Ablation of Atrial Fibrillation in Patients With Hypertrophic Cardiomyopathy: Treatment Strategy, Characteristics of Consecutive Atrial Tachycardia and Long-Term Outcome

Leon Dinshaw MD; Paula Münkler MD; Benjamin Schäffer, MD; Niklas Klatt, MD; Christiane Jungen, MD; Jannis Dickow MD; Annika Tamenchang; Ruben Schleberger MD; Simon Pecha MD; Hans Pinnschmidt, PhD; Monica Patten, MD; Hermann Reichenspurner, MD; Stephan Willems, MD; Christian Meyer MD

BACKGROUND: Atrial fibrillation (AF) is common in patients with hypertrophic cardiomyopathy (HCM) and is associated with a deterioration of clinical status. Ablation of symptomatic AF is an established therapy, but in HCM, the characteristics of recurrent atrial arrhythmias and the long-term outcome are uncertain.

METHODS AND RESULTS: Sixty-five patients with HCM (aged 64.5±9.9 years, 42 [64.6%] men) underwent AF ablation. The ablation strategy included pulmonary vein isolation in all patients and ablation of complex fractionated atrial electrograms or subsequent atrial tachycardias (AT) if appropriate. Paroxysmal, persistent AF, and a primary AT was present in 13 (20.0%), 51 (78.5%), and 1 (1.5%) patients, respectively. Twenty-five (38.4%) patients developed AT with a total number of 54 ATs. Stable AT was observed in 15 (23.1%) and unstable AT in 10 (15.3%) patients. The mechanism was characterized as a macroreentry in 37 (68.5%), as a localized reentry in 12 (22.2%), a focal mechanism in 1 (1.9%), and not classified in 4 (7.4%) ATs. After 1.9±1.2 ablation procedures and a follow-up of 48.1±32.5 months, freedom of AF/AT recurrences was demonstrated in 60.0% of patients. No recurrences occurred in 84.6% and 52.9% of patients with paroxysmal and persistent AF, respectively (P<0.01). Antiarrhythmic drug therapy was maintained in 24 (36.9%) patients.

CONCLUSIONS: AF ablation in patients with HCM is effective for long-term rhythm control, and especially patients with paroxysmal AF undergoing pulmonary vein isolation have a good clinical outcome. ATs after AF ablation are frequently observed in HCM. Freedom of atrial arrhythmia is achieved by persistent AF ablation in a reasonable number of patients even though the use of antiarrhythmic drug therapy remains high.

Key Words: ablation ■ atrial fibrillation ■ atrial tachycardia ■ catheter ablation ■ hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most frequent monogenetic cardiac disease affecting ≈1 out of 500 individuals in the general population.1 Atrial fibrillation (AF) is common in patients with HCM with a prevalence ranging between 22% and 32%, and AF episodes are often associated with a major deterioration of the functional clinical status in these patients.2-4 Thus, effective and durable rhythm control is desirable5,6 but often challenging because of the complex substrate which is determined by atrial fibrosis, atrial dilatation, or intrinsic atrial myopathy.7

See Editorial by Estes and Wong
randomized trials exist examining antiarrhythmic drug (AAD) therapy for AF prevention in HCM. Today, because of its limited long-term efficacy in permanently maintaining sinus rhythm and potential hazardous side-effects, AAD therapy remains challenging in this patient population. AF ablation has become an established therapy for symptomatic AF, and isolation of the pulmonary veins (PVs) emerged as the mainstay of the interventional or surgical treatment strategy. Several observational studies have shown that AF ablation in HCM is safe and reasonably effective despite potentially progressed atrial involvement resulting in severely enlarged atria in many cases. A recent meta-analysis of these studies found a single-procedure success of 38.7% while outcome after ≥1 procedure amounted to 51.8%. However, data on long-term outcome of AF ablation in patients with HCM undergoing multiple ablation procedures remains limited. The occurrence and the mechanism of subsequent atrial tachycardias (ATs) in these patients are largely unknown. Thus, we analyzed the recurrent atrial arrhythmias and the long-term outcome of patients with HCM undergoing AF ablation.

**METHODS**

Anonymized patient data that support the findings of this study are available from the corresponding author upon reasonable request. Consent was not obtained for data sharing, but the presented data are anonymized, and the risk of identification is minimal.

**Study Population**

A total of 65 patients with HCM undergoing catheter-based or surgical AF ablation between 2007 and 2018 at our institution were included in this study. The diagnosis of HCM was based on the current guidelines and verified in our specialized outpatient clinic for patients with HCM. The baseline parameters and the clinical functional status during symptomatic AF episodes were assessed. Echocardiographic parameters such as characteristics of left ventricular hypertrophy, systolic and diastolic function, left atrial cavity size including the left atrial volume index (left atrial volume/body surface area), functional status of the mitral apparatus, and left ventricular outflow tract obstruction were assessed according to recommendations of the European Association of Cardiovascular Imaging. Approval was received from the local ethics committee review board of the University Heart and Vascular Center Hamburg-Eppendorf.

**Protocols of Catheter Ablation and AF Surgery**

All patients gave written informed consent before the procedure. We performed transesophageal echocardiography to rule out intracardiac thrombi before the ablation. During catheter ablation, patients were under deep sedation by intravenous propofol (Propofol-Lipuro; B. Braun, Melsungen, Germany) administration and fentanyl (Fentanyl-Janssen, Neuss, Germany). After access to the left atrium (LA) by transseptal puncture bolus injections of unfractionated heparin were used to maintain an activated clotting time >300 seconds. Surface ECGs and bipolar endocardial electrograms were monitored continuously and digitally recorded (Bard Electrophysiology, Lowell, MA, USA).
At index procedure, electrical isolation of the PVs was performed by either radiofrequency energy applying a point-by-point wide antral ablation line circumferentially around each pair of ipsilateral pulmonary veins or by cryoballoon ablation aiming for isolation of the individual PVs. For radiofrequency catheter ablation, the non-fluoroscopic 3-dimensional mapping systems Ensite NavX (St. Jude Medical, St. Paul, MN, USA), Carto ( Biosense Webster, Diamond Bar, California) or Rhythmia (Boston Scientific, Charlestown, MA, USA) were used at operator’s discretion. Treatment of persistent AF primarily involved pulmonary vein isolation (PVI) and a modified stepwise approach at the discretion of the electrophysiologist, as previously described in detail. In brief, the first step of the ablation procedure was antral PVI with complete electrical isolation of the PVs. Additional targets for AF ablation in the LA consisted of complex fractionated atrial electrograms (CFAE) as well as areas of continuous local activity and bursts, temporal activation gradient between proximal and distal ablation bipoles, or areas of local spatial centrifugal activation. The desired procedural end point was the termination of AF, either directly to sinus rhythm or via atrial tachycardia (AT). Using the same criteria, mapping and ablation were performed within the coronary sinus and the right atrium if AF required.

Subsequent ATs were specifically targeted using entrainment mapping, activation mapping, and the analysis of voltage maps to guide the ablation. A multi-polar mapping catheter was used for ultra-high-density mapping, at operator’s discretion. AT was defined as an organized atrial activity with stable cycle length (CL) >180 ms, monomorphic p-waves on a standard 12-lead ECG, and consistent endocardial activation sequence. An AT with a stable CL was considered macro-reentrant when the tachycardia CL could be demonstrated around the presumed circuit and/or a consistent repeat post-pacing interval as observed. Localized reentry was defined as an atrial activity confined to an area of continuous signals on the bipoles of the mapping catheter displaying ≥85% of the tachycardia CL and showing consistent post-pacing interval (PPI) ≤30 ms after repeat entrainment pacing or demonstration of continuous rotational activation within a small area of <2 cm with each rotation encompassing 1 full CL. If a macro-reentry or a localized reentry was clearly identified during activation mapping, entrainment mapping was not always performed to confirm the diagnosis. Focal AT was recognized as an atrial activation originating from a discrete site activating the surrounding tissue centrifugally and showing other features consistent with a focal mechanism such as variation of CL ≥15% or inconsistent post-pacing interval.

We considered an AT, which remained unchanged during mapping and thus could be appropriately characterized according to above-mentioned criteria as “stable AT”. In contrast, atrial arrhythmia with frequently changing activation sequence or wavering cycle length were defined as “unstable AT”.

Linear ablation addressing the anatomical or practical arrhythmia isthmus was performed if a macro-reentrant mechanism was suspected. Localized reentry or focal ATs were ablated at the site of earliest activation based on individual characteristics of the arrhythmogenic substrate.

Repeat procedure was indicated in case of symptomatic arrhythmia recurrences and patients’ preferences. As the first step of repeat procedures, electrical isolation of the PVs was evaluated and re-established if required. In case of recurrent paroxysmal AF episodes, repeat PVI only was pursued. If patients presented with persistent AF or AT, the ablation was performed according to the protocol mentioned above.

Concomitant surgical ablation was performed in patients with AF undergoing mitral valve surgery or surgical myectomy. The indication for AF surgery as a stand-alone procedure was reserved for a selected number of patients with severely dilated LA after interdisciplinary decision of the cardiac surgeon and the electrophysiologist. Patients with paroxysmal AF received PVI. Left atrial ablation with box lesions, left atrial appendage isolation, the ablation of the left atrial isthmus, additional biatrial ablation with right atrial intercaval lesions, ablation of the cavo-tricuspid isthmus, and ablation at the right atrial appendage and the terminal crest was performed at operator’s discretion as was previously described. The energy sources applied included unipolar radiofrequency ablation (Cardioblate unipolar RF pen, Medtronic Inc.) and bipolar ablation (Cardioblate BP2 device and Cardioblate Surgical Ablation System Generator, Medtronic Inc.).

Follow-Up
All patients were monitored for peri-procedural complications throughout the procedure and during hospitalization. Follow-up was scheduled in a 3- to 6-month interval in our outpatient clinic. AF and AT recurrences were assessed using 24-hour Holter ECG recordings every 1 to 2 months. In patients with an implantable electronic cardiac device, the continuous rhythm monitoring function was used for the assessment of AF/AT recurrences. Patients were assessed for clinical status and current antiarrhythmic medication. A single AF/AT episode with a duration of >30 seconds on the 24-hour Holter ECG or an atrial high rate episode lasting longer than 5 minutes
as detected by a cardiovascular implantable electronic device such as a pacemaker or an implantable cardioverter defibrillator (ICD) was defined as AF/AT recurrence. The absence of AF/AT recurrences during the entire follow-up was considered freedom of AF/AT. If AAD therapy was continued after ablation and no further AF episodes were detected at follow-up, discontinuation of AAD therapy was recommended. Patients experiencing symptomatic recurrences with documented AF/AT or an AF burden >1% after a 3-month blanking period underwent a change of AAD or a repeat ablation at the discretion of the electrophysiologist and patients’ preference.

**Statistical Analysis**

Continuous values are reported as mean±SD or as median and range as appropriate. Group comparisons of continuous normally distributed variables was performed using the Student t-test. For group comparisons of ordinal variables, the Mann–Whitney U test was used, while dichotomous variables were compared using the Fisher exact-test. Differences in pre- and post-ablation parameters were assessed using the Wilcoxon signed-rank test for ordinal variables, while the McNemar test was used for dichotomous variables. Time to recurrence and event-free survival curves were calculated using the Kaplan–Meier estimation method. Uni- and multivariate Cox regression analyses were used to evaluate predictors for AF/AT recurrences. All statistical tests were 2-tailed. A P<0.05 was considered as statistically significant. The statistical analysis was performed using SPSS 26.0 (IBM, Chicago, IL, USA).

**RESULTS**

**Study Population**

The baseline characteristics of the study population are summarized in Table 1. At index procedure, 13 (20.0%) patients presented with paroxysmal AF and 51 (78.5%) with persistent AF. One (1.5%) patient had a primary AT when initially AF was suspected. Septal hypertrophy was diagnosed in 45 (69.2%) patients as compared with apical or concentric hypertrophy which was found in 4 (6.1%) and 16 (24.7%) of the patients, respectively. An enlarged LA was present in most of the patients with a mean volume of 110.3±55.3 mL and a LA volume index of 55.8±28.7 mL/m². In 28 (43.1%) patients an ICD was previously implanted for prevention of sudden cardiac death. In 22 (33.8%) patients the dual-chamber ICD with an atrial lead incorporated a continuous atrial rhythm monitoring function. The indication for ICD implantation was based on primary prevention in 82.1% of those patients. The majority of patients received beta-blocker therapy (80.0%), and

**Table 1. Baseline Clinical Data**

| Baseline Clinical Data                     | n=65  |
|-------------------------------------------|------|
| Age, y                                     | 64.5±9.9 |
| Sex, men, n                                | 42 (64.6) |
| BMI                                        | 27.4±5.3 |
| Arterial hypertension, n (%)               | 25 (38.4) |
| Diabetes mellitus, n (%)                   | 6 (9.2)  |
| Coronary artery disease                    | 14 (21.5) |
| Prior TIA/stroke, n (%)                    | 10 (15.3) |
| Creatinine, mg/dL                         | 1.2±0.6  |
| ProBNP, mg/L                               | 2490±2130 |
| Creatine kinase, UI/L                     | 185±159  |

Type of HCM

- Septal, n (%) | 45 (69.2) |
- Concentric, n (%) | 16 (24.7) |
- Apical, n (%) | 4 (6.1)  |
- Paroxysmal AF, n (%) | 13 (20.0) |
- Persistent AF, n (%) | 51 (78.5) |
- Primary AT, n (%) | 1 (1.5)  |
- LVEF, %        | 54.4±14.6 |
- LA diameter, mm | 54.1±12.5  |
- LA volume, mL  | 110.3±55.3 |
- LA volume index, mL/m² | 55.8±28.7 |
- Septal wall thickness, mm | 18.6±4.2  |
- Posterior wall thickness, mm | 13.4±3.2  |
- Resting gradient, mm Hg | 8.1 (0–60) |
- Stress gradient, mm Hg | 12.6 (0–62) |
- TASH           | 3 (4.6)  |
- Septal myectomy | 8 (12.3)  |
- Diastolic dysfunction
  - No            | 12 (18.5) |
  - Mild         | 19 (29.2) |
  - Moderate     | 32 (49.2) |
  - Severe       | 2 (3.1)  |
- Mitral insufficiency
  - No            | 10 (15.3) |
  - Mild         | 40 (61.5) |
  - Moderate     | 14 (21.5) |
  - Severe       | 1 (1.5)  |
- SAM of the mitral valve                     | 11 (16.9) |
- Mitral valve repair                         | 6 (9.2)  |
- Mitral valve replacement                    | 7 (10.7) |
- Family history of SCD, n (%)               | 5 (7.7)  |
- Syncope, n (%)                             | 13 (20.0) |
- SCD risk score (5-y risk of SCD in %)       | 3.7±3.2  |
- ICD                                         | 28 (43.1) |
- Primary prevention                          | 23 (32.1) |
- Secondary prevention                        | 5 (7.5)  |

Values are indicated as total number (n), percentage (%), mean±SD, or median (range). AF indicates atrial fibrillation; AT, atrial tachycardia; BMI, body mass index; BNP, B-type natriuretic peptide; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LA, left atrium; LVEF, left ventricular ejection fraction; proBNP, pro-B-type natriuretic peptide; SAM, systolic anterior motion; SCD, sudden cardiac death; TASH, transcoryonary ablation of septal hypertrophy; and TIA, transient ischemic attack.
approximately half of the patients received AAD therapy (50.7%) before ablation. The selected AAD was (Figure 1): flecainide (9.2%), amiodarone (33.8%), or verapamil (7.6%). Patients at a young age experiencing symptomatic AF episodes were primarily selected for ablation to avoid possible long-term AAD usage.

### Catheter Ablation and AF Surgery

Overall, 128 procedures were performed with a mean of 1.9±1.2 procedures per patient. Catheter ablation was conducted in the majority of cases with a total number of 119 (92.9%) procedures, as compared with a total of 9 (7.1%) AF surgeries. Procedure time, fluoroscopy time, and time of radiofrequency energy application of catheter ablation was 167.0±69.9, 27.7±18.6, and 52.1±28.2 minutes, respectively (Table 2).

The index procedure was a catheter-based ablation in 57 (87.6%) patients, whereas 8 (12.3%) patients underwent AF surgery. In 6 patients, AF surgery was accompanied by an operative mitral valve repair, mitral valve replacement, or surgical myectomy. In 2 patients, AF surgery was a stand-alone procedure. One patient had a biatrial ablation during a tricuspid and mitral valve repair as the second ablation procedure.

The index procedure involved PVI in 64 (98.5%) patients. Catheter ablation using radiofrequency energy was performed in 83.1%, while 2 (3.1%) patients underwent cryoballoon PVI at index procedure. A left atrial anterior line, connecting the mitral valve annulus to an area of dense scar in the central left atria as indicated by the voltage map, was performed in 1 (1.5%) patient with an isolated anterior left atrial macro-reentry tachycardia and no history of AF. Eleven (84.6%) patients with paroxysmal AF received PVI only with mean of 1.4±0.8 procedures. In 1 patient, CFAE ablation and ablation of ATs were performed during the third procedure. Another patient had an anterior linear ablation of a macro-reentry AT during the second ablation. During repeat ablation procedures continuous PVI of all PVs was found in 5 of 36 (13.9%) during the second, 6 of 18 (33.3%) during the third, in 5 of 10 (50.0%) during the fourth, and in one of four (25.0%) during the fifth ablation procedure. Details about the CFAE ablation and the creation of additional ablation lines beyond PVI of all patients are summarized in Figure 2. AF surgeries involved an isolated bilateral PVI in 2 patients, a left atrial ablation including PVI, box lesions and left atrial appendage excision, and left atrial isthmus ablation in 4 patients, and a biatrial ablation which additionally included right atrial intercaval lesions such as the ablation of the cavitricuspid isthmus, the right atrial appendage, and the terminal crest in 3 patients.

### Mechanism and Ablation of Atrial Tachycardia

Ablation of ATs was conducted in 25 (38.4%) patients, targeting a total of 54 ATs. Out of 47 patients in which a PVI only had been performed previously, 14 (27.7%) patients developed AT, whereas 10 of 17 (58.8%) patients with a previous ablation of CFAE presented with AT. One patient had a primary AT, as mentioned above. The mechanism was characterized as a macro-reentry tachycardia in 37 (68.5%), as a localized reentry in 12 (22.2%), or as a true focal mechanism in 1 (1.9%) of the AT in question. The mechanism was not conclusively detectable and thus not classified for the remaining 4 (7.4%) ATs. As for macro-reentry ATs, a linear ablation was performed at the LA roof (n=10), the mitral isthmus (n=11), and the anterior LA (n=16). Localized reentry ATs were identified in various different locations (Figure 3), and ablation in the left or right atrium was conducted as appropriate. These ATs were located at the atrial septum (n=3), the inferior LA (n=2), the anterior LA (n=2), near the ostium of coronary sinus (n=1), in close vicinity of the right superior PV (n=1), near the superior vena cava (n=1), at the base of the left atrial appendage (n=1), and at the posterior LA roof (n=1). A
true focal AT was located at the ostium of the coronary sinus (n=1). An additional ablation of the cavotricuspid isthmus was performed in 14 (56.0%) of those patients either empirically (n=2), because of previously reported typical atrial flutter (n=9), or after the identification of cavotricuspid isthmus dependent atrial flutter (n=3) during the electrophysiologic study (a repeat ablation of the cavotricuspid isthmus was necessary for 1 patient during a subsequent ablation procedure).

Out of the 25 patients presenting with AT, we found 15 (60.0%) with stable AT and 10 (40.0%) with unstable AT. Procedure duration and radiofrequency energy application were higher for the ablation of unstable AT as compared with stable AT, 225±58 versus 153±56 minutes (P<0.01) and 69±35 versus 48±26 minutes (P=0.03), respectively. Fluoroscopy times did not differ (33±17 versus 30±16 minutes, P=0.29).

Nine (90.0%) patients with unstable AT during the ablation procedure had undergone a previous AF ablation involving the ablation of CFAE. In those 10 patients 25 ATs occurred, of which 13 (52.0%) were characterized as macro-reentry, 8 (32.0%) as localized reentry, and 4 (16.0%) were not classified because of an inconclusive mechanism. The linear ablation for macro-reentry ATs was performed at the roof in 9, the mitral isthmus in 1, and the anterior LA in 3. The ablation of localized reentry AT was performed at the atrial septum in 3, the inferior LA in 2, near the ostium of the coronary sinus in 1, near the superior vena cava in 1, and at the posterior LA roof in 1.

In contrast, no ablation of CFAE was previously performed in 12 (80.0%) of the 15 patients with stable AT. Besides the 1 patient who presented with primary AT with a macro-reentry stable AT circling around an anterior low-voltage region, all of those patients only had PVI or cavotricuspid isthmus ablation before the ablation of the stable AT. A total of 29 ATs were reported with 24 (82.8%) described as macro-reentry, 4 (13.8%) as localized reentry, and 1 (3.4%) as a true focal AT. A linear ablation for the macro-reentry AT was performed at the roof in 7, the mitral isthmus in 12, and the anterior LA in 5. Ablation of localized...
reentry ATs was performed at the anterior LA in 2, in close vicinity of the right superior PV in 1, and at the base of the left atrial appendage in 1. The focal AT was ablated at the ostium of the coronary sinus. During the ablation primarily targeting the stable AT, a redo PVI was performed in 10 (66.6%) patients because of electrical reconnection of PVs even though AF was not reported anymore.

The occurrence of macro-reentry and localized reentry ATs were not significantly different in patients with unstable AT and stable AT (P=0.11). A redo ablation of 3 (5.5%) ATs was performed at the LA roof (n=1), the CS ostium (n=1), and the mitral isthmus (n=1).

**Long-Term Outcome**

The mean follow-up was 48.1±32.5 months after the index procedure and 30.6±26.8 months after the last ablation procedure. Continuous atrial rhythm monitoring of a previously implanted ICD was used to detect AF episodes in 22 (33.8%) patients. In the remaining 43 (66.2%) patients, the follow-up was based on sequential Holter ECG recordings. Freedom of AF/AT was found in 39 (60.0%) patients during long-term follow-up (Figure 4). No recurrences occurred in 11 (64.6%) patients with paroxysmal and 27 (52.9%) patients with persistent AF (P<0.01). In the subgroup of 25 patients with ablation of AT, we found freedom of AF/AT in 4 (40.0%) patients with unstable AT and in 9 (60.0%) patients with stable AT (P=0.43). One patient with primary AT was free of recurrences after 14 months. All patients with exclusively a surgical ablation (n=3) had arrhythmia recurrences during follow-up (2 with AF, 1 with AT). One (1.5%) patient progressed from paroxysmal to persistent AF, whereas 2 (3.1%) patients were shifted from persistent to mostly paroxysmal AF episodes.

No clinical predictors of AF/AT recurrences or clinical predictors for the occurrence of AT after AF ablation were found in univariate and multivariate Cox regression analysis. The majority of patients (92.3%) were on beta-blocker or verapamil as medical therapy for the underlying HCM. The overall usage of AADs was not reduced as shown in Figure 1 (P=0.09). After ablation class IC AAD therapy were discontinued in all patients because of hypertrophy of the ventricular septum ≥13 mm. For the suppression of AF recurrences, the antiarrhythmic medication was limited to amiodarone in 22 (33.8%) and verapamil in 2 (3.1%) patients.

---

**Figure 4.** Kaplan–Meier graph showing the atrial fibrillation/atrial tachycardia recurrence-free survival. Values are indicated as total number (n). AF indicates atrial fibrillation; and AT, atrial tachycardia.
Following the ablation of 52 (42.3%) patients with persistent AF and 13 (15.4%) patients with paroxysmal AF (with AF recurrences) received AAD therapy ($P<0.01$). Even though 6 patients were able to abandon amiodarone treatment after ablation the same number of patients required amiodarone for effective maintenance of sinus rhythm. Thus, the number of patients on amiodarone therapy remained equal before and after ablation.

The clinical functional status of most patients improved during follow-up ($P=0.0498$). Changes in pre- and post-ablation clinical functional status of every single patient are summarized in Figure 5. Freedom from symptomatic AF/AT episodes was found in 44 (67.7%) patients, whereas in 5 (7.7%) patients, asymptomatic episodes were reported after AF/AT ablation.

After a total of 119 catheter ablation procedures, 1 patient (0.8%) had a pericardial tamponade with immediate percutaneous pericardiocentesis and favorable clinical outcome. One patient (0.8%) experienced a transient ischemic attack without any residual neurological impairment. One patient (0.8%) suffered air embolization into the right coronary artery with an unremarkable clinical outcome. One patient (0.8%) had an arteriovenous fistula, which was treated surgically. No acute stroke or atrio-esophageal fistula was observed after ablation.

During follow-up, 4 (6.1%) patients died attributable to causes not related to the ablation procedure. Two (3.1%) died as a result of severe infection and septic shock of the ICD and its transvenous leads. The lethal event in these 2 patients was >24 months after the last ablation procedure, and an infectious complication related to the catheter ablation seems unlikely as mentioned in a previous work of our group. One patient (1.5%) died as a consequence of congestive heart failure after a prolonged hospitalization with hospital-related complications, and 1 (1.5%) patient suffered a severe stroke after acute obstruction of the left common carotid artery potentially because of a cardiac embolus despite oral anticoagulation with novel oral anticoagulants. In these patients the lethal event also occurred >24 months after the last ablation procedure.

**DISCUSSION**

To our knowledge, we present one of the largest single-center studies with the longest follow-up (Table 3) investigating outcome of AF ablation in patients with HCM and the mechanism of subsequent atrial arrhythmias. The main findings of this study are: (1) AF ablation is effective for long-term rhythm control in patients with HCM; (2) patients with paroxysmal AF have an especially good clinical outcome comparable with ablation of paroxysmal AF in the general population; (3) about a third of patients with HCM develop AT after the ablation of AF which are unstable in about 40% of patients; (4) while ablation of stable AT show a promising long-term outcome, in patients with unstable AT especially following CFAE ablation the efficacy of long-term rhythm control is relatively low.

**Long-Term Outcome of AF Ablation**

In patients with HCM, the occurrence of AF is common and was thought to be associated with increased mortality. A more recent study of Rowin et al reports a relatively low annual mortality <1% directly attributable to AF when applying current treatment strategies with no difference in the outcome of patients with HCM without AF. Even though the effect of rhythm versus rate control on mortality in HCM is largely unknown, this study casts a more favorable light on AF and its impact on mortality in HCM. However, recurring AF often leads to a major deterioration in clinical functional status in HCM, and thus a therapeutic strategy aiming for long-term rhythm control is desirable in most patients. As AAD therapy fails to maintain sinus rhythm durably,
Table 3. Previously Published Studies of AF Ablation in Patients With HCM Compared With the Present Study

| Author (Y)            | Study Design                  | No. of Patients, male (%) | Age, y   | Persistent AF, n (%) | LA Diameter, mm | Septal Wall Thickness, mm | Ablation Procedure | No. of Procedures | AAD Usage at Last FU, % | FU Duration, y | Occurrence of AT, % | Freedom of AF/AT, % |
|-----------------------|-------------------------------|---------------------------|----------|---------------------|----------------|--------------------------|--------------------|-------------------|------------------------|----------------|------------------|---------------------|
| Kilcaslan et al (2006) | Retrospective multicenter     | 27 (70)                   | 55±10    | 13 (48)             | 50±9           | 17±5                     | PVI                | 1.3               | 39                     | 0.9±0.6        | n.a.              | 70                  |
| Gaita et al (2007)     | Prospective cohort single-center | 26 (69)                   | 58±11    | 13 (50)             | 52±6           | 23±4                     | PVI, roof, mitral line | 1.2               | 38                     | 1.6±0.8       | 15               | 65                  |
| Di Donna et al (2010)  | Retrospective multicenter     | 61 (72)                   | 54±13    | 26 (43)             | 52±5           | 20±5                     | PVI, roof, mitral line, CTI (in 15 patients) | 1.5               | 54                     | 2.4±1.3       | 15               | 67                  |
| Derejko et al (2013)   | Prospective observational     | 30 (67)                   | 49±11    | 16 (53)             | 51±7           | 21±6                     | PVI, CTI, mitral line, roof, GFAE | 1.4               | 37                     | 1.9±1.2       | n.a.             | 53                  |
| Santangelo et al (2013) | Prospective multicenter     | 43 (67)                   | 59±8     | 31 (72)             | 47±8           | 20±4                     | PVI, box lesion, SVC isolation, CFAE, non-PV trigger | 1.6±0.7           | 24                     | 1.3 (0.7-1.6) | 37               | 94                  |
| Bassiouney et al (2015) | Retrospective single-center  | CA 79 (54), SA 68 (46)    | 55±11    | 62 (42%)            | 50±10          | 20±5                     | PVI, mitral line, roof, CTI, Cox-Maze | 1.2               | 38                     | 2.9 (1.2-5)   | 8                | 46                  |
| Dinshaw et al (2020)  | Retrospective single-center  | 65 (65)                   | 64±10    | 51 (79)             | 54±13          | 19±4                     | PVI, GFAE, AT as appropriate | 1.9±1.2           | 37                     | 4.0±2.7       | 38               | 60                  |

Values are indicated as total number (n), percentage (%), or mean±SD. AAD indicates antiarrhythmic drug; AF, atrial fibrillation; AT, atrial tachycardia; CA, catheter ablation; CFAE, complex fractionated atrial electrograms; CS, coronary sinus; CTI, cavotricuspid isthmus; FU, follow-up; HCM, hypertrophic cardiomyopathy; LA, left atrium; n.a., not available; PVI, pulmonary vein isolation; SA, surgical ablation; and SVC, superior vena cava.
the potential severe morbidity of this patient cohort. However, the ablation procedure itself has a good safety profile and a low-complication rate also in patients with HCM, which is supported by our data and which was previously shown by previous studies. Therefore, we perceive that ablation in patients with HCM with symptomatic AF is a reasonable approach for long-term rhythm control despite potential additional AAD therapy. Patients with HCM and paroxysmal AF should be treated with PVI because of the potential good long-term clinical outcome in this subgroup of patients.

Occurrence of AT After AF Ablation in HCM

In our study, about a third of patients with HCM (38.4%) undergoing AF ablation showed AT as recurring atrial arrhythmia during follow-up. Subsequent ATs are well described after ablation of AF. Gerstenfeld et al and Wasmer et al investigated the occurrence of ATs in a total of >1100 patients after circumferential antral ablation of the ipsilateral PVs and reported a prevalence of 2.9% and 4%, respectively. In contrast, a study by Deisenhofer et al found 31% of patients with ATs after circumferential PVI. In this study, however, structural heart disease was known in 58% of patients, whereas in the study of Wasmer et al, only 10% of patients with structural heart disease were included. Furthermore, in the study of Wasmer et al, patients with ATs more commonly had structural heart disease (25% versus 10%) suggesting a higher occurrence of AT after AF ablation in patients with structural heart disease.

The data about predictors of AT after AF ablation are limited. After an extensive atrial substrate modification involving CFAE and linear ablation, the occurrence of ATs is more commonly seen ranging between 24% and 40%. Recently, Ipek et al showed that right atrial dilatation is predictive for typical flutter, whereas LA dilatation, linear ablation lesions, and persistent AF were predictive for atypical flutter. We now demonstrated for the first time, to our knowledge, that patients with HCM experience a relatively high number of AT after AF ablation as compared with patients without or with another type of structural heart disease. Even after an isolated PVI, about 30% of patients have AT requiring targeted ablation. This number rises to almost 60% when an ablation of CFAE was performed previously. Clinical parameters such as LVEF, diastolic dysfunction, mitral valve insufficiency, septal wall thickness, or LA volume were not found to be predictors for the occurrence of AT in our cohort.

Mechanism of AT After AF Ablation

The mechanism of ATs has been classically described as focal or macro-reentry. More recently, we gained deeper insight into those atrial arrhythmias differentiating true focal versus localized reentry using novel mapping strategies and multipolar catheters with high-density electrogram acquisition. The critical isthmus of reentry ATs can be demonstrated in the majority of cases and the ablation of the localized or macro-reentrant AT individually planned during the procedure. Patients with HCM often have extensive structural changes resulting in sometimes severe dilatation of the atria potentially also because of an underlying primary atrial cardiomyopathy associated to hereditary cardiac disease beyond secondary changes because of a mitral insufficiency and/or diastolic dysfunction of the hypertrophied ventricle. However, the strategy for mapping and ablation of AT in patients with HCM generally does not differ as compared with the general population.

As ATs are common after AF ablation in HCM, appropriate characterization of the arrhythmia in question is essential for an optimized ablation procedure. This is surprisingly difficult in patients with HCM after AF ablation, as 40% of those patients present with unstable AT. Almost all of these patients (90.0%) had a previous CFAE ablation suggesting an initially more complex type of AF and the location of subsequent ATs are more commonly found at atypical sites such as the inferior and posterior LA. In those patients with unstable AT, a repeatedly changing cycle length and activation sequence sometimes cause the inability to characterize the atrial arrhythmia. Ablation in those cases is guided according to a multitude of criteria after entrainment-, activation- and voltage-mapping. Even though Deisenhofer et al reported a relatively large proportion of unstable AT (31%) in her study, to our best knowledge, the literature about the ablation of unstable AT is limited, and recommendations about mapping and ablation strategies do not exist.

After often prolonged ablation procedures, the unstable AT often has to be terminated by external electric cardioversion. The long-term freedom of AF/AT of 40% during follow-up in our study remains unsatisfactory, while we are not aware of any comparative results in the literature of long-term freedom of arrhythmia recurrence in this subgroup of patients. Randomized controlled studies recently questioned the role of extensive substrate ablation in patients with persistent AF. The role of CFAE or linear ablation beyond PVI in patients with HCM was not addressed in randomized trials yet. Our current results suggest that potentially the ablation of CFAE leads to unstable AT for which the current ablation strategies do not achieve a satisfactory freedom of AF/AT. This might lead to the assumption that the role and the extent of atrial substrate modification have to be substantially revisited, possibly using multipolar mapping catheters with an optimized signal.
resolution. Santangeli et al performed an extensive AF ablation in patients with HCM in their study, including PVI, isolation of the left atrial posterior wall, isolation of the superior vena cava, CFAE ablation in the LA and coronary sinus, and in redo procedures the ablation of non-PV triggers after isoproterenol challenge. Late recurrences (>1 year after the last ablation) were found in around 50% of patients, and atypical atrial flutter was the dominant mode of recurrence, occurring in almost 90% of these cases. In this study, atypical flutter was mapped and ablated in approximately two thirds of cases which is comparable to our findings. Santangeli and colleagues found that flutter termination during ablation did not predict the ablation outcome, whereas the ablation of non-PV triggers was associated with an arrhythmia-free survival benefit resulting in arrhythmia freedom in 94% of patient off AAD therapy with a median follow-up of 15 months. Thus, possibly additional ablation of non-PV triggers might play an important role in the ablation of persistent AF in HCM, which should be addressed in future studies.

In contrast, we found 60% of patients with stable AT in which the mechanism of the AT could be characterized in all cases, and the ablation was performed accordingly. In the majority (80%) of patients, only a PVI was performed during a prior ablation, and those patients had a promising long-term rhythm control with freedom of AF/AT of 60% after >24 months with only 1 (6.6%) patient on AAD therapy with amiodarone.

In summary, we perceive that all patients with HCM should primarily undergo PVI as effective rhythm control is possible in some patients, and the occurrence of stable AT is common. In case of recurrence of stable AT, a targeted ablation strategy aiming for characterization and respective ablation of the AT in addition to a redo PVI if appropriate is a reasonable approach. However, a CFAE ablation for recurrent persistent AF in HCM and a careful mapping of all subsequent ATs in case of unstable mechanisms is questionable and larger prospective multicenter trials are necessary to determine the best ablation strategy.

Limitations
The present study has several limitations: First, this is a single-center, retrospective, observational study. However, we present a relatively large patient population with a relatively long follow-up giving insights into AF ablation of patients with HCM. Second, a matched comparison with patients without HCM undergoing AF ablation was not performed in our study. As index ablation procedures go back several years, technological advancements of mapping systems and catheter design were made. Whether this influenced our results was not assessed. The differentiation between slow AF and unstable AT is challenging and was based on the best knowledge of the electrophysiologist during the procedure. Even though the diagnosis was made by at least 2 experienced electrophysiologists, interobserver bias cannot be ruled out and further mechanistically studies are warranted.

CONCLUSIONS
We conclude that AF ablation in patients with HCM is effective for long-term rhythm control. Especially patients with paroxysmal AF undergoing PVI have a good clinical outcome. The occurrence of ATs after AF ablation in HCM is high. Macro-reentry and localized reentry ATs can be demonstrated, and the ablation of stable ATs usually leads to an effective rhythm control without AAD therapy. The long-term freedom of AF/AT for persistent AF and unstable ATs in HCM is reasonable even though the optimal ablation strategy remains debatable.

ARTICLE INFORMATION
Received July 28, 2020; accepted October 16, 2020.

Affiliations
From the Department of Cardiology (L.D., P.M., B.S., N.K., C.J., J.D., A.T., R.S., M.P., C.M.) and Department of Cardiovascular Surgery (S.P., H.R.), University Heart and Vascular Center Hamburg, Hamburg, Germany; Institute of Medical Biometry and Epidemiology - University Medical Center Hamburg-Eppendorf, Hamburg, Germany (H.P.); Department of Cardiology, Asklepios Hospital St. Georg, Hamburg, Germany (S.W.); and DZHK (German Center for Cardiovascular Research), partner site Hamburg/Kiel/Lübeck, Berlin, Germany (S.W., C.M.).

Sources of Funding
None.

Disclosures
Meyer reports compensation for participation on a speaker’s bureau relevant to this topic and serving as advisory board member/consultant for Biosense Webster, Boston Scientific and Abbott. Willems reports compensation for participation on a speaker’s bureau relevant to this topic and serving as advisory board member/consultant for Boehringer Ingelheim, Bayer, Dalichi, and Abbott. The remaining authors have no disclosures to report.

REFERENCES
1. Maron BJ, Gardin JM, Flack JM, Gidding SS, Kurosaki TT, Bild DE. Prevalence of hypertrophic cardiomyopathy in a general population of young adults. Circulation. 1995;92:785–789.
2. Olivotto I, Cecchi F, Casey SA, Dotara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. Circulation. 2001;104:2917–2924.
3. Guttmann OP, Rahman MS, O’Mahony C, Anastasakis A, Elliott PM. Atrial fibrillation and thromboembolism in patients with hypertrophic cardiomyopathy: systematic review. Heart. 2014;100:465–472.
4. Kubo T, Kitaoka H, Okawa M, Hirota T, Hayato K, Yamasaki N, Matsumura Y, Yabe T, Takata J, Doi YL. Clinical impact of atrial
fibrillation in patients with hypertrophic cardiomyopathy. Results from Kochi RYOMA Study. Cir J. 2009;73:1599–1605.

5. Robinson K, Frenneaux MP, Stockins B, Karatasakis G, Polonieci JD, McKenna WJ. Atrial fibrillation in hypertrophic cardiomyopathy: a longitudinal study. J Am Coll Cardiol. 1990;56:1279–1285.

6. Bassiouny M, Lindsay BD, Leher H, Saleha W, Kleina A, Banna M, Abraham J, Shao M, Rickard J, Kani M, et al. Outcomes of nonpharmacologic treatment of atrial fibrillation in patients with hypertrophic cardiomyopathy. Heart Rhythm. 2015;12:1438–1447.

7. Calkins H, Kuck KH, Cappato R, Brugada J, Camm J, Chen S-A, Crijns HJG, Damien RJ, Davies DW, DiMarco J, et al. 2012 HRS/EHRA/ ECGA expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS) and in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS) and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm. 2012;9:692–696.e61.

8. Tendera M, Wycisk A, Schneweiss A, Polonisi L, Wodiwieck J. Effect of sotalol on arrhythmias and exercise tolerance in patients with hypertrophic cardiomyopathy. Cardiology. 1993;82:335–342.

9. McKenna WJ, Harris L, Rowland E, Kleinbeinne A, Kirklit DM, Oakley CM, Goodwin JF. Amiodarone for long-term management of patients with hypertrophic cardiomyopathy. Am J Cardiol. 1984;54:802–810.

10. Malasana G, Day JD, Bunch T. Atrial fibrillation in hypertrophic obstructive cardiomyopathy—antithrombotics, ablation and more. J Atr Fibrillation. 2009;2:210.

11. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella J, Cockburn I, Connolly S, Fox K, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37:2671–2736.

12. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, 2012;15:1438–1447.

13. Calkins H, Kuck KH, Cappato R, Brugada J, Camm J, Chen S-A, Crijns HJG, Damien RJ, Davies DW, DiMarco J, et al. 2012 HRS/EHRA/ ECGA expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS) and in collaboration with the American College of Cardiology (ACC), the American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS) and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society. Heart Rhythm. 2012;9:692–696.e61.

14. Kilicaslan F, Verma A, Saoudi N, et al. Catheter ablation of atrial fibrillation in patients with hypertrophic cardiomyopathy: a systematic review and meta-analysis. Heart. 2018;102:1533–1543.

15. Elliott PM, Anastasakis A, Borger M, Borggreve M, Cecchi F, Charron P, Hagege AA, Lafont A, Limongelli G, Marhooldt H, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35:2733–2779.

16. Cardin N, Galderisi M, Edwardsen T, Pein S, Popescu BA, A’Dreane A, Bruder O, Cosby S, Davin L, Donal E, et al. Role of modalitiy-cardiac imaging in the management of patients with hypertrophic cardiomyopathy: an expert consensus of the European Association of Cardiovascular Imaging Endorsed by the Saudi Heart Association. Eur J Heart J Cardiovasc Imaging. 2015;16:280.

17. Salukhe TV, Willems S, Dziewro I, Steven D, Hoffmann BA, Heitmann K, Rostock T. Propofol sedation administered by cardiologists without assisted ventilation for long cardiac interventions: an assessment of 1000 consecutive patients undergoing atrial fibrillation ablation. Eur Heart J. 2012;34:325–330.

18. Willems S, Klemm H, Rostock T, Brandstrup B, Ventura R, Steven D, Risius T, Lutomsky B, Meinertz T. Substrate modification combined with pulmonary vein isolation improves outcome of catheter ablation in patients with persistent atrial fibrillation: a prospective randomized comparison. Eur J Heart. 2006;27:2871–2878.

19. Nüchtrich JM, Steven D, Berner I, Rostock T, Hoffmann B, Servattus H, Sulaan A, Lüker J, Treszl A, Wegscheider K, et al. Impact of atrial fibrillation on survival in patients with paroxysmal atrial fibrillation: results from a randomized prospective study. Heart Rhythm. 2014;11:1536–1542.

20. Schaeffer B, Hoffmann BA, Meyer C, Akbulank RÖ, Moser J, Juliar M, Eckhoff C, Nüchtrich JM, Kuiklik P, Willems S. Characterization, mapping, and ablation of complex atrial tachycardia: initial experience with a novel method of high-density 3D mapping. J Cardiovasc Electrophysiol. 2013;24:978–984.

21. Nieder S, Sommer P, Böhm A, Hindricks G. Advanced mapping systems to guide atrial fibrillation ablation: electrical information that matters. J Atr Fibrillation. 2016;8:1337.

22. Sanders P, Hocini M, Jais P, Hsu LF, Takahashi Y, Rotter M, Scavée C, Pasquale J-L, Sacher F, Rostock T, et al. Characterization of focal atrial tachycardia using high-density mapping. J Am Coll Cardiol. 2015;66:2095–2100.

23. Saoudi N. A classification of atrial flutter and regular atrial tachycardia according to electrophysiological mechanisms and anatomical bases. A statement from a Joint Expert Group from the Working Group of Arhythmias of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Eur Heart J. 2001;22:1162–1182.

24. Haissaguerre M, Hocini M, Sanders P, Sacher F, Rotter M, Tkachy Y, Rostock T, Hsu LF, Böchsler P, Rother S, et al. Catheter ablation of long-lasting persistent atrial fibrillation: clinical outcome and mechanisms of subsequent arrhythmias. J Cardiovasc Electrophysiol. 2005;16:1138–1147.

25. Pech Sa, Hakti S, Subbotina I, Willems S, Reichenspurner H, Wagner FM. Concomitant surgical ablation for atrial fibrillation (AF) in patients with significant atrial dilation >55 mm. Worth the effort? J Cardiothorac Surg. 2015;10:165.

26. Dinshaw L, Schäffer B, Akbulak ÖJ, Jularic M, Hartmann J, Klett D, Gunawardene M, Münkler P, Häkki S, et al. Long-term efficacy and safety of radiofrequency catheter ablation of atrial fibrillation in patients with cardiac implantable electronic devices and transvenous leads. J Cardiovasc Electrophysiol. 2019;30:679–687.

27. Dinshaw L, Meyer G. Long-term risk of cardiovascular implantable electronic device-related infection after catheter ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2020;31:371–372.

28. Siontis KC, Geske JB, Ong K, Nishimura RA, Ommen SR, Gersh BJ. Atrial fibrillation in hypertrophic cardiomyopathy: prevalence, clinical correlations, and mortality in a large high-risk population. J Am Heart Assoc. 2014;3:e001002. DOI: 10.1161/JAHA.114.001002.

29. Guttman OP, Pavlov M, O’Mahony C, Monserratt L, Anastasakis A, Ravezzi C, Biagini E, Gimeno JR, Limongelli G, Garcia-Pavia P, et al.; Hypertrophic Cardiomyopathy Outcomes Investigators. Predictors of atrial fibrillation in hypertrophic cardiomyopathy. Heart. 2017;103:672–678.

30. Rowin EJ, Hausvater A, Link MS, Atr P, Gionfrido W, Wang W, Rastegar H, Estes NAM, Maron MS, Maron BJ. Clinical profile and
44. Okamatsu H, Ohara T, Kanzaki H, Nakajima I, Miyamoto K, Okamura M, Kornej J, Hindricks G, Arya A, Sommer P, Husser D, Bollmann A.
40. Kornej J, Hindricks G, Arya A, Sommer P, Husser D, Bollmann A.
39. Winkle RA, Jarman JWE, Mead RH, Engel G, Kong MH, Fleming W, Patrawala RA. Predicting atrial fibrillation ablation outcome: the CAAP-AF score. Heart Rhythm. 2016;13:2119–2125.
41. Kuck K-H, Brugada J, Fürnkranz A, Metzner A, Ouyang F, Chun KRJ, Elvan A, Arentz T, Bestehorn K, Pocock SJ, et al. Regional differences in referral, procedures, and outcome after ablation for atrial fibrillation in Europe: a report from the Atrial Fibrillation Ablation Pilot Registry of the European Society of Cardiology. Europace. 2016;18:191–200.
39. Winkle RA, Jarman JWE, Mead RH, Engel G, Kong MH, Fleming W, Patrawala RA. Predicting atrial fibrillation ablation outcome: the CAAP-AF score. Heart Rhythm. 2016;13:2119–2125.
40. Kornej J, Hindricks G, Arya A, Sommer P, Husser D, Bollmann A. The APPLE Score—a novel score for the prediction of rhythm outcomes after repeat catheter ablation of atrial fibrillation. PLoS One. 2017;12:e0169933.
41. Kuck K-H, Brugada J, Führenkranz A, Metzner A, Ouyang F, Chun KRJ, Elvan A, Arentz T, Bestehorn K, Pocock SJ, et al. Cryoballoon or radiofrequency ablation for paroxysmal atrial fibrillation. N Engl J Med. 2016;374:2235–2245.
42. Coseids Nielsen J, Johannessen J, Raatikainen P, Hindricks G, Walfriedsson H, Kongstad O, Pedersen S, Englund A, Hartikainen J, Mortensen LS, et al. Radiofrequency ablation as initial therapy in paroxysmal atrial fibrillation. N Engl J Med. 2012;367:1587–1595.
43. Knight BP, Novak PG, Sangigrillo R, Champagne J, Dubuc M, Adler SW, Sinharaj JT, Essebag V, Hokanson R, Kueffer F, et al. Long-term outcomes after ablation for paroxysmal atrial fibrillation using the second-generation cryoballoon. JACC Clin Electrophysiol. 2019;5:306–314.
44. Okamatsu H, Ohara T, Kanzaki H, Nakajima I, Miyamoto K, Okamura H, Noda T, Aiba T, Kusan K, Kamakura S, et al. Impact of left ventricular diastolic dysfunction on outcome of catheter ablation for atrial fibrillation in patients with hypertrophic cardiomyopathy. Circ J. 2015;79:419–424.
45. Gerstenfeld EP, Callans DJ, Dixit S, Russo AM, Nayak H, Lin D, Pulliam W, Siddique S, Marchlinski FE. Mechanisms of organized left atrial tachycardias occurring after pulmonary vein isolation. Circulation. 2004;110:1391–1357.
46. Wasmer K, Mönnig G, Bittner A, Decherding D, Zellerhoff S, Milberg P, Köbe J, Eckardt L. Incidence, characteristics, and outcome of left atrial tachycardias after circumferential antral ablation of atrial fibrillation. Heart Rhythm. 2012;9:1660–1666.
47. Deisenhofer I, Estner H, Zrenner B, Schreieck J, Weyerbrock S, Hessling G, Scharf K, Karch MR, Schmitt C. Left atrial tachycardia after circumferential pulmonary vein ablation for atrial fibrillation: incidence, electrophysiological characteristics, and results of radiofrequency ablation. Europace. 2006;8:573–582.
48. Chugh A, Oral H, Lemola K, Hall B, Cheung P, Good E, Tamirisa K, Han J, Bogen F, Pelosi F, et al. Prevalence, mechanisms, and clinical significance of macroreentrant atrial tachycardia during and following left atrial ablation for atrial fibrillation. Heart Rhythm. 2005;2:464–471.
49. Ipék EG, Marine J, Yang E, Habibi M, Chrispin J, Spragg D, Berger RD, Calkins H, Nazarian S. Predictors and incidence of atrial flutter after catheter ablation of atrial fibrillation. Am J Cardiol. 2019;124:1690–1696.
50. Anter E, McEllderry TH, Contreras-Valdes FM, Li J, Tung P, Leshem E, Haffajee CI, Nakagawa H, Josephson ME. Evaluation of a novel high-resolution mapping technology for ablation of recurrent scar-related atrial tachycardias. Heart Rhythm. 2016;13:2048–2055.
51. Luther V, Agarwal S, Chow A, Koa-Wing M, Cortez-Dias N, Carpinteiro L, de Sousa J, Balasubramaniam R, Farwell D, Jamil-Copley S, et al. Ripple-AT Study: a multicenter and randomized study comparing 3D mapping techniques during atrial tachycardia ablations. Circ Arrhythm Electrophysiol. 2019;12:e007394.
52. Verma A, Jiang CY, Betts TR, Chen J, Deisenhofer I, Mantovan R, Macle L, Morillo CA, Haverkamp W, Weerasooriya R, et al. Approaches to catheter ablation for persistent atrial fibrillation. N Engl J Med. 2015;372:1812–1822.
53. Vogler J, Willems S, Sultan A, Schreiber D, Lüker J, Servatius H, Schäffer B, Moser J, Hoffmann BA, Steven D. Pulmonary vein isolation versus defragmentation: the CHASE-AF clinical trial. J Am Coll Cardiol. 2015;66:2743–2752.