Left atrial substrate characterization in patients with atrial fibrillation and hypertrophic cardiomyopathy: evidence for an extensive fibrotic disease

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Abstract

Introduction. Data regarding the left atrial (LA) electroanatomical substrate in patients with hypertrophic cardiomyopathy (HCM) and atrial fibrillation (AF) are missing. In this electroanatomical mapping (EAM) study, we evaluated the extent of LA fibrosis and its impact on catheter ablation outcomes in patients with HCM and AF. Methods. High-density LA EAM was performed during AF in 28 consecutive patients with obstructive HCM and AF (42.9% displayed paroxysmal AF and 57.1% persistent AF). After propensity matching (PS), 28 non-HCM patients with AF were selected, and served as controls. Two different cut-off values of bipolar signal amplitude were investigated for fibrosis characterization ([?]0.25 mV and [?]0.4 mV). HCM patients underwent pulmonary vein antral isolation (PVAI) and roof line, while non-HCM patients PVAI only. Results. After the 3-month blanking period, 10 HCM patients (35.7%) displayed atrial arrhythmia recurrence. Univariate analysis revealed that the extent of LA fibrosis was the only predictor of AF recurrence. HCM patients with arrhythmia recurrence showed significantly greater low voltage areas defined as either bipolar voltage [?]0.25 mV (22.5±10% vs. 5.5±6.4%, p=0.001) or [?]0.4 mV (32+-13.9% vs. 5.9+-5.1%, p<0.001). The presence of low voltage areas [?]0.4 mV greater than 14.1% of the total LA area also predicted arrhythmia recurrence with excellent sensitivity (100%) and specificity (100%). After PS matching with non-HCM patients, patients with HCM exhibited wider fibrotic regions [?]0.25 mV compared to non-HCM patients (p=0.016). Conclusions. High-density EAM reveals extensive LA fibrotic disease in patients with HCM, an event with certain implications in catheter ablation outcomes.

Introduction

Atrial fibrillation (AF) is commonly seen in patients with hypertrophic cardiomyopathy (HCM) (˜20%).[1]Catheter ablation (CA) is a reasonable therapeutic approach in selected patients with HCM and AF (class IIa indication, Level of Evidence B).[2] Studies addressing the efficacy of AF CA in patients with HCM are limited and have demonstrated worst long-term outcomes compared to non-HCM patients.[3-7] Persistent

AF, female gender, age, New York Heart Association (NYHA) functional class, LA enlargement, and left ventricle (LV) outflow tract obstruction have been proposed as predictors of AF recurrence following catheter ablation in this specific population.[3-5] Pulmonary vein (PV) isolation only appears insufficient to improve the long-term arrhythmia survival in HCM patients, possibly due to extensive LA remodeling.[6]

Among AF patients undergoing catheter ablation, atrial tissue fibrosis assessed by delayed enhancement magnetic resonance imaging was independently associated with arrhythmia recurrence.[8]The presence of LA cardiomyopathy estimated by high-density electroanatomical mapping (EAM) has been associated with AF relapse following catheter ablation.[9,10] Data regarding the EAM LA substrate in patients with HCM and AF are missing. In this high-density EAM study, we evaluated for the first time the extent of LA fibrosis and its impact on catheter ablation outcomes in patients with HCM and AF.

Methods

Patients

Consecutive patients with obstructive HCM planned for radiofrequency AF CA between January 2016 and March 2020 were enrolled, and prospectively studied. Patient demographics, medical history, medications, echocardiographic data [interventricular septum (IVS) thickness, left ventricular end-diastolic diameter (LVEDD), LA diameter, LA volume, left ventricular outflow tract (LVOT) gradient, and left ventricular ejection fraction (LVEF)], and procedural data were collected in all cases. HCM patients were propensity score (PS) matched to patients without HCM (non-HCM) who underwent AF CA, and served as control group.

The diagnosis of HCM was based on 2-dimensional echocardiography and defined by a wall thickness [?]15 mm or [?]13mm in patients with a documented family history of HCM that is not explained by another cardiac or systemic disease capable of producing the magnitude of hypertrophy.[11] LVOT obstruction was defined as an outflow tract gradient [?]30 mmHg at rest or during Valsalva maneuver, standing or exercise.[11]

The institutional ethics committee approved the study protocol, and written informed consent was obtained from all patients.

Left atrial electroanatomical mapping and catheter ablation procedure

Patients were under conscious sedation. Transesophageal echocardiography was performed in all subjects to exclude LA thrombus. The procedure has been described in details elsewhere.[10,12] After a single transseptal puncture, an activated clotting time (ACT) more than 300 seconds was maintained by intravenous heparin bolus (100 IU/kg) and infusion. A 20-pole catheter (Pentaray, interelectrode spacing 2-6-2 mm, Biosense Webster) and an open-tip irrigated radiofrequency (RF) catheter with tip-integrated contact force (CF) sensor (Thermocool SmartTouch, D curve, 1-6-2mm; Biosense Webster) were used for mapping and ablation, respectively. After reconstructing the three-dimensional geometry of the left atrium (LA) (Carto 3; Biosense Webster), high-density bipolar voltage mapping was performed during AF using the 20-pole multielectrode mapping catheter. In patients presented in sinus rhythm, burst atrial pacing from distal coronary sinus (CS) at a cycle length of 200 to 150ms was used to induce atrial fibrillation (AF). The Biosense Webster Confidense module process was used to collect points with the following filter settings: (a) force >6 g; (b) catheter stability, acquiring points when the catheter location was stable (position stability 2.5mm); (c) density 1mm, minimizing acquisition points when the catheter is not being moved or collecting denser points if a higher setting is chosen; (d) tissue proximity indicator, which uses impedance measurements to determine the electrode proximity to cardiac tissue. The CS was mapped with a steerable decapolar catheter (DECANAV, interelectrode spacing 2-8-2 mm, Biosense Webster). As the ablation catheter has a different electrode size and spacing and generally underestimates the true electrogram voltage compared with the multielectrode catheters, we made every attempt to collect all points using the multipolar catheter rather than the ablation catheter to maintain consistency within the map. Criteria for an adequate LA shell were more than 2000 points (mean number of points: 2323±862) that were homogenously distributed to delineate the entire chamber of the LA. We mapped regions with low-amplitude signals with greater point density

to more precisely delineate the extent of endocardial electroanatomic scar areas. With a band pass filter set at 30 to 500 Hz, each acquired point was classified according to the peak-to-peak bipolar electrogram voltage. Two different cut-off values of bipolar signal amplitude were investigated for scar fibrotic area characterization. Areas displaying low amplitude bipolar signals [?]0.25 mV (1^{st} low voltage definition) and [?]0.4 mV (2^{nd} low voltage definition) were defined as scar fibrotic regions. We divided the LA into the following regions: (1) left PV-LA junction; (2) right PV-LA junction; (3) roof; (4) posterior; (5) inferior; (6) anterior (including LA appendage); and (7) left septum (**Figure 1**). Confluent regions of bipolar low voltage were measured using the standard surface area measurement tool on the CARTO 3 software. The proportion of the mapped LA surface exhibiting low voltage bipolar signals was expressed as a percentage of the overall mapped LA surface area, except the four PVs. All measurements were performed during the index ablation procedure.

HCM patients underwent pulmonary vein antral isolation (PVAI) with intention to minimize not isolated posterior and roof line, while non-HCM patients PVAI only. Point-by-point ipsilateral PVAI was performed using the real-time automated display of radiofrequency applications (Visitag; Biosense Webster) with predefined settings for catheter stability (2.5mm for 10 seconds) and minimum CF (60% of time >7 g). Radiofrequency energy was delivered in a power-controlled mode with maximum 40W for 20 seconds on the posterior wall and maximum 40W for 30 seconds on the anterior wall and the roof of the LA (irrigation of 30 ml/min) (EP Shuttle ST, Stockert GmbH, Freiburg, Germany). If we could not terminate AF to a regular rhythm (sinus rhythm or atrial tachycardia), we performed electrical cardioversion. Entrance and exit block of the PVs as well as bidirectional block of the roof line were confirmed after sinus rhythm was restored.

Post-ablation care and follow-up

Pericardial effusion was ruled out by transthoracic echocardiography on the day of the procedure and 24-hours later. Twelve-lead electrocardiogram, 24-hour Holter and echocardiography were regularly performed 1, 3, 6, 9, and 12 months after discharge and every 6 months thereafter, with additional visits when patients described palpitations. Arrhythmia recurrence was defined as any atrial arrhythmia (AF or atrial tachycardia including cavotricuspid right atrial flutter) after a 3-month blanking period from the index procedure.[2] A repeated procedure was offered in all patients with arrhythmia recurrence. All patients were followed up for at least 18 months after the first procedure.

Statistical analysis

The normality of continuous data was assessed using the Shapiro–Wilk test. Categorical variables were reported as frequency (%) while continuous variables as mean +- Standard Deviation (SD). The Chi-square or Fisher's exact test was used to compare categorical variables, as appropriate. Student's t test or the Mann–Whitney U test was used to compare continuous variables, as appropriate. Receiver operator characteristic (ROC) curves were plotted to find the optimal cut-off values for predicting arrhythmia recurrence. Propensity score (PS) matching analysis was performed to reduce the impact of potential confounding factors. PSs were derived to match patients at a 1:1 ratio. Patients were matched according to age, sex, LA diameter, and AF type. Analysis was performed using SPSS software version 23.0 (IBM Corp., Armonk, NY, USA) and XLSTAT statistical software for excel. The statistical significance was set at a two-tailed P-value of [?] 0.05.

Results

A total of 28 consecutive patients with obstructive HCM [mean age: 58.3+-11.3 years, males: 21 (75%)] were enrolled in the study. Regarding AF type, 12 patients (42.9%) displayed paroxysmal AF (PAF) and 16 (57.1%) persistent and long-standing persistent AF (non-PAF). All patients were on amiodarone before ablation, and it was stopped 3 months after the index procedure. After this period, amiodarone was restarted in patients with arrhythmia recurrence. Beta-blocker were used in all patients. After PS matching had been performed, 28 non-HCM patients were selected [(mean age: 53+-14 years, males: 22 (78.5%)], and served as control group.

After the 3-month blanking period, 10 HCM patients (35.7%) displayed an atrial arrhythmia recurrence, while

18 patients (64.3%) remained in sinus rhythm. The baseline clinical, echocardiographic, electrophysiologic and procedural characteristics of HCM patients with and without arrhythmia recurrence are provided in **Table 1** . Specifically, sinus rhythm was maintained in 75% of PAF and 56.3% of non-PAF patients. All subjects with arrhythmia relapse underwent a repeated procedure (3 patients for AF, 5 patients for LA micro- or macro-reentrant atrial tachycardia, and 2 patients for cavotricuspid right atrial flutter). After 1.35 catheter ablation procedures per patient, 8 HCM patients (28.5%) had an arrhythmia recurrence, while 20 HCM patients (71.5%) remained in sinus rhythm at the end of follow-up period (39.1+-15.1 months). There were no procedural related complications. Univariate analysis revealed that the only predictor of AF recurrence was the extent of LA fibrosis. Specifically, patients with arrhythmia recurrence showed significantly greater low voltage areas defined as either bipolar voltage [?]0.25 mV (22.5+-10% vs. 5.5+-6.4%, p=0.001) or [?]0.4 mV (32+-13.9% vs. 5.9+-5.1%, p<0.001) compared to those who remained in sinus rhythm (**Table 2 and Figure 2**). ROC analysis demonstrated that the presence of low voltage areas [?]0.25 mV greater than 13.1% of the total surface area predicts AF recurrence with high sensitivity (100%) and specificity (88.9%), while the existence of low voltage areas [?]0.4 mV greater than 14.1% of the total LA area also predicts arrhythmia recurrence with great sensitivity (100%) and specificity (100%). The fibrotic areas of non-PAF patients were significantly wider compared to PAF patients by using the 0.4mV cut-off value (16.5+-13.8% vs. 9.4+-13.7%, p=0.03), but not for the 0.25mV cut-off value (11.5+-6.0% vs. 8.4+-12.8%, p=0.19). Detailed data regarding the location of fibrotic areas in relation to LA segments in subjects with HCM are provided in Table 2. After PS matching with non-HCM patients who underwent AF catheter ablation, patients with HCM exhibited wider low voltage areas based on the 0.25mV criterion compared to non-HCM patients (9.7+-10.7% vs. 2.8+-3.2%, p=0.016). No statistically significant differences were seen using the 0.4mV criterion (12.4+-14.3% Vs. 5.9+-5.3%, p=0.116). A comparison of low voltage areas with respect to specific LA segments in patients with and without HCM, before and after PS matching, is depicted in **Table 3** .

Discussion

The main findings of the present study are the following:

1. HCM patients with arrhythmia recurrence exhibit significantly wider fibrotic areas compared to those who remained in sinus rhythm;
2. The presence of fibrotic areas greater than 13.1% ([?]0.25 mV voltage criterion) or 14.1% ([?]0.4 mV voltage criterion) predict arrhythmia recurrence with high sensitivity and specificity;
3. LA fibrosis is the only predictor of arrhythmia recurrence following catheter ablation in patients with obstructive HCM;
4. HCM patients with AF display significantly broader fibrotic areas compared to a PS matched control population of non-HCM patients and AF.

The development of AF in HCM is multifactorial and has been related to LA enlargement, increased LA pressure, LVOT obstruction, and LA fibrosis as detected by late gadolinium enhancement cardiac MR (LGE-CMR).[1,13,14] This complex pathophysiology of AF in HCM possibly explains the high recurrence rates observed following catheter ablation of the arrhythmia. In a meta-analysis of five studies, the single-procedure success rate (free from any atrial arrhythmia) was only 38.7% in patients with HCM compared to 49.8% in controls.[3] Outcomes after multiple procedures increased to 51.8% compared to 71.2% in controls. Repeat procedures and antiarrhythmic drugs are more frequently needed in patients with HCM to prevent arrhythmia relapse.[3]

Recent LGE-CMR studies have demonstrated the presence of LA fibrosis in HCM patients, and especially in those with AF.[13,14]The extent of LA LGE has been significantly correlated with the extent of LV LGE, suggesting that either the LA fibrosis is the result of LV fibrosis or both of them are manifestations of the same pathophysiologic process.[5] Atrial fibrosis is the most important predictor of ablation failure beyond PV isolation.[9] PV and posterior wall isolation alone have been shown to be insufficient to obtain satisfactory long-term results.[6] In addition, non-PV triggers have been demonstrated in the majority of HCM patients with arrhythmia recurrence, a finding that supports the appropriateness of a more extensive ablation beyond

PV isolation to improve the arrhythmia-free survival.[6] These findings are possibly related to an extensive LA cardiomyopathy in this specific population.

In this high-density EAM study, we evaluated for the first time the extent of LA fibrosis and its impact on catheter ablation outcomes in patients with HCM and AF. Irrespective of the bipolar voltage cut-off value used for fibrosis characterization ([?]0.25 mV or [?]0.4 mV), HCM patients with arrhythmia relapse exhibited wider fibrotic regions compared to those who remained in sinus rhythm. By using the [?]0.4 mV bipolar voltage criterion, the presence of low voltage areas more than 14.1% of the total LA area predicted AF recurrence with an excellent sensitivity (100%) and specificity (100%). We additionally showed that non-paroxysmal AF patients exhibit significantly wider diseased areas compared to paroxysmal AF patients. HCM patients exhibited larger low voltage areas compared to the PS matched control population of non-HCM patients. These findings have important implications in AF catheter ablation outcomes. In cases with extensive fibrosis, substrate modification aiming at scar homogenization or isolation or LA compartmentalization may be need to improve long term outcomes following catheter ablation.[8,9] The existence of LA voltage areas [?]0.4 mV more than 10% of the total LA surface area has been shown to predict arrhythmia recurrence following PVAI even for paroxysmal AF patients.[10] In a similar high-density EAM study, we have demonstrated that substrate modification aiming specific electrograms within low voltage areas ([?]0.4 mV) leads to AF termination in 23% of patients with persistent AF and improved long-term free-survival from any atrial arrhythmia.[12]

Clinical implications

The fibrotic process possibly plays a crucial role in the development and maintenance of AF.[8,9] Keeping in mind that only young patients with paroxysmal AF and less dilated atria display better long-term outcomes,[3-5] the presence of LA cardiomyopathy with respect to the progression of the disease might have important implications in ablation outcomes. HCM patients undergo catheter ablation late in the course of their disease (median of 5.9 years after the diagnosis of atrial arrhythmias),[3] and therefore an extensive structural and electrical remodeling including LA enlargement and fibrosis is possibly present at the time of catheter ablation. The present findings suggest that patients with obstructive HCM exhibit LA cardiomyopathy that affects long-term ablation outcomes. We postulate that catheter ablation should be performed at the early stages of AF (paroxysmal phase) where the development of LA cardiomyopathy is less likely.

Limitations

This study has potential limitations. First, the number of HCM patients is relatively small. Second, our clinical follow-up regarding arrhythmia recurrence following catheter ablation was based on 12-lead electrocardiogram and 24-hour Holter monitoring, and therefore the true recurrence rates may have been underestimated. Third, the identification of fibrotic substrate using EAM is not fully developed, and displays several limitations.[15] The measured voltage depends on the rhythm (sinus rhythm vs. atrial pacing vs. AF), the contact of the electrode to the tissue, the thickness of the atrial myocardium, the electrode size and spacing, the wave front direction, and other variables.[15] However, in our study, two low bipolar voltage criteria were used for tissue characterization (the strict criterion of [?]0.25 mV and the less strict but more commonly used of [?]0.4 mV). Finally, we did not use LGE-CMR in order to confirm that LA regions with low bipolar voltage [?]0.4 mV or [?]0.25 mV represent true atrial scar. However, EAM during AF has been shown to correlate well with atrial scar detected by LGE-CMR.[16]

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Tables

Table 1. Baseline clinical, echocardiographic and electrophysiologic characteristics of patients with HCM according to arrhythmia recurrence following catheter ablation.

	AF recurrence (n= 10, 35.7%)	**No AF recurrence (n= 18, 64.3%)**	**P-Value**
Demographics	**Demographics**	**Demographics**	**Demographics**
Age (years)	54.3±12.4	60.3±10.3	0.16
Males (%)	6 (60%)	14 (77.8%)	0.53
BMI (Kg/m^2)	29.2±4.4	29.9±6.1	0.74
AF type	**AF type**	**AF type**	**AF type**
Paroxysmal (%)	3 (30)	9 (50)	0.28
Persistent (%)	6 (60)	9 (50)	
Long-standing persistent (%)	1 (10)	0 (0)	

	AF recurrence (n= 10, 35.7%)	**No AF recurrence (n= 18, 64.3%)**	**P-Value**
Echocardiographic parameters	**Echocardiographic parameters**	**Echocardiographic parameters**	**Echocardiographic parameters**
IVS thickness (mm)	16.3±1.8	15.5±2.0	0.40
LVEDD (mm)	45.4±6.2	46.7±5.1	0.61
LA diameter (mm)	48.4±3.7	46.5±4.5	0.33
LA volume (ml)	136.7±13.7	126.1±14.7	0.18
LVOT gradient (mmHg)	41.8±1.8	43.7±2.7	0.06
LVEF (%)	55±5.8	59.3±8.5	0.11
Medications	**Medications**	**Medications**	**Medications**
Amiodarone (%)	9 (90)	11 (61.1)	0.19
Anticoagulation regimen	**Anticoagulation regimen**	**Anticoagulation regimen**	**Anticoagulation regimen**
Dabigatran (%)	1 (10)	4 (22.2)	0.32
Apixaban (%)	4 (40)	3 (16.7)	
Rivaroxaban (%)	2 (20)	8 (44.4)	
Acenocoumarol (%)	3 (30)	3 (16.7)	
Medical History	**Medical History**	**Medical History**	**Medical History**
Stroke (%)	1 (10)	1 (5.6)	1.0
Hypertension (%)	3 (30)	12 (66.7)	0.11
Diabetes Mellitus (%)	1 (10)	2 (11.1)	1.0
Dyslipidemia (%)	2 (20)	8 (44.4)	0.25
Procedural data	**Procedural data**	**Procedural data**	**Procedural data**
Complications (%)	0 (0)	0 (0)	-
Procedure time (min)	139±99.1	114.7±92.9	0.36

Abbreviations. AF: atrial fibrillation; BMI: body mass index; HCM: hypertrophic cardiomyopathy; IVS: interventricular septum; LA: left atrium; LVOT: left ventricular out-flow tract; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter.

Table 2. Comparison of LA low voltage areas in patients with HCM according to AF recurrence following catheter ablation.

	AF recurrence (n= 10, 35.7%)	**No AF recurrence (n= 18, 64.3%)**	**P-Value**	
1st low voltage criterion: bipolar signals [?]0.25mV	**1st low voltage criterion: bipolar signals [?]0.25mV**	**1st low voltage criterion: bipolar signals [?]0.25mV**	**1st low voltage criterion: bipolar signals [?]0.25mV**	**1st low voltage criterion: bipolar signals [?]0.25mV**
Total low voltage area (%)	22.5±10	5.5±6.4	0.001	
Anterior wall (%)	7.2±2.8	1.3±2	0.001	
Posterior wall (%)	7.3±5.2	2.6±5.1	0.023	
Inferior wall (%)	3.1±1.3	0.1±0.3	<0.001	
Roof (%)	2.3±1.6	1.0±1.4	0.043	
Septum (%)	2.7±1.9	0.6±0.6	0.022	

	AF recurrence (n= 10, 35.7%)	**No AF recurrence (n= 18, 64.3%)**	**P-Value**	
2nd low voltage criterion: bipolar signals [?]0.4mV	**2nd low voltage criterion: bipolar signals [?]0.4mV**	**2nd low voltage criterion: bipolar signals [?]0.4mV**	**2nd low voltage criterion: bipolar signals [?]0.4mV**	**2nd low voltage criterion: bipolar signals [?]0.4mV**
Total low voltage area (%)	32±13.9	5.9±5.1	<0.001	
Anterior wall (%)	8.3±3.3	1.9±2.2	0.001	
Posterior wall (%)	8.8±4.1	1.6±1.7	<0.001	
Inferior wall (%)	8.2±7.2	0.2±0.6	<0.001	
Roof (%)	3.2±1.4	1.3±1.5	0.022	
Septum (%)	3.7±2.4	1.1±1.0	0.022	

Abbreviations. AF: atrial fibrillation; HCM: hypertrophic cardiomyopathy; LA: left atrium.

Table 3. Comparison of low voltage areas between patients with and without HCM, before and after PS matching.

	Before PS matching	**Be**
	HCM patients (n=28)	**Co**
1st low voltage criterion: bipolar signals [?]0.25mV	**1st low voltage criterion: bipolar signals [?]0.25mV**	**1st**
Total LA area (%)	9.7±10.4	5.2
Anterior wall (%)	2.8±3.4	1.2
Posterior wall (%)	3.8±5.4	1.1
Inferior wall (%)	0.9±1.5	1.5
Roof (%)	1.3±1.6	0.5
Septum (%)	1.2±1.4	0.8
2nd low voltage criterion: bipolar signals [?]0.4mV	**2nd low voltage criterion: bipolar signals [?]0.4mV**	**2n**
Total LA area (%)	12.4±13.9	8.6
Anterior wall (%)	3.5±3.7	2.1
Posterior wall (%)	3.4±4.0	1.9
Inferior wall (%)	2.2±4.9	2.4
Roof (%)	1.8±1.7	1.0
Septum (%)	1.7±1.8	1.3

Abbreviations. AF: atrial fibrillation; HCM: hypertrophic cardiomyopathy, LA: left atrium; PS: propensity score.

Legends

Figure 1. 3-D anatomical compartmentalization of the LA into seven segments in antero-posterior (A) and postero-anterior (B) views: (1) left PV-LA junction; (2) right PV-LA junction; (3) roof; (4) posterior; (5) inferior; (6) anterior (including LA appendage); and (7) left septum. EAM: electroanatomical; LA: atrium; LAA: left atrial appendage; LIPV: left inferior pulmonary vein; LSPV: left superior pulmonary vein; RIPV: right inferior pulmonary vein; RSPV: right superior pulmonary vein; PV: pulmonary vein.

Figure 2. A1-A2: High-density EAM demonstrating severe LA fibrotic disease (extensive low bipolar voltage areas) in a patient with HCM, persistent AF and arrhythmia recurrence following catheter ablation

as detected using either the [?]0.25 mV low voltage criterion (A1) or the [?]0.4 mV low voltage criterion (A2). **B1-B2:**High-density EAM in a patient with HCM, paroxysmal AF and sinus rhythm maintenance following catheter ablation showing minimal left atrial disease as detected using the [?]0.25 mV low voltage criterion (B1) and mild (wider low voltage areas) using the [?]0.4 mV low voltage criterion (B2). AF: atrial fibrillation; EAM: electroanatomical mapping; HCM: hypertrophic cardiomyopathy; LA: left atrium.