

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/crvasa



Původní sdělení | Original research article

Catheter ablation for atrial fibrillation – Single center experience

Luděk Haman, Hana Dostálová, Petr Pařízek

I. interní kardioangiologická klinika, Lékařská fakulta Univerzity Karlovy v Hradci Králové a Fakultní nemocnice Hradec Králové, Hradec Králové, Česká republika

INFORMACE O ČLÁNKU

Historie článku:
Došel do redakce: 17. 10. 2012
Přepracován: 10. 11. 2012
Přijat: 12. 11. 2012
Dostupný online: 19. 11. 2012

Keywords: Atrial fibrillation Catheter ablation Quality of life

ABSTRACT

Aims: Catheter ablation (CA) has become standard therapy for atrial fibrillation, especially for paroxysmal atrial fibrillation. Precise single center follow-up (FU) data (especially long-term FU data) are published infrequently.

Methods: We studied 303 consecutive patients (172 males, 131 females, mean age 57 years) who underwent catheter ablation for atrial fibrillation (489 procedures) in years 2004–2012. Clinical examination, ECG, 24-h or 7-day Holter monitoring and quality-of-life (QoL) measurement (EQ-5D) was performed at 3-, 6-, 12-, 18- and 24-month FU.

Results: FU data longer than 6 months after the first procedure are available for 135 patients with paroxysmal, 84 patients with persistent and 48 patients with long-standing persistent AF. The success rate after 6 months after the first procedure (sinus rhythm without AA drugs, no arrhythmias) was 48% for paroxysmal, 43% for persistent and 44% for long-standing persistent AF. The complication rate was 3.3% (16 patients, no deaths, no pulmonary vein stenosis, 5 incidents of pericardial effusion treated with pericardiocentesis; 1 transitory ischemic attack; the remainder were local complications in the groin). The success rate after the last procedure (mean FU 24 ± 16 months, 1.6 procedure per patient) was 80% for paroxysmal and 58% for persistent and long-standing persistent AF. QoL increased significantly in all groups of patients. Conclusion: With the standard procedure we can achieve acceptable results (success rate 60–80% with re-

Conclusion: With the standard procedure we can achieve acceptable results (success rate 60–80% with repeated procedures) with low complication rate even in a "lower volume" center. In selected patients (with paroxysmal AF preferring interventional treatment) CA can be recommended as first-line therapy for rhythm control. CA improves QoL in our patients with AF. As there is no gold standard to measure QoL in AF patients, EQ-5D seems to be a simple, quick and useful tool.

SOUHRN

Cíle: Katetrizační ablace se stala standardní léčbou fibrilace síní (FS), zvláště její paroxysmální formy. Přesná data dlouhodobého klinického sledování po výkonu jsou publikována ojediněle.

Metody: V období 4/2004–8/2012 podstoupilo v našem centru katetrizační ablaci FS 303 po sobě následujících pacientů (172 mužů, 131 žen, průměrný věk 57 let, celkem 489 výkonů). Nemocní byli sledováni (klinické vyšetření, EKG, 24hodinové či 7denní holterovské vyšetření, kvalita života pomocí dotazníku EQ-5D) po 3, 6, 12, 18 a 24 měsících po ablaci.

Adresa: Doc. MUDr. Luděk Haman, Ph.D., I. interní kardioangiologická klinika, Lékařská fakulta Univerzity Karlovy v Hradci Králové a Fakultní nemocnice Hradec Králové, Sokolská 581, 500 05 Hradec Králové, e-mail: haman@fnhk.cz

DOI: 10.1016/j.crvasa.2012.11.007

L. Haman et al. 561

Výsledky: Déle než šest měsíců po výkonu bylo sledováno 135 nemocných s paroxysmální FS, 84 pacientů s perzistující FS a 48 pacientů s dlouhodobě perzistující FS. Úspěšnost (sinusový rytmus, bez antiarytmické terapie, bez arytmií za monitorace) po prvním výkonu byla 48 % pro paroxysmální FS, 43 % pro perzistující a 44 % pro dlouhodobě perzistující FS. 3,3 % výkonů bylo provázeno komplikací – pětkrát perikardiální výpotek řešený perikardiocentézou, jedna transitorní ischemická ataka, ostatní lokální komplikace v třísle. Úspěšnost po poslední proceduře (průměrné sledování 24 ± 16 měsíců, 1,6 procedury na pacienta) byla 80 % pro paroxysmální a 58 % pro perzistující a dlouhodobě perzistující FS. Kvalita života se signifikantně zvýšila ve všech skupinách pacientů.

Klíčová slova: Fibrilace síní Katetrizační ablace Kvalita života Závěry: Se standardní procedurou je možné dosáhnout akceptovatelných výsledků (úspěšnost 60–80 %, včetně reablací) s nízkým rizikem komplikací i v "méně objemových" centrech. U vybraných nemocných (s paroxysmální FS, preferujících intervenční léčbu) může být katetrizační ablace doporučena jako léčba první volby. Katetrizační ablace zlepšuje kvalitu života pacientů s fibrilací síní. Vzhledem k absenci specifického nástroje k měření kvality života pacientů s FS, může být EQ-5D použit jako jednoduchá, rychlá a validní pomůcka.

© 2012, ČKS. Published by Elsevier Urban and Partner Sp. z o.o. All rights reserved.

Introduction

Catheter ablation (CA) has become standard therapy of atrial fibrillation (AF), especially for paroxysmal AF. Despite a high number of re-ablation procedures (30–50%), success is reported in 80–95% in patients with paroxysmal AF and in 50–85% in patients with long-standing persistent AF; furthermore, the complication rate is low (4–6%) [1–3]. Precise single center follow-up (FU) data (especially long-term FU data) are published infrequently.

Methods

Patient characteristics

The group consisted of 303 consecutive patients (172 males, 131 females, mean age 57 years) studied from April 2004 to August 2012. All patients underwent an electrophysiology study and CA for paroxysmal (157 patients), persistent (duration 1–12 months, 94 patients) and long-standing persistent (duration > 12 months, 52 patients) AF. Patients resistant to a minimum of two antiarrhythmic (AA) drugs were treated with catheter ablation until 2006; subsequently, patients resistant to one AA drug received CA. All patients signed written informed consent documents.

Electrophysiological procedure and catheter ablation

Magnetic resonance imaging was performed in all patients before the procedure (except 4 patients with implanted pacemaker, where computed tomography was used). AA drugs were discontinued minimally 5 days (1–3 months for amiodarone) before the procedure; in patients with the long-standing persistent form of AF, amiodarone was usually discontinued after the procedure. All patients underwent transesophageal echocardiography within 24 hours before the procedure to exclude thrombi in the left atrial appendage. All patients received effective oral anticoagulation for at least 4 weeks before ablation. Low molecular weight heparin (LMWH) anticoagulation replaced oral anticoagulants 2–3 days before CA.

Patients were studied in a conscious state with analgosedation (fentanyl and diazepam intravenously until 2010; subsequently fentanyl, diazepam, and propofol intravenously). A decapolar catheter was inserted through the right femoral vein into the coronary sinus. Two long sheaths (FAST-CATH Transseptal, 8,5F, St. Jude Medical, Minnetonka, MN, USA; PREFACE 8F, Biosense Webster Inc., Diamond Bar, CA, USA) were inserted to the left atrium transseptally, via the right femoral vein. After the last femoral vein puncture, an intravenous bolus of heparin (5000 units) was administered. After the first transseptal puncture, an additional intravenous bolus of heparin (dose complementary to 100 units per kg) followed by infusion or additional boluses were administered to maintain an activated clotting time of 300–350 seconds.

All procedures were done by one operator. Electroanatomical maps of the left atrium were constructed using a non-fluoroscopic navigation system (CARTO XP, CARTO3 from March 2011, Biosense Webster Inc., Diamond Bar, CA, USA) in all patients. Radiofrequency (RF) lesions were delivered with an irrigated-tip catheter (Navistar Thermocool, Biosense Webster Inc.). RF energy was titrated up to 25 W (to 23 W on the posterior wall); the irrigation rate was 20 ml/min. Ablation lesions created circumferential lines around the antra (ostia) of the pulmonary veins (PV) in patients with paroxysmal AF; in persistent and long--standing persistent AF patients, additional ablation lines were created (roof line, mitral isthmus line). In some patients ablation of fractionated electrograms and ablation inside the coronary sinus was performed. The endpoint of the PV ablation was PV isolation confirmed with a circular catheter (LASSO, Biosense Webster Inc. or Optima Plus, IBI, St. Jude Medical). The endpoint of linear and substrate ablation was termination of AF (directly or via left atrial flutter) or completion of these lines after electrical cardioversion in patients who were still in AF at the end of ablation.

Post-ablation management

All patients were discharged on oral anticoagulants and continued this therapy for at least two to three months. Clinical examination, ECG and 24-h or 7-day Holter monitoring was performed at 3-, 6-, 12-, 18- and 24-month FU. AA drug therapy was discontinued 1–3 months after the procedure (if it was not discontinued before the procedure). Patients with recurrent AF underwent reablation 6 months after the first procedure.

Quality-of-life measurement

Quality of life was measured prospectively with the European Quality of Life Group instrument – EQ-5D, Czech version. The objective portion, EQ-5D index, measures mobility, self-care, usual activities, pain/discomfort and anxiety/depression on a 0 to 1 scale using the European value set [4]; the subjective portion, EQ VAS (visual analog scale of 0–100) was measured before CA and during FU visits; in cases of re-ablation, measurements were re-initiated.

Statistical analysis

Continuous measurements are presented as the mean \pm standard deviation. Data obtained before and during the follow-up were compared by means of Student's t-test or Kruskal-Wallis Multiple-Comparison Z-Value Test (using NCSS statistical program). A *p*-value < 0.05 was considered statistically significant.

Results

Magnetic resonance imaging results

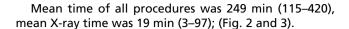
3D reconstruction proved in 80% of our patients common ostium of left sided PV (dominantly shorter – 1–2 cm, in 18% longer than 2 cm). In 6% of patients accessory right middle PV was proved. 6% of patients had common ostium of left and right sided PV. In one patient common ostium of left sided PV and right inferior PV from the posterior wall was proved.

Transesophageal echocardiography results

311 patients underwent transesophageal echocardiography the day before the procedure. In two patients CA was canceled because of thrombus in atrial appendage. In 6 patients severe mitral or aortic regurgitation was newly diagnosed and these patients underwent surgical correction with MAZE procedure.

Procedural data

From April 2004 to August 2012 303 patients underwent catheter ablation of AF, including redo procedures totally 489 procedures were performed (1.6 procedure per patient, Fig. 1).



Clinical characteristic

CA for paroxysmal AF was performed in 157 patients (mean age 57 years), for persistent AF in 94 patients (mean age 58 years) and for long-standing persistent AF in 52 patients (mean age 57 years). Duration of symptoms, previous antiarrhythmic drug therapy, type of symptoms, echocardiographic parameters and concomitant diseases are shown in Table 1.

Complications

The complication rate was 3.3% (16 patients, no deaths, no pulmonary vein stenosis, 5 incidents of pericardial effusion treated with pericardiocentesis; 1 transitory ischemic attack; the remainder were local complications in the groin (Table 2). Four pericardial effusions became symptomatic within 2–6 h after the end of the procedure, in one patient late tamponade was observed more than 48 h after the procedure. Three out of the local complications in the groin were treated surgically. All complications were treated successfully without any further consequences.

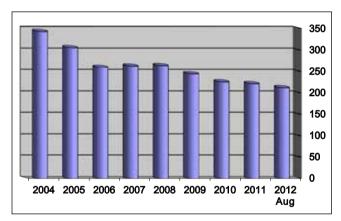


Fig. 2 - Mean time of the procedure (min).

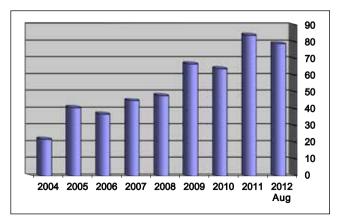


Fig. 1 - Number of procedures 2004-2012.

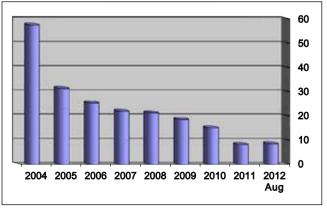


Fig. 3 – Mean X-ray time (min).

L. Haman et al. 563

Table 1 – Clinical characteristic of the patients group (mean, min, max).							
	Paroxysmal	Persistent	Long-standing persistent	Total			
Patients	157	94	52	303			
No of procedures	243	155	91	489			
Age	56 (25–80)	56 (25–77)	58 (37–72)	57			
Symptoms (years)	7 (0–41)	6 (0–28)	5 (0–27)	6			
Amiodarone	28 (18%)	27 (29%)	19 (37%)	74 (24%)			
Beta-blockers	67 (43%)	46 (49%)	41 (79%)	154 (51%)			
Propafenon	31 (20%)	14 (15%)	3 (6%)	48 (16%)			
Sotalol	20 (13%)	12 (13%)	4 (8%)	36 (12%)			
No drugs	39 (25%)	12 (13%)	1 (2%)	50 (17%)			
Palpitations	147 (94%)	65 (69%)	31 (60%)	243 (80%)			
Dyspnoe	67 (43%)	49 (52%)	39 (75%)	155 (51%)			
Weakness	41 (26%)	21 (22%)	6 (12%)	68 (22%)			
Fatigue	26 (17%)	24 (26%)	13 (25%)	63 (21%)			
Chest pain	35 (22%)	11 (12%)	4 (8%)	50 (17%)			
No symptoms	2 (1%)	9 (10%)	4 (8%)	15 (5%)			
LA (mm)	42 (29–55)	46 (36–61)	47 (36–62)	44 (29–62)			
EF (%)	64 (35–75)	59 (23–75)	51 (20–70)	60 (20–75)			
Mitral regurgitation (grade 1–4)	2 (0–4)	2 (1–4)	2 (1–4)	2 (1–4)			
Hypertension	87 (55%)	59 (63%)	32 (62%)	178 (59%)			
IHD	10 (6%)	10 (11%)	5 (10%)	25 (8%)			
Cardiomyopathy	6 (4%)	5 (5%)	13 (25%)	24 (8%)			
Thyreopathy	22 (14%)	16 (17%)	8 (15%)	46 (15%)			
Stroke/TIA	5 (3%)	5 (5%)	3 (6%)	13 (4%)			
CHADS ₂ score	1 (0–5)	1 (0–3)	1 (0–4)	1 (0–5)			

EF - ejection fraction; IHD - ischemic heart disease; LA - left atrium; TIA - transitory ischemic attack.

Table 2 – Complications of catheter ablation.								
	Paroxysmal	Persistent	Long-standing persis- tent	Total				
Patients	157	94	52	303				
No of procedures	243	155	91	489				
Pericardial effusion	2	2	1	5 (1.0%)				
Stroke/TIA	0	1	0	1 (0.2%)				
Local complication treated surgically	0	2	1	3 (0.6%)				
Local complication	4	3	0	7 (1.4%)				

Catheter ablation results

Serial Holter monitoring was performed in all patients, 7-day Holter monitoring was also performed in 15% of patients.

FU data longer than 6 months after the first procedure are available for 135 patients with paroxysmal, 84 patients with persistent and 48 patients with long-standing persistent AF. The success rate after 6 months after the first procedure (defined as in sinus rhythm without AA drugs, no arrhythmias during serial Holter monitoring) was 48% for paroxysmal, 43% for persistent and 44% for long-standing persistent AF (Table 3).

Catheter ablation was repeated in 53 patients (39%) with paroxysmal, 39 patients (46%) with persistent and 22 patients (46%) with long-standing persistent AF (1 redo procedure in 78 patients, 2 redo in 23 patients, 3 redo in 10 patients and 4 redo in 3 patients) because of recurrence of AF or atrial tachycardia (AT) after linear ablation. Reason for AF recurrence was dominantly PV reconnection or ectopic activity in previously non-isolated PV.

Recurrence of AF more than 12 months after the procedure was documented in 10 patients with paroxysmal (7%), in 17 patients with persistent (20%) and in 12 pa-

Table 3 – Results of catheter ablation (4/2004–4/2012).							
	Paroxysmal	Persistent	Long-standing persis- tent	Total			
Patients	135	84	48	267			
Success rate 6 months after the first procedure							
– SR	65 (48%)	36 (43%)	21 (44%)	122 (46%)			
– paroxysmal AF	67 (50%)	31 (37%)	10 (21%)	108 (40%)			
– AF/AT	3 (2%)	17 (20%)	17 (35%)	37 (14%)			
Total success rate including redo procedures							
– SR	108 (80%)	49 (58%)	28 (58%)	185 (69%)			
– paroxysmal AF	26 (19%)	27 (32%)	11 (23%)	64 (24%)			
– AF/AT	1 (1%)	8 (10%)	9 (19%)	18 (7%)			

AF – atrial fibrillation; AT – atrial tachycardia; SR – sinus rhythm.

tients with long-standing persistent AF (25%). Five patients died during the FU, all because of malignancy.

The success rate (defined as in sinus rhythm without AA drugs and without arrhythmias during monitoring) after the last procedure (mean FU 24 ± 16 months, min 6, max 90 months) was 80% for paroxysmal and 58% for persistent and long-standing persistent AF. Additional 7% of patients (6% in paroxysmal AF group, and 8% in persistent and long-standing persistent AF group) were asymptomatic with documented AF paroxysms during monitoring.

Quality-of-life measurement

The EQ-5D index increased in patients with paroxysmal, persistent, and long-standing persistent AF following CA (from 0.79 to 0.94; from 0.81 to 0.94; and from 0.75 to 0.85 respectively, p < 0.05). The EQ VAS also increased in all groups of patients after CA (from 65 to 87; from 61 to 82; and from 55 to 74 respectively, p < 0.05). Significant changes on both measures were more pronounced in patients with successful CA than in unsuccessful patients (EQ-5D index – from 0.79 to 0.95; from 0.75 to 0.84 respectively; EQ VAS – from 64 to 88; from 54 to 68 respectively, p < 0.01).

Discussion

The left atrial anatomy is complex. A detailed understanding of this anatomy is essential for a safe and effective AF ablation procedure. There is a significant inter- and intrapatient variability in the number; size and bifurcation of the PVs. Supernumerary right PVs are present in 18–29% of the patients, common trunk of left-sided PVs in more than 30% of patients [5]. Higher number of left common trunk in our group is a methodological difference, because we count also short common trunk, which is a frequent finding in the majority of patients. Anatomical variability supports routine use of imaging in AF ablation procedures (CT or MR image integration, intracardiac ultrasound, etc.).

Number of procedures is gradually increasing, faster increase in our center is limited by financial resources.

Time of the procedure and X-ray time decreased gradually, faster decrease was observed after learning curve and in case of X-ray time also after upgrade to CARTO3 navigation system in March 2011.

The efficacy of AF ablation in comparison with antiarrhytmic drug therapy was proved in a large number of non-randomized clinical trials and in several prospective randomized clinical trials. Results of randomized trials were examined in recent meta-analyses [6]. Overall, the success rate was 77.8% in the ablation arm as compared with 23.3% in the control group. Also recent worldwide survey monitoring outcome and safety features of AF ablation reports a 70% efficacy rate free of antiarrhythmic drugs and an additional 10% efficacy rate in the presence of previously ineffective antiarrhythmic drugs. The second procedure was required in every third patient and ablation of paroxysmal AF was associated with a 35% and 66% larger probability of success as compared to ablation of persistent and long-standing persistent AF [7]. Success rate in our group of patients is comparable with these results. Lower numbers of the first procedure success rate and higher number of redo procedures are clearly influenced by learning curve. We followed all patients from the beginning of AF ablation procedures in our center and during learning curve we did not achieve complete PV isolation in many patients. Higher number of redo procedures is also explainable by our emphasis to freedom of AF and not only to freedom of symptoms. We recommend redo procedure also to asymptomatic patients with AF recurrence in order to reduce the need for anticoagulation therapy.

CA of AF is one of the most complex interventional electrophysiologic procedures and the risk associated with AF ablation is higher than for ablation of other arrhythmias. The overall complication rate in last worldwide survey [7] was 4.5% (25 procedure-related deaths [0.15%], 213 episodes of tamponade [1.31%], 115 transient ischemic attacks [0.71%] and 37 strokes [0.23%]). Our complication rate 3.3% per procedure (5.3% per patient) is fully comparable with published results. Majority of our complications are local complications in the groin. All complications were treated successfully without further consequences. The use of standard technique of wide circumferential lesions with 3D navigation from the beginning and lower power used in left atrium and especially on the posterior wall contributes to lower complica-

L. Haman et al. 565

tion rate. Lower power settings are contributive to longer procedure time, but we prefer safety first principle. We also do not count atrial tachycardia after linear ablation as a complication but as some kind of intermediate product of our ablation between AF and sinus rhythm. Using the low power on the posterior wall, we did not provide any other prevention of atrioesophageal fistula than periprocedural administration of proton pump inhibitors.

Formal assessment of quality of life has played an increasingly important role in the evaluation of ablation outcomes. A number of single-center nonrandomized studies have demonstrated significant and sustained improvements in QoL following catheter ablation. Also three randomized clinical trials demonstrated superiority of CA over antiarrhythmic drug treatment which was associated with significant improvement QoL relative to baseline, with restoration to levels at or above population norms [8-10]. Direct comparison with our results is not possible because these studies used different QoL questionnaires (most often SF 36). Nevertheless, the descriptive capacity of SF 36 and EQ-5D is similar [11]; in addition the EQ-5D is simpler and less time-consuming (the principal factors for our use of this generic instrument in our center). Significantly, lower initial values in our patients with all AF subtypes showed clear impairment of QoL before CA. After CA, the QoL of patients with long-standing AF improved nearly to that of the reference population, and patients with paroxysmal and persistent AF improved significantly above the values of the reference population. After successful CA, AF patients reached highly above-average QoL values; furthermore, even patients with persistent symptoms improved (probably because of less frequent symptoms or better effect of AA drugs), although not to normal values.

Limitations

Several limitations of this study must be noted. Our single center non-randomized study included a small number of patients, especially those with long-standing persistent AF. Also, the average age of our patients is lower than in the typical AF population. 24-month mean follow-up may be insufficient for a long-term evaluation of the effect of catheter ablation.

Conclusion

Despite a lot of unsolved questions catheter ablation of AF is an accepted method of treatment of symptomatic AF patients, especially with paroxysmal form. With the standard procedure we can achieve acceptable results (success rate 60–80% with repeated procedures) with low complication rate even in a "lower volume" center. CA improves QoL in our patients with AF. As there is no gold standard to measure QoL in AF patients, EQ-5D seems to be a simple, quick; and useful tool.

Most important thing in AF patient's management is a proper indication of ablation procedure, i.e. to select patients, who will benefit most. According to guidelines [12], CA can be considered in selected patients as first-line therapy for rhythm control, i.e. those with paroxysmal AF preferring interventional treatment with low risk profile for procedure-associated complications.

Funding

This work was partially supported by the Ministry of Health of the Czech Republic (MZO00179906) and by the Charles University Research project PRVOUK 37/03.

References

- [1] C. Pappone, V. Santinelli, Atrial fibrillation: state of the art, The American Journal of Cardiology 96 (2005) 59L–64L.
- [2] M.D. O'Neill, M. Wright, S. Knecht, et al., Long-term follow-up of persistent atrial fibrillation ablation using termination as a procedural endpoint, European Heart Journal 30 (2009) 1105–1112.
- [3] M. Fiala, J. Chovancík, D. Wojnarová, et al., Results of complex left atrial ablation of long-lasting persistent atrial fibrillation, Journal of Interventional Cardiac Electrophysiology 23 (2008) 189–198.
- [4] W. Greiner, T. Weijnen, M. Nieuwenhuizen, et al., A single European currency for EQ-5D health states. Results from a six country study, The European Journal of Health Economics 4 (2003) 222–231.
- [5] H. Mlcochova, J. Tintera, V. Porod, et al., Magnetic resonance angiography of pulmonary veins: implications for catheter ablation of atrial fibrillation, Pacing and Clinical Electrophysiology 28 (2005) 1073–1080.
- [6] C. Bonanno, M. Paccanaro, L. La Vecchia, et al., Efficacy and safety of catheter ablation versus antiarrhythmic drugs for atrial fibrillation: a meta-analysis of randomized trials, The Journal of Cardiovascular Medicine 11 (2010) 408–418.
- [7] R. Cappato, H. Calkins, S.A. Chen, et al., Updated worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation, Circulation. Arrhythmia and Electrophysiology 3 (2010) 32–38.
- [8] O.M. Wazni, N.F. Marrouche, D.O. Martin, et al., Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of symptomatic atrial fibrillation. A randomized trial, The Journal of the American Medical Association 293 (2005) 2634–2640.
- [9] P. Jais, B. Cauchemez, L. Macle, et al., Catheter ablation versus antiarrhythmic drugs for atrial fibrillation: the A4 study, Circulation 118 (2008) 2498–2505.
- [10] D.J. Wilber, C. Pappone, P. Neuzil, et al., Comparison of antiarrhythmic drug therapy and radiofrequency catheter ablation in patients with paroxysmal atrial fibrillation: A randomized controlled trial, The Journal of the American Medical Association 303 (2010) 333–340.
- [11] C. Quercioli, G. Mesina, E. Barbini, et al., Importance of sociodemographic and morbidity aspects in measuring health-related quality of life: performance of three tools, The European Journal of Health Economics 10 (2009) 389–397.
- [12] A.J. Camm, G.Y.H. Lip, R. De Caterina, et al., 2012 focused update of the ESC Guidelines for the management of atrial fibrillation, European Heart Journal 33 (2012) 2719–2747.