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Impact of monitoring on detection of arrhythmia recurrences in the ESC-EHRA EORP atrial fibrillation ablation long-term registry

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Aims Monitoring of patients after ablation had wide variations in the ESC-EHRA atrial fibrillation ablation long-term (AFA-LT) registry. We aimed to compare four different monitoring strategies after catheter AF ablation.

Methods and results The ESC-EHRA AFA-LT registry included 3593 patients who underwent ablation. Arrhythmia monitoring during follow-up was performed by 12-lead electrocardiogram (ECG), Holter ECG, trans-telephonic ECG monitoring (TTMON), or an implanted cardiac monitoring (ICM) system. Patients were selected to a given monitoring group according to the most extensive ECG tool used in each of them. Comparison of the probability of freedom from recurrences was performed by censored log-rank test and presented by Kaplan–Meier curves. The rhythm monitoring methods were used among 2658 patients: ECG ($N = 578$), Holter ECG ($N = 1874$), TTMON ($N = 101$), and ICM ($N = 105$). A total of 767 of 2658 patients (28.9%) had AF recurrences during follow-up. Censored log-rank test discovered a lower probability of freedom from relapses, which was detected with ICM compared to TTMON, ECG, and Holter ECG ($P < 0.001$). The rate of freedom from AF recurrences was 50.5% among patients using the ICM while it was 65.4%, 70.6%, and 72.8% using the TTMON, ECG, and Holter ECG, respectively.

Conclusion Comparing all main electrocardiographic monitoring methods in a large patient sample, our results suggest that post-ablation recurrences of AF are significantly underreported by TTMON, ECG, and Holter ECG. The ICM estimates AF ablation recurrences most reliably and should be a preferred mode of monitoring for trials evaluating novel AF ablation techniques.

Keywords Atrial fibrillation • Ablation • Recurrence • Rhythm monitoring • EHRA registry

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What's new?

- A comparison of the yield of all main electrocardiographic monitoring methods was performed in a large patient sample undergoing catheter ablation for atrial fibrillation.
- Post-ablation recurrences of atrial fibrillation are significantly underreported by 12-lead electrocardiogram, Holter ECG, and trans-telephonic ECG monitoring.
- Implanted cardiac monitoring system estimates atrial fibrillation recurrences most reliably.

Introduction

The atrial fibrillation ablation long-term (AFA-LT) registry, conducted by the European Heart Rhythm Association (EHRA) and the EURObservational Research Program (EORP) department of the European Society of Cardiology (ESC), provided detailed information on contemporary atrial fibrillation (AF) ablation in a real-world setting and also highlighted wide variations in the monitoring of patients after ablation.[1] During follow-up, several available methods were used for monitoring: 12-lead electrocardiogram (ECG), Holter ECG, trans-telephonic ECG monitoring (TTMON), or an implanted cardiac monitoring (ICM) system.[1] ESC Guidelines consider prolonged monitoring reasonable to detect episodes of AF.[2] Previous studies discuss the importance of duration and intensity of arrhythmia monitoring for the detection of AF.[3–5] Therefore, an ancillary analysis was planned to evaluate the impact of monitoring duration on detection of arrhythmia recurrences in a large cohort of patients. We hypothesized that non-continuous rhythm monitoring overestimates AF ablation results. Moreover, several studies suggested limitations of follow-up strategies which were based solely on symptoms after AF ablation because of high incidence of silent arrhythmia recurrence or poor correlation between symptoms and arrhythmia.[6,7] Incidence of asymptomatic AF after catheter ablation was also reported to increase significantly up to 36% at 12 months of follow-up.[7] On the other hand, at 6- to 12-month follow-up, 7-day Holter or TTMON detected significantly more patients with AF recurrences after ablation than 24-h Holter ECG monitoring.[8–10]

In this ancillary analysis, we aimed to compare four different ECG monitoring strategies after catheter AF ablation.

Methods

The AFA-LT registry is a prospective, multicentre, observational registry of consecutive patients undergoing an ablation procedure for AF at 104 centres in 27 countries, members of the European Society of Cardiology.[1] Study design and participants, data collection and definitions are described elsewhere.[1] The patient cohort included 3593 patients with paroxysmal (67.6%), persistent (27.4%), and long-standing persistent (5.0%) AF treated with ablation.

Registry data for the ancillary analysis were obtained through review of electronic case report forms in order to capture information for baseline clinical characteristics, procedural and post-procedural data, and follow-up. Baseline clinical characteristics, technical characteristics of the ablation procedure, and medical treatment during follow-up are described in a previous publication.[1]

Follow-up

Follow-up was performed by clinical evaluation and monitoring methods. Arrhythmia recurrence was defined as an electrocardiographically documented episode of AF or atrial flutter, which lasted at least 30 s.[1] Cavotricuspid isthmus-dependent flutter was excluded from all definitions, and a blanking period of 3 months was employed after ablation.[1] It was detected by at least one of the following monitoring methods: 12-lead ECG, Holter ECG, TTMON, and ICM. Some patients were thus assessed with more than one monitoring method. Therefore, the criteria for selecting patients to a given monitoring group were defined according to the tool that enabled the most extensive ECG recording in the following order of increasing intensity: 12-lead ECG, Holter ECG, TTMON, and ICM. For the purpose of the analysis, patients were divided, respectively, into four groups according to the most continuous type of monitoring during their follow-up. However, the electronic case report forms of the AFA-LT registry did not capture details about the duration of the Holter ECG or the frequency of use of each of the non-implantable systems. Various monitoring strategies were compared to assess their diagnostic value for the detection of arrhythmia recurrence.

Statistical analysis

Statistical analysis was performed using SAS statistical software version 9.4 (SAS Institute, Inc., Cary, NC, USA). Categorical variables were expressed using counts and percentages. Frequencies of different monitoring methods were compared using the Fisher's exact test. *P*-values <0.05 are considered statistically significant. Comparison of the probability of freedom from recurrences was performed by censored log-rank test and presented by Kaplan–Meier curves.

Results

Monitoring methods

Considering the duration of monitoring, Holter ECG ($N = 1874$ patients; 70.5%) was the most frequently used method, followed by 12-lead ECG ($N = 578$ patients; 21.7%), ICM ($N = 105$ patients; 4.0%), and TTMON ($N = 101$ patients; 3.8%) (*Table 1*). It predominated and was the most commonly used technique in all types of AF as follows: for paroxysmal AF (1283/1799 patients; 71.3%), persistent AF (514/735 patients; 69.9%), and long-standing persistent AF (77/124 patients; 62.1%).

Among paroxysmal AF patients (*Table 1*), the following distribution of the remaining monitoring methods was found: 12-lead ECG (369/1799 patients; 20.5%), ICM (79/1799 patients; 4.4%), and TTMON (68/1799 patients; 3.8%). The frequency of use of the monitoring methods after ablation of persistent AF was 23.0% for 12-lead ECG (169/735 patients) vs. 4.4% (32/735 patients) for TTMON and 2.7% (20/735 patients) for ICM. Long-standing persistent AF patients were monitored with 12-lead ECG with an incidence of 32.3% (40/124 patients) vs. ICM (6/124 patients; 4.8%) and TTMON (1/124 patients; 0.8%). There were significant differences in the use of the different monitoring modalities in patients with paroxysmal, persistent, and long-standing persistent AF (*Table 1*).

Follow-up

The median duration of follow-up was 12.4 months (interquartile range 11.9–13.4) after the procedure.[1] Results of follow-up in the AFA-LT registry are presented in a flowchart (*Figure 1*). The number of patients who completed their follow-up and also received

Table 1 Methods used for rhythm monitoring of patients with different types of atrial fibrillation during follow-up in the AFA-LT registry

Completed follow-up with rhythm monitoring (*N* = 2658)	Paroxysmal AF (*N* = 1799)	Persistent AF (*N* = 735)	Long-standing persistent AF (*N* = 124)	*P*-value
ECG (*N* = 578)	369/1799 (20.5%)	169/735 (23.0%)	40/124 (32.3%)	0.009[a]
Holter ECG (*N* = 1874)	1283/1799 (71.3%)	514/735 (69.9%)	77/124 (62.1%)	
TTMON (*N* = 101)	68/1799 (3.8%)	32/735 (4.4%)	1/124 (0.8%)	
ICM (*N* = 105)	79/1799 (4.4%)	20/735 (2.7%)	6/124 (4.8%)	

AF, atrial fibrillation; ECG, electrocardiogram; ICM, implanted cardiac monitoring system; *N*, number; TTMON, trans-telephonic ECG monitoring.
[a]*P* = 0.121 (paroxysmal vs. persistent AF); *P* = 0.008 (paroxysmal vs. long-standing persistent AF); and *P* = 0.016 (persistent vs. long-standing persistent AF).

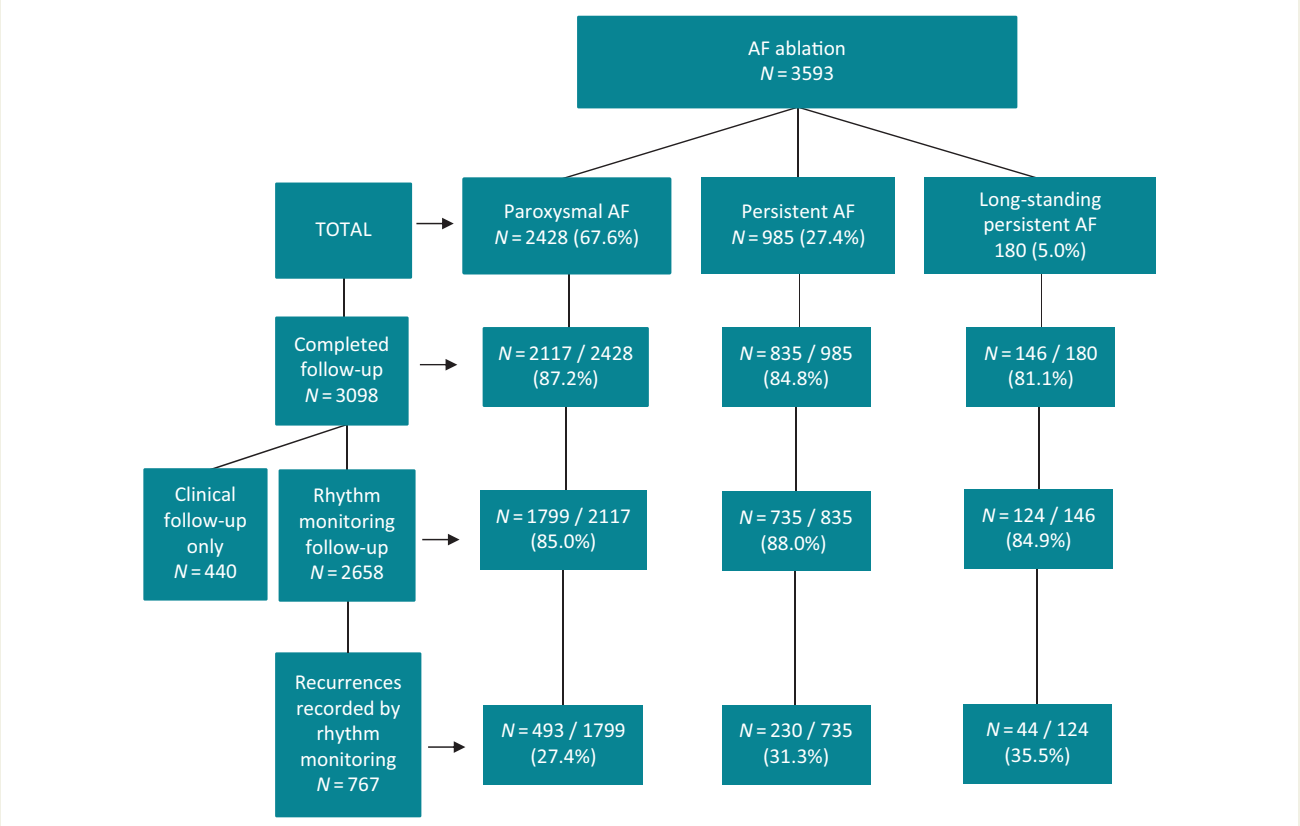

Figure 1 A flowchart of patient follow-up after ablation of paroxysmal, persistent, and long-standing persistent AF in the AFA-LT registry with *N* of patients. AF, atrial fibrillation; *N*, number.

ECG-based rhythm monitoring was 2658 of 3098 (85.8%), while 440 patients (14.2%) underwent clinical follow-up alone. The rates of follow-up evaluations were similar in patients with paroxysmal, persistent, and long-standing persistent AF, 87.2%, 84.8%, and 81.1% of the patients, respectively. The corresponding rate of rhythm monitoring was 85.0%, 88.0%, and 84.9% among the patients with paroxysmal, persistent, and long-standing persistent AF. Of the 2658 patients who underwent rhythm monitoring, 767 (28.9%) experienced recurrences during follow-up. Recurrences were slightly higher in long-standing persistent AF (44/124 patients; 35.5%) and persistent AF (230/735 patients; 31.3%) than in paroxysmal AF (493/1799 patients; 27.4%). The diverse proportions of various monitoring techniques among the patients with and without recurrences after ablation of paroxysmal, persistent, and long-standing persistent AF are presented in *Table 2*.

The Kaplan–Meier curves for the four groups with monitoring follow-up (12-lead ECG, Holter ECG, TTMON, and ICM) and censored log-rank test (*Figure 2*) showed that a lower probability of

Table 2 Proportions of various monitoring techniques among the patients with and without recurrences after ablation of paroxysmal, persistent, and long-standing persistent atrial fibrillation in the AFA-LT registry

Rhythm monitoring methods	Paroxysmal AF		Persistent AF		Long-standing persistent AF	
	With recurrences, n/N (%)	Without recurrences, n/N (%)	With recurrences, n/N (%)	Without recurrences, n/N (%)	With recurrences, n/N (%)	Without recurrences, n/N (%)
ECG	90/493 (18.3)	279/1306 (21.4)	65/230 (28.3)	104/505 (20.6)	15/44 (34.1)	25/80 (31.3)
Holter ECG	344/493 (69.8)	939/1306 (71.9)	139/230 (60.4)	375/505 (74.3)	27/44 (61.4)	50/80 (62.5)
TTMON	19/493 (3.9)	49/1306 (3.8)	16/230 (7.0)	16/505 (3.2)	0/44 (0.0)	1/80 (1.3%)
ICM	40/493 (8.1)	39/1306 (3.0)	10/230 (4.3)	10/505 (2.0)	2/44 (4.5)	4/80 (5.0)

AF, atrial fibrillation; ECG, electrocardiogram; ICM, implanted cardiac monitoring system; *N*, number; TTMON, trans-telephonic ECG monitoring.

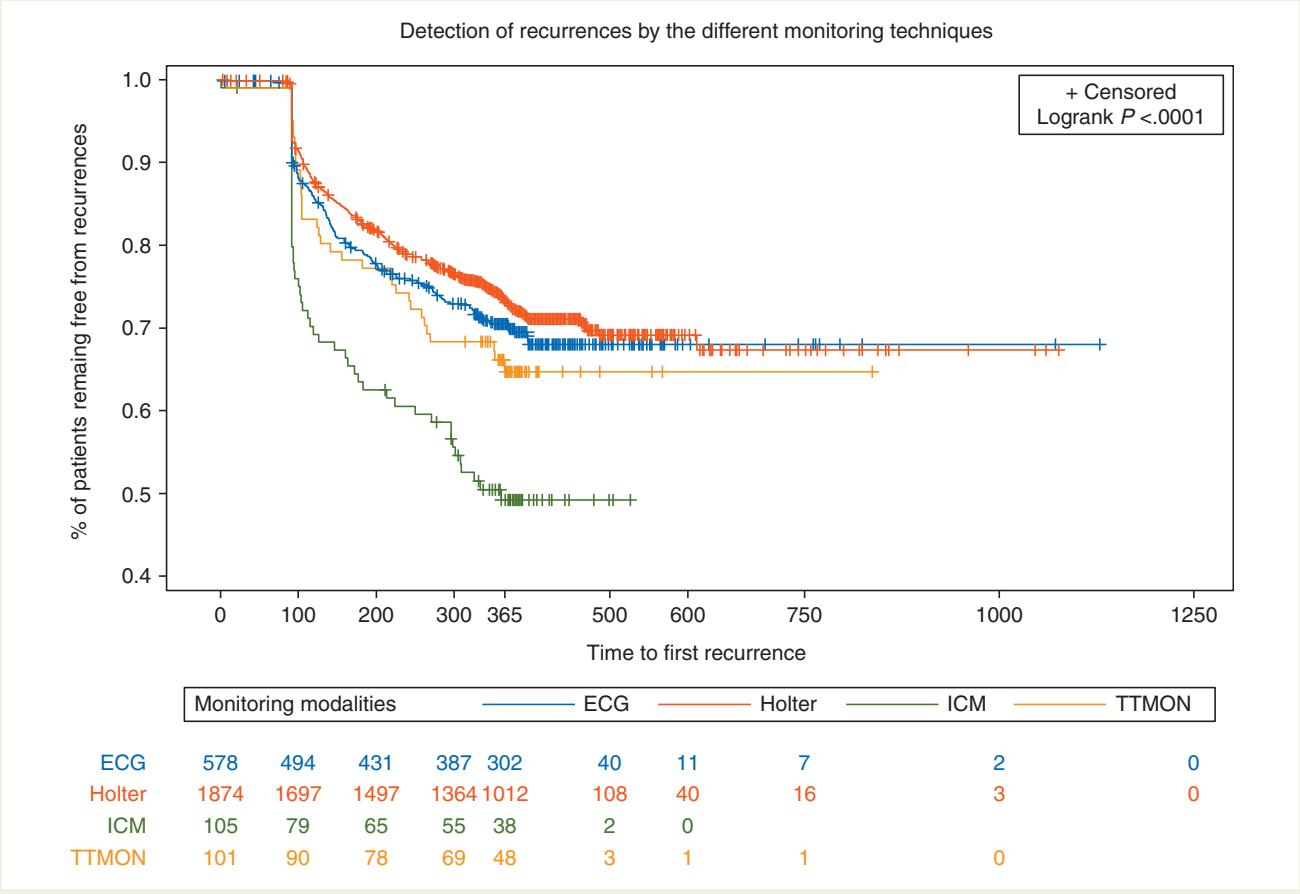

Figure 2 Kaplan–Meier curves to the end of follow-up for atrial fibrillation recurrences detected with the various methods: 12-lead ECG, Holter ECG, ICM system, and TTMON. ECG, electrocardiogram; ICM, implanted cardiac monitoring; TTMON, trans-telephonic ECG monitoring.

freedom from recurrences was detected with ICM compared to TTMON, ECG, and Holter ECG ($P < 0.001$). Moreover, the total success rate of AF ablation as determined by ICM was 50.5%, while the corresponding rates with non-continuous AF monitoring systems (TTMON, ECG, and Holter ECG) were 65.4%, 70.6%, and 72.8%, respectively.

Discussion

Major findings

In this ancillary analysis of the prospective AFA-LT registry, we confirmed that continuous intensive monitoring performed with ICM after AF ablation detected arrhythmia recurrences in half of the

patients during the 1-year follow-up. In contrast, significantly less arrhythmia recurrences were detected with intermittent monitoring strategies such as TTMON, ECG, and Holter ECG, which are mostly used in clinical practice, suggesting that non-continuous AF monitoring methods may overestimate the antiarrhythmic effect of AF ablation. Current guidelines recognize more intensive monitoring as a factor with a greater likelihood of detecting AF, and they also clearly recommend minimum monitoring requirements for follow-up after AF ablation.[11] In making these recommendations, the expert committee encouraged more intensive follow-up with more frequent Holter recordings and/or extended ECG monitoring.

Methods for arrhythmia monitoring

The AFA-LT registry revealed low rates of follow-up evaluations, which were relatively similar in patients with paroxysmal, persistent, and long-standing persistent AF, 87.2%, 84.8%, and 81.1% of the patients, respectively. The corresponding rate of rhythm monitoring was 85.0%, 88.0%, and 84.9% of the patients who underwent a follow-up. However, it is important to notice that a significant number of patients ($N = 440$; 14.2%) did not receive any electrocardiographic monitoring during follow-up.

Generally, the main monitoring methods were Holter ECG (70.5%), followed by ECG (21.7%), ICM (4.0%), and TTMON (3.8%). The electronic case report forms of AFA-LT registry did not contain details about the duration of the Holter ECG. Therefore, the duration of Holter ECG monitoring was not included in comparisons of the monitoring methods. Nevertheless, we discovered through censored log-rank test that ICM detected a significantly higher number of patients with recurrences compared to ECG, Holter ECG, and TTMON. In fact, there was a trend towards a lower AF detection rate with Holter-based follow-up strategy compared to 12-lead ECG only. A possible explanation for this result might be the implementation of symptom-triggered ECG in a substantial number of the patients.

Use of ECG monitoring tools is essential to assess AF ablation success.[11] Furthermore, high incidence of silent arrhythmia recurrence or poor correlation between symptoms and arrhythmia was found after ablation in several previous studies.[6,7,10,12–14] Our prospective, multinational, observational registry supports the results of previous studies which demonstrated that continuous and more intensive monitoring can better detect AF.[8–10,13–16] However, a main strength of our study is the demonstration of these effects not only in a much larger patient population but also in a generalizable setting across many countries in different European geographies and across many centres with significant variation of volumes and with application of follow-up techniques based on clinical routine.

Kottkamp *et al.*[8] detected significantly more AF recurrences using 7-day ECG recording compared with classic 24-h ECG directly after ablation as well as 3 and 6 months after ablation in patients with paroxysmal AF. In a similar way, Holter monitoring with duration of <4 days missed a great portion of recurrences in another study and seemed to be less accurate in the detection of post-interventional arrhythmia recurrence.[9] A prospective short-term follow-up study demonstrated that half of the patients with atrial arrhythmia recurrence after catheter ablation had asymptomatic episodes.[10] These results were confirmed in the AFA-LT registry, which showed that over half of the population (56.6%) became asymptomatic after the AF ablation.[1] The strategy to reduce symptoms may be acceptable for common clinical practice where symptom relief is a main indication for catheter ablation, and anticoagulation strategy is determined rather by risk factors and not by the actual rhythm. However, for clinical studies comparing efficacy of different tools or strategies, continuous ECG monitoring should be the most appropriate method. A recently published expert consensus statement underlines that the importance of asymptomatic AF episodes depends on the purpose of the clinical trials.[11] Thus, the writing group concludes that detection of asymptomatic AF could be of little relevance if the aim of the study is a decrease of symptoms. On the contrary, identification of asymptomatic AF recurrence is of crucial importance if the study objective is to reduce the associated risks of AF (stroke, heart failure), and to change the therapy.[11]

The significance of extended cardiac monitoring was proved in a study which demonstrated that TTMON with a daily 30-s ECG detected more AF relapses than ECG and 24-h Holter ECG.[10] Moreover, the short-term success of ablation decreased from 86% to 72%.[10] In another study, TTMON which was performed once every 2 days showed a 25% rate of asymptomatic AF episodes after ablation, whereas ablation success rate from a follow-up with TTMON was comparable (at around 50%) to the success rate estimated from a follow-up with 7-day Holter ECG.[13] Use of continuous monitoring with ICM revealed higher incidence of AF recurrences and lower success rate (42% at the end of the 3-month post-ablation period).[14] In a similar way, ICM resulted in higher AF detection during the first 6 months after ablation in a pilot study.[15] However, observations exist that long-term subcutaneous implantable loop monitors show false-positive AF detection because of sinus arrhythmia or oversensing of myopotentials, T-waves, and premature beats.[15] Accuracy of AF detection is also influenced by undersensing of beats, limited memory, and determination of arrhythmia episodes ≥2 min.[17,18]

Nevertheless, ICM provided an assessment of long-term AF burden and late recurrences, including asymptomatic episodes that might have implications for further patient management.[11]

A certain degree of non-compliance with guidelines for monitoring after AF ablation was established in the AFA-LT registry. Outcome results of follow-up demonstrated that 10–13% of the patients after AF ablation had no monitoring including 12-lead ECG. Patients' non-compliance and lack of homogeneity and control during follow-up are possible explanations for these results. In addition, newer technologies (smartwatch, smartphone, internet-enabled mobile ECG, and self-applied wearable ECG patch) might have positive impact on post-ablation monitoring.[19]

Limitations

In the interpretation of the results, it should be considered that there was no direct comparison of different monitoring strategies in the individual patient. Thus, the results may have been confounded by several factors such as different success rates among the different centres. Nevertheless, the consistency of our findings with previous literature reports lets us assume that the observed differences correspond to true differences in the detection rates of arrhythmia recurrences by the different monitoring methods. Furthermore, the study design of the AFA-LT registry did not include rhythm monitoring at baseline so that the treatment effects might be biased. Therefore, the robustness of some of the comparative statistical analyses could be

weak. Moreover, the selection of patients to a given monitoring group was performed in this ancillary analysis according to the tool that enabled the most extensive ECG recording. This approach may have introduced some bias.

Our study has also limitations that are inherent to such a large registry. For instance, we do not have sufficient data on frequency and duration of the different monitoring modalities. This represents a lack of precision. In addition, information on further details of the applied monitoring techniques such as type, duration, and number of Holter recordings, types of trans-telephonic monitoring or loop recorders, and programming parameters were not available in the registry. The participating centres had different experience in AF ablation and follow-up monitoring with ECG-based methods, devices, and programming. All of these factors resulted in diverse patient populations.

Despite the recommended and wide application of a 30-s threshold for the definition of AF recurrences that was also applied in our registry, several data question the clinical usefulness of this definition. Recent studies demonstrate a relation between reduction of arrhythmia burden and improvement of general health following ablation showing the limitations of this dichotomic criterion for the management of patients following ablation.[20]

In the AFA-LT registry, there was no information as well whether the episodes of arrhythmia recurrences were symptomatic. There were some disproportions in size among the patient groups belonging to each monitoring type, which is a reflection of the real-life situation where the choice of the follow-up monitoring system is presumably related to a lot of uncontrolled reasons, mostly unknown: local monitoring system availability, perception of need of intense or occasional monitoring by both the responsible physician and the patient, severity of the underlying disease, individual economic issues, logistical situations, patient's compliance and ability of understanding and managing a device.

Conclusion

Comparing all main electrocardiographic monitoring methods in a large patient sample undergoing AF ablation, our results suggest that post-ablation recurrences of AF are significantly underreported by TTMON, ECG, and Holter ECG. While intermittent ECG monitoring is acceptable for common clinical follow-up of the patients, the ICM should be a preferred mode of monitoring for trials evaluating novel AF ablation techniques for improved patient management since it estimates AF ablation recurrences most reliably.

Supplementary material

Supplementary material is available at *Europace* online.

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Smartphone electrocardiograms reveal painful left bundle branch block syndrome and illustrate associated electrophysiological phenomena

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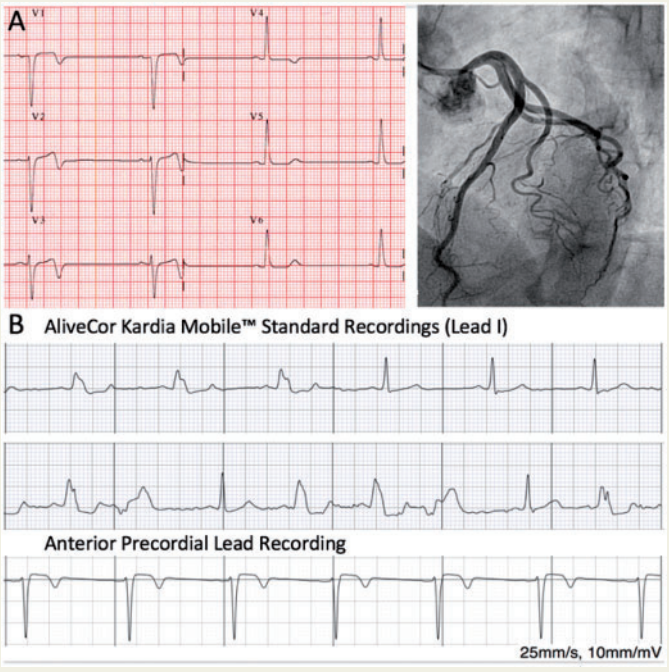
A 69-year-old lady presented with exertional chest discomfort. A 12-lead ECG indicated anteroseptal T wave inversion (TWI) (*Panel A*, left), suspicious for Wellens' syndrome. However, cardiac catheterization (*Panel A*, right) and echocardiography were normal. Her symptoms persisted and she purchased a smartphone electrocardiogram (EGM) device (AliveCor KardiaMobile™, USA). Recordings revealed that her pain coincided with the sudden onset and resolution of left bundle branch block (LBBB) (*Panel B*, top EGM). 'Painful LBBB Syndrome' is an increasingly recognized entity and is easily missed following a reassuring ischaemic evaluation. These single lead recordings also illustrate associated electrophysiological phenomena. The LBBB is rate related (*Panel B*, top EGM), suggesting a phase 3 block. Resolution occurs at a lower rate than onset, due to 'linking phenomenon' whereby concealed retrograde invasion of the bundle occurs from the contralateral side. Premature ventricular contractions allowed time for the LBBB to recover (*Panel B*, middle), consistent with aforementioned explanations for 'functional' block. The TWI was also demonstrated on the KardiaMobile™ by recording an anterior precordial lead (*Panel B*, bottom). Known as 'cardiac memory', TWI transiently occurs after a period of abnormal ventricular activation. In summary, smartphone-based EGM's continue to improve our diagnostic capability and can illustrate complex electrophysiological phenomena.



The full-length version of this report can be viewed at: https://www.escardio.org/Education/E-Learning/Clinical-cases/Electrophysiology.