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Original article

Burden-based classification of atrial fibrillation predicts multiple-procedure success of pulmonary vein isolation

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ABSTRACT

Background: Catheter ablation of atrial fibrillation (AF) by means of pulmonary vein isolation (PVI) focuses on the PVs as the putative trigger of AF. However, which classification should be used to identify patients that are most suitable for PVI is uncertain. The aim of the study was to evaluate rhythm-, burden-, and anatomically-based classification schemes to predict success rates after up to two procedures of an ablation strategy strictly aimed at isolation of the PVs.
Methods: Patients with paroxysmal or non-longstanding persistent AF undergoing PVI-only ablation with the option of one repeat PVI in case of AF recurrence were included. An AF burden score (AFB) was determined based on frequency, episode duration, and number of previous cardioversions and then categorized as minimal, mild, moderate, or severe. Two- and three-dimensional anatomical assessment of the left atrium (LA) was performed based on pre-interventional imaging by computed tomography or magnetic resonance imaging.
Results: Of 195 patients analyzed, 24 presented with recurrence after the last intervention (12%, median follow up: 16 ± 11 months). In multivariable analysis, a more than 6-fold increase of risk for AF recurrence was identified for patients with a severe compared to a mild AFB [hazard ratio: 6.241 (95% confidence interval: 1.914–20.167, $p = 0.002$)]. In contrast to univariable analysis, no other parameter was associated with recurrence in multivariable analysis.
Conclusions: Burden-based (AFB) classification was identified as a significant predictor for AF recurrence even after repeat PVI, while neither anatomical parameters nor the established rhythm-based classification of paroxysmal and persistent AF did.

Introduction

Atrial fibrillation (AF) is considered to be primarily initiated by pulmonary vein (PV) triggers and sustained by the atrial myocardium [1]. Consequently, PV isolation (PVI) is established as first-line therapy in patients with paroxysmal AF [2]. In patients with persistent AF, additional ablation lesions have commonly been performed to modify the left atrial (LA) substrate. The randomized STAR AF II study, however, has shown that in patients with persistent AF, additional ablation beyond PVI of the substrate (such as lines and ablation of complex fractionated atrial electrograms) increased procedure time but did not improve outcomes [3]. These and more recent studies confirmed PVI only as an accepted therapy even for persistent AF [4,5]. Nevertheless, patients with persistent AF are shown to have a higher AF recurrence rate than patients with paroxysmal AF [6].

To characterize the different stages of AF, a rhythm-based classification of AF is commonly performed based on the guidelines of the European Society of Cardiology (ESC) and the American Heart Association (AHA)/American College of Cardiology (ACC) as

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paroxysmal, persistent, or long-standing persistent AF dependent on the duration of the AF episodes [7–9]. In addition to this rhythm-based classification, anatomical discriminators have been identified to have the potential to predict the outcome after catheter ablation and in particular after PVI [10,11]. They have been detected as predictors for success after catheter ablation [6], but are not yet used as discriminators to define the ablation strategy. These classification schemes, however, have never been compared with regard to their ability to determine patients that benefit the most from a PVI-only ablation approach, especially when a repeat PVI to close the electrical gaps around the PVs is allowed.

The aim of the current study was to investigate the value of rhythm-, burden-, and anatomically-based classifications to predict success rates after up to two procedures of an ablation strategy strictly aimed at isolation of the PVs.

Methods

In this retrospective analysis, we analyzed consecutive patients included in our prospective 'Basel Atrial Fibrillation Pulmonary Vein Isolation' (BEAT-AF-PVI) cohort study, undergoing PVI-only using radiofrequency (RF) and cryoballoon (CB) technology. The local ethics committee on human research approved our study and written informed consent was obtained from all patients.

The endpoint of this study was AF recurrence after a maximum of two PVI-only ablations. Exclusion criteria were substrate-based ablations (e.g. lines and complex fractionated atrial electrograms) for the first and the repeat procedure or a history of any previous left atrial procedure (surgical or percutaneous).

Rhythm-based classifications

The AF type at baseline was initially classified according to the ESC/EHRA guidelines of 2010 [8] and retrospectively re-classified after the ESC/EHRA guidelines of 2016 either as paroxysmal or persistent AF [2]. Whereas any cardioversion and AF duration >7 days triggered patients to be defined as persistent in the 2010 ESC guidelines, patients with any cardioversion within 7 days after onset were still classified as paroxysmal according to the 2016 ESC guideline which is in line with the 2014 AHA/ACC/HRS guideline [9].

Burden-based classification

AF burden was graded based on a questionnaire for the structured clinical assessment of the patient as recently shown [12]. Symptomatic AF burden was characterized based on the duration of the episode [minutes (1 point), hours (2 points), most of the day (3 points), all day (4 points)], the symptomatic frequency [<4 times per year (1 point), monthly (2 points), once a week (3 points), two or more days a week (4 points), daily (5 points)] and the number of electrical cardioversions [1 (1 point), 2 (2 points), 3 (3 points), >3 (4 points)]. These measures were summarized and classified as a minimal (1) (1–3 points), mild (2) (4–6 points), moderate (3) (7–9 points), and severe (4) (≥10 points) AF burden score (AFB).

Anatomical classification

All patients underwent pre-procedural imaging with cardiac magnetic resonance imaging (cMRI; $n = 131$) or computed tomography (CT; $n = 64$), depending on individual eligibility and scanner availability. A transthoracic and transesophageal echocardiogram to rule out left atrial thrombus and to determine LA diameter in the parasternal long axis (PLAX) was performed the day before the intervention in all patients.

Cardiac magnetic resonance imaging

cMRI was performed on 1.5 T scanners (Magnetom Avanto/Magnetom Espree, Siemens, Erlangen, Germany). After breath-hold, T1-weighted spoiled gradient echo sequence (FLASH) in coronal orientations covering the whole LA were acquired before and after contrast agent application (2 ml/s flow, Multihance, 0.1 mmol/kg, Bracco, Milan, Italy). cMRI parameters were: TR 3.7 s, TE 1.3 ms, flip angle 25°, Bandwidth 63.6 kHz. Acquisition matrix was 380 × 380 pixels, reconstruction matrix 512 × 512 pixels, and voxel size 2.25 × 2.25 × 1.2 mm. Slice thickness was 1.2 mm with 20% overlap.

Computed tomography

CT scans were performed on either a 64-slice scanner (Somatom Sensation 64 or Somatom Definition AS+) or a 128-slices Somatom Flash scanner (all three Siemens). First a coronal and a sagittal scout were acquired, followed by an injection of 60 ml i.v. contrast agent and image acquisition (3.5 ml/s flow rate, Ultravist 370, Bayer AG, Leverkusen, Germany). Reconstructions were performed after the scan with a 512 × 512 matrix, a slice thickness of 1 mm and a soft tissue kernel.

Left atrial assessment

Geometrical assessment of the LA from cMRI and CT was performed as described recently [6]. Briefly, a 3D model of the LA was created using a semi-automatic, threshold-based region-growing algorithm in Aquarius Intuition software (Terarecon, Foster City, CA, USA). From this model, the LA volume was automatically calculated. Additionally, it was corrected by the body surface area for indexed LA volume (LAVI). Sphericity (as the deviation from an ideal sphere) was assessed by comparing the LA to a fitted sphere (SpS) and ellipsoid (SpE) as recently described [6]. The principal axis of the ellipsoid was used to characterize the lateral (long-axis SpE), craniocaudal, and transverse/anterior (short-axis SpE) extension of the LA.

2D measurements [maximal lateral diameter (LAT 2D), anterior–posterior diameter (AP 2D), area (AREA 2D), and circumference (CIRC 2D)] were performed on axial slices.

Pulmonary vein isolation

PVI only were performed using an irrigated-tip radiofrequency ablation catheter in combination with a 3D mapping system (Carto3, Biosense Webster, Diamond Bar, CA, USA) or cryoballoon (CB) catheters [13]. Briefly, for radiofrequency PVI, the geometrical reconstruction of the LA of the mapping system and the imported reconstruction from MRI or CT were used to guide the continuous circumferential antral ablation around the ipsilateral PVs. Confirmation of PVI based on entrance block was performed using a variable 20 pole circumferential mapping catheter (Lasso Nav, Biosense Webster).

CB-PVI was performed using the Arctic Front and the Arctic Front Advance (Medtronic, Fridley, MN, USA) using the inner-lumen circular catheter (Achieve, Medtronic). At the physician's discretion, freezing cycles with a duration of 180 or 240 s were performed. Confirmation of PVI based on entrance block was performed using a circumferential or inner-lumen mapping catheter.

Follow up and assessment during repeat procedure

A blanking period of 3 months was applied. Follow up included outpatient clinic visits at 3, 6, and 12 months and included a detailed history, physical examination, 12-lead electrocardiogram (ECG), 24-h Holter monitoring, and 4 or 7 day Holter at 12 months and every 12 months thereafter. In patients with symptomatic recurrences, ECGs and 24-h Holter monitoring was performed to document the tachycardia. Episodes of AF (>30 s) or any sustained left atrial tachycardia (AT) were counted as recurrences.

The majority of patients with recurrence of AF after an initial PVI showed reconnection of the veins [14]. To address this "technical failure" of the index ablation to create a persistent isolation of the PVs, one repeat PVI procedure per patient was allowed after a blanking period of 3 months using a focal RF catheter in combination with the Carto3 system. The reconnection of the PV was identified using the circular mapping catheter (Lasso Nav) re-isolated at the antral level around the PV. A minimum follow up of 6 months after the last intervention was required.

Statistical analysis

Baseline characteristics of patients are shown as the number and percentage affected for categorical variables and as the mean ± one standard deviation (SD) and median for continuous variables. For continuous variables, comparisons were made using Student's *t*-test, Mann–Whitney *U* test, or one-way ANOVA, as appropriate. Discrete variables were compared using the chi-squared test. Univariable and multivariable Cox regression analysis was performed to assess the associations between the variables and AF/AT recurrence. For the multivariable Cox proportional-hazard model, an automated hierarchical stepwise forward selection approach, starting with the most significant variable from univariable analysis, with a *p*-value of <0.05 as entry criteria was used. In addition to this "uncorrected model" of the multivariable Cox proportional-hazard model, we corrected for the potential confounders age, sex, body mass index (BMI), and history of cardiovascular risk factors including hypertension (HT), coronary artery disease (CAD), diabetes and hypercholesteremia in the "adjusted model". A *p*-value <0.05 was considered to indicate statistical significance. All analyses were performed using SPSS (IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY, USA).

Results

Patient population

From June 2010 until May 2014, 220 consecutive patients were primarily selected after initial procedure. Of the 98 patients with recurrence of AF after this first procedure (45%), 25 patients without repeat procedure were excluded from the analysis (Fig. 1).

Repeat PVI was performed between December 2010 and June 2016. Of the remaining 195 patients included in the analysis, 146 were male (75%) with a mean age of 60.1 ± 9.4 years. All baseline characteristics are summarized in Table 1.

Median follow up after the last PVI (including first and repeat procedure) was 16 ± 11 months. During this period, 24 of the 195 patients (12%) showed recurrence of AF or LA tachycardia after the last ablation (1.3 ± 0.5 procedures per patient).

AF classification

Based on the 2010 ESC guidelines, 137 patients were classified as paroxysmal AF and 58 as persistent AF. Re-evaluation based on the 2016 guidelines led to 6 newly classified patients with

Table 1
Baseline characteristics of study population.

Baseline	*N* = 195
Age [years]	60.1 ± 9.4 (61)
Male sex	146 (74.9)
BMI [kg/m^2]	26.9 ± 4.7 (25.8)
Paroxysmal AF (2010 ESC guidelines)	137 (70.3)
Paroxysmal AF (2016 ESC guidelines)	143 (73.3)
Risk factors	
Hypertension	114 (58.5)
Diabetes	14 (7.2)
Coronary artery disease	13 (6.7)
Hypercholesterolemia	73 (37.4)
CHA2DS2-VASC	
0	45 (23.1)
1	62 (31.8)
2	45 (23.1)
3	28 (14.4)
4	12 (6.2)
5	3 (1.5)
>6	0 (0)
Duration of AF (months)	50 ± 61 (26)
PLAX [mm]	41 ± 6 (40)
AF frequency	
<4 times per year	7 (3.6)
Monthly	20 (10.3)
Once a week	51 (26.2)
Twice or more per week	60 (30.8)
Daily	54 (27.7)
Unclear	3 (1.5)
AF duration	
Minutes	58 (29.7)
Hours	92 (47.2)
Most of the day	8 (4.1)
All day	33 (16.9)
Unclear	4 (2.1)
Cardioversions	
0	142 (72.8)
1	32 (16.4)
2	13 (6.7)
3	4 (2.1)
>3	3 (1.5)
Unclear	1 (0.5)
AFB	
(1) Minimal	9 (4.6)
(2) Mild	120 (61.5)
(3) Moderate	47 (24.1)
(4) Severe	15 (7.7)
Unclear	4 (2.1)

Values are *n* (%) for categorical and mean ± standard deviation and median (median) for continuous variables.
AF, atrial fibrillation; AFB, AF burden score; BMI, body mass index; PLAX, parasternal long-axis.
Duration of AF was defined as the time interval between the first diagnosis of AF and pulmonary vein isolation.

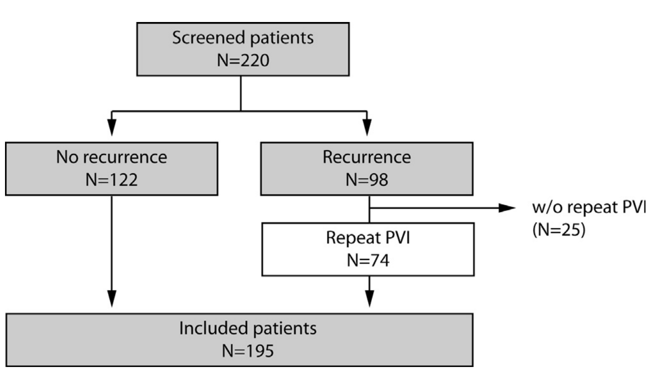

Fig. 1. Flowchart of patient selection. PVI, pulmonary vein isolation.

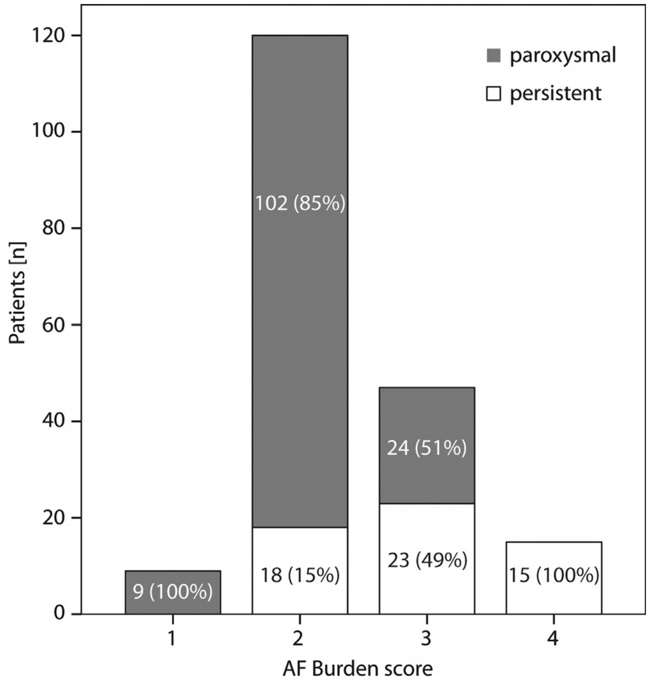

Fig. 2. Categorical distribution of AF type of the European Heart Rhythm Association/European Society of Cardiology guidelines from 2010 based on the AF burden score (1: minimal; 2: mild; 3: moderate; 4: severe). AF, atrial fibrillation.

paroxysmal AF due to cardioversion within 7 days after onset. AF score was 1 in 9 patients (4.6%), 2 in 120 patients (61.5%), 3 in 47 patients (24.1%), and 4 in 15 patients (7.7%), respectively. The percentage of paroxysmal and persistent patients classification over AFB are summarized in Fig. 2.

We did not identify any difference in AF recurrence between paroxymal and persistent AF after PVI only either for the classification according to the 2010 or to the 2016 guidelines. Classified based on the 2010 guidelines, succes rate of the paroxysmal and persistent groups were 89% and 84%, respectively. In contrast, a significant difference between patients with and without AF recurrence was observed for the AFB classification ($p = 0.026$, Table 2).

There was a trend toward a longer duration of AF since first detection in patients suffering from a recurrence of AF after PVI, but this was not statistically significant.

Anatomical assessment

The mean values of LAT 2D, AP 2D, and AREA 2D and CIRC 2D were 7.5 ± 3.1 (7.3) cm, 3.4 ± 0.8 (3.4) cm, 21.4 ± 5.9 (20.9) cm^2, and 18.7 ± 2.3 (18.9) cm, respectively. Mean sphericity from the fitted ellipsoid (SpE) was 87.7 ± 6.2 (89.0) and 80.7 ± 3.5 (80.9) from the sphere (SpS). Mean LA volume and the calculated LAVI were 103.0 ± 30.9 (98.3) ml and 51.0 ± 14.2 (49.5) ml/m^2. LA size in parasternal long axis (PLAX) from transthoracic echocardiography was 41.2 ± 6.4 mm. The area from 2D measurement (AREA 2D), the length of the short axis from SpE, the LA volume and the LAVI were significantly different between the groups. The LA size in parasternal long-axis from echocardiography (PLAX) was not different between the groups (Table 3).

Relationship between anatomy and AF classification

A significant difference was observed for LA volume for the four AFB groups ($p < 0.001$). LA volume was 86.1 ± 16.4 (89.6) for minimal, 96.5 ± 25.7 (92.7) for mild, 111.8 ± 34.5 (109.8) for moderate, and 136.1 ± 27.2 (128.7) for severe AFB, respectively (Fig. 3).

Predictive models

Univariable analysis

In univariable analysis, only the anatomical measures, namely the short axis [hazard ratio of (HR) 1.168 (95% confidence interval [95% CI] 1.037–1.316), $p = 0.010$], LA volume [HR 1.013 (95% CI 1.002–1.025), $p = 0.024$], LAVI [HR 1.037 (95% CI 1.011–1.064), $p = 0.005$], AP 2D [HR 1.641 (95% CI 1.012–2.662), $p = 0.045$], and Area 2D [HR 1.075 (95% CI 1.007–1.147), $p = 0.030$] were identified as significant predictors of AF recurrence after PVI. None of the rhythm-based parameters showed statistical significance. A summary is shown in Table 4.

Multivariable analysis

In the adjusted analysis, corrected for sex, age, and BMI as well as cardiovascular risk factors (HT, CAD, diabetes, and hypercholesteremia), the AFB was identified as the only independent predictor for AF recurrence. In detail, an HR for recurrence of AF of 6.241 (95% CI: 1.914–20.167, $p = 0.002$) for the severe compared to the mild AFB was identified (Table 4). None of the anatomical parameters nor the rhythm-based classification were identified to predict AF recurrence. These results were confirmed by the uncorrected analysis.

Table 2
AF classification in patients with and without recurrence of AF.

AF classification	Recurrence	No recurrence	*p*-Value
2010 guidelines			0.375
Paroxysmal ($n = 137$)	15 (11%)	122 (89%)	
Persistent ($n = 58$)	9 (16%)	49 (85%)	
2016 guidelines			0.200
Paroxysmal ($n = 143$)	15 (10%)	128 (90%)	
Persistent ($n = 52$)	9 (17%)	43 (83%)	
AFB			0.026
(1) Minimal	0	9 (100%)	
(2) Mild	11 (9%)	109 (91%)	
(3) Moderate	8 (17%)	39 (83%)	
(4) Severe	5 (67%)	10 (33%)	
Duration of AF (months)	60 (15–107)	24 (8–65)	0.092

AF, atrial fibrillation; AFB, AF burden score.
Values are *n* (%) for categorical and median (95% CI) for continuous variables.

Table 3
Differences in anatomical parameters between patients with and without recurrence of atrial fibrillation (12 months and maximal follow up).

Parameter	Recurrence	No recurrence	*p*-Value
LAT 2D (cm)	7.56 (6.88–8.05)	7.23 (6.66–7.90)	0.311
AP 2D (cm)	3.58 (3.04–4.21)	3.33 (2.88–3.92)	0.123
AREA 2D (cm^2)	23.3 (19.6–26.0)	20.5 (17.0–24.7)	**0.047**
CIRC 2D (mm)	192.5 (178.3–205.8)	188.5 (168.5–203.0)	0.144
Long axis SpE (mm)	85.8 (80.2–92.4)	86.6 (78.6–92.8)	0.737
Short axis SpE (mm)	41.8 (38.0–46.2)	37.8 (34.2–40.9)	**0.013**
SpE (%)	91.7 (86.7–92.7)	88.2 (85.0–91.6)	0.054
SpS (%)	82.6 (79.2–83.7)	80.7 (78.8–82.9)	0.115
LA volume (ml)	110.0 (87.3–128.7)	95.4 (79.7–118.5)	**0.040**
LAVI (ml/m^2)	54.4 (48.7–69.1)	48.7 (39.6–57.2)	**0.004**
PLAX (mm)	42 (38–47)	40 (37–45)	0.453

AP 2D, anterior–posterior diameter; AREA 2D, LA area; CIRC 2D, LA circumference; LA, left atrium; LAT 2D, maximal lateral diameter; LAVI, left atrial volume indexed; PLAX, parasternal long-axis; SpE, sphericity (ellipsoid); SpS, sphericity (sphere).
Values are given as median (95% CI).

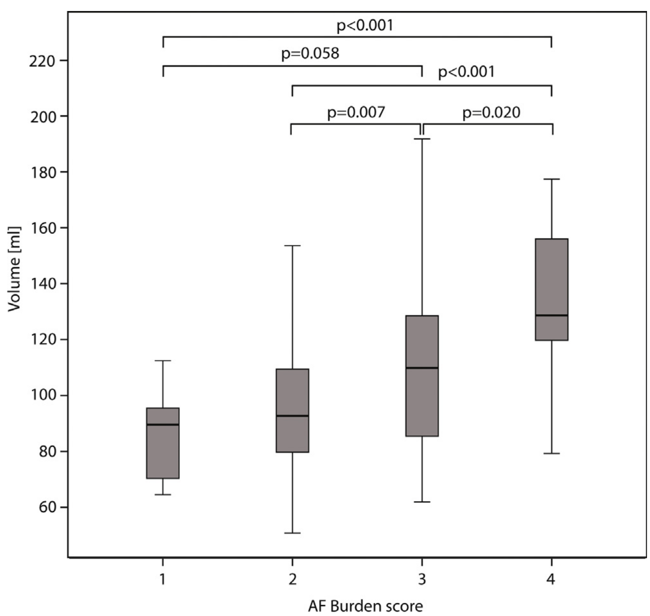

Fig. 3. Volume measures for the four classes of AFB. 1: minimal; 2: mild; 3: moderate; 4: severe. AFB, atrial fibrillation burden.

Discussion

To the best of our knowledge, this is the first study investigating rhythm-, burden-, and anatomically based classifications to predict success rates after up to two procedures of an ablation strategy strictly aimed at isolation of the PVs for both procedures (no linear lesions, no ablation of complex atrial electrograms, or others). In this retrospective analysis of consecutive AF patients, we report the following main findings: (1) both, burden-based classification and 3D anatomical parameters showed the potential to predict multiple procedure success rate in univariable analysis. (2) In multivariable analysis corrected for several confounders, the AFB was identified as the only significant predictor of multiple-procedure-success. (3) Finally, the rhythm-based distinction between paroxysmal and persistent AF according to the current guidelines is not predictive of AF recurrence.

Technical failure versus failure of treatment strategy

Recurrence of AF after catheter ablation has been shown to be mainly linked to PV reconnection [14]. This could be regarded as technical failure of the procedure targeting persistent isolation of the PVs, which we aimed to address in our study by allowing a second intervention to close the gaps in the isolation line around the PVs. Of note, all patients showed at least one reconnected PV during repeat procedure. It has been shown that repeat PVI procedures increase the effectiveness of AF ablation [15], which was also confirmed in our study. In contrast, other studies showed recurrence of AF despite persistent isolation of the PVs [16,17]. In our study, recurrence of AF after two procedures was considered as failure of the treatment strategy of PVI itself and might prompt physicians to identify and ablate ectopic non-PV triggers, to perform additional lesions to modify LA substrate (e.g. roof or posterior wall lesion, ablation of complex fractionated electrograms) or to switch to a completely different treatment strategy (e.g. rate control). However, the STAR AF II study showed that performing additional lesions after PVI did not improve the outcomes after PVI in patients with persistent AF. One possible explanation for this observation might be the categorization based on the current established rhythm-based classification of AF. As shown in Fig. 2, the group of persistent AF showed a wide distribution over 3 of the 4 AFB scores. Furthermore, this group of persistent AF can still be composed of a very inhomogeneous group with either PV-triggered AF without or only little substrate or clearly remodeled LA tissue with low voltage areas [18].

AF classification

Based on the current guidelines, characterization and classification of the AF type plays a central role in the diagnosis and clinical management of AF. A quantitative rhythm-based characterization of AF defined by the frequency and duration of the AF episodes is difficult to measure since only a short time interval is covered even when using Holter monitoring resulting in underestimation of AF density [19]. Long-term continuous monitoring using implantable loop recorders allows for more reliable quantification but is not yet widely applicable in the global population of AF patients mainly due to its costs [20]. In clinical practice, the classification is performed based on patient-reported symptoms using the scoring system of the EHRA/ESC or AHA/HRS guidelines. Whereas in the 2010 guidelines, any cardioversion of the patient triggered to be classified as persistent AF, the EHRA/ESC and AHA/HRS classification of 2014 and 2016, respectively, allowed cardioversion within 7 days after detected onset to be still classified as paroxysmal AF. Furthermore, the classification in the 2010 guidelines did not define how to classify patients showing both characteristics of AF, whereas the more recent guidelines specified to use the most frequent pattern. This change in classification over time might have resulted in differences in categorization and above all uncertainty of the classification, as

Table 4
Univariable and multivariable Cox regression analysis.

Parameter	Univariable analysis		Multivariable analysis Uncorrected model		Multivariable analysis Adjusted model[a]	
	Hazard ratio (HR) (95% CI)	*p*-Value	Hazard ratio (HR) (95% CI)	*p*-Value	Hazard ratio (HR) (95% CI)	*p*-Value
Male sex	0.285 (0.127–0.639)	0.003	0.027 (0.095–0.543)	**0.001**	0.215 (0.077–0.599)	**0.003**
Age [years]	1.063 (1.007–1.121)	0.026			1.036 (0.981–1.094)	0.204
BMI [kg/m^2]	0.994 (0.910–1.085)	0.890			0.980 (0.902–1.066)	0.641
HT	3.854 (1.211–11.335)	0.014			3.330 (1.049–10.573)	**0.041**
CAD	1.964 (0.584–6.611)	0.275			2.428 (0.496–11.895)	0.274
Diabetes	3.625 (1.224–10.738)	0.020			2.534 (0.707–9.079)	0.153
Hypercholesteremia	1.339 (0.594–3.020)	0.482			0.663 (0.270–1.627)	0.370
AF classification						
Persistent 2010	1.448 (0.633–3.311)	0.381				
Paroxysmal 2016	1.707 (0.746–3.906)	0.205				
AFB						
(2) Mild (reference)		0.078		**0.015**		**0.025**
(4) Severe	4.077 (1.409–11.797)	0.010	6.306 (2.057–19.334)	**0.001**	6.214 (1.914–20.167)	**0.002**
(3) Moderate	1.760 (0.703–4.402)	0.227	1.482 (0.592–3.712)	0.401	1.589 (0.593–4.259)	0.357
(1) Minimal	0	0.979	0	0.978	0.000 (0.000–)	0.978
Duration of AF (months)	1.002 (0.997–1.007)	0.340				
Anatomical						
Long axis [mm]	1.016 (0.953–1.083)	0.632				
Short axis [mm]	1.168 (1.037–1.316)	0.010				
SpS [%]	1.085 (0.960–1.226)	0.193				
SpE [%]	1.062 (0.980–1.150)	0.145				
Volume [ml]	1.013 (1.002–1.025)	0.024				
LAVI [ml/m^2]	1.037 (1.011–1.064)	0.005				
AP 2D [cm]	1.641 (1.012–2.662)	0.045				
LAT 2D [cm]	0.991 (0.870–1.128)	0.887				
AREA 2D [cm^2]	1.075 (1.007–1.147)	0.030				
CIRC 2D [cm]	1.015 (0.997–1.033)	0.114				

AF, atrial fibrillation; BMI, body mass index; HT, hypertension; CAD, coronary artery disease; AFB, atrial fibrillation burden score; LA, left atrium; LAT 2D, maximal lateral diameter; AP 2D, anterior–posterior diameter; AREA 2D, LA area; CIRC 2D, LA circumference; SpE, sphericity (ellipsoid); SpS, sphericity (sphere); LAVI, left atrial volume indexed; PLAX, parasternal long-axis.
[a] Adjusted for sex, age, BMI and for history of cardiovascular risk factors (HT, CAD, diabetes, and hypercholesteremia).
AFB 2 (mild) served as reference to which the other categories were compared.

shown in our study with a reclassification of 6 patients. The value of this widely adopted classification scheme has already been questioned [21].

A more detailed classification of the symptomatic AF burden based on a questionnaire was first proposed by Koci et al. and applied in a modified version [6,12]. In our study, AF patients classified as paroxysmal as well as persistent were distributed over 3 of the 4 AFB scores, confirming the marked variability of the conventional classification schemes as suggested recently [21]. In particular, the subgroup with an AFB of 3 (moderate), consisting mainly of patients with AF episodes lasting several hours, with a frequency of more than 2 days but less than 7 days a week, is equally composed of paroxysmal or persistent AF patients based on the conventional “dichotomous” classification. It is conceivable that this more detailed analysis and more precise representation of the burden of AF resulted in the parameter AFB as opposed to the conventional classification to be identified as a predictor for recurrence of AF after PVI.

Anatomy

Change in LA size was identified as an independent risk factor for incident AF more than 30 years ago [22]. Over the recent years, multiple imaging based criteria were evaluated regarding outcome after PVI, focusing on both 2D and 3D parameters [10,11]. In our study, we included scores of measures to quantify the LA anatomy based on CT, cMRI, and echocardiography [10,11].

Although by no means correctly assessing LA size, 2D measurements of the LA on transthoracic echocardiography have been identified as predictors of recurrence of AF after PVI [23]. In addition, 3D parameters such as LA volume or sphericity, which probably characterize LA anatomy even better than 2D measurements, were identified as predictors [10,11]. In our study in univariable analysis, 2D and 3D parameters were also predictive of AF recurrence after PVI. However, in multivariable analysis corrected for cardiovascular risk factors, these effects disappeared completely. None of the anatomical parameters was identified as predictor for recurrence which is in contrast to other recent studies [6,10]. This might at least in part be explained by the different ablation approach in these studies. Furthermore, the anatomical neighborhood influences left atrial dilatation via skeletal landmarks such as the sternum and the spine or the left ventricular outflow tract/aortic root and the descending aorta making the anatomy potentially less precise in describing the LA remodeling with AF [24]. Another explanation might be the relationship of LA dimensions to cardiovascular risk factors and especially hypertension, for which the model is corrected [25].

Clinical implications

Based on the findings from multivariable analysis, the symptomatic AFB score, which can be easily assessed during medical examination, helps to identify patients that are most suitable for PVI in terms of multiple-procedure success rate. Primarily, patients with a low number of short-lasting symptomatic AF episodes were found to have a high multiple-procedure success rate after a PVI-only approach, and, importantly, this was independent of the classification as paroxysmal or persistent AF.

This fact might especially be helpful to identify patients who are most suitable for an ablation approach with a simple ablation tool strictly designed to isolate the PVs. However, this still needs to be confirmed in a prospective study. Furthermore, whether a substrate-based ablation or the identification and ablation of non-PV triggers is the most suitable strategy for the patients with AF recurrence needs further investigation.

Limitations

This is a single center, retrospective analysis of prospectively acquired registry data collected between 2010 and 2016. Consequently, different generations of the catheter types were included and differences in the procedural workflow might have occurred. Furthermore, just as for the conventional classification of AF, the AFB is a qualitative and subjective, symptom-triggered parameter and consequently might underestimate the true AF burden. In addition, it can be applied only in symptomatic AF patients. Despite allowing a repeat procedure to close gaps in the lesion around the PVs, permanency of isolation of the PVs after the repeat procedure cannot be proven. As in other studies using 24-h or 7-day Holter recordings during follow up, possible AF recurrences in patients with only short episodes of AF might remain undetected due to the relatively short absolute duration of electrocardiographic monitoring which might result in an overestimation of the success rate in this patient group. Finally, differences to other studies regarding the predictors of AF recurrence could also in part be explained by the number and type of statistical adjustment of covariates.

Conclusion

Based on multivariable analyses, AFB score was identified as a predictor of AF recurrence after electrical isolation of the PVs after two procedures. In contrast, anatomical parameters and the conventional classification into paroxysmal and persistent AF were not identified as predictors of AF recurrence.

Conflicts of interest

Maurice Pradella, Florian Spies, Tobias Reichlin, Ivan Zeljkovic, Steffen Blum, Bram Stieltjes, Jens Bremerich, Philip Haaf, Stefan Osswald and Sven Knecht – no conflict of interest.

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