The impact of basic atrial rhythm during catheter ablation of atrial fibrillation on clinical outcomes: Lessons from the German Ablation Registry

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Abstract

Background: The impact of basic atrial rhythm (sinus rhythm [SR] vs. atrial fibrillation [AF]) during AF ablation on efficacy and safety is unknown.

Methods: about 3375 patients from the German Ablation Registry undergoing first-time AF ablation were divided according to the type of AF and the basic atrial rhythm during the ablation procedure: paroxysmal AF (PAF) and SR [group Ia], PAF and AF [group Ib]), persistent AF and SR (IIa), and persistent AF and AF (IIb).

Results: Patients in SR (n = 2312 [67%]) underwent cryoballoon ablation more often (Ia vs. Ib p = .002 and IIa vs. IIb p = .010, whereas in patients in AF (n = 1063 [33%]) radiofrequency (RF)-based ablation (Ia vs. Ib p = .006 and IIa vs. IIb p = .014) including left and/or right atrial substrate modification was more frequently performed. Depending on the basic rhythm there was no difference regarding arrhythmia recurrence during long-term follow-up. For patients suffering from persistent AF acute procedure-related complications were more often documented when ablated in AF (9.1% vs. 4.6%, p = .012), which was mainly driven by the higher occurrence of pericardial effusion/tamponade. For patients suffering from persistent AF, favorable results were found regarding 366-day Kaplan–Meier estimates of...
Atrial fibrillation (AF) is the most common arrhythmia worldwide and catheter ablation of AF is an established and effective treatment option. Different ablation tools for pulmonary vein isolation (PVI) such as radiofrequency (RF) current in conjunction with a three-dimensional (3D) mapping system or the cryoballoon (CB), as well as different ablation strategies such as stand-alone PVI or PVI plus additional substrate modification have already been evaluated.

However, limited data are available on the impact of the basic intraprocedural atrial rhythm (sinus rhythm [SR] or AF) on procedural efficacy and safety as well as on long-term clinical outcomes. In general, left atrial contraction and diastolic compliance are significantly reduced during AF, which on the other hand might enhance catheter stability and more efficacious lesion creation. Therefore, the index atrial rhythm might play an important role with regard to acute efficacy as well as for clinical long-term results of AF ablation.

The study reports on the impact of catheter ablation of AF according to the basic periprocedural atrial rhythm from a real-world multicentre prospective registry.

### METHODS

#### 2.1 German ablation registry structure

The German Ablation Registry is a prospective, multicenter non-profit registry led by the "Institut für Herzinfarktforschung" (IHF, Ludwigshafen, Germany). Project development and management, data acquisition, and clinical monitoring were organized by the IHF. Out of 55 participating German centers, 41 provided cases with AF catheter ablation.

The study was approved by local ethics boards. Patients gave written informed consent for registry participation. Data acquisition was conducted on a web-based platform.

#### 2.2 Patient selection

Patients undergoing first catheter ablation for symptomatic AF between 2007 and 2010 were enrolled. Patients were divided into four groups according to the underlying type of AF based on the patient’s medical history and the basic atrial rhythm at the beginning of the ablation procedure: paroxysmal AF (PAF and SR [group Ia], PAF and AF [group Ib]), persistent AF and SR (IIa), and persistent AF and AF (IIb), respectively (Figure 1). Data were analyzed for procedural characteristics and safety as well as acute efficacy and long-term clinical outcome.

Ablation procedures were performed according to institutional standards. Before the procedure, transthoracic and transoesophageal echocardiography was performed to rule out intracardiac thrombi and to assess the LA diameter. In patients on vitamin-K antagonists, anticoagulation was stopped before ablation and bridging was performed with low molecular-weight heparin. Periprocedural activated clotting times (ACT) of 250 to 300 s were targeted. Procedures were performed under deep sedation using midazolam, sufentanyl, and/or continuous propofol infusion. Performance of pre-interventional imaging, the use of a 3D mapping system and selection of the ablation system (RF or cryoballoon [CB] ablation) were at the discretion of the operators. PV isolation (PVI) was the cornerstone of all ablation procedures. Additional ablation strategies including the creation of right atrial (RA) and LA linear lesions, or ablation of complex fractionated atrial electrograms (CFAEs) were at the discretion of the operator. The postprocedural anticoagulation...
management and antiarrhythmic drug therapy (AAD) were conducted according to local institutional standards.

### 2.4 Registry management and clinical follow-up

Physicians and study nurses at participating sites entered data for baseline characteristics, and procedural details during hospital stay (see Supplement 1 for further details). A centralized telephone follow-up was conducted after 12 months applying a standardized protocol (see Supplement 2 for further details). Adverse events during follow-up were collected. Information about the occurrence and type of symptoms, patient satisfaction, and patient safety was obtained in a personal interview. Patient satisfaction was categorized as “improved,” “unchanged,” and “worsened.” Patients not reached at their given address were traced with the help of local municipal authorities.

### 2.5 Endpoints

In-hospital outcomes of interest were acute procedural success (defined as successful PV isolation) and safety. Long-term outcomes of interest were a long-term procedural success (defined as the absence of arrhythmia recurrence during the follow-up period), patient survival and long-term safety as well as patient satisfaction (defined as subjective patient well-being).

Potential periprocedural complications were categorized as severe, moderate, and minor (see Table S1 for further details).

Adverse events (AE) during follow-up were categorized as serious, moderate, and minor (see Table S2 for details).

Long-term safety was specified as 12-month MACE rate (composite endpoint of death and myocardial infarction), MACCE rate (composite endpoint of death, myocardial infarction, and stroke) and a quadruple endpoint (composite endpoint of death, myocardial infarction, stroke, and major bleeding).

### 2.6 Statistical analysis

Continuous data are described as means ± standard deviation (SD), if normally distributed, or as medians and interquartile range (IQR; first and third quartile). Categorical data are described as absolute and relative frequencies.

Differences in categorical variables were compared between the patient groups with the Pearson χ² test, those of continuous variables with Mann–Whitney–Wilcoxon test. For rates of in-hospital complications, Fisher’s exact test was used.

### TABLE 1 Baseline characteristics of patients suffering from paroxysmal AF

| Variable | Group Ia (n = 1985) | Group Ib (n = 355) | p value |
|----------|---------------------|-------------------|---------|
| Age (years) | 62 (IQR 53–68) | 62 (IQR 54–68) | .25 |
| Male gender | 1256 (63%) | 231 (65%) | .52 |
| Cardiomyopathy | 46 (2%) | 18 (5%) | .003 |
| Valvular disease | 96 (5%) | 38 (11%) | <.001 |
| CAD | 347 (18%) | 49 (14%) | .089 |
| Renal insufficiency | 8/349 (2%) | 2/72 (3%) | .81 |
| Diabetes mellitus | 150 (8%) | 27 (8%) | .97 |
| Arterial hypertension | 206/350 (59%) | 43/72 (60%) | .89 |
| CHA2DS2-VASc score | 1.7 ± 1.3 | 1.9 ± 1.4 | .44 |
| Cardiac device | 114 (6%) | 29 (8%) | .079 |

Note: Values are medians (25th, 75th percentile; interquartile range (IQR)), mean ± SD, or n (%). Definition of the different groups: PAF and SR (group Ia), PAF and AF (group Ib).

Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; PAF, paroxysmal atrial fibrillation; SR, sinus rhythm.

aData only available for 307 (16%) and 61 (17%) patients.

The Kaplan–Meier method was used to estimate the 12-month MACE rate (composite endpoint of death and myocardial infarction), MACCE rate (composite endpoint of death, myocardial infarction, and stroke) and a quadruple endpoint (composite endpoint of death, myocardial infarction, stroke, and major bleeding), based on the reported event dates. The aforementioned outcomes were compared between patient groups using the log-rank test.

Statistical calculations were based on available data and cases at the time of follow-up. Documentation of baseline and procedural characteristics was more than 99% complete unless indicated in the tables.

All statistical comparisons were two-sided, and a p value < .05 was considered statistically significant. Analyses were performed using the Statistical Analysis System (SAS, Version 9.4, SAS Institute Inc.).

### 3 RESULTS

#### 3.1 Patient cohorts and baseline parameters

A total of 3375 patients were analyzed. About 2340 patients suffered from PAF, out of whom 1985 (85%) were in SR (Ia) and 355 (15%) in AF (Ib) at the beginning of the procedure. The 1035 patients suffered from persistent AF, out of whom 327 (32%) were in SR (Iia) and 708 (68%) in AF (Iib) at the beginning of the procedure.

There were no significant differences regarding relevant baseline characteristics between patients in SR versus AF. The presence
TABLE 2  Baseline characteristics of patients suffering from persistent AF

| Variable                  | Group Ia (n = 327) | Group Ib (n = 708) | p value |
|---------------------------|--------------------|--------------------|---------|
| Age (years)               | 64 (IQR 56–69)     | 63 (IQR 56–69)     | .81     |
| Male gender               | 242 (74%)          | 515 (73%)          | .67     |
| Cardiomyopathy            | 24 (7%)            | 45 (6%)            | .56     |
| Valvular disease          | 30 (9%)            | 57 (8%)            | .54     |
| CAD                       | 67 (21%)           | 150 (21%)          | .80     |
| Renal insufficiency       | 1/59 (2%)          | 1/39 (1%)          | .74     |
| Diabetes mellitus         | 28 (9%)            | 60 (8%)            | .96     |
| Arterial hypertension     | 39/59 (66%)        | 64/95 (67%)        | .67     |
| CHA2DS2-VASc scorea       | 1.8 ± 1.2          | 1.9 ± 1.4          | .80     |
| Cardiac device            | 17 (5%)            | 39 (6%)            | .84     |

Note: Values are medians (25th, 75th percentile; interquartile range (IQR)), mean ± SD, or n (%). Definition of the different groups: persistent AF and SR (group Ia) and persistent AF and AF (group Ib).

Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease; SR, sinus rhythm.

aData only available for 49 (15%) and 86 (12%) patients.

of cardiomyopathy or valvular heart disease was more often documented in patients of group Ib than in patients of group Ia.

In total patients with persistent AF were older and suffered from cardiac comorbidities more often when compared to patients with paroxysmal AF.

Detailed patients’ baseline characteristics are provided in Tables 1, 2, and 3.

TABLE 3  Baseline characteristics depending on type of AF

| Variable                  | Persistent AF (n = 1035) | Paroxysmal AF (n = 2340) | p value |
|---------------------------|--------------------------|--------------------------|---------|
| Age                       | 64 (IQR 56–69)           | 62 (IQR 53–68)           | <.001   |
| Male gender               | 757 (73%)                | 1487 (64%)               | <.001   |
| Cardiomyopathy            | 459 (44%)                | 746 (31%)                | <.001   |
| Valvular disease          | 87 (8%)                  | 134 (6%)                 | .004    |
| CAD                       | 217 (21%)                | 396 (17%)                | .005    |
| Renal insufficiency       | 2/152 (1%)               | 10/421 (2%)              | .43     |
| Diabetes mellitus         | 88 (9%)                  | 177 (8%)                 | .35     |
| Arterial hypertension     | 103/154 (67%)            | 249/422 (60%)            | .086    |
| CHA2DS2-VASc scorea       | 1.8 ± 1.3                | 1.7 ± 1.3                | .48     |

Note: Values are medians (25th, 75th percentile; interquartile range (IQR)), mean ± SD, or n (%).

Abbreviations: AF, atrial fibrillation; CAD, coronary artery disease.

aData only available for 135 (13%) and 368 (16%) patients.

TABLE 4  Detailed procedural data for patients with paroxysmal AF

| Variable                  | Group Ia (n = 1985) | Group Ib (n = 355) | p value |
|---------------------------|--------------------|--------------------|---------|
| Procedure duration (min)  | 170 (IQR 120–210)  | 175 (IQR 130–225)  | .23     |
| Fluoroscopy duration (min)a | 28 (IQR 19–42)   | 29 (IQR 19–42)     | .80     |
| Radiation dose (cGy·cm²)b  | 3561 (IQR 1780–7018) | 3584 (IQR 1769–7240) | .61     |
| Ablation modality         |                      |                    |         |
| RF                        | 1419 (72%)          | 279 (79%)          | .006    |
| CB                        | 537 (27%)           | 68 (19%)           | .002    |
| Others                    | 28 (1%)             | 8 (2%)             | .24     |
| Cardiac imaging before procedure | 514 (27%) | 94 (27%) | .76 |

Note: Values are medians (25th, 75th percentile; interquartile range (IQR)), or n (%). Definition of the different groups: PAF and SR (group Ia), PAF and AF (group Ib).

Abbreviations: AF, atrial fibrillation; CB, cryoballoon; CFAE, complex fractionated electrograms; PAF, paroxysmal atrial fibrillation; PVI, pulmonary vein isolation; RF, radiofrequency; SR, sinus rhythm.

aData only available for 1786 (90%) and 334 (94%) patients.

3.2 | Procedural data

Overall, patients in SR were more often treated with the CB than with RF current (Ia vs. Ib: 537/1985 [27%] vs. 68/355 [19%], p = .006; Ia vs. Ib:52/327 [16%] vs. 73/708 [10%], p = .010). In contrast, RF-based catheter ablation was more frequently performed than CB ablation in patients in AF (Ia vs. Ib:1419/1985 [72%] vs. 279/355 [79%], p = .002; Ia vs. Ib:273/327 [84%] vs. 630/708 [89%], p = .014). Circumferential PVI was performed in all patients of either group. Additional (left and/or right atrial) linear lesions were significantly more often created in group Ib than in group Ia (74/354 [21%] vs. 203/1985 [10%], p < .001). For patients suffering from persistent AF, a difference was only found in LA lesion creation (1419/1985 [72%] vs. 279/355 [21%] vs. 203/1985 [10%], p < .001). Circumferential PVI was performed in all patients of either group. Additional (left and/or right atrial) linear lesions were significantly more often created in group Ib than in group Ia (74/354 [21%] vs. 203/1985 [10%], p < .001). For patients suffering from persistent AF, a difference was only found in LA lesion creation (1419/1985 [72%] vs. 279/355 [21%] vs. 203/1985 [10%], p < .001).
in patients with persistent AF median fluoroscopy time was slightly longer when presenting in AF at the beginning of the procedure (36 [IQR 21–59] vs. 30 [21–48] minutes; \( p = .014 \)).

Detailed procedural data are shown in Tables 4 and 5.

### 3.3 Acute procedure-related complications

For patients suffering from PAF there were no significant differences in the incidences of acute severe, moderate, and minor complications when comparing SR versus AF. The total incidence of complications was 8.4% (167 patients) in group Ia and 9.0% (32 patients) in group Ib (\( p = .68 \)). Detailed information on types of procedure-related complications for group Ia and Ib are shown in Table 6. No patient of group Ia or Ib died during the procedure or the hospital stay.

For patients suffering from persistent AF the total incidence of acute procedure-related complications was 4.6% (15/327 patients) in group IIa and 9.1% (64/707 patients) in group IIb (\( p = .012 \)). Moderate complications were significantly more often documented for patients ablated in AF (4% vs. 1%, \( p = .017 \)). This difference was mainly driven by the occurrence of pericardial effusion/tamponade (8 [1.3%] vs. 0 [0%]; \( p = .057 \)). However, the total incidence of severe procedure-related complications did not differ between group IIa and IIb (1% vs. 1%, \( p = 1.0 \)). Detailed information on types of procedure-related complications for patients of group IIa and IIb are shown in Table 7. One patient of group IIb died during the hospital stay.

### 3.4 Arrhythmia recurrences during hospital stay and long-term clinical outcomes

Clinical long-term follow-up was available for 1941/1985 (97.8%) patients of group Ia and 349/355 (98.3%) patients of groups Ib.
TABLE 7  Acute procedure-related complications in patients suffering from persistent AF

| Variable                        | Group Ia (n = 327) | Group Ib (n = 708) | p value |
|---------------------------------|--------------------|--------------------|---------|
| Severe complications*           | 4 (1.2)            | 9 (1.3)            | 1.0     |
| Myocardial infarction           | 0 (0)              | 0 (0)              | n.d.    |
| Stroke                          | 1 (0.3)            | 3 (0.4)            | 1.0     |
| Major bleeding requiring intervention | 3 (0.9)         | 6 (0.6)            | 1.0     |
| Moderate complications*         | 4 (1.3)            | 26 (4.4)           | .017    |
| Transient ischemic attack       | 0 (0)              | 1 (0.2)            | 1.0     |
| Aneurysma spurium, AV fistula   | 2 (0.6)            | 12 (1.7)           | .25     |
| Infection at puncture site      | 0 (0)              | 1 (0.2)            | 1.0     |
| Clinically relevant pericardial effusion/tamponade | 0 (0) | 8 (1.3) | .057 |
| Periprocedural, total AV-Block  | 1 (0.3)            | 1 (0.2)            | 1.0     |
| Pneumothorax                    | 0 (0)              | 2 (0.3)            | .55     |
| Phrenic nerve palsy             | 1 (0.3)            | 0 (0)              | .34     |
| Pulmonary vein stenosis         | 1 (0.3)            | 1 (0.2)            | 1.0     |
| Atrio-esophageal fistula        | 0 (0)              | 0 (0)              | n.d.    |
| Minor complications*            | 5 (1.6)            | 22 (3.7)           | .10     |
| Minor bleeding                  | 4 (1.3)            | 22 (3.7)           | .056    |
| AV-Block I*                     | 1 (0.3)            | 0 (0)              | .34     |

Note: Values are n (%). p values were calculated by Fisher’s exact test. Abbreviations: AF, atrial fibrillation; AV, atrioventricular.

*Severe complications: Data available for 327 (100%) and 708 (100%) patients. Moderate complications: Data available for 304 (86%) and 595 (84%) patients. Minor complications: Data available for 304 (85%) and 598 (85%) patients.

FIGURE 2  The impact of basic rhythm on arrhythmia-free survival off antiarrhythmic drugs during long-term clinical follow-up. AF, atrial fibrillation; SR, sinus rhythm

(p = .53) and for 321/327 (98.2%) patients of group Ila and 691/707 (97.7%) patients of group IIb (p = .66). Median overall follow-up duration was 454 (403; 526) days in group Ia and 460 (404; 536) days in group Ib (p = .42) and 456 (407; 534) days in group Ila and 464 (410; 540) days in group IIb (p = .42).

Clinical arrhythmia recurrence (AF-related symptoms and either ECG documentation or documented initiation of medical therapy) was documented in 860/1906 (45%) patients of group Ia and 165/346 (48%) patients in group Ib (p = .38) and in 159/317 (50%) patients of group Ila and 321/675 (48%) patients of group IIb (p = .44). Recurrence of atrial tachyarrhythmias (reliable documentation via ECG) was seen in 809/1906 (42%) patients of group Ia and 158/346 (46%) patients of group Ib (p = .27) and in 150/317 (47%) patients of group Ila and 304/675 (45%) patients of group IIb (p = .50).

At the end of follow-up, 31% of patients in group Ia and 32% of the patients in group Ib (Class I, III or IV; p = .75) and 38% of patients in group Ila and 32% of patients in group IIb (p = .067) were still on AAD therapy.

Detailed data on the clinical long-term follow-up—freedom from documented arrhythmia off ADD—are depicted in Figure 2. In addition, data on arrhythmia-free survival rates off AAD depending on the energy source used (RF vs. CB-based AF-abelation) is represented in Figure 3.

A total of 22% of patients in group Ia and 27% of patients in group Ib (p = .023) as well as 27% of patients in group Ila and 25% of patients in group IIb (p = .44) underwent reactivation procedure during follow-up.

3.5  Arrhythmia related symptoms, rehospitalization, and patient satisfaction during long-term follow-up

Clinical follow-up regarding arrhythmia-related symptoms was available for 94% of follow-up survivors. In conclusion, 82% of patients in group Ia and 83% of patients in group Ib (p = .65) and 77% of patients in group Ila and 77% of patients in group IIb (p = .94) specified no arrhythmia-related symptoms or regression of symptoms at the end of follow-up.

There was no different between the groups regarding overall rehospitalization (44% vs. 46%, p = .60) and 51% vs. 47%, p = .23) as well as cardiovascular-related rehospitalization (33% vs. 35%, p = .75) and 43% vs. 36%, p = .19) during follow-up.

3.6  Patient survival and long-term safety

When comparing groups Ia and Ib, the respective 366-day Kaplan–Meier estimates were 0.3% and 0.3% (hazard ratio [HR] 0.90, 95% confidence interval [CI] 0.11–7.72, log-rank p = .92) for all-cause-mortality, 0.3% and 0.3% (HR 1.08, 95% CI 0.13–8.99, log-rank p = .94) for MACE (death and myocardial infarction), 0.5% and 0.9% (HR 0.60, 95% CI 0.17–2.18, log-rank p = .43) for
MACCE (death, myocardial infarction, and stroke), and 1.4% and 1.1% (HR 1.22, 95% CI 0.4–3.48, log-rank p = .71) for quality endpoints (death, myocardial infarction, stroke, and major bleeding). There were no significant differences between groups Ia and Ib in overall moderate and severe complications during follow-up. However, patients of group Ib experienced significantly more often systemic thromboembolism and/or moderate bleeding during long-term follow-up (1/331 [0.3%] vs. 0/1820 [0%]; p = .019 and 11/332 [3.3%] vs. 21/1819 [1.2%]; p = .003) than did patients of group Ia. For patients of groups IIa and IIb, respective 366-day Kaplan–Meier estimates were 0% and 0.7% (log-rank p = .13) for all-cause mortality, 0% and 1.0% (log-rank p = .071) for MACE, 0% and 2.0% (log-rank p = .011) for MACCE, and 0.3% and 3.0% (log-rank p = .006) for quadruple endpoints. For patients with persistent AF presenting in AF (group IIb) a significant difference regarding overall moderate and severe nonfatal complications during follow-up was found (50/529 [9.5%] vs. 15/275 [5.1%]; p = .030 and 20/642 [3.1%] vs. 1/306 [0.3%]; p = .006, respectively). There were numerically more transient ischemic attacks (TIAs) and strokes documented in group IIb when compared with IIa (0.6% vs. 0% for TIAs and 1.1% vs. 0%). However, this did not reach statistical significance (p = .17 for TIAs and p = .067 for strokes).

### DISCUSSION

The present study analyzes the impact of the intraprocedural atrial rhythm (SR or AF) on the acute and long-term efficacy and safety of catheter ablation of AF in a prospective multicenter registry. Our main findings are as follows:

1. At the beginning of the ablation procedure, patients suffering from paroxysmal AF presented in SR more often than did patients suffering from persistent AF (85% vs. 32%).

2. Patients presenting in SR were more often treated with the CB, regardless of the underlying type of AF (paroxysmal vs. persistent AF), whereas RF ablation was more often performed in patients presenting in AF.

3. In general, basic atrial rhythm did neither affect total procedure time, nor fluoroscopy time, nor cumulative radiation dosage.

4. There was no significant difference in arrhythmia-free survival during 1-year follow-up between patients presenting in SR and those presenting in AF.

5. For patients suffering from persistent AF and ablated in SR a more favorable acute and long-term safety profile was observed when compared to ablation in AF.

4.1 Procedural parameters and acute procedure-related complications

In patients with persistent AF, the overall acute procedure-related complication rate was higher when ablated in AF (54 [9.1%] vs. 15 [4.6%], p = .012). This difference was mainly driven by the occurrence of pericardial effusion or tamponade (8 [1.3%] vs. 0 [0%], p = .057). A potential explanation is a higher proportion of patients in this cohort in whom ablation strategies extending beyond PVI were performed. Moreover, patients with persistent AF were older and had more comorbidities than PAF patients. We can only speculate that more extensive ablation strategies applied in this cohort were the reason for longer fluoroscopy times, whereas in general basic rhythm did not influence procedural parameters in our analyses.

In general, data on the incidence of complications of RF versus CB-based ablation and more complex ablation as compared with stand-alone PVI are conflicting. While several studies have shown similar complication rates for more complex ablation strategies, others describe enhanced rates of cardiac tamponade or of minor and major complications in general. Furthermore, PVI guided by balloon systems might be associated with a lower risk of tamponades.
as compared to point-by-point RF-ablation. In addition, there is data revealing the higher number of transseptal punctures in RF ablation as a potential source and reason for a higher incidence of cardiac tamponades.

4.2 | The role of basic atrial rhythm during AF-ablation procedures on long-term clinical outcome

In principle, left atrial contraction and diastolic compliance are both significantly reduced during AF and therefore potentially associated with beneficial effects for catheter ablation such as enhanced catheter stability and, thus, more effective lesion creation. Therefore, the index atrial rhythm might play a significant role with regard to acute lesion efficacy (i.e., procedure times) of the ablation procedure itself and also for the durability of lesions and thus for long-term clinical results.

Recently, Reissmann et al. published data focusing on the impact of atrial rhythm during CB-based PVI and could confirm that the performance of CB-based PVI during AF results in lower nadir CB temperatures and a trend towards higher durability of PVI when compared with patients ablated in SR. The significantly lower nadir CB temperature in the AF group during their study indicates that reduced atrial contractility during AF might be beneficial for balloon-tissue contact and more effective energy transfer.

Interestingly, data on the impact of the intraprocedural heart rhythm during point-by-point RF ablation are inconsistent. RF ablation is more complex and certain anatomic areas and spots such as the ridge of the lateral PVs might be difficult to reach and it might be particularly difficult to stabilize the catheter during ablation. Therefore, it is conceivable that atrial rhythm during ablation as well as atrial contractility might play a more significant role during ablation procedures using point-by-point RF ablation. In our analysis, there were no significant differences in arrhythmia-recurrence rates during follow-up, which might be considered a surrogate for lesion quality and durability. On the other hand, patients admitted and ablated in AF might have a more progressed form of AF such as persistent or longstanding persistent AF and thus a potentially higher grade of atrial substrate which is associated with less beneficial clinical outcomes.

4.3 | Long-term safety and mortality

For patients undergoing AF ablation during SR a more favorable long-term safety profile was observed, especially when analyzing patients with persistent AF. For patients of group IIb 7 deaths, 2 myocardial infarctions, 7 strokes, and 11 severe bleedings were found, whereas for patients of group IIa only one major bleeding was documented, which—for itself—was shown to be not statistically significant. However, respective 366-day Kaplan-Meier estimates for MACCE and the quadruple endpoints showed statistically significant differences in favor of group IIa when compared to IIb.

In general, mortality is higher in patients with persistent AF than in patients with PAF and is mainly driven by comorbidities and age. Interestingly, in our analysis, numerically more deaths were documented for patients suffering from persistent AF when ablated in AF compared with patients ablated during SR, although this difference was not statistically significant. However, for patients with persistent AF ablated in AF, poorer results were found for MACCE (death, myocardial infarction, and stroke) and quadruple endpoints (death, myocardial infarction, stroke, and major bleeding). These differences in safety outcomes are among others driven by the increased incidence of stroke in this cohort. Stroke is mainly influenced by increased age and distinct comorbidities, which are both known to be more common in patients with persistent AF and patients with an increased AF burden. However, the CHA2DS2-VASc score, which is currently the recommended risk score for anticoagulation assessment in AF patients, was similar in groups IIa and IIb. Another aspect might be a higher rate of electrical cardioversions during the ablation procedure in patients of group IIb. Electrical cardioversion is associated with potential stunning of the left atrial appendage and therefore might lead—at least transiently—to a higher stroke risk even when treated with anticoagulants.

4.4 | Limitations

Data acquisition was conducted in this prospective registry based on voluntary participation of centers and patients, and in a non-randomized fashion. Moreover, the follow-up was carried out according to local standards and therefore data acquisition might affect the study findings.

5 | CONCLUSIONS

Patients undergoing AF ablation in SR were more often treated with the CB, regardless of the underlying type of AF (paroxysmal vs. persistent), whereas in patients in AF at the beginning of the ablation procedure RF-based ablation including (right and/or left atrial) substrate modification was more often performed. However, basic atrial rhythm did not affect total procedure time, fluoroscopy time, and cumulative radiation dosage. Regarding arrhythmia-free survival during 1-year follow-up, there was no difference between patients presenting in SR and those presenting in AF at the beginning of an AF-ablation procedure. However, for patients suffering from persistent AF a more favorable acute and long-term safety profile was observed when ablated in SR.

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DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION
Additional Supporting Information may be found online in the supporting information tab for this article.

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