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Posterior wall substrate modification using optimized and contiguous lesions in patients with atrial fibrillation

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Abstract

Background: *Radiofrequency (RF) linear ablation at the left atrial (LA) roof and bottom to isolate the LA posterior wall using contiguous and optimized RF lesions was evaluated. Achieving isolation of the LA posterior wall is challenging as two continuous linear lesion sets are necessary.*

Methods: *Forty consecutive patients with symptomatic atrial fibrillation (AF) and arrhythmia substrates affecting the LA posterior wall underwent posterior wall isolation by linear lesions across the roof and bottom. The cohort was divided into two groups: group 1 (20 patients) linear ablation guided by contact force (CF) only; group 2 (20 patients) guided by ablation index (AI) and interlesion distance.*

Results: *Bidirectional block across the LA roof and bottom was achieved in 40/40 patients. Additional endocardial RF applications in 5 patients from group 1 vs. 3 patients from group 2 resulted in posterior wall isolation in all patients. Procedure duration was almost equal in both groups. CF and AI were significantly higher in group 2 for the roof line, whereas no statistical difference was found for the bottom line. AI-guided LA posterior wall isolation led to a significantly lower maximum temperature increase. The mean AI value as well as the mean value for catheter-to-tissue CF for the roof line were significantly higher when AI-guided ablation was performed. Standard deviation in group 2 showed a remarkably lower dispersion.*

Conclusions: *Ablation index guided posterior wall isolation for substrate modification is safe and effective. AI guided application of the posterior box lesion allows improved lesion formation.* (Cardiol J 2022; 20, 6: 917–926)

Key words: atrial fibrillation, catheter ablation, posterior wall isolation, ablation index, contact force

Introduction

Catheter ablation for persistent atrial fibrillation (PERS) is challenging and is associated with only a moderate outcome [1–4]. The mechanisms initiating and perpetuating atrial fibrillation (AF) are still not completely understood and therefore, ablation strategies are heterogeneous [1, 2, 5]. Several observations have led to individual mechanistic insights in AF management and arrhythmia associated cardiac remodeling which emphasizes

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the need for personalized paths in AF management. The posterior left atrial (LA) wall has a common embryological origin with the pulmonary veins (PVs) and therefore a comparable arrhythmogenic potential, especially when there is evidence of myocardial fibrosis [3, 6, 7]. A beneficial effect of the LA posterior wall isolation (PWI) has been demonstrated among patients who underwent surgical AF therapy [8], whereas conflicting outcome data exist regarding the value of LA PWI adjunctive to or beyond PV isolation (PVI) performing endocardial ablation [9–12]. However, there is sparse data reporting the feasibility, safety and efficacy of LA PWI as performing linear ablation in the LA remains challenging. Bidirectional block across LA lines should be the ablation endpoint [13], but this is only achieved in a limited number of patients [14] and incomplete electrical block can contribute to the development of an iatrogenic arrhythmia substrate [15]. One of the most relevant drawbacks in performing posterior wall substrate modification is the risk of collateral damage to the esophagus [16]. Consequently, the theoretical advantages of PWI have to be balanced against the undisputed risk of major complications or incomplete electrical block across the applied lines resulting in proarrhythmic effects and arrhythmia recurrence [6]. Recently, new studies have reported an ablation approach in performing anatomical point-by-point radiofrequency (RF) ablation based on an indirect evaluation of lesion depth and delivery of contiguous RF lesions [17, 18]. Focusing on PVI, it has been shown that acute and late PV reconnection resulted from an insufficient ablation index (AI) and/or from interlesion distance being too far [17]. This has also been reported from catheter ablation procedures performing linear lesion sets across the LA roof, anterior wall and mitral isthmus [19, 20]. However, these criteria on minimal AI and maximal interlesion distance have not yet been evaluated and not been validated for substrate modification at the LA posterior wall. Thus, the aim of this study was to evaluate feasibility and efficacy of AI-guided isolation of the posterior wall in patients suffering from PERS.

Methods

A total of 40 consecutive patients with drug-refractory PERS and a relevant amount of bipolar low-voltage affecting the LA posterior wall were included in this prospective observational analysis. AF was defined as persistent if episodes lasted > 7 days or required electrical or pharmacological cardioversion after ≥ 48 h from onset [13]. The mean AF duration before the procedure was assessed by comprehensive review of the patients' records including 12-lead-electrocardiograms and doctors' letters. In this study AI was assessed and evaluated exclusively for PWI by means of linear lesion sets across the LA roof and bottom beyond proof or successful PVI. All patients were ablated at our institution. Written informed consent was obtained from each patient and the current study complies with the Declaration of Helsinki and was approved by the institutional review board. LA thrombus formation was ruled out prior to ablation in all patients. All procedures were performed on uninterrupted oral vitamin K anticoagulants with a target international normalized ratio of 2.0–3.0 on the day of the procedure, direct oral anticoagulants were discontinued the day of the procedure and resumed the same day after ruling out pericardial effusion. Catheter ablation was performed under deep sedation with bolus of midazolam and fentanyl and a continuous infusion of propofol. In all patients, preprocedural magnetic resonance imaging was performed to guide the intervention and to visualize the anatomical location and course of the esophagus. A 6 F diagnostic catheter was inserted distal into the coronary sinus (CS) via the right femoral vein. Double transseptal puncture using 8.5 F SL1 sheaths (SJM, St. Paul, Minnesota, USA) and a modified Brockenbrough technique was performed as previously described in detail [21]. Unfractionated heparin was administered according to the patient's weight to maintain an activated clotting time ≥ 300 s.

Map acquisition

After transseptal puncture, a multipolar mapping catheter (Lasso or PentaRay, Biosense-Webster Inc., Diamond Bar, CA, USA) and an open-tip irrigated RF catheter (8 Fr) with tip-integrated contact force (CF) sensor (Thermocool SmartTouch SF, Biosense-Webster Inc.) were positioned in the LA. Subsequent calibration of CF catheter, respiratory gating, and three-dimensional geometry of the LA (Carto System®, Biosense Webster Inc.) were performed using ultra high-density mapping aiming for > 1000 mapping points for the estimation of bipolar LA voltage (Fig. 1). Bipolar voltage maps were created during sinus rhythm. In patients with PERS, sinus rhythm was restored by transthoracic direct electrical cardioversion at the beginning of the procedure. For the LA voltage map, the bipolar voltage reference interval was set between 0.05 and 0.5 mV. The definition of low-voltage areas included one of the two following

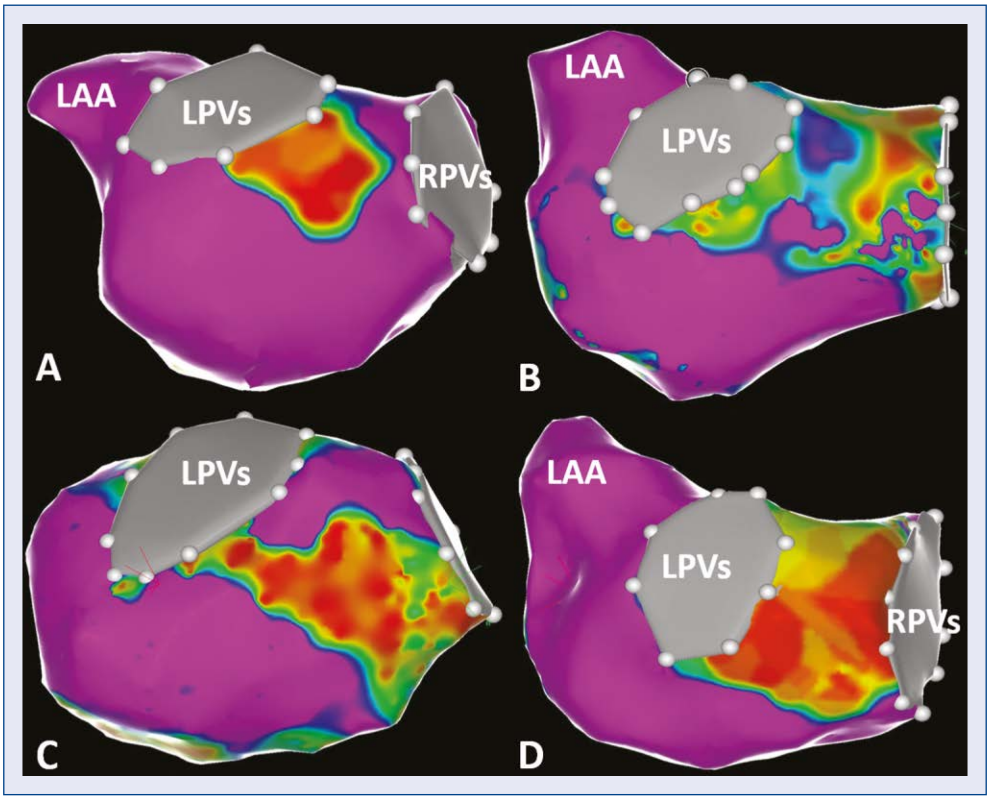

Figure 1. Typical examples for areas with left atrial bipolar low voltage using ultra-high density mapping; **A.** Native bipolar low-voltage suggestive for fibrosis, **B.** Bipolar low voltage at the posterior wall after previous radiofrequency--guided pulmonary vein isolation (PVI); **C.** Diffuse distribution of native bipolar low voltage; **D.** Localization of bipolar low voltage following previous cryoballoon-guided PVI; posterior-anterior view; bipolar voltage reference interval was set as < 0.5 mV; LAA — left atrial appendage; LPVs — left-sided pulmonary vein; RPVs — right-sided pulmonary veins.

criteria: (1) absence of voltage or a bipolar voltage amplitude ≤ 0.05 mV, indistinguishable from noise; (2) low-voltage "abnormal" areas were defined with an amplitude ≤ 0.5 mV, as previously reported [22]. The total individual amount of LA bipolar low voltage was measured using the area measurement tool. Patients with PERS undergoing a first catheter ablation procedure underwent PVI first. In patients undergoing a repeated ablation procedure, electrical isolation of the PVs was checked with the Lasso or PentaRay catheter and electrical reisolation of the PVs was performed if reconnection had occurred. Afterwards LA linear ablation at the roof and the bottom was subsequently performed to achieve posterior wall isolation if low-voltage areas were detected.

Ablation procedure

Catheter ablation was performed with an open-irrigated tip catheter (Thermocool SmartTouch SF, Biosense Webster Inc.). After reconstruction of the LA, each PV ostium was identified by selective PV angiography and ablation was performed. Following PV ablation, PWI started with a linear lesion set across the LA roof from the superior aspect of the left PVs to the superior aspect of the right-sided PVs (Fig. 2). Irrigated RF was delivered, targeting a maximum temperature of 43°C, a maximum power level of 35 W and an infusion rate of 20 mL/min. The bottom line was drawn from the most inferior aspect of the left-sided PVs to the inferior aspect of the right PVs aiming for coverage the complete area of bipolar low-voltage within posterior wall (Fig. 2). The bottom line was applied with a maximum power limited to 30 W. Patients were divided into two groups according to the ablation protocol. In patients of group 1 (n = 20), lesion creation was guided by contact force targeting 10–40 g, aiming for local signal attenuation of ≥ 80% at each point [23, 24]. These procedures were used to calculate an individual AI for posterior wall isolation. However, the performing physician was blinded to all AI values. In patients of group 2 (n = 20), all procedures were guided by AI target values (AI roof

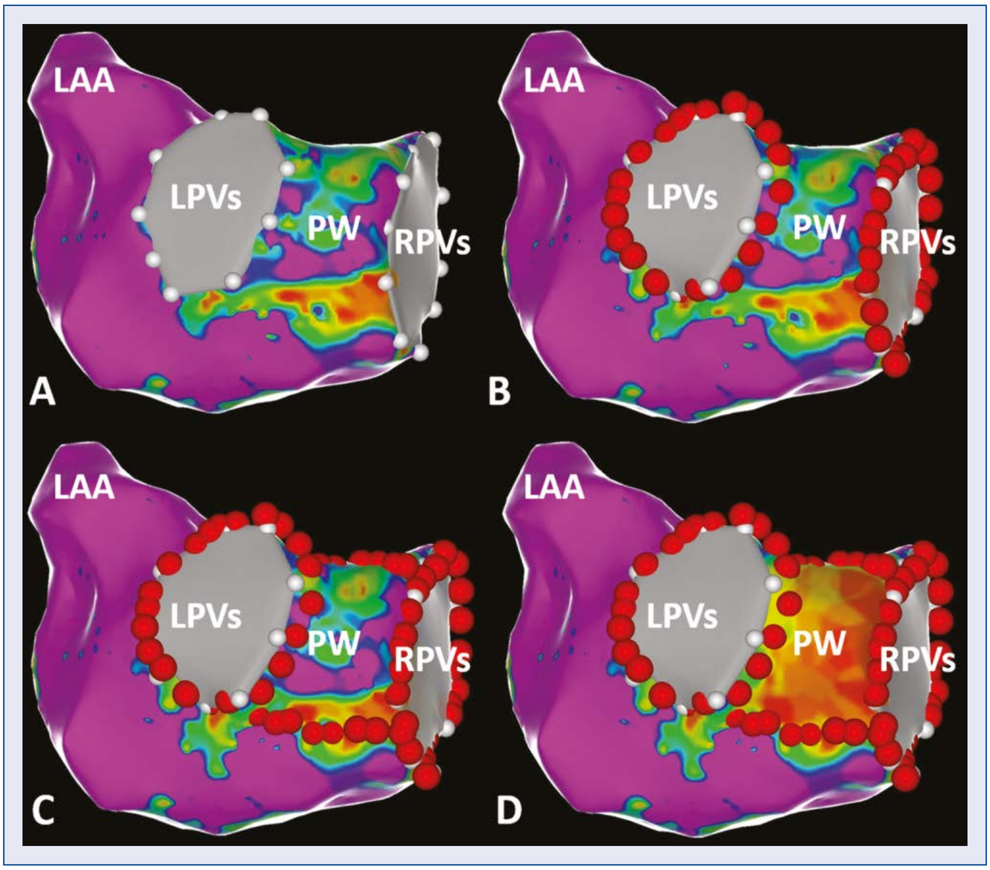

Figure 2. Patient specific example for ablation index (AI)-guided posterior wall isolation; **A.** After reconstruction of the left atrial (LA), each pulmonary vein (PV) ostium was identified; **B.** Pulmonary vein isolation was performed using AI; **C.** Posterior wall (PW) isolation started with a linear lesion set across the LA roof from the superior aspect of the left PVs (LPVs) to the superior aspect of the right-sided PVs (RPVs). The inferior line was drawn from the most inferior aspects of the left-sided PVs to the inferior aspects of the right PVs aiming for coverage of the complete area of bipolar low-voltage within PW isolation; **D.** Repeat voltage mapping to confirm isolation of the posterior box; LAA — left atrial appendage.

line: 550; AI bottom line: 400), and targeting an interlesion distance ≤ 6 mm (Fig. 2). Conduction block along the lines was validated in sinus rhythm by widely spread double potentials along the whole lines, pacing manoeuvres (including entrance- and exit-block) and repeated voltage mapping,including area measurement, of the isolated posterior box (Fig. 2D). Procedural success was subsequently reconfirmed after a minimum waiting period of 30 min. All patients were followed-up in the outpatient clinic 3, 6 and 12 months after ablation. At each visit they were asked for any symptoms suggestive for arrhythmia recurrence or discomfort during respiration. Moreover, a 72 h-Holter electrocardiogram was routinely performed in all patients to monitor arrhythmia recurrence and AF burden. Following a 3-month blanking period, recurrence was defined as any symptomatic episode of atrial tachycardia/AF lasting > 30 s.

Statistical methods

Continuous variables are reported as means ± standard deviation and were compared with the Student t test for unpaired groups as required, and dichotomic variables as percentage and compared with χ^2 test of the Fisher test as required. A p value < 0.05 was considered as statistically significant.

Results

Patients' characteristics

Forty consecutive patients (65% male), mean age 64 ± 9 years, that were routinely referred to our hospital for LA ablation procedures due

Table 1. Baseline characteristics of all patients and their respective p-values.

	Group 1 (CF)	Group 2 (AI)	P
Age [years]	63 ± 8	64 ± 17	0.37
Male	10 (50%)	16 (80%)	0.09
Left ventricular ejection fraction [%]	52 ± 13	53 ± 4	0.37
Left atrial diameter [mm]	44.3 ± 0.7	45 ± 1.9	0.22
Mean AF-duration prior ablation [months]	7 ± 2	8 ± 3	0.14
Amount of bipolar low voltage of the PW [%]	18 ± 12	20 ± 10	0.46
Ejection fraction [%]	53.8 ± 0.6	54.0 ± 0.7	0.83
Arterial hypertension	13 (65%)	15 (76%)	0.73
Congestive heart failure	2 (10%)	2 (10%)	1.0
Diabetes mellitus	2 (10%)	3 (15%)	1.0
Coronary artery disease	5 (25%	4 (20%)	1.0
CHA_2DS_2VASC Score	1.3±1.1	1.±1.2	0.16
Previous AAD	12 (60%)	14 (70%)	0.74
Beta-blockers	16 (80%)	17 (85%)	1.0
Previous ablations:			
Pulmonary vein isolation	9 (45%)	12 (60%)	0.53
LAMRT	1 (5%)	0	1.0
Cavotricuspid isthmus	3 (15%)	6 (30%)	0.45

AAD — antiarrhythmic drugs; AF — atrial fibrillation; LAMRT — left atrial macro-reentrant tachycardia; PW — posterior wall

to PERS. Mean left ventricular ejection fraction was 53 ± 5% and LA diameter was 45 ± 7 mm. A significant low-voltage area at the posterior LA wall was detected in all patients. The groups did not differ significantly in terms of age, sex and cardiovascular risk factors. Baseline characteristics are reported in Table 1.

Procedural data and success

For this study, analysis of the procedural data of all patients included a total of 601 RF applications. The whole procedure duration was comparable between both groups with 98 ± 23 min in group 1 and 92 ± 9 min in group 2, respectively ($p = 0.10$). This was also the fact for the mean fluoroscopy time (group 1: 4.2 ± 1.6 min; group 2: 4.1 ± 1.9 min; $p = 0.87$). Although there was no significant difference in terms of procedural duration, a remarkably lower variation in the AI-guided ablations was observed.

Acute isolation of the posterior wall was achieved in all cases. Bidirectional block of the roof line required a total of 5 ± 3 RF applications in group 1 and 4 ± 1 RF applications in group 2 ($p = 0.44$). For the bottom line, a mean of 10 ± 7 RF applications was required in group 1 and 10 ± 5 RF applications in the AI-guided group ($p = 0.84$). There was no significant difference focussing on ablation duration for bidirectional block across the roof (1.9 ± 1.1 min group 1 vs. 1.5 ± 0.8 min group 2; $p = 0.14$) or the bottom line (3.5 ± 3.1 min group 1 vs. 3.5 ± 1.6 min group 2; $p = 0.95$). First-pass block of the roof line was achieved in the majority of patients (n = 17 in CF-group and n = 18 in AI group). First-pass block of the bottom line, resulting in LA posterior wall isolation was observed in 15/20 patients in group 1 (75%) and 17/20 patients in group 2 (85%; $p = 0.43$). No electrical reconduction of the posterior wall was found after the waiting period of 30 min in patients who underwent AI-guided posterior box isolation. In contrast, reconduction requiring reablation was observed in 3 (15%) patients from group 1. Gaps in the ablation lines were identified from signal mapping and pacing maneuvers in all cases. RF applications inside the box were not necessary.

Of note, AI-guided LA PWI led to significantly lower maximum temperature rises measured at the catheter tip (roof line: 27 ± 1.4°C group 1 vs. 25 ± 1.7°C group 2; $p < 0.01$; bottom line: 27 ± 1.2 group 1 vs. 25 ± 1.7°C group 2; $p < 0.01$). Furthermore, the mean AI value (roof line: 482 ± 108 group 1 vs. 549 ± 74 group 2; $p < 0.01$; bottom line: 442 ± 127 group 1 vs. 428 ± 99 group 2; $p < 0.01$)

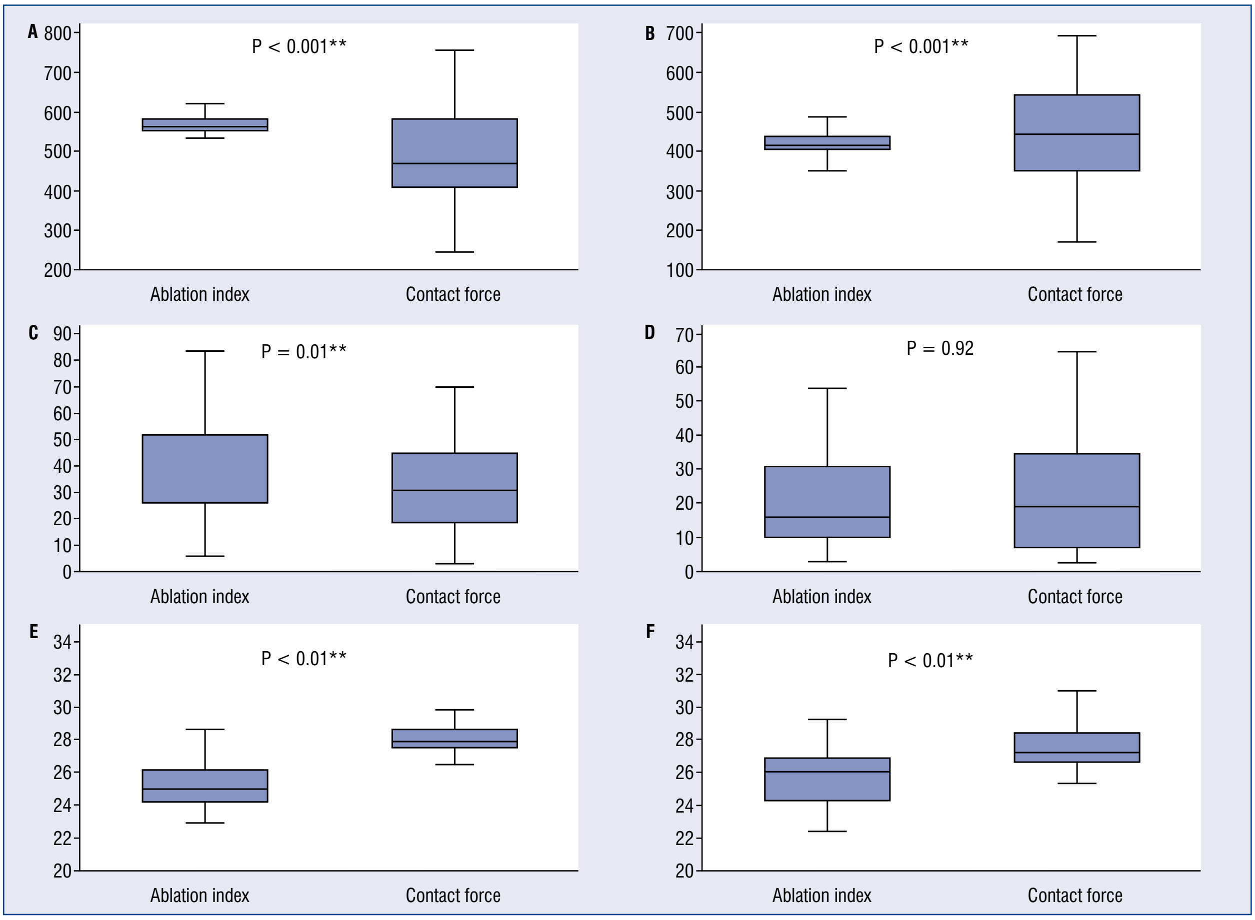

Figure 3. Box-plots depicting the mean values for ablation index (AI), catheter-tip to tissue contact force and maximum temperature rising for both groups. Values for the roof line are listed on the left side, values for the bottom lines are shown on the right. **A.** Ablation index roof line; **B.** Ablation index bottom line; **C.** Catether tip-to-tissue contact force roof line [g]; **D.** Catether tip-to-tissue contact force bottom line [g]; **E.** Maximum temperature roof line [°C]*; **F.** Maximum temperature bottom line [g]. The AI was significantly higher in the AI-group and the maximum temperature rise was significantly lower, respectively (for both p < 0.01). In addition, the contact force administered for the roof line was significantly higher in the AI-guided group. Of note, the variance in the AI-guided group was very small indicating a very good reproducibility of lesion application and formation using the AI; *As measured from the catheter tip; **Significant.

as well as the mean value for catheter-to-tissue contact force for the roof line (32 ± 18 group 1 vs. 39 ± 17 group 2; p = 0.01) were significantly higher when performing AI-guided catheter ablation. Besides these statistically significant differences mentioned above, the data highlighted even more the important benefit of using AI-guided posterior wall isolation in terms of safety and reproducible efficacy, as the AI variance creating each ablation lesion was remarkably low (Fig. 3). All procedural parameters are summarized in Table 2. No relevant complications were recorded during or after the intervention.

During a mean follow-up period of 12.1 ± 1.8 months, 16/20 (80%) and 18/20 (90%) patients were free of any arrhythmia recurrence in both group 1 and group 2, respectively. Focusing on arrhythmia recurrence, 2/4 patients from group 1 presented with LA macro-reentrant tachycardia (LAMRT), one patient presented with AF and LAMRT and another patient with AF. In contrast, 2 patients with AF recurrence were observed in group 2.

Discussion

Main findings

This is the first study systematically evaluating the use of AI guided LA posterior wall substrate modification aiming for electrical isolation of the posterior wall. Four major findings are reported in this study: First, AI guided PWI for substrate modification in AF patients is safe and reproducibly

Table 2. Procedural data and their respective p-value.

	Group 1 (CF)	Group 2 (AI)	P
Procedure duration [min]	98 ± 23	92 ± 9	0.10
Fluoroscopy time [min]	4.2 ± 1.6	4.1 ± 1.9	0.87
Ablation time [total]	2.7 ± 2.5	2.5 ± 1.6	0.67
Ablation time [min]:			
Roof line	1.9 ±1.1	1.5 ± 0.8	0.14
Bottom line	3.5 ± 3.1	3.5 ± 1.6	0.95
Length [mm]:			
Roof line	115 ± 70	90 ± 50	0.06
Bottom line	207 ± 98	210 ± 186	0.73
No of RF applications:			
Roof line	4 ± 3	4 ± 1	0.92
Bottom line	10 ± 7	10 ± 5	0.84
Contact force [g]:			
Roof line	32 ± 18	39 ± 17	0.01*
Bottom line	21 ± 16	22 ± 16	0.92
Ablation index:			
Roof line	482 ± 108	549 ± 74	< 0.01*
Bottom line	442 ± 127	428 ± 99	< 0.01*
Maximal temperature:			
Roof line	27 ± 1.4	25 ± 1.3	< 0.01*
Bottom line	27 ± 1.2	25 ± 1.7	< 0.01*

*Significant; AI — ablation index; CF — contact force; RF — radiofrequency

effective. Second, performing AI-guided LA linear lesions across the LA roof and bottom in patients with PVI results in a high rate of first-pass PWI. Third, using target AI values results in a significant decrease of temperature exposure during lesion formation at the posterior wall. Fourth, AI guided application of the posterior box lesion set is assigned by improved lesion formation focussing on CF and AI.

Left atrial posterior wall isolation: Technically challenging

The STAR AF trial [1, 25] failed to demonstrate a relevant benefit of LA lines and ablation of complex fractionated atrial electrograms beyond PVI in patients with PERS. However, catheter ablation aiming for LA PWI was not part of the study. Approaches of PWI include box isolation, single ring isolation, and debulking ablation [9]. A recent meta-analysis from Thiyagarajah et al. [9] demonstrated that acute LA PWI as a procedural endpoint was achieved in 78.5% with a pooled estimate of 70.9% in 12 studies [26–37]. The authors reported pooled estimates for 12-months freedom from any arrhythmia recurrence of 65.3% and 61.9% for patients with PERS, respectively. In the present study acute procedural success was achieved in all patients and recurrence free survival during the follow-up period was 80% and 90%, respectively. In this context, it is well known that incomplete bidirectional conduction block has been associated with an increase in subsequent arrhythmia during follow-up [14, 15]. In the recent study, even respecting the criteria for contiguity and AI in group 2, complete block across the roof in 90% of patients and in 85% at the bottom line after a single linear lesion set was achieved. The very high success rate of first-pass block of both LA lines in the current study can probably be explained by the specific anatomy of the LA roof with a thin wall thickness ranging from 3.5 to 6 mm and relatively smooth inferior parts of the posterior wall [38], which finally render the posterior wall quite suitably for a strategy aiming at transmurality and contiguity of RF lesions. Moreover, and as demonstrated in Figure 3A and B, AI-guided ablation lesions were created with a remarkably lower variance in target values at the roof and bottom line as compared to CF-guided ablation alone (Fig. 3).

Left atrial posterior wall ablation: The narrow ridge between effectiveness and risk

Hypothesized herein, that AI-guided lesion formation at the LA posterior wall could be helpful in avoiding complications in these high-risk procedures. In their meta-analysis Thiyagarajah et al. [9] reported that 15 major complications were found across 1667 ablation procedures aiming for PWI. Pericardial effusion requiring drainage or cardiac tamponade were observed in 10 patients, cerebrovascular events in 3 patients, and atrio-esophageal fistulas in 2 patients [9, 33]. There are multiple approaches to PWI with different strategies of power delivery, RF application time, image integration, endpoints and in the context of temperature monitoring for the esophagus [9]. In the present study, no major complication was observed using an AI of 400 for ablation at the posterior wall. In this context, Figure 3E and F emphasize that a significant lower maximum temperature rise was observed performing ablation guided by AI in line with improved lesion formation (Fig. 3E, F). In studies focusing on RF ablation in the canine heart, Nakagawa et al. [39, 40] found that the RF lesion depth was accurately (± 1 mm) described by a logarithmic function of CF, RF power and application time. However, today AI-guided AF ablation does not take into account atrial wall thickness and individual distribution of fibrosis in the logarithmic function, although these factors may play an important role in the initialization and maintenance of PERS [41, 42]. Based on the current findings and those discussed above we would like to address the need for personalized paths in catheter based PERS management in terms of efficacy and safety and therefore suggest a shift to the current AI approach to a substrate-based index taking into account the individual LA architecture as well as the amount and distribution of fibrosis.

The potential benefit of both continuous and optimized RF lesions

Recently, several studies reported beneficial effects of AI-guided ablation approaches for PVI with respect to periprocedural workflow, acute procedural success (first-pass PVI) and freedom from arrhythmia recurrence [18, 43–45]. Focusing on LA RF lesions, Taghji et al. [18] demonstrated that for durable PVI, the maximum interlesion distance should not exceed 6 mm and the minimal AI should be ≥ 400 at the posterior and ≥ 550 at the anterior aspects of the PVs. Beyond PVI, Santoro et al. [20] reported interesting data about the feasibility and safety of LA anterior line ablation using AI and interlesion distance measurement with shorter ablation time, shorter overall RF application time and a reduced number of RF applications to achieve anterior line bidirectional block. Another study by Wolf et al. [19] evaluated LA linear ablation using contiguous and optimized RF lesions for linear ablation across the LA roof and the posterior mitral isthmus. The authors concluded, that their ablation approach resulted in a high rate of first-pass block at the roof but not at the mitral isthmus. The present data confirms the results from Wolf et al. [19] with respect to linear lesion sets across the LA roof and also emphasizes the beneficial effects of an AI-guided approach in terms of workflow improvement, transmural lesion formation and estimation of reproducible AI target values (Fig. 3). The same effect was observed for the bottom line leading to consecutive LA PWI (Fig. 3). Consequently, this AI-guided approach resulted in PWI as a consequence of roof and inferior lines without the additional need of ablation inside the box. Based on these findings, we hypothesize that AI-guided linear ablation aiming for LA PWI respecting strict criteria of contiguity and indirect lesion assessment would also improve achievement of both acute and durable bidirectional block across linear lesion sets resulting in persistent PWI.

Limitations of the study

This is a single-center study with a limited number of patients. Although no safety-related issues were observed, larger studies are necessary to validate the safety and efficacy of this protocol for LA posterior wall substrate modification. Previous ablation for PVI may have affected the atrial tissue at the posterior wall differently according to previous RF- or cryoballoon-guided PVI (Fig. 1). However, high density mapping was performed in all patients to visualize the area of bipolar low voltage on the posterior wall representing scarred or fibrotic tissue. Another limitation might be the lack of a direct luminal esophageal temperature monitoring during PWI in the present study. Luminal esophageal temperature is not performed in clinical routine during AF ablation at our center due its potential compound role in the context of lesion formation.

Conclusions

Ablation index-guided LA PWI for substrate modification in AF patients is safe and reproducibly effective. Furthermore, AI-guided application of the posterior box lesion set is featured by improved lesion formation with respect to CF, AI and temperature development. The present findings suggest AI-guided ablation is safe, effective and transmural linear LA RF lesions across the posterior LA wall.

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Conflict of interest: None declared

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