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Predictors of Short and Long Term Recurrences of Paroxysmal AF after Radiofrequency Ablation. Is Blanking Period Really Benign?

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Abstract

Background: Following pulmonary vein isolation for paroxysmal atrial fibrillation (PAF), early recurrences of atrial arrhythmias (ERAA) are frequent, classified benign as a part of a blanking period. But recently it seems that there is increased incidence of late recurrences in patients with ERAA but mechanism is still unknown.

Purpose: To assess the incidence and risk factors for early and late AF recurrences post AF ablation and the impact of these ERAA on long-term success.

Methods: Thirty-six consecutive patients (age 45 ± 11 years, 72% males) undergoing RF ablation for PAF. They were followed up in hospital for 2 days post ablation then every week for one month. Subsequent follow-up visits consisted of clinical interview, ECGs, and 24h Holter monitoring every 3 months were done for one year. Extended Holter monitoring was done for patients with palpitations. Any episode of symptomatic or asymptomatic documented atrial tachyarrhythmia > 30 seconds was considered recurrence.

Results: Prevalence of ERAA during first 3 months was 47.2%, while late AF recurrence was 25%. 35% of patients with ERAA had late AF recurrence. ≥ 2 attacks of ERAA during the blanking period had significant diagnostic performance in prediction of late AF with sensitivity 44% and specificity 100% (p value=0.05) and also long procedural time (with sensitivity 89% and specificity 63% (p value=0.049). Multivariate logistic regression showed that frequent ERAA attacks was the only significant factor that increases the risk of late AF recurrence (p value =0.008, OR= 4.39, 95% CI=1.48–12.99).

Conclusion:ERAA in blanking period may be associated with increased risk for late AF recurrence. Frequent episodes of early recurrences (≥ 2 attacks) is a strong predictor for late AF recurrence. These data should be considered during follow up of the patients with paroxysmal AF after ablation.

Introduction

Catheter ablation incorporating pulmonary vein isolation (PVI) is an established treatment for symptomatic atrial fibrillation (AF). Current guidelines recommend catheter ablation for drug-refractory AF in adults, and as first-line therapy in selected patients with paroxysmal AF[1-3]. However, there is a wide variety of success rates reported after the catheter ablation and recurrence of AF remains an important problem[4-5].There are currently limited, and conflicting data on the incidence of asymptomatic AF recurrences post-AF ablation. Some studies have suggested that the incidence of asymptomatic AF recurrence is common post-ablation, even in patients who were previously quite symptomatic. Thus, these recurrences are generally censored and known more colloquially as blanking period[6-8]. However, other studies have reported that asymptomatic recurrences post-AF ablation are uncommon[9]. Several studies proposed several procedural predictors of AF recurrence after the procedure [10-11]. However, because AF type (paroxysmal, persistent, and long-standing persistent AF), ablation strategy, patient characteristics, and data analyses were highly heterogeneous in those studies, the results were not consistent. In addition, AF recurrences during the first weeks after AF ablation were treated as a non-significant factor. But nowadays they are regarded to have an impact on long-term PVI failure[12-13].

This study was designed to further study the incidence and risk factors for early and late AF recurrence post-ablation and assess the impact of early AF recurrences on long term success.

Key Words

Paroxysmal Atrial Fibrillation, AF Recurrence, RF Ablation, Blanking period, Long Term AF Freedom

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Methods

Study population

This was a prospective single centre study which included 36 consecutive patients who underwent radiofrequency catheter ablation (RFCA) of symptomatic paroxysmal AF at cardiology department in Ain shams university hospitals during the period from 2015 till 2017. Exclusion criteria included patients unwilling to give study consent and those with persistent AF, history of organized atrial tachycardia (AT) or atrial flutter (AFL), or previous history of AF ablation.

Trans-oesophageal echocardiography was performed in all patients to rule out left atrial (LA) thrombus before ablation. In patients on

vitamin K antagonists, anticoagulation was stopped 3 days before ablation and replaced by intravenous heparin to maintain a partial thromboplastin time of 2–3 times of the normal value, or bridged with low-molecular weight heparin. The procedure was performed under therapeutic INR values of ≤ 2. The study was performed under general anaesthesia after obtaining informed written consent from the patients.

Mapping

First, trans-septal access to the left atrium was obtained with standard techniques. Repetitive intravenous heparin was administered to maintain an activated clotting time of 300 to 350 s. Mapping and catheter ablation of AF were performed using 3D electro-anatomical (3D EA) mapping system (CARTOR 3 system, Biosense Webster, Diamond Bar, CA, USA) Simultaneous surface ECG and bipolar intracardiac electrogram (EGM) recordings (filtered between 30 and 500 Hz) were amplified and displayed using the Prucka CardioLab System (GE Medical Systems, Milwaukee, WI, USA).

Mapping was performed during sinus rhythm using a 3.5-mm–tip catheter (ThermoCool Navi-Star, Biosense Webster Inc., Diamond Bar, CA) to create an anatomical map. In each case, we tried to obtain an evenly distributed map throughout the left atrium.

After 3D reconstruction of the LA, each pulmonary vein (PV) ostium was tagged on the map. Lasso catheter was positioned across the ostium of each PV aiming at recording pulmonary vein potentials (PVPs).

RF-ablation protocol

RF- ablation approach chiefly involved pulmonary vein isolation (PVI) in all patients. PVI was performed first at the antrum of left PVs followed by the right sided PVs using RF energy of 25-30 Watts with an external irrigation flow rate of 15-17 ml/min. RF current was applied continuously with repositioning of the catheter tip every 30-60 seconds. Special caution was done at the posterior wall near the oesophagus as power was reduced to 25 Watts with continuous repositioning of the catheter tip every 20 seconds. Disappearance or dissociation of PV potentials on Lasso catheter was defined as acute PVI success (exit block).

After ablation, Patients who had AF during the study underwent electrical cardioversion (CV) in order to verify PVI in SR, and PVI was reassessed in all patients after a 30-minute waiting period. Confirmation of PVI was defined by the absence of PVPs on the Lasso catheter during pacing from a coronary sinus or an LA catheter (Entrance block) and Failure of capturing the atrium through pacing from all poles of Lasso catheter inside each PV (Exit block).

After a 30-minute waiting period, a 40 mg bolus of adenosine triphosphate was injected to unmask any dormant PV conduction. The subsequent response was assessed for each PV using the lasso mapping catheter. If no dormant conduction was detected, the procedure was consideredsuccessful, and the patients were defined as acute PVI responder.

If dormant conduction was detected, an additional targeted RF ablation was done at sites of transient or sustained reconnection in each affected pulmonary vein until dormant conduction could no longer be elicited.

No antiarrhythmic drugs were prescribed after the procedure to avoid the effect of medications on recurrence. The patients underwent continuous, in-hospital ECG monitoringfor 2–4 days following the procedure. The first outpatientclinic visit was one week after the ablation procedure. Subsequentfollow-up visits consisted of a clinical interview, ECGs,and 24-h Holter monitoring every week for 3 months, followed by every 3 months for 12 months, at the cardiologyclinic. Patients with palpitations were encouraged to do extended Holter monitoring for up to 7 days.

Any episode of AF that lasted more than 30 seconds documented with surface ECG or Holter monitoring was considered a recurrence. AF recurrence was further subdivided into asymptomatic and symptomatic AF.

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 20 , IBM Corp., Chicago, USA, 2009.

Descriptive statistics were done for quantitative data as minimum and maximum of the range as well as mean± SD (standard deviation) for quantitative normally distributed data, median and 1st and 3rd inter-quartile range for quantitative non-normally distributed data, while it was done for qualitative data as number and percentages.

Inferential analyses were done for quantitative variables using independent groups with normally distributed data and Mann whiteny U in cases of two independent groups with non-normally distributed data. In qualitative data, inferential analyses for independent variables were done using Fisher's Exact test for differences between proportions with small expected numbers. ROC curve was used to evaluate the performance of different tests differentiate between certain groups. Logistic regression model was used to find out independent factors affecting recurrence. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant. Sensitivity = (True positive test / Total positive golden) x 100, Specificity = (True negative test / Total negative golden) x 100.

Results

Patient Characteristics

Patient characteristics are depicted in [Table 1]

The age of the study population was 45.3 ± 11.4 years. Twenty six (72.2%) patients were males while 10 (27.8%) were female.

Nineteen patients (52.8%) of the study population had arterial hypertension (HTN), five patients (13.9%) had diabetes Mellitus (DM), and six patients (16.7%) were smokers. Only one patient (2.8%) had hypertrophic cardiomyopathy (HCM) while the rest of

Table 1: Baseline clinical characteristics, procedural data and post procedural follow up of the study population

Characteristic	Study population (no.36)
Age at ablation time (years)	45.3 ± 11.4
Gender	
Male	26 (72.2%)
Female	10 (27.8%)
Arterial hypertension(HTN)	19 (52.8%)
Diabetes Mellitus (DM)	5 (13.9%)
Smoking	6 (16.7%)
Thyroid disease	0
Structural heart disease	1 (2.8%)
IHD	0
DCM	0
HCM	1
VHD	0
AF	
Duration since first attack(years)	4.4±3.3
Frequency per month	3.64 ± 1.18
EHRA score	EHRA II: 2 (5.6%) EHRA III: 34 (94.4%)
LAD (mm)	42.75 ± 5.02
LVEF%	65.47 ± 3.07
Vitamin K antagonists	30 (83.3%)
No. of AADs	1 (1-3)
Betablockers	1 (2.8%)
Class I AAD	20 (55.6%)
Class III AAD	16 (44.4%)
Fluroscopy time (minutes)	44.2 ± 27.9
Procedural time (minutes)	167.3 ± 30.6
PVI attempted	36/36 (100%)
PVPs (Exit block)	36 (100%)
Eliminated	29 (80.5%)
Dissociated	8(19.4%)
Entrance block	36 (100%)
First 3 months post AF ablation (Blanking period)	
Incidence of AF	17 (47.2%)
Number of attacks	
Single attack	13 (76.5%)
Two attacks	2 (11.7 %)
>2 attacks	2 (11.7 %)
Symptomatic AF	12 (70.5%)
Need for cardio-version	5 (41.6 %)
AF recurrence over 12 months (after blanking period)	
Incidence of AF	9 (25%)
Symptoms	9 (25 %)
Response to AADs	5 (55.5 %)
Need for Redo AF Ablation	4 (44.4 %)

AF: atrial fibrillation; IHD: ischemic heart disease, DCM: dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy; VHD: valvular heart disease; LAD: left atrial diameter; mm: millimeter; LVEF: left ventricular ejection fraction; AADs: antiarrhythmic drugs; PVI: pulmonary vein isolation; PVPs: pulmonary vein potentials.

patients (97. 8%) had normal structural heart. All study population had normal thyroid profile and no history of thyroid disease. There was no history of thromboembolic events or familial history of AF< 55 years.

Median time interval from first AF diagnosis to index ablation procedure (AF duration) was 43.5 ± 27 months with a frequency of 3.64 ± 1.18 times/month. As regards EHRA score[1], 34 patients (94.4%) had symptomatic AF graded as EHRA score III.

The median number of antiarrhythmic drugs (AAD) prior to ablation was one (range 1-3). Vitamin K antagonists were used in thirty patients (83.3%) while the rest of patients didn't take any anticoagulants as CHA2DS2-VASC score[1] was 0.

Pre-procedural Echocardiographic parameters [Table 1]

Left atrial longitudinal diameter (LAD) was 42.75 ± 5.02 mm (ranged from 32 to 56 mm), while left ventricular systolic function (LV EF) was 65.47 ± 3.07 %.

Mapping and Ablation outcomes [Table 1]

Mapping and ablation were guided by 3D LA mapping using Carto 3 system in all study populations. Complete PVI was achieved in all procedures of 36/36 patients and no additional lines were needed. Entrance and exit blocks were achieved in all procedures (100%). Total fluoroscopy time was 44.21± 27.9 minutes and total procedural time was 167.36 ± 30.69 minutes.

Follow-Up

Follow up was for 2–4 days following the procedure. The first outpatientclinic visit was one week after the ablation procedure. Subsequentfollow-up was every week for 3 months followed by every 3 months for 12 months, at the cardiology clinic.

The blanking period (first three months after AF ablation) [Table 1]

Atrial arrhythmias occurred in 17 patients (47.2%). 13 out of 17 patients (76.5%) had only one attack, while 4 patients (23.5%) had more than one attack. 12 patients(70.5%) were symptomatic while 5 patients (29.5%) were asymptomatic. Cardioversion was needed in 5 out of 12 patients (41.6%). But no antiarrhythmic drugs were described as maintenance therapy based on the current study design.

Follow up After blanking period till 12 months: [Table 1]

Nine patients (25%) had AF recurrence during follow up over 12 months. five of 9 patients (55.5%) who had AF recurrence responded to pharmacological treatment in form of Amiodarone while redo AF ablation was done in four patients (44.4%). Three patients (8.3%) had AF recurrence between 3-6 months, 5 patients (13.8%) had AF recurrence between 6-9 months, while one patient (2.7%) had AF recurrence between 9-12 months.

Redo AF ablation procedures

A redo AF ablation was performed in 4/36 (11%) patients. In these procedures, PV re-connections were observed in 4/4 (100%) patients. Therefore, RF ablation was done at sites of reconnection in each affected pulmonary vein.

Predictors of AF recurrence during first 3 months (blanking period): [Table 2]

HTN was present in 13 out of 17 patients who had atrial tachyarrhythmia during blanking period with p value 0.007. Those

Table 2: Predictors of AF recurrence during blanking period

Parameters	Patients with atrial arrhythmias (No. 17)	Patients without atrial arrhythmias (No.19)	P value
Age	45.7 ± 12.1	44.9 ± 11.1	^0.84
Gender			
Male	12 (70.6%)	14 (73.7%)	§0.83
Female	5 (29.4%)	5 (26.3%)	
DM	2 (11.8%)	3 (15.8%)	§0.72
HTN	13 (76.5%)	6 (31.6%)	§0.007*
Smoking	1 (5.9%)	5 (26.3%)	§0.10
AF			
Age of onset of AF (years)	41.3±11.6	42.0 ±10.5	^0.84
Time interval from first AF diagnosis to AF ablation (years)	4.4±2.7	2.9±1.5	^0.043*
Frequency per month (median/IQR)	4 (4–5)	3(2–4)	#0.003*
EHRA score II-III	17 (100%)	19(100%)	§0.93
LAD (mm)	44.5 ± 5.1	41.1 ± 4.36	^0.036*
LV EF%	65.53 ± 3.20	65.4 ± 3.02	^0.92
Fluoroscopic time	38.5 ± 20.9	49.5 ± 33.1	^0.26
Procedural time	175.8 ± 28.1	159.7 ± 31.5	^0.12
Late AF recurrence after blanking period	6 (35.3%)	3 (15.8%)	§0.255

AF: atrial fibrillation; LAD: left atrial diameter; mm: millimeter; LVEF: left ventricular ejection fraction; PVI: pulmonary vein isolation.
^Independent t-test, #Mann Whitney test, § Fisher's Exact, *Significant.

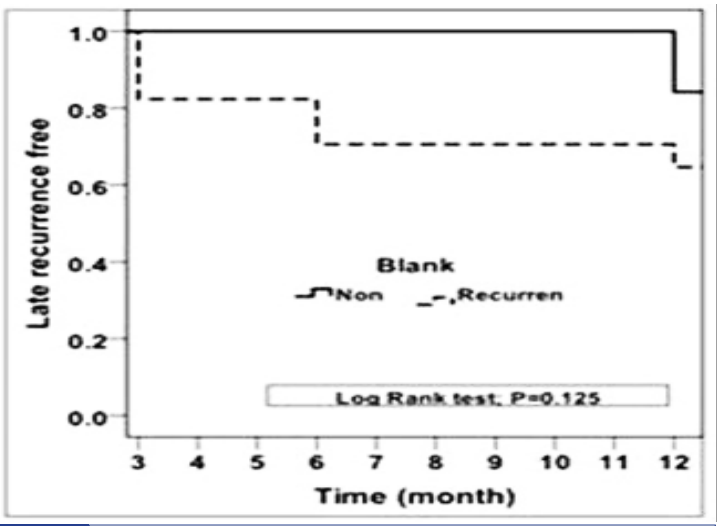

Figure 1: The Kaplan–Meier estimate Arrhythmia-free survival and 95% confidence intervals after RF ablation of PAF in patients with atrial arrhythmias detected during the blanking period (dashed line) and the patients without any arrhythmias during the blanking period (continuous line) over 12 months. Numbers indicate remaining patients without AF recurrence at each time point.

patients had also longer interval from first AF diagnosis to AF ablation and more frequent AF attacks per month before ablation than those without atrial tachyarrhythmia (p value= 0.043 and 0.003, respectively). In addition, Left atrial longitudinal diameter (LAD) was significantly larger in the patients who had atrial tachyarrhythmia than those without (p value=0.036).

Six out of 17 patients (35.3%) with atrial arrhythmias during blanking period had late AF recurrence while 3/19 patients (15.8%) without atrial arrhythmias had late AF recurrence (p value=0.255). [Table 2] and[Figure 1].

Diagnostic performance of these factors in prediction of AF recurrence during blanking period ([Table 3] and [Figure 2]):

Frequent AF attacks per month before ablation had significant diagnostic performance in prediction of recurrence during blanking period with sensitivity 82.4% and specificity 68.4% (p value=0.005) with cutoff value ≥ 4 attacks /month.

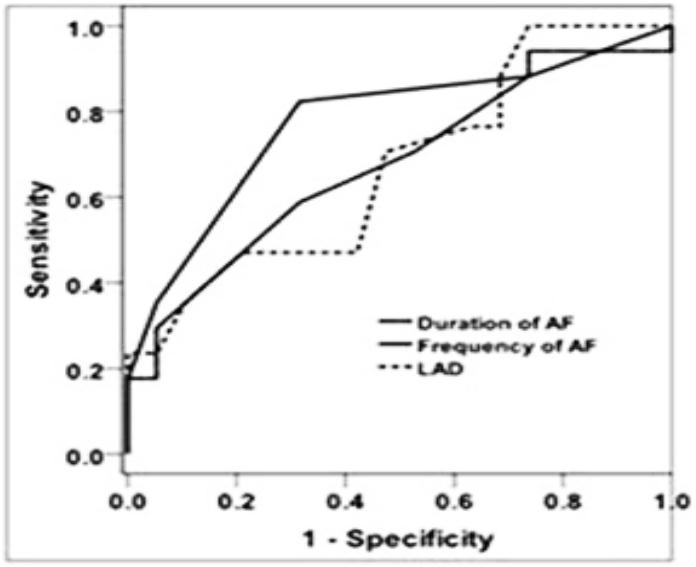

Figure 2: ROC curve for factors predicting the incidence of atrial arrhythmia during the blanking period post AF ablation.

Table 3: Diagnostic performance of the factors in prediction of AF recurrence

Factors	AUC	SE	95% CI	P	Cut off	Sensitivity	Specificity
Prediction of AF recurrence during blanking period							
Time interval from first AF diagnosis to AF ablation (years)	0.676	0.091	0.498–0.855	0.071	≥3.5	0.588	0.684
Frequency of AF per month before ablation	0.776	0.081	0.616–0.935	0.005*	≥4.0	0.824	0.684
LAD (mm)	0.670	0.090	0.493–0.848	0.081	≥37.5	1.000	0.263
Prediction of AF recurrence over 12 months follow up							
Age at time of first AF diagnosis (years)	0.704	0.106	0.496–0.911	0.071	≥42.5	0.667	0.741
Duration of procedure (minutes)	0.718	0.087	0.547–0.889	0.049*	≥177.5	0.889	0.630
Frequency of AF attacks during blanking period	0.720	0.115	0.494–0.946	0.05*	≥2.0	0.444	1.000

AF: atrial fibrillation; LAD: left atrial diameter; mm: millimeters

LAD ≥37.5 mm is the cutoff value, that is associated with high incidence of AF recurrence in the blanking period with sensitivity 100%, specificity 26.2% but p value =0.081.

After adjustment of all factors using Multivariate logistic regression, we found that: HTN is an independent risk factor for atrial arrhythmia during the blanking period (OR 7.042, 95% CI = 1.602-30.9 with p value 0.01). Frequency of AF attacks per month (≥ 2 attacks per month) is also an independent risk factor (OR 24.5, 95% CI = 2.57–234.25 with p value 0.005), in addition to, the Time interval from first AF diagnosis to AF ablation (≥ 3.5 years) is an independent risk factor (OR 9.71, 95% CI = 1.06–89.34 with p value 0.045).

Predictors of late AF recurrence over 12 months post AF ablation: [Table 4]

The patients with late AF recurrence post ablation had older age (43.8±10 years) than those without AF recurrence (40.4±11.6 years) [p value= 0.046].

LAD was also significantly larger in patients who had AF recurrence (46.08 ± 5.25 mm) than those without recurrence (41.08 ± 4.05 mm) with P value 0.003.

Table 4: Predictors of late AF recurrence over 12 months follow up

Parameters	Patients with atrial arrhythmias (No. 9)	Patients without atrial arrhythmias (No.27)	P value
Age	46.1 ± 10.9	43.7 ± 12.6	^0.57
Gender			
Male	7 (77.8%)	19 (70.4%)	§1.000
Female	2 (22.2%)	8 (29.6%)	
HTN	3 (33.3%)	16 (59.3%)	§0.255
DM	2 (22.2%)	3 (11.1%)	§0.581
Smoking	2 (22.2%)	4 (14.8%)	§0.627
Structural heart disease (HCM)	1 (11.1%)	0 (0%)	§0.250
AF			
Age at onset of AF	43.8±10.0	40.4±11.6	^0.046*
Time interval from first AF diagnosis to AF ablation (years)	4.4±3.3	3.4±1.8	^0.216
Frequency per month (median/IQR)	4 (3 –5)	3 (3–4)	#0.103
EHRA score II-III	9 (100%)	25 (92.6%)	§1.000
No. of AADs before ablation			
One	2 (22.2%)	23 (85.2%)	
Two	4 (44.4%)	3 (11.1 %)	§0.146
> 2	3 (33.3 %)	1 (3.7%)	
LAD (mm)	46.1 ± 5.2	41.1 ± 4.1	^0.003*
LV EF%	64.8 ± 3.2	65.7 ± 2.9	^0.38
Procedural time (minutes)	184.4±15.7	161.7±32.5	^0.009*
Atrial arrhythmia in blanking period	6 (66.7%)	11 (40.7%)	§0.255
Number of AF attacks during the blanking period (median/IQR)	2.5 (1.0–3.3)	1 (1–1)	#0.003*

AF: atrial fibrillation; HTN: arterial hypertension; DM: Diabetes Mellitus; AADs: antiarrhythmic drugs; LAD: left atrial dimensions; mm: millimeter; LVEF: left ventricular ejection fraction; PVI: pulmonary vein isolation.

Procedural time was longer in patients with AF recurrence (184.4±15.7 min.) than those without (161.7±32.5 min.) with p value 0.009.

There is no statistical difference in incidence of atrial arrhythmias during the blanking period between the patients with late AF recurrence and the patients without recurrence (P value =0.255). But, we found that patients with late AF recurrence had more frequent AF attacks during the blanking period than those without late recurrence [p value= 0.003]

Diagnostic performance of these factors in prediction of late AF recurrence ([Table 3] and [Figure 3])

Longer procedural time had significant diagnostic performance in prediction of late recurrence with sensitivity 89% and specificity 63% (p value=0.049).≥ 2 AF attacks during the blanking period also had significant diagnostic performance in prediction of late AF with a sensitivity of 44% and specificity of 100% (p-value 0.05). After adjustment of all factors using multivariate logistic regression(Table 5), we found that: Frequency of AF attacks during the blanking period was the only significant factor that increases the risk of late AF recurrence (p-value 0.008, OR 4.39, 95% CI 1.48–12.99).

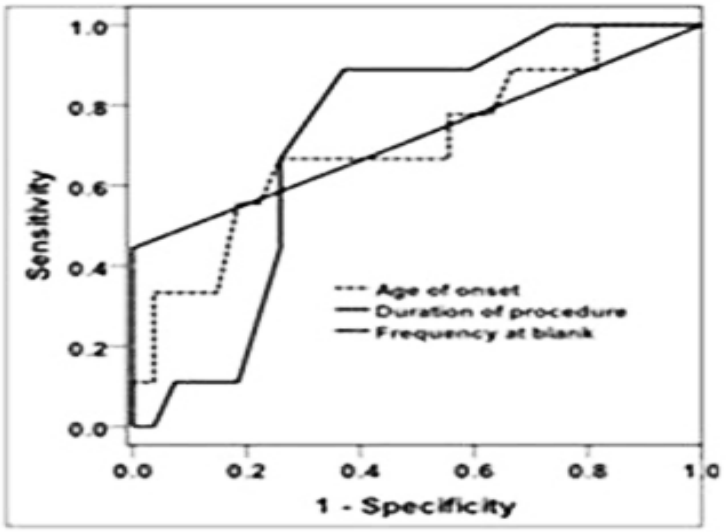

Figure 3: ROC curve for factors predicting late AF recurrence over 12 months follow up post AF ablation.

Table 5: Logistic regression for factors affecting AF recurrence

Factors	β	SE	P	OR (95% CI)
Factors affecting AF recurrence during blanking period				
Time interval from first AF diagnosis to AF ablation (≥3.5 years)	2.27	1.13	0.045*	9.71 (1.06–89.34)
Frequency of AF per month before ablation (≥2 per month)	3.20	1.15	0.005*	24.54 (2.57–234.25)
HTN	2.99	1.16	0.010*	7.42 (1.602-30.9)
Factors affecting late AF recurrence over 12 months				
Frequency of AF attacks during blanking period	1.48	0.55	0.008*	4.39 (1.48–12.99)

β: Regression coefficient, SE: Standard error, OR: Odds ratio, CI: Confidence interval, *Significant

Discussion

Main study findings

This prospective study is characterized by in hospital continuous ECG monitoring for patients with paroxysmal AF after RF ablation for 2-4 days. Then the first outpatient clinic visit was one week after the ablation procedure. Subsequent follow-up was every week for 3 months at the cardiology outpatient clinic then every 3 months for 12 months. Patients with palpitations were encouraged to do extended Holter monitoring up to 7 days. In order to study if there was a correlation between early AF recurrence and long term AF freedom.

We found that prevalence of AF during first 3 months (blanking period) was 47.2%, while late AF recurrence was 25% in the study population. Frequent AF attacks during the blanking period were associated with increased risk for late AF recurrence after RF ablation of PAF and these results suggested that AF during blanking period is not benign as it was considered in previous studies.

Previous studies have investigated clinical predictors of ablation success in a population with both paroxysmal and persistent AF [14-16] or only with persistent AF[17]. In 2010, an important systematic review[18] was published for the predictors of AF recurrence. They evaluated 25 studies with a multivariable analysis, and concluded that non-paroxysmal AF might be a clinically useful proxy for a combination of confounded variables, none of which alone were an independent predictor of AF recurrence. The evaluation was limited because of the large heterogeneous nature of this study. Persistent AF is a very different pathophysiological entity requiring more ablation lesions so indications for ablation, ablation strategy and endpoint of the procedure were highly heterogeneous. Therefore, it is likely to have different predictors of success. All these reasons make the results of these studies are contradictory.

In the current study, we focused only on paroxysmal AF (PAF) as PAF is the best indication for ablation and PVI is a widely accepted strategy for it. To our knowledge, a very few studies[19] evaluated predictors of recurrence post AF ablation in patients with only paroxysmal AF.

Prevalence and significance of early recurrences during blanking period

Prevalence of AF was 47.2% during first 3 months in this study which is similar to results of several previous trials ranged from 35 to 45%[20-24].

The current study demonstrate that 64.7% of patients who experienced early recurrences did not experience a late AF recurrence requiring treatment. Many previous studies also reported that up to 60% of patients with an early recurrence did not go on to have late recurrences[25-26]. Vasamreddy et al.[25]found that 45% of patients with ER experienced long-term success following AF ablation; but if patients with asymptomatic recurrences were included, this reduced to only 20% of patients. Klemm et al.[26]included only patients with paroxysmal AF like the current study but In thier study, all patients had 24 hours ambulatory monitoring at 1, 3, 6, 9, and 12 months following the procedure while we had more intensive follow up protocol included symptomatic and asymptomatic recurrences.

In the current study, the patients with atrial arrhythmias during the blanking period had higher arterial blood pressure, larger LAD, more frequent AF attacks and longer interval from first diagnosis of AF till ablation compared to the patients without atrial arrhythmias. But we found that the only predictors for AF during this period were LAD, Time interval from first AF diagnosis to AF ablation and Frequency of AF per month before ablation. LAD ≥37.5 mm is the cutoff value with sensitivity 100%, specificity 26.2% while Time interval from first AF diagnosis to AF ablation (≥ 3.5 years) had sensitivity 59% and specificity 68%. However, Frequent AF attacks per month (≥4 per months) before ablation was the most significant predictor for AF recurrence during blanking period with high sensitivity 82.4% and specificity 68% (P value 0.005).

Multivariate analysis showed the independent risk factors that increase the incidence of AF were HTN, frequent AF attacks per month and longer interval from first AF diagnosis to AF ablation. Our explanation is that these factors reflect the extent of atrial remodeling. The current study was one of few studies that detected predictors for AF during blanking period like Masuda et al [27] and Lellouche et al[22] while some other studies do not find any risk factors like Lodziński et al[23]. Our explanation for impact of frequency of AF attacks and duration as predictors is tendency to postpone AF ablation till failure of pharmacological treatment because of high cost of this procedure in Egypt.

Follow up over 12 months

In the current study, the patients with late AF recurrence had larger LAD and showed older age at time of first AF diagnosis, longer procedural time and more frequent AF attacks in the blanking period compared to the patients with recurrence. But we found that the only predictors for late AF recurrence were age at time of first AF diagnosis, procedural time and Frequency of AF attacks during the blanking period.

≥42.5 years is the cutoff value for age at time of first AF diagnosis with a sensitivity of 67% and specificity of 74%. Procedural time of ≥177.5 minutes had a sensitivity of 89% and specificity of 63% (p-value 0.049).In addition, frequent AF attacks during blanking period (≥2 attacks) was a significant predictor with a sensitivity of 44% and a high specificity of 100% (p-value 0.05).

Multivariate analysis showed the only independent risk factor that increase the incidence of late AF recurrence was Frequency of AF attacks during the blanking period (p value =0.008, OR= 4.39, 95% CI=1.48–12.99). This may explain why not all patients with early recurrences in blanking period will experience late recurrences, as it depends on frequency of AF attacks during this period.

Prior data have demonstrated that AF recurrence shortly after PVI may not portend ultimate outcome[24,28]; a period referred to as the "blanking period," ranging from 1–3 months. However, AF monitoring during this period has been highly variable. Therefore, the practical and working definition of this period remained elusive.

O'Donnell et al.[13] examined AF recurrence after PVI with an ECG obtained at various time intervals following PVI and suggested clinical recovery was complete by 3 months. While several recent studies revealed that early recurrence during blanking period is associated with late AF recurrence[29,32] Willems, et al.[31] analyzed also the clinical significance of early recurrence episodes occurring at different times throughout the blanking period in patients who were enrolled in the Adenosine Following Pulmonary Vein Isolation to Target Dormant Conduction Elimination (ADVICE) trial. They found that ablation success rate at one year was significantly higher in patients who had no early recurrences (77.2% 1-year freedom from AF), while rates of success were lower as early recurrence occurred later within the blanking period. In addition, Jaskson et al. [32]reported that early recurrence which occurs later (>2 weeks after ablation) in the blanking period as well as the occurrence of multiple episodes throughout the blanking period are strong predictors of late arrhythmia recurrence.

Conclusion

Early atrial arrhythmia recurrences in blanking period may be associated with increased risk for late AF recurrence. Frequent episodes of early recurrences (≥ 2 attacks) is a strong predictor for late AF recurrence. These data should be considered during follow up of the patients with paroxysmal AF after ablation.

Study limitations

This study includes a relatively small number of patients. We needed longer term recordings for more precise detection of asymptomatic recurrences, besides, the follow up period is not long enough that some very late recurrence may be ignored. Therefore, the AF recurrence maybe underestimated and some underlying risk factors may be neglected or less studied. However, the results may be clinically important.

Disclosures

Dr. Lamyaa Allam (author A) declares that she has no conflict of interest. Dr. Mazen Tawfik (Author B) declares that he has no conflict of interest .Dr. Ayman Morttada (author C) declares that he has no conflict of interest.

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