Kardiologia Polska 2013; 71, 3: 247–252; DOI: 10.5603/KP.2013.0036 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Evaluation of factors affecting persistence of atrial fibrillation in patients with concomitant atrial flutter treated with percutaneous radiofrequency current ablation of the right atrial cavotricuspid isthmus

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Abstract

Background: Atrial fibrillation (AF) and atrial flutter (AFL) often coexist. In some patients, AF remission is seen after successful percutaneous radiofrequency current ablation of the cavotricuspid isthmus (CTI).

Aim: To evaluate factors affecting AF remission in patients with typical AFL and concomitant AF who underwent CTI ablation.

Methods: The study included consecutive 69 patients with typical AFL and concomitant clinically documented AF who underwent successful CTI ablation in 2003–2010. Based on the follow-up data from medical records and telephone interviews, the patients were divided into two groups: with persistent AF (group A) and with remission of AF (group B). This distinction was based on arrhythmia symptoms reported by the patient, such as palpitation or irregular heartbeat, and confirmed electrocardiographically (12-lead ECG or Holter monitoring).

Results: Group A included 47 patients, and group B included 22 patients. The two groups did not differ significantly in regard to the New York Heart Association (NYHA) functional class and concomitant diseases including diabetes, ischaemic heart disease, previous myocardial infarction and arterial hypertension. The two groups also did not differ by echocardiographically determined mean left ventricular ejection fraction (LVEF) and left atrial dimension (43.5 ± 9.27 vs. 39.27 ± 5.76, p = 0.075). Multivariate logistic regression did not identify any independent risk factors of AF persistence after CTI ablation. Univariate logistic regression also did not show arterial hypertension, type 2 diabetes, previous myocardial infarction, LVEF, left ventricular dimension or age to affect AF persistence after successful ablation.

Conclusions: Based on the results of our study, we were unable to identify factors determining remission of AF coexisting with AFL in patients after percutaneous CTI ablation. These findings may indicate the need for complex ablation procedure (involving both CTI and pulmonary venous ostia ablation) in patients in whom these two arrhythmias coexist.

Key words: atrial fibrillation, atrial flutter, radiofrequency current ablation

Kardiol Pol 2013; 71, 3: 247–252

INTRODUCTION

Atrial fibrillation (AF) and atrial flutter (AFL) are two types of supraventricular tachyarrhythmia that often coexist. It has been estimated that AF is also present in about 60% of patients with AFL. In addition, AFL is seen in about 25–35% of patients with AF. Coexistence of AF and AFL leads to faster ventricular rate

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Received: 03.10.2011 **Accepted:** 31.10.2011

during arrhythmia and more frequently results in the development of tachyarrhythmic cardiomyopathy [1]. Waldo et al. [2] showed that both AF and AFL may be manifestations of the same electrical heart disease. Studies confirmed AF remission after successful cavotricuspid isthmus (CTI) ablation in patients with concomitant AF and AFL. Others reported persistence of AF after successful ablation of AFL [3–5]. Indications for ablation in patients with concomitant AF and AFL have not been clearly defined yet [6].

The purpose of the study was to evaluate effects of successful CTI ablation and determine factors affecting AF remission in patients with typical AFL and concomitant AF.

METHODS

This was a retrospective study based on the analysis of medical records and telephone interviews. The study population was divided into two groups: group A with persistent AF after CTI ablation, and group B with remission of AF.

Study population

The study included 69 consecutive patients with clinically documented typical AFL and concomitant AF. The inclusion criterion was the presence of typical AFL and AF in conventional electrocardiogram (ECG) and/or Holter monitoring.

Clinically predominant arrhythmia was AFL. In all patients included into the study, an invasive electrophysiological study with concomitant successful radiofrequency catheter ablation (RFCA) of the CTI was done. The procedures were performed in 2003–2010. Mean patient age was 57.5 years (range 23–78 years, standard deviation ± 14), and the study group included 66% men and 34% women. Ultimately, patients were included into the group A when medical records (outpatient, in-hospital, or obtained from other centres) indicated persistence of arrhythmia in the available ECG recordings.

In all patients, left ventricular ejection fraction (LVEF) and left atrial dimension were determined echocardiographically. Left atrial dimension was determined in a parasternal view as this measure could be obtained from the available medical records.

Electrophysiological study and ablation

In all patients invasive electrophysiological study and RFCA of the CTI was performed using the anatomical method after obtaining a written informed consent. Nine procedures were performed using the classical approach, 32 procedures with the use of the CARTO electroanatomic system (Biosense Webster, Inc.), and 28 procedures with the of the LocaLisa system (Medtronic, Inc.). The choice of the method was left to the discretion of the operator. Two leads were used during the procedure, a 10-polar catheter (which was placed in the coronary sinus) or a Halo catheter (which was placed along the tricuspid annulus), and an ablation catheter. Procedural endpoint was defined as obtaining bidirectional conduction block through the CTI and inability to induce AFL with continuous pacing at the cycle length of 300 ms, 250 ms, and the AFL cycle length. In group A, mean procedure duration was 101.86 ± 45.17 (range 35–210) min, exposure time was 14.3 ± 11.57 (range 1–43.4) min, and the absorbed radiation dose was 261.83 ± 309.06 (range 15–1782) mGy. In group B, these values were 103.81 ± 50.69 (40–240) min, 16.15 ± 12.79 (2.43–49) min, and 204.63 ± 176.02 (20–717) mGy. Postprocedural anticoagulation was used according to the current guidelines. All patients received antiarrhythmic drug therapy after the procedure. An ECG was recorded on the discharge day in all patients.

Follow-up

Mean duration of follow-up was 1013 ± 271.529 days. The first outpatient visit was within 1 month after the procedure, and next visits were at 3 and 6 months. The schedule of the following visits was determined by the treating physician depending on the clinical status of the patient. During telephone interviews in 2009–2010, patients were asked about the name and the surname, the date of the procedure, whether the patient is able to differentiate between AF and AFL (based on the regularity of palpitations felt), and whether any of these arrhythmias persisted. If the answer was positive, the patient was asked how frequent AF episodes were and whether they were confirmed by a physician. Patients were also questioned whether arrhythmias were accompanied by symptoms, what their severity was after the procedure, whether hospital admissions were necessary after the ablation (when and for what reason), what their concomitant diseases and current medications were, and whether they underwent pacemaker, implanted cardioverter-defibrillator or cardiac resynchronisation therapy device implantation. Among symptoms suggesting arrhythmia recurrence indicating the need for a 24-hour Holter ECG monitoring at an outpatient follow-up visit, we considered palpitation (with regular or irregular heartbeat), fatigue, decreased exercise tolerance, syncope, and dizziness. Arrhythmia confirmed in standard ECG, Holter monitoring or printouts of the events recorded by the implanted devices was taken as the evidence of AF persistence during the follow-up.

Statistical analysis

Statistical analyses were performed using the Statistica Version 6 software (StatSoft, Inc.). We used the Student *t* test for unpaired samples, k-ratio test for differences between proportions, and nonparametric tests. Multivariate analysis was performed using a logistic regression model. $P \leq 0.05$ was considered statistically significant.

RESULTS

Group A included 47 (68% of the study group) patients with AF persisting after the ablation, and group B included 22 (32%) patients with AF remission. Both groups were relatively similar in terms of demographic parameters (Table 1)

Table 1. Comparison of demographic data in groups A and B

Parameter	Group A	Group B	P
Age [years]	56.36 ± 13.88 (23–78)	58.82 ± 14.92 (27–78)	NS
Height [cm]	171.26 ± 8.16 (156–191)	170.05 ± 6.9 (153–182)	NS
Body mass [kg]	82.21 ± 15.45 (54–120)	78.74 ± 17.24 (49–115)	NS
Male gender	32 (68%)	14 (64%)	NS

Mean values ± SD and ranges (in parentheses) or patient numbers and percentages (in parentheses) are given.

Table 2. Comparison of concomitant diseases and selected echocardiographic parameters in groups A and B

Condition/parameter	Group A	Group B	P
Arterial hypertension	19 (41%)	8 (36%)	NS
Ischaemic heart disease	16 (36%)	5 (23%)	NS
Myocardial infarction	7 (16%)	5 (23%)	NS
Ischemic stroke/transient ischaemic attack	3 (6%)	1 (4.5%)	NS
Diabetes	5 (11%)	3 (14%)	NS
Left ventricular ejection fraction [%]	47.62 ± 11.07	47.92 ± 13.16	NS
Left atrial dimension in a parasternal view [mm]	43.5 ± 9.27	39.27 ± 5.76	NS

Mean values ± SD and ranges (in parentheses) or patient numbers and percentages (in parentheses) are given.

Table 3. Comparison of the risk of thromboembolic events as estimated using the CHADS2 in groups A and B

CHADS2 score (points)	Group A	Group B	P
0	11 (23%)	6 (27.2%)	NS
1	12 (25.5%)	5 (22.7%)	NS
2	19 (40%)	7 (31.8%)	NS
3	4 (8.5%)	3 (13.6%)	NS
4	1 (2.1%)	1 (4.5%)	NS
5	0	0	
6	0	0	

Patient numbers and percentages (in parentheses) are given; CHADS2 — congestive heart failure, hypertension, age, diabetes, stroke (doubled)

and concomitant diseases such as type 2 diabetes, arterial hypertension, and previous myocardial infarction, stroke, or transient ischaemic attack (Table 2). Ischaemic heart disease was insignificantly more common in Group A compared to Group B (36 vs. 23%). Selected echocardiographic parameters also did not show any significant differences (Table 2), although left atrial dimension was larger in Group A compared to Group B (43.5 vs. 39.27 mm, an insignificant difference at $p = 0.075$).

We also compared patients in both groups in regard to the risk of thromboembolic events as estimated using the CHADS2 score (Table 3) and drug therapy used (Table 4) and we found no significant differences. During the follow-up, patients were treated with angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists, class IC, II, III, and IV antiarrhythmic drugs, and statins.

Multivariate logistic regression did not identify any independent risk factors of AF persistence after CTI ablation. Univariate logistic regression also did not show arterial hypertension, type 2 diabetes, previous myocardial infarction, LVEF, left ventricular dimension or age to affect AF persistence after successful CTI ablation (Table 5).

Table 4. Comparison of drug therapy used after cavotricuspid isthmus ablation in groups A and B

Medication class	Group A	Group B	P
Angiotensin-converting enzyme inhibitors	16 (37%)	7 (32%)	NS
Statins (HMG-CoA reductase inhibitors)	12 (28%)	5 (23%)	NS
Angiotensin receptor antagonists	1 (2%)	2 (9%)	NS
Class IC antiarrhythmic drugs	11 (26%)	4 (17%)	NS
Class II antiarrhythmic drugs	29 (67%)	13 (59%)	NS
Class III antiarrhythmic drugs	10 (23%)	4 (17%)	NS
Class IV antiarrhythmic drugs	1 (2%)	2 (9%)	NS

Patient numbers and percentages (in parentheses) are given; HMG-CoA — 3-hydroxy-3-methyl-glutaryl-CoA reductase

DISCUSSION

Atrial fibrillation and flutter are frequently coexisting supraventricular arrhythmias that have a complex pathomechanism and are closely related to each other [1, 7]. Published data regarding AF persistence after successful AFL ablation are inconsistent. Some data indicate that if both arrhythmias coexist before the procedure, CTI ablation may result in AF remission in about 30–50% of patients [3, 4]. In our study, this proportion was 31.9% (22/69 patients) during a relatively long, 3-year follow-up.

Important data regarding relations between AFL and AF were obtained in a metaanalysis by Perez et al. [4]. These authors showed that in a population of patients with AFL

Table 5. Univariate logistic regression analysis in patients with concomitant atrial fibrillation and atrial flutter treated with cavotricuspid isthmus ablation

Analysed parameter	Hazard ratio (95% confidence interval)
Arterial hypertension	0.81 (0.28–2.37)
Type 2 diabetes	1.27 (0.26–6.08)
Previous myocardial infarction	1.6 (0.43–5.96)
Left ventricular ejection fraction	0.99 (0.94–1.06)
Left atrial dimension	0.90 (0.80–1.03)
Age	1.01 (0.97–1.05)

p = NS

and AF that was similar to the one evaluated in the present study, AF persisted after successful CTI ablation in 52.7% of patients. Interesting data are also available regarding patients with isolated AFL. Following successful ablation of this arrhythmia, AF de novo developed in 23.1% of these patients. During initial years of follow-up, this proportion was lower compared to the rate of AF in patients with AFL and AF, but at 5 years it was similar in both groups. These data support the notion of a common pathomechanism of both arrhythmias. Surprisingly, creation of a bidirectional block with the CTI was a risk factor for AF. The same metaanalysis indicated that established risk factors for AF in multivariate analyses in many studies included presence and duration of AF before RFCA, reduced LVEF, left atrial enlargement, arterial hypertension, younger patient age and participation in endurance sports [4]. Studies also showed increased prevalence (though nonsignificantly) of arterial hypertension and left atrial dilatation in patients in whom AF did not remit after CTI. Somewhat different data were reported by de Melo et al. [8] who found that the rate of AF after CTI ablation in patients with concomitant AFL and AF was similar to that among patients with isolated AFL (30.8% and 30%, respectively). In that study, predictors of AF included the presence of persistent or permanent (duration > 3 years) AFL.

Schmieder et al. [3] also reported a significant, 33% reduction of AF episodes after CTI ablation in patients with concomitant AF and AFL. Similarly to our findings, Moreira et al. [9] found that AF persisted in 69% of patients with a history of AF and AFL who underwent CTI ablation. Ellis et al. [10] found *de novo* AF in 82% of patients with a history of AFL only who underwent ablation. In our study, however, both uni- and multivariate analyses did not identify factors affecting AF remission after CTI ablation. The above cited studies indicate that in some patients, AF and AFL are two forms of the same electrical atrial disease.

An interesting concept was presented by Waldo et al. [2] who observed that the development of isthmus-dependent AFL required previous occurrence of AF resulting in a functional block between the two venae cavae. If a CTI block is present after the ablation, atrial arrhythmias may not evolve into isthmus-dependent AFL but with the presence of an ectopic focus and electrical atrial remodelling they may manifest as AF.

In addition, a stable re-entry circuit resulting in AFL may induce or sustain AF if its cycle length is sufficiently short to result in so-called fibrillatory conduction [2]. Also the use of class IC and III antiarrhythmic drugs in patients with AF may result in the development of typical AFL [2, 11, 12].

In view of these relations between AF and AFL, numerous studies were performed with the aim of identifying factors affecting AF persistence after CTI ablation. Such factors may include mitral regurgitation, left atrial enlargement, patient age < 65 years, and LVEF < 50% [13–15]. Another issue is the development of de novo AF in patients who underwent CTI ablation due to AFL.

Taking into account this close relationship between both arrhythmias, Wazni et al. [16] suggested an alternative treatment approach. They performed pulmonary vein isolation (PVI) only in half of their patients, and pulmonary venous ostial ablation together with CTI ablation in the remaining patients. During short-term follow-up, AFL occurred in 55% of patients and AF in 30% of patients in the isolated PVI group. In the combined ablation group, AFL remission was noted in all patients, and AF persisted in 35% of patients. During a longer-term follow-up (> 8 weeks), proportion of patients with persisting AF and AFL was similar in both groups. In the isolated PVI group, AFL persisted in only 5% of patients, and AF in 11% of patients, while in the combined ablation group, these proportions were 0% and 14% of patients, respectively. Results of this study suggest that AFL remission may be expected in some patients after PVI, which is most likely related to ablation of an arrhythmogenic focus within pulmonary veins. Of note, the cited analysis showed no significant differences between groups in regard to demographic data, concomitant diseases, presence of a structural cardiac disease, AF type, and duration of symptoms. As CTI ablation procedure involves less risk for the patient, we attempted to identify factors affecting AF remission after ablation. We analysed the following variables: the number of previous myocardial infarction, presence of stable coronary artery disease, diabetes, and arterial hypertension, the New York Heart Association (NYHA) functional class, and medications used. However, we did not find any significant differences between the two study groups and thus we were unable to identify patients in whom AF remission would be more likely.

Of note, AF rate after CTI ablation increases with time, which might reflect progressive atrial disease and the degree of electrical remodelling [10].

As AF occurs so commonly after CTI ablation, complex invasive treatment of both AF and AFL should be considered in some patients with both arrhythmias. Currently available data do not allow precise identification of factors predisposing to AF remission after CTI ablation, and AF may be present in up to 30–80% of such patients [17, 18]. Our study also did not

identify such predictors. According to the current guidelines, CTI ablation should be performed in patients with AF and coexisting AFL in whom the decision to proceed with PVI is made only after unsuccessful attempts of drug therapy directed at AF, while ablation is the treatment of choice in isolated AFL [1, 19]. It should be remembered, however, that PVI places the patient at a higher risk, as the rate of serious complications is 4%, and the success rate is only about 60–70% [20]. In addition, long-term effectiveness of PVI decreases with duration of follow-up, and the mean number of ablation procedures is 2 per patient [20, 21]. With successful treatment of both arrhythmias, the risk of their serious sequelae is decreased, including that of thromboembolic complications, development of tachyarrhythmic cardiomyopathy, heart failure, and death.

Limitations of the study

The main limitation is the retrospective nature of our study. The study protocol did not allow detection of asymptomatic AF recurrences during follow-up, which might have led to underestimation of the true recurrence rate. Unfortunately, the same problem has occurred in many other studies. Asymptomatic AF accounts for about 12% of all AF episodes and is associated with the same prognosis as symptomatic AF [22]. Certainly, arrhythmia recurrences would be more precisely detected by 7-day Holter monitoring performed routinely in the study group at 1, 6, and 12 months, or using an event recorder implanted biennially. With these optimal diagnostic approaches, it would be possible to create a reliable clinical database. Another limitation of our study protocol was the inability to identify a subset of patients in whom AFL occurred for the first time after a class IC or III antiarrhythmic drug was administered. In addition, some arrhythmia diagnoses might have been imprecise due to the fact that some information was collected by telephone interview directly from the patient and not from the medical records, and available ECG recordings were not uniformly verified by a cardiac electrophysiologist. In addition, the study population was relatively small, which might have affected the lack of statistical significance in uni- and multivariate analyses.

CONCLUSIONS

Based on the results of our study, we were unable to identify factors determining remission of AF coexisting with AFL in patients after RFCA of the CTI. These findings may indicate the need for complex ablation procedure (involving both CTI ablation and PVI) in patients in whom these two arrhythmias coexist. A multicentre registry allowing standardised evaluation and verification of supraventricular arrhythmia recurrences in patients after CTI ablation is needed to determine risk factors for AF recurrence, quality of life indicators, and pharmacoeconomic parameters.

Conflict of interest: *Beata Średniawa is a consultant for Medtronic Bakken Research Centre.*

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Ocena czynników wpływających na utrzymywanie się migotania przedsionków u pacjentów ze współistniejącym trzepotaniem przedsionków poddanych przezskórnej ablacji cieśni dolnej prawego przedsionka

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Streszczenie

Wstęp: Migotanie (AF) i trzepotanie przedsionków (AFL) są często współistniejącymi arytmiami. U części chorych po skutecznej przezskórnej ablacji prądem o wysokiej częstotliwości cieśni prawego przedsionka (CTI) obserwuje się przypadki remisji AF.

Cel: Celem pracy była ocena czynników wpływających na remisję AF u chorych z typowym AFL i współistniejącym AF, poddanych zabiegowi ablacji CTI.

Metody: Do badania włączono kolejnych 69 chorych z typowym AFL i współistniejącym udokumentowanym klinicznie AF, poddanych skutecznemu zabiegowi ablacji CTI. Chorych leczono w latach 2003–2010. Na podstawie danych obserwacyjnych i uzyskanych za pomocą telefonicznej ankiety pacjentów podzielono na 2 grupy: grupę z utrzymującym się AF (grupa A) i grupę z remisją AF (grupa B). Kryterium grupującym były odczuwane przez chorego objawy arytmii, takie jak: „kołatanie serca" i uczucie niemiarowego rytmu serca potwierdzone elektrokardiograficznie (EKG, badanie metodą Holtera).

Wyniki: W grupie A było 47, a w grupie B — 22 pacjentów. Obie grupy nie różniły się istotnie statystycznie pod względem klasy czynnościowej wg NYHA i występowania chorób współistniejących, odpowiednio: cukrzycy, choroby niedokrwiennej serca, przebytego zawału serca i systemowego nadciśnienia tętniczego. W obu grupach także nie różniła się istotnie (oceniana echokardiograficznie) średnia wartość frakcji wyrzutowej lewej komory (LVEF) i średnicy lewego przedsionka (ten ostatni parametr 43,5 ± 9,27 *vs.* 39.27 ± 5,76; p = 0,075). W wieloczynnikowym modelu regresji logistycznej nie wyłoniono niezależnych czynników ryzyka utrzymywania się AF po ablacji CTI. Również w jednoczynnikowej regresji logistycznej nie stwierdzono, aby nadciśnienie tętnicze, cukrzyca typu 2, przebyty zawał serca, LVEF, wymiar lewej komory i wiek wpływały na utrzymywanie się AF po skutecznej ablacji.

Wnioski: Na podstawie uzyskanych wyników nie można wyróżnić czynników determinujących remisję współistniejącego z AFL migotania przedsionków u chorych po przezskórnej ablacji CTI. Wyniki te mogą wskazywać na konieczność wykonania kompleksowego, jednoczesnego zabiegu ablacji (CTI i ablacji ujść żył płucnych) u chorych, u których arytmie te współistnieją.

Słowa kluczowe: migotanie przedsionków, trzepotanie przedsionków, ablacja prądem o wysokiej częstotliwości

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Praca wpłynęła: 03.10.2011 r. **Zaakceptowana do druku:** 31.10.2011 r.