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Targeting Bachmann's bundle in hybrid ablation for long-standing persistent atrial fibrillation: a proof of concept study

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Abstract

Background Catheter-based or surgical procedures in patients with long-standing persistent atrial fibrillation (LSPAF) remain a challenge. As a result, different approaches including hybrid (surgical and endocardial) ablation have been developed. Bachmann's bundle (BB) is a mainly epicardial structure capable of sustaining arrhythmic reentry that could be involved in the development and perpetuation of atrial fibrillation. We investigated the efficacy and safety of an adjunctive BB ablation in LSPAF patients undergoing hybrid ablation.

Methods In a two-arm non-randomized study, consecutive LSPAF patients undergoing epicardial isolation of pulmonary veins with left atrial posterior wall (box lesion) with (n = 30, BB group) and without additional BB ablation (n = 30, CONV group) were enrolled in the study. All patients underwent an endocardial procedure within 6 weeks post-surgery to assess for potential lesion gaps and additional atrial substrate modification. The primary endpoint was freedom from AF through 12 months of follow-up.

Results The two-staged hybrid ablation was successfully completed in all patients. One-year freedom from atrial arrhythmias recurrence rates was 96.6% in the BB group vs 76.6% in the CONV group ($p = 0.025$). At procedure completion, 30 (100%) and 17 (56%) patients had a spontaneous cardioversion in BB and CONV group, respectively ($p < 0.001$). No significant differences in quality of life or complication rates were observed.

Conclusions This initial experience shows, for the first time, that adjunctive BB ablation in the setting of hybrid ablation for LSPAF is a feasible and effective approach in increasing maintenance of sinus rhythm without increasing complication rates.

Keywords Atrial fibrillation ablation · Long-standing persistent atrial fibrillation · Hybrid ablation · Bachmann's bundle · Posterior wall isolation

1 Introduction

Patients with long-standing persistent atrial fibrillation (LSPAF) represent a major challenge for both cardiologist and cardiac surgeons [1, 2]. Despite continuous improvements, catheter-based procedures have shown poor outcomes and may need repeated transcatheter procedure to achieve sinus rhythm [3]. Surgical minimally invasive approach combining a surgical epicardial and a transcatheter endocardial ablation has emerged as alternative treatment, with encouraging results [4–6].

Electrical isolation of the left atrial posterior wall ("box lesion") represents the target of the epicardial approaches. Nevertheless, other cardiac structures outside the posterior wall might play a role in the atrial fibrillation (AF) genesis, i.e., the ligament of Marshall, the left atrial appendage, or the superior vena cava.

Bachmann's bundle (BB) is a muscular structure comprising of parallel-aligned myocardial strands, connecting the right and left atrial walls. It represents the main pathway of

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interatrial conduction, and its disruption may result in various atrial tachyarrhythmias. Surgical isolation of the BB does not require additional blunt dissection since, during an epicardial approach, it is easily accessible just beneath the descending aorta. BB may be involved in the pathogenesis and sustaining of a number of unstable reentrant circuits, and it has been hypothesized that its isolation could prevent induction of stable AF [7–9].

The aim of this study was to explore the feasibility, effectiveness, and safety of adding BB ablation to a predetermined right and left atrial lesion sets, in the setting of a two-staged hybrid ablative approach as first-line strategy in LSPAF.

2 Methods

2.1 Study population

From September 2016 to April 2017, 60 consecutive patients underwent two-staged hybrid ablation at the Anthea Hospital, GVM Care & Research, Bari, Italy, and were followed up for 1 year to monitor recurrences. Patients were included on the basis of the following criteria: (A) symptomatic LSPAF as defined by current guideline [10], (B) AF refractory to the maximal tolerated doses of antiarrhythmic therapy, and (C) at least 1 failed electrical or pharmacologic cardioversion attempt during the 6 months preceding the surgical evaluation. Left atrial dimension indexed to body surface area exceeding 35 mm/m^2 was considered an exclusion criterion.

The study was designed as a two-arm non-randomized interventional study. All enrolled patients underwent epicardial isolation of the pulmonary veins and of the left atrial posterior wall ("box lesion"). The study cohort (BB group = 30 patients) underwent surgical ablation with additional ablations targeting the BB. For comparison, BB group patients' outcomes were compared with the historical cohort (CONV group) comprising 30 consecutive patients who underwent the same surgical lesions without BB ablation.

All patients underwent a staged endocardial ablation within 6 weeks after the surgical procedure with the goal of verifying or ablating: (A) the surgical lines and completing the isolation if needed, (B) additional right and left atrial substrate modification, and (C) other triggers of AF. Each ablation strategy was performed by the same operators in both groups. All procedures were performed by expert operators, with >10 years of experience both parts of the staged procedure, to correct for a potential learning curve effect. GVM Care & Research ethical board approved the study, and all patients gave written informed consent for procedure and study enrollment.

2.2 Epicardial approach

All patients were required to be on oral anticoagulant therapy for at least 4 weeks before the scheduled surgery and were asked to withdraw oral anticoagulation therapy 3 days before the procedure. Enoxaparin sodium (100 IU/kg twice daily) was administered until the evening before surgery, as per surgical protocol. Oral anticoagulant therapy was recommenced the day following surgery.

2.2.1 Surgical box lesion

A circumferential lesion set was delivered anterior to the PVs in an attempt to isolate the PVs and posterior left atrium (box lesion set) according to a previously described approach [5]. Briefly, after general anesthesia, transesophageal echocardiography was performed to rule out an atrial thrombus before surgery. A 3–4-cm right minithoracotomy was performed at the 3rd intercostal space level, and a soft-tissue retractor was applied. Thoracoscopic camera was used in all the cases, and the pericardium was opened above the right phrenic nerve. The oblique sinus was entered through blunt dissection. The Estech COBRA Fusion™ 150 Surgical Ablation System (Estech, San Ramon, CA) was used in all the patients.

The introducer with the magnetic tip was pushed into the transverse sinus until the left atrial appendage was passed. The second introducer was then advanced into the oblique sinus until its tip hinged the first introducer. Care was taken to avoid lesion of the atrial appendage, and pulmonary veins were encircled with the ablation probe. The device used suctioned to stabilize the contact with the epicardium and achieve uniform energy delivery. A circular box lesion was created with bipolar and unipolar radiofrequency energies. Different patterns of energy delivery are available with the device used; in our series, ablation was performed by 2 energy applications lasting 150 s each. These were followed by a 60-s application after the probe was moved circumferentially, to achieve complete closure of the box lesion. All the cases were performed off-pump. After the probe was withdrawn, efficacy assessment was usually done by measurement of conduction across the lesion. Conduction block was routinely tested for by recording signals from the posterior wall of the left atrium; if conduction block was not present, additional lesions were delivered. The chest was closed after hemostasis and insertion of a drain.

2.2.2 Bachmann's bundle ablation

An adjunctive BB ablation was performed in the BB group. Bachmann bundle was ablated by introducing the magnetic tip below the ascending aorta and above the roof of the left atrium and then advanced until the base left atrial appendage. No further dissection was required. The ablation line goes from

the left to the right atrial appendage behind the non-coronary aortic sinus, and efficacy assessment was done by measurement of conduction across the line (Fig. 1).

As for the box lesion, the second introducer was advanced into the oblique sinus until its tip hinged the first introducer. Ablation was performed with 2 energy bipolar and unipolar applications, each lasting 150 s. Radiofrequency (RF) lesions have been performed using the maximum power and duration allowed by the device. BB ablation was tested with pacing across the ablate lesions of the BB, with success defined as entrance block without any sharp, and discernible electrograms throughout the entire ablated region other than far field.

2.3 Endocardial ablation

Catheter ablation was performed on an uninterrupted oral anticoagulant regimen 2 to 6 weeks after the surgical procedure. All patients received the procedure under general anesthesia and esophageal temperature monitoring with a dedicated tripolar catheter (Esotherm, Fiab). Heparin boluses were administered during the procedure to achieve an activated coagulation time above 300 s. Mapping and ablation were performed using an electroanatomic mapping system (CARTO, Biosense Webster, Diamond Bar, CA, USA). A detailed bipolar voltage map of the left atrium was obtained. All points were acquired point-by-point using the ablation catheter to ensure adequate catheter tissue contact by contact force (8–10 g). Radiofrequency was applied using an open irrigated tip catheter with power output up to 35 W in the posterior wall and up to 45 W in the remaining atrial sites (Fig. 2).

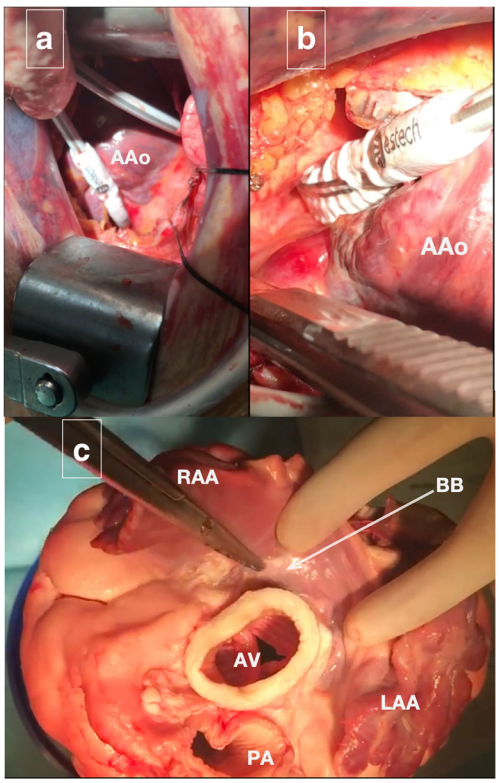

Fig. 1 Panels **a**, **b**. Intraoperative view of the magnetic tip of Estech COBRA Fusion™ 150 Surgical Ablation System passing below the ascending aorta. See text for further details. Panel **c** Pictured here is a heart with some dissection that reveals the anatomic layout of Bachmann's bundle stretching across the interatrial groove. AAo ascending aorta; RAA right atrial appendage; LAA left atrial appendage; AV aortic valve; PA pulmonary artery

Entrance block was defined by complete elimination, or dissociation of pulmonary vein (PV) potentials, determined by the circular mapping catheter positioned in the pulmonary veins and posterior wall. Endocardial ablation was first directed to possible gaps in the surgical lesions. Finally, the procedure was completed with: (a) ablation of the Marshall ligament, (b) roof and anterior mitral lines, (c) coronary sinus and superior vena cava isolation, and (d) intercaval and cavotricuspid isthmus. After restoration of sinus rhythm, linear lesions were assessed for bidirectional block with further ablation performed as required to achieve block. High rate pacing, with a cycle length up to atrial effective refractory period for at least 10 s, was used to induce atrial arrhythmias and ablation of all the residual atrial arrhythmias was performed.

2.4 Follow-up

Oral anticoagulation was resumed on the evening after the surgical procedure and was not discontinued during the endocardial procedure.

At discharge, patients received an ECG recorder (PM 100 Eumaco or Cardio B Gima) and were instructed to obtain a 30-s ECG once a day and a further ECG record in case of symptomatic palpitations. Information from internal loop recorders was available in 6 patients.

The follow-up visits were scheduled at 3, 6, and 12 months in our center. Visits consist of 12-lead ECG, 24-h Holter, transthoracic echocardiography, and physical examination. Oral anticoagulants were discontinued according to the CHA_2DS_2-VASc score after a minimum of 3 months. Antiarrhythmic therapy was reassessed at first follow-up visit, and, in presence of an ECG showing sinus rhythm on the day of the follow-up visit, was suspended.

Functional New York Heart Association (NYHA) class and quality of life were assessed before surgery and at last follow-up (1 year) by administration the EQ visual analogue scale (EQ VAS) for quantitative analysis (www.euroqol.org).

2.5 Endpoints

Efficacy endpoint was freedom from AF or other supraventricular arrhythmias (lasting >30 s) at 1-year follow-up. Because early recurrences of AF may be a transient phenomenon, a 3-month blanking period was used. Safety endpoints

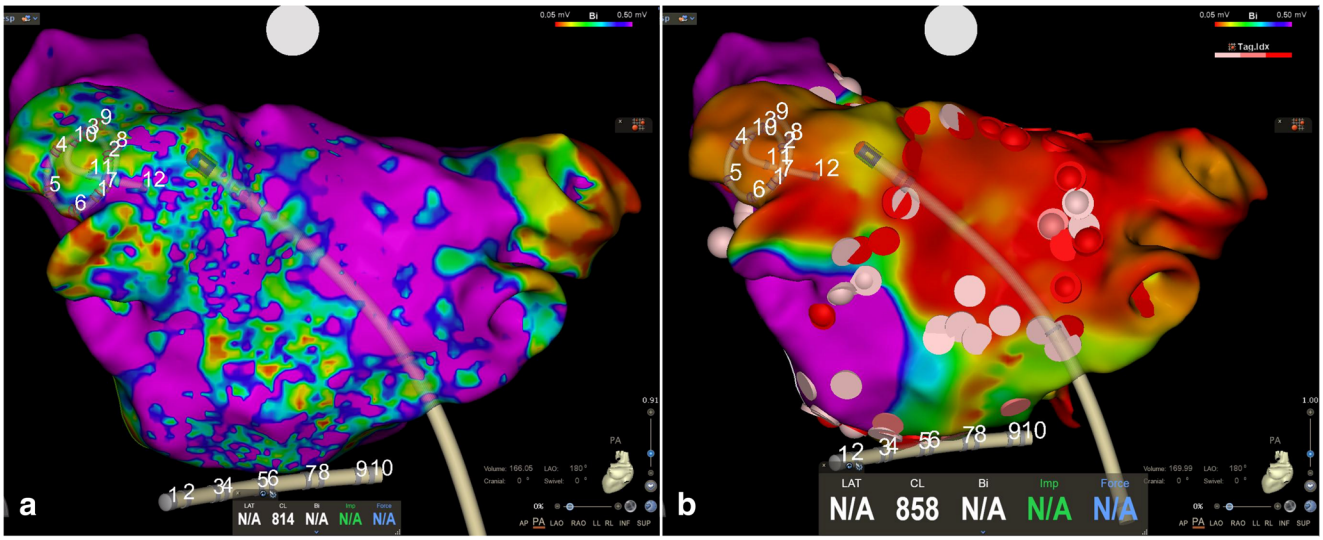

Fig. 2 Example of a 3D bipolar voltage map (CARTO picture/posteroanterior view) obtained with multielectrode catheter and ablation catheter. Regions in purple represent normal myocardium; other colored regions represent low-voltage areas (voltage cutoff 0.05–0.5 mV). **a** Substrate map obtained before RF ablation shows the surgical lesion set. **b** Post-RF ablation map of the same patient shows wide area antral PV ablation and concomitant isolation of the posterior left atrial wall

were incidence of mortality, morbidity, or other procedure-related complications.

2.6 Statistical analysis

Continuous data are presented as mean ± standard deviation (SD) or as median (interquartile range). Categorical data are summarized using absolute values (percentage). Continuous variables were tested for normal distribution with the Shapiro–Wilk test. Non-continuous variables expressed as proportions were compared with using χ^2 analysis or Fisher's exact test, as appropriate. Intergroup comparisons were performed using a the 2-tailed Student *t* test (continuous variables) or the χ^2 test/Fisher test (categorical variables) for unpaired data. Paired non-parametric exact methods were used to compare the change in QoL over time for each patient. Long-term survival was described with the Kaplan–Meier method, and comparisons were made by use of the log-rank statistic. All *P*-values were two-sided, with a *p*-value of < 0.05 was considered to indicate statistical significance.

3 Results

3.1 Baseline characteristics

A total of 60 consecutive patients with symptomatic long-standing persistent AF referred for hybrid ablation were included in the study, with 30 patients per arm. Baseline demographics and clinical characteristics are reported in Table 1 and presented no significant intergroup difference.

3.2 Epicardial ablation

The surgical ablation was performed with a mean operative time of 101.3 ± 25.7 min. In the BB group, Bachmann's bundle ablation was performed in all patients. At the end of the epicardial ablation, 56 patients (93.3%) needed electrical cardioversion for sinus rhythm restoration, 27/30 (90%) in the Bachmann's group, and 29 (96.6%) in the conventional group (p = NS).

Mean hospital stay was 8 ± 3 days, with no differences between the two groups. Twenty-three patients (38%) were discharged in sinus rhythm, and anti-arrhythmic drugs (AADs) were administered in all patients: 52 (86.7%) were treated with amiodarone and 8 (13.3%) with flecainide.

Post-operative complications (i.e., within 30 postoperative days) are reported in Table 2. One patient (BB group) had a serious bleeding requiring surgical revision; the source was identified at the level of the chest drain site insertion. One patient (CONV group) had delirium 1 day after surgery, with a normal brain CT. Two patients (3.3%), one per group, had pneumothorax, with a need for drainage. Two patients (3.3%), one per group, developed superficial wound dehiscence. Right phrenic nerve paresis was observed in 3 patients in the BB group (10.0%) and 2 in the CONV group (6.6%) (p=NS). Four of these patients had complete regression of phrenic nerve function after a maximum of 5 months. No patient required sternotomy, and no significant differences in serious postoperative complications were observed between groups.

Table 1 Baseline characteristics

	CONV group $n = 30$	BB group $n = 30$	P
Age, y/o (IQR)	63 (21)	66 (18)	0.43
Female, *n* (%)	19 (63.3)	23 (76.6)	0.78
BSA, m^2 (SD)	1.8 (0.25)	1.9 (0.23)	0.72
Hypertension, *n* (%)	19 (63.3)	15 (50)	0.73
NIDDM, *n* (%)	8 (26.6)	1 (3.3)	0.06
Hypercholesterolemia, *n* (%)	10 (33.3)	15 (50.0)	0.54
Smoking history, *n* (%)	20 (66.6)	10 (33.3)	0.2
Previous TIA stroke, *n* (%)	1 (3.3)	1 (3.3)	1.00
GFR > 85 mL/min, *n* (%)	28 (93.3)	25 (83.3)	0.91
Previous PCI, *n* (%)	2 (6.6)	0	0.5
LVEF ≤ 50%, *n* (%)	3 (10)	5 (16.6)	0.77
CHA2DS2-VASc score, mean (SD)	3.3 ± 1.1	3.4 ± 1.0	0.72
AF duration (months), mean (SD)	23.2 ± 8.1	24.9 ± 8.9	0.43
Left atrial dimension, mm (SD)	45.5 (3.1)	45.8 (2.8)	0.71
Left atrial dimension, mm/m^2 (SD)	24.9 (4.3)	25.4 (3.8)	0.82
Class I (a, b, c) antiarrhythmic drugs, *n* (%)	20 (66.6)	18 (60)	0.96
Class II antiarrhythmic drugs, *n* (%)	3 (10)	5 (16.6)	0.77
Class III antiarrhythmic drugs, *n* (%)	25 (83.3)	30 (100)	0.76

AF atrial fibrillation, *BB* Bachmann bundle, *BSA* body surface area, *GFR* glomerular filtration rate, *IQR* interquartile range, *LVEF* left ventricle ejection fraction, *NIDDM* non-insulin dependent diabetes mellitus, *SD* standard deviation, *TIA* transient ischemic attack, *PCI* percutaneous coronary intervention

3.3 Endocardial ablation

All patients underwent an endocardial catheter ablation as second step procedure, after a median time from surgery of 34 (IQR) days. At the time of endocardial ablation, 26 (43%) patients were in sinus rhythm, 27 (45%) in AF, and 7 (12%) patients in atypical atrial flutter. No significant differences in rhythm type at endocardial ablation presentation were observed between the two groups.

Table 2 Periprocedural outcomes

	CONV group ($n = 30$)	BB group ($n = 30$)	P
Death	0	0	-
Patients transfused, *n* (%)	1 (3.3)	0	1.00
Mechanical intubation time, h (IQR)	6 (6)	5 (5.2)	0.76
ICU LOS, h (IQR)	23 (29.3)	26 (19.4)	0.52
Total LOS, day (IQR)	8 (2)	5 (4)	0.21
Delirium, *n* (%)	1 (3.3)	0	1.00
Temporary pacing, *n* (%)	1 (3.3)	0	1.00
Superficial wound dehiscence, *n* (%)	2 (6.6)	0	0.5
Phrenic nerve palsy	2 (6.6)	3 (10.0)	1.00
Re-exploration for bleeding, *n* (%)	1 (3.3)	0	1.00
Lung complications, *n* (%)	1 (3.3)	1 (3.3)	1.00
Predischarge AF, *n* (%)	4 (13.3)	3 (10)	1.00

Other abbreviations are in Table 1

ICU intensive care unit, *LOS* length of stay, *TIA* transient ischemic attack

At the beginning of the endocardial procedure, complete isolation of the posterior LA wall was observed in 22 (36%) patients ($n = 10$ in BB group, $n = 12$ in conventional group (p=0.59). Achievement of electrical box isolation required endocardial ablation of the septal aspect of the box in 14/38 patients (36%), of the roof of the box in 12/38 patients (31%), of the lateral aspect of the box in 23/38 patients (60%), and of the inferior aspect of the box in 32/38 patients (84%). After the box lesion, spontaneous restoration of the sinus rhythm occurred in 2 patients of the Bachmann's group.

A bidirectional conduction block across the mitral isthmus line was achieved in all patients in the Bachmann's group compared with 21 patients (70%) in the conventional group (p=0.039). All patients received ablation of the ligament of Marshall, coronary sinus septal intercaval, cavo-tricuspidal isthmus, and superior vena cava isolation. Finally, 3 patients in Bachmann's group and 2 patients in conventional group received additional ablations for focal atrial arrhythmias.

Total duration of the endocardial ablation was (126 ± 42 min) in BB group vs 143 (±39 min) in the CONV group (p = 0.11). Average hospital stay resulted 2.6 days in BB group vs 2.5 days for the CONV group (p = 0.84). During endocardial ablation, a spontaneous restoration of sinus rhythm was observed in all patients ($n = 16$) in the BB group versus 5 patients

(28%) in the CONV group ($p < 0.001$). Patients in the CONV group still presenting AF ($n = 9$) or atrial flutter ($n = 4$) were successfully converted to sinus rhythm by electrical cardioversion.

After completion of endocardial ablation, incremental atrial pacing was conducted to test arrhythmia inducibility. Sustained atrial arrhythmias (lasting >30 s) were observed in 1/30 patients in the Bachmann's group (3.6%), versus in 19/30 patients (64.4%) in the CONV group (p= 0.0025). No major complications were recorded during the endocardial procedures. Three patients showed modest groin hematoma that non-required intervention or transfusion. No periprocedural thromboembolic events were observed in either group.

3.4 Follow-up

After the two-stage ablations, all patients were discharged in sinus rhythm. No patient was lost during follow-up, and all patients completed the 1-year follow-up. Four patients ($n = 1$ in BB group; $n = 3$ in CONV group) experienced early recurrences within the blanking period (<3 months). At the first evaluation after discharge, P-wave duration, morphology, and PR intervals were measured to assess atrial and atrioventricular conductions. Specifically, no significant differences were found in terms of (1) P-wave duration: 78.3 ± 18.9 (BB) vs 80.0 ± 16.0 (CONV) (p=0.835) and (2) PR interval: 166.2 ± 36.0 (BB) vs 161.0 ± 44.0 (CONV) (p=0.632). Apart from 1 patient with no clear visible P-waves (post-ablation junctional rhythm), no significant alterations in P-wave morphology were found in both groups, with P-waves mostly upright in inferior leads, negative or biphasic in V1, and negative in aVR. The 1-year success rate free of AAD was 96.6% in BB Group and 76.6% in the CONV group (p=0.025). A Kaplan–Meier curve of arrhythmia-free survival for both groups was reported in Fig. 3. No deaths or thromboembolic events were recorded.

Quality of life (QoL) questionnaire EQ-5D-3L was obtained from all patients. There was no statistically significant difference between groups (Supplementary Material).

4 Discussion

Although various ablative strategies have been designed over the last years [11–15], the success rate of catheter ablation in patients with LSPAF remains low, with wide variations in ablation techniques among operators. Increasing evidence suggests that the hybrid approach could represent a more aggressive, but greatly effective treatment for such patients [16].

The current report is the first study to date describing the adjunctive role of BB ablation in patients with LSPAF refractory to medical therapy. It resulted in the following important findings: (A) Bachmann's bundle ablation in the setting of a two-staged hybrid ablation is safe and highly effective with 96% of patients being arrhythmia-free at 12 months, off AADs, and without a need for re-ablation. (B) Adding this surgical ablation target, where the BB is supposed to be anatomically located, was easy to perform without a significant increase in procedural time and did not require further blunt dissection. (C) BB ablation does not increase the risk of periprocedural complications.

The 12-month success rate observed in the CONV group is consistent with prior reports. Muneretto et al. reported an 88% success rate at 1 year, and in the past, the same group described a 90% success rate with a sequential-staged approach [5, 17]. Kress et al. achieved an AF-free survival of 72% at median follow-up of 16 months [18]. Other authors [19, 20] achieved sinus rhythm in over 80% of the patients and resulted in substantial left atrial and left ventricular reverse remodeling, improvement in the ejection fraction, functional status, and even a decrease in the NT-pro BNP serum levels after 12 months.

It is noteworthy that adjunctive BB ablation resulted in 96% of the patients being arrhythmia-free, off AADs, and without a need for re-ablation. Bachman's bundle may be involved in a number of unstable re-entrant circuits, and it has been hypothesized that an effective lesion of the BB would prevent induction and maintenance of AF. Structural changes of BB may cause longitudinal dissociation of adjacent muscle fibers, facilitating re-entry and hence the development of AF [7]. In addition, BB ablation implies a greater amount of ablated tissue reducing the critical mass necessary to sustain AF and may eliminate "driver tachycardias" and arrhythmogenic foci outside the pulmonary veins.

Notably, no complications were specifically attributable to the adjunctive BB ablation. Across the two cohorts, 5 patients experiences phrenic nerve injury. Among those, 4 patients completely recovered within follow-up periods normally reported in the literature. The last patient remained asymptomatic during follow-up. Additionally, although absolute values of pre- and post-PR intervals have not been routinely measured, no post-procedural, stable, atrioventricular block occurred in our cohort, and pacemaker implantation was performed, despite the extensive ablation lesion set. Further studies are necessary to evaluate the effect of BB ablation on atrioventricular conduction delay.

We found a significant difference between the two groups in spontaneous conversion to sinus rhythm during the staged endocardial ablation and in terms of subsequent arrhythmia inducibility. In the BB group, all patients converted to sinus rhythm during the endocardial ablation, and none needed cardioversion. This represents a major finding if we consider that only 5 patients in the conventional group converted to sinus rhythm during the ablation while 13 patients needed electrical cardioversion. Differences in inducibility rate between groups were even more impressive, especially considering the

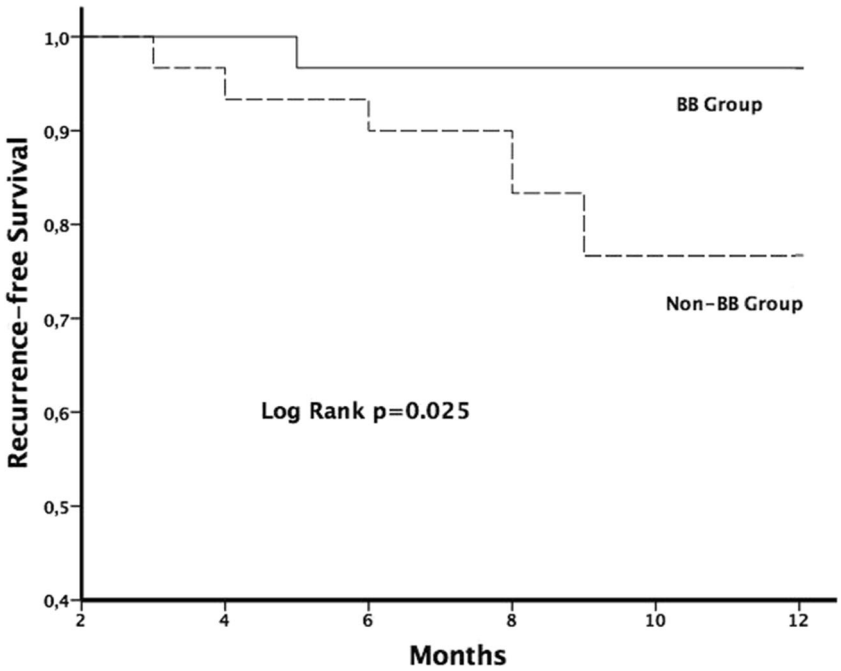

Fig. 3 Kaplan–Meier estimates of AF recurrence-free survival. AF episodes within 3 months after were excluded from the analysis. Freedom from AF was significantly higher in BB group. AF, atrial fibrillation; BB, Bachman bundle

aggressive protocol of induction used in our study: only one patient remained inducible in the BB group compared with 19/30 patients in the conventional groups. These observations suggest that BB plays a major role in the perpetuation of atrial fibrillation and should prompt to include the ablation of BB in the ablation schemes used for LSPAF. Moreover, data related to AF duration were similar in the two groups; therefore, it is unlikely that duration of AF may have had a relevant impact on different success outcomes after ablation in the two groups, with or without BB ablation. Of note, a more anterior BB line could result in inadvertent isolation of the left atrial appendage (LAA) when paired with the box lesion, and this may contribute to the higher success rate in our BB cohort [21]. Generally, however, additional touch-up RF ablations are needed to completely isolate LAA. Unfortunately, routine assessment of LAA isolation was not part of the study protocol, and further studies regarding the impact of anterior BB line on LAA isolation are required.

Of note, no significant differences were found in the two groups in terms of atrial and atrioventricular activations, assessed as P-wave duration and morphology and PR interval, suggesting no significant impact on atrioventricular electrical coupling after BB ablation.

In our case series, no thromboembolic events were observed at 12-month follow-up; this is probably due to a consistent anticoagulation regime and to the relative low numerosity of our population. Large sample size studies should be issued to properly address this topic. In 7 patients of the CONV group, mitral isthmus line was not successfully completed after catheter ablation. One of them had AF recurrence; however, this number was too small for any meaningful conclusion. Leftward extensions of the BB bifurcate to pass to either side of the left atrial appendages: it is our opinion that BB ablation could have facilitated in some way the mitral isthmus block obtained in all patients of the BB group.

4.1 Limitations

This is a single-center non-randomized study and has all the inherent limitations associated this design. Furthermore, the small sample size might account for the failure to detect differences between groups in all the QoL scores.

We may also have underestimated the recurrence rate because of asymptomatic undocumented arrhythmia episodes and because implantable loop recorders were not routinely used. However, many prior studies of AF ablation have not systematically looked for asymptomatic episodes of recurrent atrial fibrillation on a daily basis, and the entire population was composed of late-persistent atrial fibrillation, in which the pretest probability of being in AF was elevated; even a single ECG in sinus rhythm therefore represents a non-insignificant rule out test for atrial recurrence. Although LAA electrical isolation may have followed an anterior BB ablation, unfortunately, a circular mapping catheter was not routinely placed in the LAA to assess its electrical activity during the procedure; therefore, specific data about LAA could not be provided in a consistent fashion. Moreover, the study may be underpowered to detect significant differences in QoL, due to its sample size, although QoL is a weak endpoint to assess catheter ablation outcomes. Despite not having data on AF burden, we acknowledge that its reduction may significantly improve QoL, since AF is not a binary entity in its clinical manifestation. Finally, percutaneous ablation was performed 2 to 6

weeks after the surgical approach, and in some cases, full "maturation" of the surgical scars may have not happened.

5 Conclusions

Bachmann's bundle ablation in the setting of a two-staged hybrid ablation is a safe and highly effective first-line treatment for patients with long-standing persistent AF, with 96% of patients being arrhythmia-free 1 year after the procedure. Pending further trials with a longer and continuous follow-up, this study suggests the major role of BB in the substrate maintaining LSPAF even after an extensive biatrial ablation.

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References

1. Muneretto C, Bisleri G, Rosati F, Krakor R, Giroletti L, Di Bacco L, et al. European prospective multicentre study of hybrid thoracoscopic and transcatheter ablation of persistent atrial fibrillation: The HISTORIC-AF trial. Eur J Cardio-Thoracic Surg. 2017;52:740–5. https://doi.org/10.1093/ejcts/ezx162.
2. Mohanty S, Di Biase L, Mohanty P, Trivedi C, Santangeli P, Bai R, et al. Effect of periprocedural amiodarone on procedure outcome in patients with longstanding persistent atrial fibrillation undergoing extended pulmonary vein antrum isolation: results from a randomized study (SPECULATE). Heart Rhythm. 2015;12:477–83. https://doi.org/10.1016/j.hrthm.2014.11.016.
3. Sorgente A, Tung P, Wylie J, Josephson ME. Six year follow-up after catheter ablation of atrial fibrillation: a palliation more than a true cure. Am J Cardiol. 2012;109:1179–86. https://doi.org/10.1016/j.amjcard.2011.11.058.
4. Nasso G, Moscarelli M, Fattouch K, Zebele C, Iacopino S, Fiore F, et al. Mid-term performance of bipolar radiofrequency ablation for isolated atrial fibrillation through a right minithoracotomy. Semin Thorac Cardiovasc Surg. 2017;29:160–72. https://doi.org/10.1053/j.semtcvs.2017.01.005.
5. Muneretto C, Bisleri G, Bontempi L, Cheema FH, Curnis A. Successful treatment of lone persistent atrial fibrillation by means of a hybrid thoracoscopic-transcatheter approach. Innov Technol Tech Cardiothorac Vasc Surg. 2012;7:254–8. https://doi.org/10.1097/IMI.0b013e31826f0462.
6. Muneretto C, Bisleri G, Bontempi L, Curnis A. Durable staged hybrid ablation with thoracoscopic and percutaneous approach for treatment of long-standing atrial fibrillation: a 30-month assessment with continuous monitoring. J Thorac Cardiovasc Surg. 2012;144:1460–5. https://doi.org/10.1016/j.jtcvs.2012.08.069.
7. Van Campenhout MJH, Yaksh A, Kik C, De Jaegere PP, Ho SY, Allessie MA, et al. Bachmann's bundle a key player in the development of atrial fibrillation? Circ Arrhythm Electrophysiol. 2013;6:1041–6. https://doi.org/10.1161/CIRCEP.113.000758.
8. Kumagai K, Khrestian C, Waldo AL. Simultaneous multisite mapping studies during induced atrial fibrillation in the sterile pericarditis model: insights into the mechanism of its maintenance. Circulation. 1997;95:511–21. https://doi.org/10.1161/01.CIR.95.2.511.
9. Kumagai K, Uno K, Khrestian C, Waldo AL. Single site radiofrequency catheter ablation of atrial fibrillation: Studies guided by simultaneous multisite mapping in the canine sterile pericarditis model. J Am Coll Cardiol. 2000;36:917–23. https://doi.org/10.1016/S0735-1097(00)00803-2.
10. Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: executive summary. J Interv Card Electrophysiol. 2017;50. https://doi.org/10.1007/s10840-017-0277-z.
11. Dewire J, Calkins H. Update on atrial fibrillation catheter ablation technologies and techniques. Nat Rev Cardiol. 2013;10:599–612. https://doi.org/10.1038/nrcardio.2013.121.
12. Forleo GB, De Martino G, Mantica M, Carreras G, Parisi Q, Zingarini G, et al. Clinical impact of catheter ablation in patients with asymptomatic atrial fibrillation: the IRON-AF (Italian Registry on NavX Atrial Fibrillation Ablation Procedures) study. Int J Cardiol. 2013. https://doi.org/10.1016/j.ijcard.2013.06.132.
13. Dukkipati SR, Neuzil P, Kautzner J, Petru J, Wichterle D, Skoda J, et al. The durability of pulmonary vein isolation using the visually guided laser balloon catheter: multicenter results of pulmonary vein remapping studies. Heart Rhythm. 2012;9:919–25. https://doi.org/10.1016/j.hrthm.2012.01.019.
14. Kuck KH, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun J, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. J Cardiopulm Rehabil Prev. 2016;36:393–4. https://doi.org/10.1056/NEJMoa1602014.
15. Cox JL, Churyla A, Malaisrie SC, Pham DT, Kruse J, Kislitsina ON, et al. A hybrid maze procedure for long-standing persistent atrial fibrillation. Ann Thorac Surg. 2019;107:610–8. https://doi.org/10.1016/j.athoracsur.2018.06.064.
16. Marchlinski F, Kumareswaran R. Hybrid ablation for atrial fibrillation: better or just different? JACC Clin Electrophysiol. 2017;3:350–2. https://doi.org/10.1016/j.jacep.2016.12.020.
17. Bisleri G, Rosati F, Bontempi L, Curnis A, Muneretto C. Hybrid approach for the treatment of long-standing persistent atrial fibrillation: electrophysiological findings and clinical results. Eur J Cardio-Thoracic Surg. 2013;44:919–23. https://doi.org/10.1093/ejcts/ezt115.
18. Kress DC, Erickson L, Choudhuri I, Zilinski J, Mengesha T, Krum D, et al. Comparative effectiveness of hybrid ablation versus endocardial catheter ablation alone in patients with persistent atrial fibrillation. JACC Clin Electrophysiol. 2017;3:341–9. https://doi.org/10.1016/j.jacep.2016.10.010.
19. Budera P, Osmancik P, Herman D, Zdarska J, Talavera D, Mala A, et al. Midterm outcomes of two-staged hybrid ablation of persistent and long-standing persistent atrial fibrillation using the versapolar epicardial surgical device and subsequent catheter ablation. J Interv Card Electrophysiol. 2017;50:187–94. https://doi.org/10.1007/s10840-017-0286-y.
20. Toplisek J, Pernat A, Ruzic N, Robic B, Sinkovec M, Cvijic M, et al. Improvement of atrial and ventricular remodeling with low atrial fibrillation burden after hybrid ablation of persistent atrial fibrillation. Pacing Clin Electrophysiol. 2016;39:216–24. https://doi.org/10.1111/pace.12791.
21. Park HC, Lee DI, Shim J, Choi JI, Kim YH. The clinical efficacy of left atrial appendage isolation caused by extensive left atrial anterior wall ablation in patients with atrial fibrillation. J Interv Card Electrophysiol. 2016;46:287–97. https://doi.org/10.1007/s10840-016-0116-7.