

MB-LATER score as a useful tool for prediction of arrhythmia recurrence after radiofrequency catheter ablation of atrial fibrillation – clinical application

Milan Marinković¹, Aleksandar Kocijančić¹, Vladan Kovačević¹, Miroslav Mihajlović¹, Jelena Simić¹, Nikola Isailović¹, Anja Radunović¹, Vera Vučićević², Tatjana Potpara^{1,3}, Nebojša Mujović^{1,3}

¹Cardiology Clinic, Clinical Center of Serbia, Belgrade, Serbia; ²Center for Anesthesiology Clinical Center of Serbia Belgrade Serbia; ³School of Medicine, University of Belgrade, Belgrade, Serbia

Abstract

Atrial fibrillation (AF) is most frequent sustained cardiac arrhythmia in general population. It is well established that crucial task for management of these patients is prevention of AF-related complications. One of the most important management strategies represents catheter ablation in order to reduce AF burden, to achieve symptomatic and functional improvement, and in some patient (e.g. heart failure) to reduce overall mortality. Several prognostic scores were developed for AF recurrence prediction after catheter ablation of AF. Role of these scores might be better optimization of long-term follow-up and deciding on discontinuation of oral anticoagulant therapy and stopping of antiarrhythmic drugs after the procedure, thus identification of patients at risk for arrhythmia recurrence may be extremely important. Numerous clinical factors are associated with arrhythmia recurrence and some of those are used for developing rhythm-outcome specific scores. MB-LATER score was retrospectively derived for prediction of arrhythmia recurrence after catheter ablation of AF, and in this article, we are going to discuss its utilization in clinical practice.

Key words

atrial fibrillation, catheter ablation, prognostic scores, arrhythmia recurrence

Introduction

Atrial fibrillation (AF) is the most common arrhythmia diagnosed in general population and is associated with increased morbidity and mortality.¹ Radiofrequency catheter ablation (RFA) represents well established and effective method for invasive treatment of AF, that provides better quality of life compared to antiarrhythmic therapy.² Today we have more data on the importance of RFA of in AF patients with heart failure (HF), where it significantly contributes to the reduction of the risk of rehospitalization due to HF, HF progression and reduction of overall mortality.³ Furthermore, it seems that RFA of AF might have important role in risk reduction for thromboembolic events in patients with AF shown in some observational studies, but we currently lack randomized studies powered to prove this.⁴⁻⁶ Given these potential benefits, approach to invasive treatment must be balanced due to potential complication of the procedure and relatively high arrhythmia recurrence rate after RFA of AF that ranges from 20-40%.¹

Identification of patients at risk for arrhythmia recurrence may be extremely important in terms of anticoagulant therapy and appropriate rhythm monitoring

strategy after RFA. Numerous clinical factors are associated with arrhythmia recurrence after RFA of AF, most commonly older age, non-paroxysmal AF, left atrial (LA) size, gender, coronary artery disease (CAD), hypertension (HTA), diabetes mellitus (DM), metabolic syndrome (MS), chronic kidney disease (CKD), HF and early recurrence of AF (ERAF) after procedure.⁷ Several prognostic scores have been developed to predict individual risk of recurrence of AF after catheter ablation.⁸ Some of them are rhythm-outcome specific scores like: ALARMEC, BASE-AF₂, APPLE, CAAP-AF, and MB-LATER.⁹⁻¹⁴ MB-LATER score is derived by our group and validated in several external cohorts.¹⁵ We found that our score has significant clinical implications, since it was initially developed to predict very late recurrences of AF - VLRAF (more than 12 months post AF ablation), but also it has been externally validated and showed a significant but modest predictive ability for late recurrence of AF (more than 3 months post-AF ablation).^{12,15} Therefore MB-LATER score could be used for adequate discussion of the expected results of RFA before procedure with our patients as well as to develop an adequate follow-up strategy for these patients after the procedure.

The purpose of this paper is to summarize available tools for risk stratification for arrhythmia recurrence after RFA

of AF. Here we discuss the clinical implementation of MB-LATER score in two cases from our practice and so far, published data on other rhythm-outcome specific scores for the purpose of more comprehensive understanding and adequate managing of these patients.

Case presentation

CASE 1. A 68 year-old Caucasian male with history of HTA was evaluated at our department for highly symptomatic palpitations. First episode of arrhythmia was registered three years before admission to our department, at that time he was examined at emergency room and 12-lead ECG showed AF with fast ventricular response. Rhythm control was achieved by administration of propafenone i.v. (1.5 mg/kg). Propafenone was advised for long-term rhythm control, and also dabigatran (150 mg, bid) was introduced for stroke prevention (CHA₂DS₂-VASc = 2). Further, coronary angiography was performed and revealed no significant coronary artery disease. Propafenone was transiently effective, and in the past 12 months before the procedure he had 4 episodes of AF, longest duration up to 12 hours. Physical examination at admission revealed normal findings. Echocardiography showed no structural heart disease; LA diameter was 45 mm and ejection fraction (EF) was preserved. Chest X-ray was unremarkable. Baseline laboratory investigations including serum electrolytes, complete blood count, liver and renal function tests were normal, except dyslipidaemia. There was a history of smoking up to 20 cigarettes per day and no history of

alcohol or drug abuse. Family history revealed that his brother suffered from stroke of unknown cause. Given the previous history of the disease, resistance to medical therapy and highly symptomatic episodes of AF catheter ablation was performed. Propafenone was discontinued ≥ 5 half-lives before the procedure. Dabigatran was omitted 24 hours before the procedure. RF catheter ablation was performed under conscious sedation. The quadripolar catheter was inserted into the distal coronary sinus as electroanatomical landmark. Via the right femoral vein three sheaths were introduced, transseptal puncture (TSP) was carried out with a long needle and sheath (BRK1/BRK1-XS, Swartz SL0/SL1, St Jude Medical, MN, USA) and navigation of the ablation catheter was performed with a long steerable sheath (8.5 Fr Agilis NXT, St Jude Medical, MN, USA). Pulmonary vein (PV) activity was assessed with a circular 20-polar catheter inserted through the long non-steerable sheath. Anatomical LA map was created, and fusion with the CT scan was performed (Ensite Precision, St Jude Medical). Ablation was performed using RF energy (TactiCath Quartz catheter, 7 Fr, St Jude Medical, MN, USA). Strategy of ablation was ipsilateral circumferential antral pulmonary vein isolation (PVI, Figure 1A). RF application were delivered 1–2 cm outside from the ipsilateral PV ostia (30W, 43C, flow rate 17 ml/min). Electrical PVI was achieved as endpoint of this procedure, and patient was observed in the lab for the 30 min after the last RF application (standard protocol in our electrophysiology lab as previously published).¹² Patient was discharged two days later, without any post-procedural complications during hospital stay.

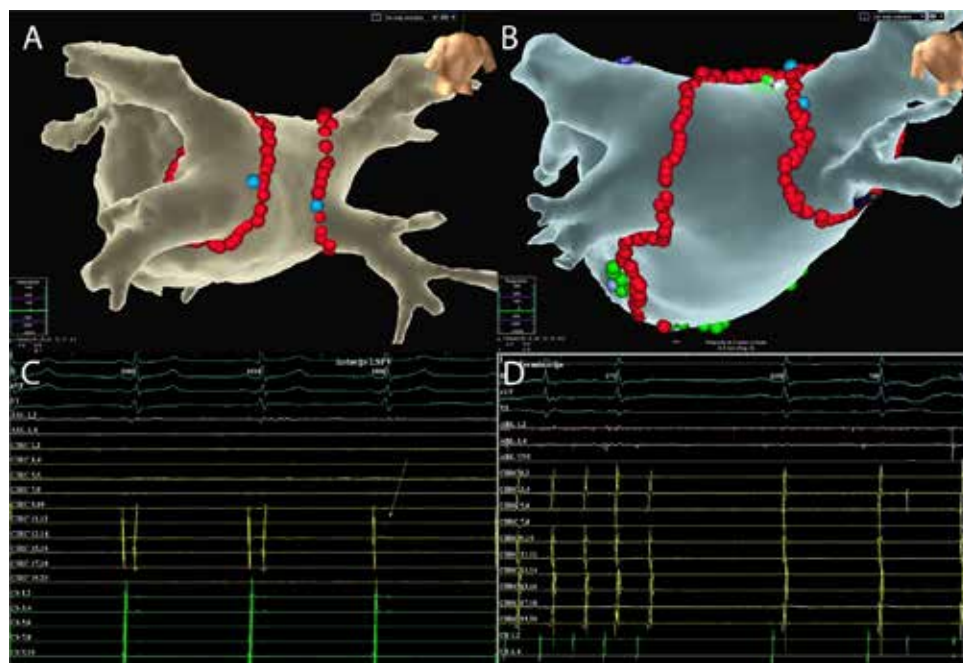


Figure 1. Panel A displays PVI ablation lesion set as ablation strategy in patient presented as Case 1 (PV isolation circumferential lines, encircling the ipsilateral PV pairs). Panel B displays ablation lesion set as ablation strategy in patient presented as Case 2 (PVI + additional substrate ablation). Panels A and B showing the posterolateral and posterior view of the LA model fused with computed tomography image. Radiofrequency lesions were tagged as the 4-mm diameter red balls. On panel B additional substrate ablation is presented (roof line connects the most cranial points of the left-sided and right-sided PVI circles; mitral line extends from the lateral mitral annulus to anteroinferior segment of left PVI, adjacent to left inferior PV ostium). Panel C presents the intracardiac signals and a moment of left sided PVI (yellow arrow) in patient presented as Case 1. Panel D points the moment of AF termination during procedure in patient presented in Case 2.

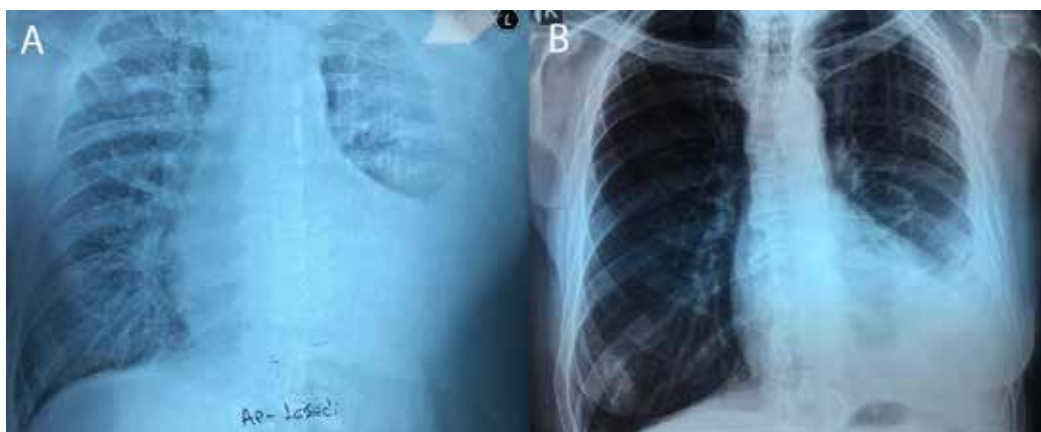


Figure 2. Chest X-ray of patient presented as Case 2. A – on admission before therapy; B – at discharge after correction of medical therapy and RF ablation of atrial fibrillation

MB-LATER score for this patient was 1 (for male gender). During the first three months after RFA therapy with propafenone and dabigatran was continued and thereafter stopped. Patient had scheduled follow-up visits consisting of physical examination, 12-lead ECG and 24-hour Holter-recording at discharge, 1, 3 and 6 months after the procedure, and every 6 months thereafter. During two years of follow-up no arrhythmia recurrence was registered, patient was symptom and drug free during that time, which could be expected based on the predictive ability of MB-LATER score.

CASE 2. A 71-year-old woman with a history of paroxysmal AF was admitted at our department due to first episode of congestive HF. She complained of reduced exercise tolerance over the past two months. ECG at admission showed AF with ventricular response of 120 bpm and presence of left bundle branch block (LBBB) as new finding. Baseline laboratory findings were normal except slightly elevated liver and renal parameters. Thyroid hormones were in reference range.

The physical examination revealed a continuous arrhythmia, silent heart sounds, bilateral pretibial edema. The X-ray showed enlargement of the heart with a reduced transparency of lung parenchyma and left sided pleural effusion, **Figure 2**. Echocardiogram revealed LV dilatation (EDD=59 mm, ESD=44 mm) with global hypokinesia (EF=35%) and markedly enlarged LA=51 mm. Immediately intensive parenteral therapy was started after admission including digitalis, beta blocker, amiodarone and diuretics. Likewise, low molecular weight heparin was induced instead of warfarin and anti-Xa level was monitored. After initial clinical improvement CAD was excluded after coronary angiography. Despite comprehensive therapy, patient remains symptomatic and decision was made to refer for RF catheter ablation of persistent AF during same hospitalization.

Catheter ablation was performed in the same fashion as previously described except that in this patient, after the isolation of the PV, additional ablation of the substrate was performed. Endocardial LA roof and mitral isthmus ablation was performed using 30 W, with the applications lasting 60–120 s in the same location. Endpoint that involved achieving linear conduction block on both lines and PV isolation was reached (**Figure 1B**

– lesion set during RF ablation). Patient was discharged on amiodarone as adjuvant therapy.

One month after the procedure ERAF was registered on scheduled Holter ECG monitoring (persistent AF). We performed electrical cardioversion due to ERAF during “blanking” period. Considering clinical characteristic of this patient we realize that this patient had the value of MB-LATER score of 4 (persistent AF, LBBB, LA>47 mm, ERAF), which does not necessarily mean failure of interventional treatment but in these situations, we are committed to discuss success rate and potential risk with the patient, and also to closely monitor these patients. Three months after the procedure patient reported significant symptomatic and functional capacity improvement. Echocardiogram confirmed reduction of LV dimensions (EDD=56 mm, ESD=39 mm) and increase of EF=50%. At the end of the first year of follow-up amiodarone induced hyperthyroidism was established, so amiodarone was suspended. Two months later she suffered from late recurrence of AF, which is why the procedure was repeated. In the redo procedure reconnection of left PVs was found, and PVs were reisolated. During additional two years of follow-up there were no registered episodes of AF.

Discussion

In this paper, we have presented two cases from our clinical practice that reflect the applicability of the MB-LATER score in everyday clinical work. Our experience and available data indicate that the application of such scores could be important in the treatment of these patients.

PVI represents a cornerstone of RFA for AF. The main limitations of procedure are its invasive nature with potential serious complications and the achievement of durable PVI lesion. PVI alone may be insufficient for successful rhythm control in approximately a third of patients who underwent CA of AF. As a result, relatively high rate of recurrent atrial arrhythmias post-CA is registered and repeat CA procedures are often necessary to achieve optimal treatment success.^{1,16} The reliable application of prediction models of post-ablation AF recurrence might improve the pre-procedural selection of patients which are the most suitable candidates for CA and planning of the optimal rhythm monitoring strategy

Table 1. The score components included in prediction model

	HF*	HTA	AGE	DM	CVA	CAD	Enlarged LA	AF type/history	ERAF	SEX	COPD/Smoking	CKD	Metabolic sy/ BMI	AADs
<i>Rhythm specific scores</i>														
BASE-AF₂							✓	✓	✓		✓		✓	
ALARMc	✓						✓	✓				✓	✓	
APPLE	✓		✓				✓	✓				✓		
CAAP-AF			✓			✓	✓	✓		✓				✓
MB-LATER	✓						✓	✓	✓	✓				

HF, heart failure; HTA, hypertension; DM, diabetes mellitus; CVA, cerebrovascular accident; CAD, coronary artery disease; LBBB, left bundle branch block; LA, left atrium; AF, atrial fibrillation; ERAF, early recurrence of atrial fibrillation; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; BMI, body mass index; AAD, antiarrhythmic drug;

* HF included cardiomyopathy, congestive HF, reduced left ventricular ejection fraction and LBBB.

and drug therapy during post-CA follow-up.¹⁶ These models should not represent limiting factor for the treatment of these patients, but should indicate what to expect from the intervention and how to monitor and manage these patients during follow-up after RF ablation.

To our knowledge, so far five rhythm specific scores are identified (ALARMc, BASE-AF₂, APPLE, CAAP-AF, and MB-LATER score). Each of these scores encompasses components which are significantly associated with increased risk of arrhythmia recurrence after RF ablation of AF (Table 1).

The ALARMc score (NPAF, normalized LA area >10.25, eGFR <68 ml/min, metabolic syndrome and cardiomyopathy) had a good predictive ability of AF recurrence during a 2-year follow-up after redo procedure (AUC: 0.657)¹⁷. Original score included a nonstandard definition of NPAF, renal failure, metabolic syndrome and LA enlargement, and was applied to the patients undergoing the first RF ablation. Further studies added presence of cardiomyopathy to this score, and externally validated the score.¹⁸ All four studies found that arrhythmia recurrence rate is increased with higher ALARMc score. The main remark was related to the normalized LA area cut-off.¹⁸⁻²¹

The BASE-AF₂ score was derived to predict recurrences in AF patients after cryoballoon ablation. A BASE-AF₂ score ≥3 points was significantly associated with AF recurrences (AUC: 0.94). Variables included in the score were: BMI > 28 kg/m², LA diameter >40 mm, current smoking, early AF recurrence post-CA, duration of AF history of >6 years, and non-paroxysmal type of AF. One of the objections is the use of ERAF as a score component, bearing in mind that ERAF is post festum phenomenon, and therefore cannot be used for baseline assessment.⁹

The APPLE score includes age ≥ 65 years, persistent AF, impaired eGFR (<60 mL/min/1.73 m²), LA diameter ≥ 43 mm, EF < 50%. This score was derived and validated for first (AUC: 0.634) and repeated procedure (AUC: 0.557).^{10,14} It has been shown that the score not only predicts arrhythmia recurrence but also can provide additional information about the presence of low-voltage areas in the LA, as a valuable marker of negative electrophysiological remodeling as substrate for AF initiation

and perpetuation.²² APPLE score has been validated in several external cohorts showing similar results. In one external validation APPLE score was compared with the MB-LATER score, and both scores showed good predictive ability in the ROC curve analysis (AUC 0.716, *P* = 0.002 vs AUC 0.782, *P* < 0.001) for the prediction of VLRAF.¹²

The CAAP-AF score was developed to predict AF freedom after RF ablation of AF. CAD, LA diameter, age, presence of persistent, or long-standing persistent AF, antiarrhythmics failed and female sex were included in to this predictive model. Score was initially derived in large cohort of patient (n=1125) of which majority was referred for first RFA. The score is then internally validated (n=937), with similar results as in the derivation cohort (2-year Kaplan-Meier AF-free rates by CAAP-AF scores were as follows: 0 = 100%, 1 = 87.0%, 2 = 89.0%, 3 = 91.6%, 4 = 90.5%, 5 = 84.4%, 6 = 70.1%, 7 = 71.0%, 8 = 60.7%, 9 = 68.9%, and ≥10 = 51.3%)(11). The score has been recently evaluated in two external cohorts, and it showed a good predictive ability for LRAF.^{15,23}

The MB-LATER score has been developed to predict VLRAF after CA. Male sex, bundle branch block, LA diameter ≥47 mm, clinical type of AF (0 point for paroxysmal, 1 point for persistent, and 2 points for longstanding persistent AF), and early recurrent AF (ERAF) were included in the MB-LATER score. Each variable except clinical type of arrhythmia scores 1 point (maximum points is 6).¹² The MB-LATER score showed good predictive ability for VLRAF (AUC = 0.782, *p* < 0.001. MB-LATER score of ≥2 had the best predictive value for VLRAF with 75.0% sensitivity, 72.6% specificity.¹² After derivation, the score has been validated in an internal cohort of patients and compared to other scores providing better predictive accuracy for VLRAF than the other scores. The score was externally validated in four studies, and MB-LATER showed the largest net benefit compared to the other scores.^{15,21,23,24} MB-LATER is the first score specifically designed for patients free of arrhythmia recurrence at 1 year after ablation. Those patients are often subjected to a less intensive clinical follow-up beyond 1-year post ablation, and some of them are at increased risk for cardiovascular events, most commonly due to discontinuation of anticoagulant therapy.

Important component of MB-LATER score is ERAF, which was found to be independent predictor for LRAF also in external validation cohorts.^{15,23} Although ERAF is not suitable for baseline risk stratification due to postprocedural appearance, MB-LATER score is very suitable in routine clinical practice because of its simplicity owing to readily available variables.^{12,15,16}

Besides ERAF, some of the MB-LATER score components, such as AF clinical type and LA enlargement, have been already identified as independent predictors of AF recurrence following ablation and were incorporated in other scoring models.^{9,10,18,25-27} HF is also one of the most common components of these clinical scores (Table 1). This does not mean that these patients are not good candidates for RF ablation of AF, on the contrary those patients might have significant benefit from the procedure.⁽³⁾ Simplicity is what each prediction model should provide with the aim to facilitate implementation in everyday practice. Some components of other scores (for example normalized LA volume) require additional pre-procedural work-up (CT, appropriate software and complex mathematical model for calculation), thus limiting its applicability.^{12,16}

These clinical scores have also significant role reflected in decision-making regarding the use of anticoagulant and antiarrhythmic therapy. Although recurrence of the arrhythmia carries only nonsignificant trend for increased thromboembolic risk,²⁸ current recommendations suggest to continue long-term oral anticoagulation therapy in all patients with CHA₂DS₂-VASc ≥ 2 , regardless of the AF ablation outcome.¹ Interestingly, in one observational retrospective multicenter study has been observed that all thromboembolic events following AF ablation occur in patients who experienced arrhythmia recurrence in contrast to patients who did not have arrhythmia recurrence (4% vs. 0%, $p < 0.001$).²⁹

Conclusion

Despite we have interesting tools for risk stratification for AF recurrence after RF ablation, one should make final decision about procedure in agreement with patient after consideration of all potential benefits and harms of the procedure. Adequate patient selection for the procedure is of great importance considering high arrhythmia recurrence rate after ablation, significant costs, availability of medical care, long radiation exposure time and potentially serious complications that may occur during AF ablation procedure.

Since the strategy of AF ablation and follow-up management differ significantly among EP centers,¹ we need additional studies to prospectively validate and compare all these scores in independent external cohorts in order to determine their relative predictive ability for post-CA recurrence and achieve clinical utility.

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Sažetak

MB-LATER skor kao koristan predictor ponovne pojave aritmija posle radiofrekventne kateter ablacija atrijalne fibrilacije - klinička primena

Milan Marinković¹, Aleksandar Kocijančić¹, Vladan Kovačević¹, Miroslav Mihajlović¹, Jelena Simić¹, Nikola Isailović¹, Anja Radunović¹, Vera Vučićević², Tatjana Potpara^{1,3}, Nebojša Mujović^{1,3}

¹Klinika za kardiologiju, Klinički centar Srbije, Beograd, Srbija; ²Centar za anesteziju, Klinički centar Srbije, Beograd, Srbija; ³Medicinski fakultet, Univerzitet u Beogradu, Beograd, Srbija

Atrijalna fibrilacija (AF) je najčešća dugotrajna aritmija u opštoj populaciji. Dobro je poznato da je jedan od osnovnih zadataka u lečenju bolesnika sa AF prevencija komplikacija povezanih sa aritmijom. Kateterska ablacija AF predstavlja važnu strategiju u lečenju ovih bolesnika sa ciljem eliminacije aritmije, odnosno redukcije vremena provedenog u aritmiji. Nakon intervencije kod značajnog broja bolesnika se registruje unapređenje simptomatskog i funkcionalnog statusa, a u podgrupi bolesnika sa srčanom insuficijencijom dolazi i do redukcije ukupnog mortaliteta. Razvijeno je nekoliko prognostičkih scoring sistema za predikciju pojave recidiva aritmije nakon kateterske ablacije AF. Uloga ovih modela je u eventualnoj boljoj optimizaciji dugoročnog praćenja ovih bolesnika kao i odlučivanju vezanom za obustavljanje antikoagulantne i antiaritmijske terapije nakon intervencije. Brojni faktori su definisani do sada kao prediktori recidiva aritmije, a neki od njih su korišćeni za razvoj skorova specifičnih predikciju recidiva aritmije nakon kateterske ablacije. MB-LATER skor je kreiran u retrospektivnoj studiji sa ciljem predikcije recidiva aritmije nakon kateterske ablacije AF. U ovom radu ćemo prikazati njegovu primenu u kliničkoj praksi.

Ključne reči: atrijalna fibrilacija, radiofrekventna kateter ablacija, prognostički skor, recidiv aritmija