What is the real atrial fibrillation burden after catheter ablation of atrial fibrillation? A prospective rhythm analysis in pacemaker patients with continuous atrial monitoring

Daniel Steven*, Thomas Rostock, Boris Lutomsky, Hanno Klemm, Helge Servatius, Imke Drewitz, Kai Friedrichs, Rodolfo Ventura, Thomas Meinertz, and Stephan Willems

Department of Cardiology, University Heart Centre Hamburg, Martinistr. 52, Hamburg 20246, Germany

Received 11 August 2007; revised 7 January 2008; accepted 10 January 2008; online publish-ahead-of-print 9 February 2008

See page 964 for the editorial comment on this article (doi:10.1093/eurheartj/ehn108)

Aims
Rhythm follow-up after catheter ablation of atrial fibrillation (AF ablation) is mainly based on Holter electrocardiogram (ECG), tele-ECG or on patients symptoms. However, studies using 7-day Holter or tele-ECG follow-up revealed a significant number of asymptomatic recurrences. Thus, the aim of this study was to analyse continuous atrial recordings in pacemaker patients with an incorporated Holter function before and after AF ablation in order to determine all AF recurrences and thereby the ‘real’ success rates.

Methods and results
The study comprised 37 patients (64.6 ± 10 years) with prior pacemaker/implantable cardioverter defibrillator (ICD) implantation including an atrial Holter function referred for AF ablation. Holter data were obtained and correlated to patients’ symptoms before and every 3-month after AF ablation. AF recurrence was defined as an atrial high frequency episode of less than 330 ms (180 b.p.m.) lasting longer than 30 s. The ablation procedure consisted of pulmonary vein isolation (PVI) in patients with paroxysmal atrial fibrillation (PAF, n = 20) and additional substrate modification aiming arrhythmia termination in patients with persistent or inducible AF after PVI as well as in patients with a history of long-lasting persistent AF (PersAF, n = 17). The mean atrial Holter monitoring period was 7.4 ± 3.3 months before and 13.5 ± 4.2 months after ablation with an overall AF burden of 33.7% prior to ablation. During follow-up, AF burden decreased from 17.3–0.65% (P = 0.001) in PAF patients and from 57.4 to 13.9% (P = 0.024) in patients with PersAF. Complete AF freedom was observed in 85% (17 patients) of PAF patients and 59% (10 patients) in patients with PersAF. The absence of symptoms correlated well with documented freedom of AF.

Conclusion
In the present study we could show, that freedom from AF can be achieved by catheter ablation in a high percentage of patients even with PersAF. Continuous atrial monitoring reveals AF ablation success rates comparable with those assessed by clinical evaluation. Symptomatic freedom of AF correlated well with the actual freedom of AF at least in this highly symptomatic patient cohort.

Keywords
Atrial fibrillation • Ablation • Pacemaker • Atrial Holter recording

Introduction
Pulmonary vein (PV) isolation has emerged as an effective therapy for paroxysmal atrial fibrillation (PAF) with success rates ranging between 60 and 80%.1 In patients with persistent AF (PersAF), there is growing evidence that additional substrate modification is necessary to achieve similar results as reported for PAF patients.2,3 The electrophysiological endpoints are electrical
the devices used for Holter diagnosis in these studies performed ad infinitum and patient-independent recording of the atrial rhythm. Implanted dual-chamber devices are assumed to have a high appropriate detection rate of atrial high frequency episodes. Thus, the aim of this study was to investigate the real recurrence rates of AF ablation by continuous atrial monitoring using those devices with atrial Holter monitoring function.

Methods

Study population

Between February 2005 and April 2006 a total number of 304 patients underwent AF ablation in our institution (Figure 1). Thirty-seven (mean age 64.6 ± 10 years, 20 male) of them had independently undergone prior pacemaker implantation due to sick-sinus-syndrome (53%), atrioventricular conduction block (13%), pharmacological treatment for AF with consecutive bradycardia and pacemaker implantation (16%) or underwent implantable cardioverter defibrillator (ICD) implantation for ventricular tachycardia (13%). In two patients (5%) atrioventricular (AV)-node ablation has been performed in a different institution and AF ablation was due to persistent symptoms and progressive heart failure. All of the devices were equipped with software algorithms allowing continuous atrial rhythm monitoring and electrogram (EGM) storage for retrospective analysis. Twenty patients had PAF with episodes lasting less than 7 days without prior history of external cardioversion. Seventeen patients had persistent or chronic AF with episodes lasting longer than 7 days and a prior history of at least one external cardioversion.

The patients had not responded to 3 ± 1 antiarrhythmic drug including amiodarone. Twelve patients had a structural heart disease and none of them had history of any thromboembolic event. The mean left atrial (LA) diameter was 43 ± 5 mm; the mean left ventricular (LV) function was 51 ± 13% (Table 1). There was no significant difference in baseline clinical data at the time point of the index procedure between both groups, unless LV function, which was lower in the group of patients with PersAF (Table 2).

Electrophysiologic study

All patients gave written informed consent. Antiarrhythmic drugs (AAD), with the exception of amiodarone, were stopped at least five half-life times before the study. Oral anticoagulation (international normalized ratio 2–3) was administered for at least 1 month, and transesophageal echocardiography for exclusion of an LA thrombus was performed prior to the procedure. During ablation procedure three catheters were used: (i) a 6Fr quadripolar diagnostic catheter (Xtrem, Ela Medical, Montrouge, France) positioned in the coronary sinus (CS), (ii) a decapolar diagnostic catheter for circumferential mapping of the PVs (Lasso, Biosense-Webster, Diamond Bar, CA, USA), and (iii) a 3.5 mm irrigated-tip ablation catheter (Thermocool, Biosense-Webster, Diamond Bar, CA, USA). Two long sheaths (SL0, SJM, St Paul, MN, USA) continuously flushed with heparinized normal saline were used for stabilizing the catheters in the LA. Following transseptal puncture and application of 70 units/kg of heparin, the activated clotting time (ACT) was measured and maintained between 250 and 300 s during the entire procedure. Surface ECGs and bipolar endocardial electrograms were monitored continuously and stored on a computer-based digital amplifier/ recorder system (Bard Electrophysiology, Lowell, MA, USA). Filter settings were set for 30–500 Hz; online callipers and a sweep speed of 100 mm/s were used.

Catheter ablation

The techniques used for pulmonary vein isolation (PVI) have been previously described. In brief, the PVs were electrically isolated individually or as pairs of ipsilateral veins. The circumferential PV mapping catheter was placed in an ostial position at each PV, and ablation was guided by recording of the PV potentials during radiofrequency (RF) delivery. RF energy was delivered through a Stockert generator (Biosense-Webster) in a temperature-controlled mode and limited to 48°C using a maximal power of 30 W. Electrical PVI was confirmed by the abolition or dissociation of the PV potentials demonstrated by the circumferential mapping catheter.

In patients with PersAF, ablation was continued after PVI using a modified stepwise ablation approach as implemented by Haissaguerre et al. Complex fractionated atrial electrograms were mapped and ablated throughout both atria and within the CS. Ablation endpoints were (i) local elimination of fractionation, (ii) transformation of local fractionation to discrete electrogram configuration, and (iii) termination of AF by either conversion to an atrial tachycardia (AT) or to sinus rhythm. LA lines were created only in case of conversion to AT involving the LA roof or the mitral isthmus. Cavotricuspid isthmus ablation has been performed in all patients.

Pacemaker settings

Only patients with pacemakers including a continuous Holter monitoring were selected for the study analysis (BiotronikC60/Philips II DR, VitatronC60/C60/ T70, MedtronicC60 InSync III Marquis). The detection of atrial high frequency episodes is based on a five out of eight beat analysis in case of the MedtronicC60. Kappa 900. In all other
devices a beat-to-beat analysis is performed. The baseline settings for detection of atrial high frequency episodes were similar in all of the pacemaker models and remained unchanged after AF ablation. Every detected high atrial frequency episode of $330 \text{ ms} (180 \text{ beats per minute})$ lasting for longer than $30 \text{ s}$ with an atrial sensitivity of $0.5 \text{ mV}$ was assumed as an episode of AF. AF burden is defined as the overall percentage of AF during the observed period. Manual interpretation of all documented episodes (EGM) was performed to avoid misdiagnose atrial flutter or AT of AF. The following Holter information was obtained prior to the procedure and at patients’ follow-up visits: (i) mean and longest duration of AF episodes, (ii) duration of recording prior to the procedure, and (iii) programmed atrial as well as ventricular sensitivity, respectively. No overdrive suppression or other device related prevention algorithms have been programmed after ablation.

Follow-up

Patients were discharged on oral anticoagulation, which was continued until at least 6 months consecutive AF-free interval was documented. In patients with PAF, AADs have been discontinued after the procedure. Patients with PersAF were kept on AADs for the first 4 weeks after AF ablation.

All patients were seen in our outpatient clinic every 3 months after ablation for pacemaker data collection and anamnestic survey. The stored atrial high frequency episodes were analysed and the AF burden calculated by the device was obtained. All stored EGM were analysed in order to avoid misdiagnosis of AF and AT. All stored data had been reset after each interrogation to avoid follow-up data overlap. At each follow-up visit, a detailed evaluation of the current medication and the patients’ symptoms suggestive for potential AF recurrences was performed.

Statistical analysis

Continuous variables are reported as mean ± standard or as median and percentiles if appropriate. Normally distributed variables were compared using the independent Student’s t-test. Otherwise comparisons between both the groups (PAF and PersAF) were performed using the Mann–Whitney U test. The comparison within groups has been performed using the Friedman test for more than two time points. For two repeated measurements, the paired Wilcoxon test was used. Categorical variables were stated as absolute and relative frequencies and were compared using the $\chi^2$ test. As we performed an exploratory data analysis, the results were interpreted nominatively and no further adjustment for multiple testing was performed. All tests were two-tailed. A P-value of $<0.05$ was considered as statistically significant. The statistical analysis was performed using SPSS 13.0 (SPSS Inc., IL, USA).

Results

Ablation procedure

In all patients, all PVs have been targeted and successfully isolated by using a mean fluoroscopy time of $45 \pm 20 \text{ min} \ (\text{PAF} 36 \pm 19 \text{ min} / \text{PersAF} 48 \pm 20 \text{ min})$ and a mean procedure duration of $209 \pm 106 \text{ min} \ (\text{PAF} 144 \pm 34 \text{ min} / \text{PersAF} 219 \pm 90 \text{ min})$, including right atrial isthmus ablation in all patients.
Seventeen patients (54%) required defragmentation of complex fractionated electrograms after PVI. In 13 (76.5%) of them, AF termination could be achieved by catheter ablation (six patients to sinus rhythm (SR), seven patients to AT). No procedure related complications occurred. All patients were on antiarrhythmic medication prior to ablation.

**Follow-up**

**Overall study population**

The mean observation time of rhythm analysis prior to the index procedure was 7.4 ± 3.3 months. All patients completed the 12 months follow-up. The overall AF burden decreased from a mean of 33.7% at the index procedure to a mean of 6.3% at the 12-months follow-up visit in the overall study population. The mean duration of AF episodes was reduced from 4 (0.2/300) days to 0.35 (0/0.9) days in patients with AF recurrences in the same period. Oral anticoagulation was discontinued in 26 (70%) patients (PAF \( n = 17 \), PersAF = 9). At the time point of the 12-months follow-up, nine patients (53%) have been free of AAD PersAF group, while 13 patients in the PAF group (65%) have not taken any further antiarrhythmic medication (Table 1).

**Paroxysmal atrial fibrillation**

In 17 (85%) patients, no further AF episodes were recorded during the entire follow-up period (Figure 3). In the remaining three patients (15%), AF burden decreased from 15.5% at the index procedure to 4.3% after 12 months. The number of AF-free patients between 3- and 6-months follow-up visit increased from 12 (60%) to 16 (80%).

All symptomatic patients had at least one episode of AF documented in the Holter recordings during each follow-up. None of the patients, who reported to be asymptomatic, had any AF recurrences. During the entire follow-up a significant reduction in AF burden has been shown (5.5 \( \times \) 10 – 13).

**Persistent atrial fibrillation**

Two of 17 patients underwent a redo procedure during follow-up. Ten (59%) patients with PersAF had no AF recurrence (AF burden 0%) (Figure 3), while the remaining seven patients experienced AF recurrences. However, the AF burden was significantly reduced from 57.4% at the time of the index procedure to 13.9% at the 12-months follow-up visit (\( P = 0.024 \)) (Figure 4). During time course of follow-up, a significant reduction in AF burden has been shown (2.9 \( \times \) 10 – 9). Two patients had atrial high frequency episodes that have been classified as AT during the manual EGM and ECG interpretation. These patients subsequently underwent catheter ablation for these tachycardias and were not accounted as AF recurrence accordingly. In another two patients, AF recurrence was paroxysmal with episodes lasting no longer than 7 days and without the need for external cardioversion. As described in the paroxysmal group, there have been no patients with AF or AT episodes in the Holter who denied having had any symptomatic recurrence of AF.
Discussion

The present study provides new information on recurrent arrhythmic events following AF ablation in patients with paroxysmal and PersAF. First, catheter ablation of AF led to a complete freedom from AF in 85% of patients with PAF and in 59% of PersAF patients as proven by permanent atrial monitoring. Second, a symptom-based follow-up is reliable to identify patients with AF recurrences after AF ablation, at least in a cohort with highly symptomatic AF. Finally, even in patients with AF recurrences a significant decrease in AF burden was achieved.

Reliability of conventional follow-up

Conventional follow-up strategies are limited by non-continuous atrial rhythm monitoring, i.e. Holter ECG and tele-ECG, associated with an uncertain number of undetected and asymptomatic AF recurrences. Previous investigators who observed a significant amount of asymptomatic AF recurrences hypothesized that success rates of AF ablation procedures assessed by conventional rhythm monitoring potentially are overestimated.\(^{13}\) Thus, there is an ongoing discussion on mid- and long-term results after AF ablation arguing that 50% of AF episodes and 38% of patients remain asymptomatic after AF ablation.\(^{13,14}\) However, the present study revealed that none of the patients with pacemaker documentation of AF recurrence remained completely asymptomatic during the entire follow-up.

In concert with previous reports, the present study revealed a considerable higher number of documented AF episodes after AF ablation as compared with lone anamnestic survey exploring AF recurrences.\(^{7,14}\) In a study using tele-ECG follow-up after AF ablation, we observed 46% of asymptomatic AF episodes. However, only 9% of those patients remained completely asymptomatic during lone anamnestic follow-up indicating that symptomatic and asymptomatic episodes may occur in the same patient. Thus, patients’ interrogation identifies 91% of patients who experienced AF recurrences.

Very recently, Verma et al.\(^{15}\) published their data on pacemaker patients undergoing AF ablation demonstrating that 30% of patients had documented asymptomatic recurrences. Nevertheless, those episodes mostly lasted for less than 60 s. In this study however, no differentiation between patients with paroxysmal and PersAF in terms of the ablation strategy and its respective follow-up has been made. Furthermore, arrhythmia recurrence detection was limited by the count of pacemaker mode-switch activations.

The limited reliability of conventional follow-up has been also reported by Hindricks et al. demonstrating that 36% of patients with both, paroxysmal and PersAF had asymptomatic AF episodes after catheter ablation.\(^{13}\) However, potential reasons for the discrepancy between this study and our results are:

(i) In the study of Hindricks et al., 72% of patients were on beta-blocker therapy, which potentially diminished patients’ perception of AF recurrence.\(^{13}\)

(ii) Moreover, in their study, patients’ symptoms were assessed in close relation with each documented AF episode whereas in the present study, the patients where cumulatively interrogated after a period of 3-months, increasing the likelihood of perception of at least one symptomatic AF episode during this 3-months period.

(iii) Finally, AF perception often is different in patients with PAF and PersAF necessitating specific follow-up strategies with respect to the AF entity.

Previous studies using pacemaker-based follow-up after AF ablation have been performed by Pürerfellner et al.\(^{16,17}\) Although these studies are limited by a small number of included patients (12 and 14, respectively), continuous atrial monitoring revealed a significant reduction of AF burden. However, not all PVs were routinely targeted and post-ablation treatment consisted of early redo procedures, continuation of antiarrhythmic drug therapy and preventive pacing algorithms.

Freedom and reduction of atrial fibrillation burden by catheter ablation

In the first study of catheter ablation of long-standing PersAF aiming arrhythmia termination by Haïssaguerre et al.\(^{18}\) the change from PersAF to paroxysmal atrial tachyarrhythmias after the ablation has been reported. In our study, three patients with PersAF demonstrated only short-lasting AF episodes during follow-up. Thus, those patients potentially reach the goal of complete AF freedom after a second procedure for PAF presumably due to conduction recovery of the PVs. However, follow-up is limited by a small number of patients and further studies are needed to verify this hypothesis.

An important issue of follow-up after AF ablation is the differentiation of the type of recurrent arrhythmia. In our study, seven out of 17 patients with PersAF demonstrated arrhythmia recurrences during follow-up. Nonetheless, manual interpretation of pacemaker EGM and 12-lead ECG revealed an AT as the recurrent arrhythmia in two patients, resulting in a total number of 12 patients being free of AF. Hence, even if complete arrhythmia freedom was not achieved, a redo procedure may result in overall arrhythmia elimination by selective catheter ablation of these subsequent tachycardias.\(^{19}\)

Limitations

The data provided in this study are based on continuous atrial Holter monitoring that are exclusively obtained by an implanted pacemaker with monitoring algorithms. A potentially remaining limitation in terms of ‘follow-up continuity’ might be the miss of an arrhythmogenic episode due to electrode undersensing of atrial potentials during AF or AT. However, since all patients also documented AF episodes prior to the ablation procedure this issue seemed to be therefore a minor limitation.

Despite no patient with AF recurrence being asymptomatic during the follow-up, no information can be provided in terms of symptom correlation of the documented AF burden prior to ablation, although all patients included in the study were highly symptomatic.

The differentiation between AF and AT was performed by manual interpretation of the stored pacemaker EGM. Since an accurate interpretation of P-wave morphologies is not feasible by intracardiac Holter monitoring the diagnosis of AF/AT was based on the regularity of the atrial cycle length. Hence, potential mis-diagnosis of AF/AT might be a possible issue in some cases, e.g. in patients with very regularized AF cycle lengths. However, patients with AT usually present with their arrhythmia (mainly...
atrial flutters) to a follow-up visit, providing the possibility to document the AT in a 12-lead surface ECG.

**Conclusion**

AF ablation in both PAF and PersAF seems to be a safe and feasible approach in patients with implanted pacemaker/ICD devices. Continuous atrial monitoring revealed that a high number of patients with PAF and a considerable proportion of PersAF patients had no recurrences during a follow-up period of 1 year.

Furthermore, these data demonstrate that symptomatic freedom of AF correlates well with the actual freedom of AF after AF ablation and thus complete freedom from AF is appropriately asserted by conventional follow-up, at least in this selected cohort of highly symptomatic patients.

**Conflict of interest:** D.S., T.R., B.L. and S.W. report having received lecture honoraria from St Jude Medical, St Paul, Minn. The other authors report no conflicts.

**References**


