of predictors of complications associated with AF ablation

Overall, 1243 AF ablation procedures were analyzed, the median age was 62 years (55-69 years), 32% were females, and 32% had persistent AF. Hypertension was present in 70% of the patients, while diabetes mellitus, coronary artery disease, and prior stroke occurred in 16%, 11%, and 6%, respectively. Median left ventricular ejection fraction was 57% (55-60%). Previous AF ablation was performed in 18% of the cases.

Vitamin K antagonist was used in 69% and direct oral anticoagulant in 30% of the cases. Antiarrhythmic drug therapy was amiodarone in 8%, propafenone in 2%, and sotalol in 2% of the patients.

The majority of ablations (95%) were performed with the radiofrequency point-by-point method, while nMARQ catheter was used in 2% and cryoballoon in 3% of the cases. ICE catheter was inserted in 13% of the procedures to rule out intracardiac thrombus and / or to assist the transseptal puncture. Additional ablation lines were drawn in 23% of the procedures.

Incidence of complications

Most complications occurred during the same hospitalization when the ablation was performed. Certainly, pulmonary vein stenoses were diagnosed only during the follow-up of the patients; and there was one case of a late pericardial effusion diagnosed on the 15th postprocedural day. The incidence of overall and major complications in the case of de novo and repeat procedures are shown in Table 1.

Type of complication	Number of complications of de novo ablations (total n= 1022)	Number of complications of repeat procedures (total n=221)	Summary (total n= 1243)
Major complications	18	17	35 (2.82%)
Pericardial tamponade	8	10	18 (1.45%)
Stroke / transient ischemic attack	5	1	6 (0.48%)
Pseudoaneurysm of femoral artery	4	1	5 (0.40%)
Pulmonary vein stenosis	0	3	3 (0.24%)
III. degree atrio-ventricular block	0	2	2 (0.16%)
Arteriovenous fistula	1	0	1 (0.08%)
Phrenic nerve palsy	0	0	0
Atrio-esophageal fistula	0	0	0
Procedure-related death	0	0	0
Minor complications	33	17	50 (4.02%)
Pericardial effusion	17	11	28 (2.25%)
Groin hematoma	16	6	22 (1.77%)
Overall complications	51	34	85 (6.84%)

Table 1. Distribution of complications associated to initial (de novo) and repeated AF ablation procedures.

Predictors of complications

We analyzed patients' baseline characteristics and procedural characteristics to evaluate the predictors of complications. Univariate analysis for overall complications showed that age≥65 years (p=0.0231), female gender (p=0.0438), hypertension (p=0.0488), CHA_2DS_2-VASc score≥2 (p=0.0156) and previous AF ablation procedure (p<0.0001) was associated with a higher risk for adverse events. Multivariate analysis for overall complications showed that the only independent predictor of overall complications was previous AF ablation procedure (OR 3.13; 95% CI 1.95-5.03; p<0.0001). A similar analysis was performed to determine the predictors of major complications. According to our results, the only independent predictor of major complications was the previous AF ablation procedure (OR 3.65; 95% CI 1.84-7.24; p<0.0001). The results of the multivariate analysis are shown in Table 2.

Examined parameter	**P-value**	**OR (95% CI)**
Overall complications		
Female	0.3550	1.25 (0.78-2.00)
Hypertension	0.1060	1.59 (0.91-2.81)
Age ≥ 65 years	0.0900	1.50 (0.94-2.40)
Previous AF ablation	< **0.0001**	**3.13 (1.95-5.03)**
Major complications		
Previous AF ablation	< **0.0001**	**3.65 (1.84-7.24)**

Table 2. Multivariate analysis for predictors of adverse events associated with AF ablation procedures.
Abbreviations: AF= atrial fibrillation, CI= confidence interval, OR= odds ratio.

Conclusions

Our retrospective analysis showed that the CARTO electroanatomical mapping system is safe and effective in guiding catheter ablation of FAT-s. Success rates were higher in the case of CARTO-enhanced procedures compared to procedures guided by conventional fluoroscopy-based mapping.

AF is the most common sustained cardiac arrhythmia. Our analysis revealed that the rate of complications for AF ablation in our Electrophysiology Laboratory is within the previously reported range. The only independent predictor of complications was the previous AF ablation procedure in our series.

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Clinical effectiveness of primary prevention implantable cardioverter-defibrillators: results of the EU-CERT-ICD controlled multicentre cohort study

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