Atrial Fibrillation Catheter Ablation Versus Surgical Ablation Treatment (FAST)

A 2-Center Randomized Clinical Trial

Lucas V.A. Boersma, MD, PhD, FESC; Manuel Castella, MD, PhD; WimJan van Boven, MD;
Antonio Berruezo, MD; Alaaddin Yilmaz, MD; Mercedes Nadal, MD; Elena Sandoval, MD;
Naiara Calvo, MD; Josep Brugada, MD, PhD, FESC; Johannes Kelder, MD;
Maurits Wijffels, MD, PhD; Lluís Mont, MD, PhD, FESC

Background—Catheter ablation (CA) and minimally invasive surgical ablation (SA) have become accepted therapy for antiarrhythmic drug–refractory atrial fibrillation. This study describes the first randomized clinical trial comparing their efficacy and safety during a 12-month follow-up.

Methods and Results—One hundred twenty-four patients with antiarrhythmic drug–refractory atrial fibrillation with left atrial dilatation and hypertension (42 patients, 33%) or failed prior CA (82 patients, 67%) were randomized to CA (63 patients) or SA (61 patients). CA consisted of linear antral pulmonary vein isolation and optional additional lines. SA consisted of bipolar radiofrequency isolation of the bilateral pulmonary vein, ganglionated plexi ablation, and left atrial appendage excision with optional additional lines. Follow-up at 6 and 12 months was performed by ECG and 7-day Holter recording. The primary end point, freedom from left atrial arrhythmia >30 seconds without antiarrhythmic drugs after 12 months, was 36.5% for CA and 65.6% for SA ($P=0.0022$). There was no difference in effect for subgroups, which was consistent at both sites. The primary safety end point of significant adverse events during the 12-month follow-up was significantly higher for SA than for CA (n=21 [34.4%] versus n=10 [15.9%]; $P=0.027$), driven mainly by procedural complications such as pneumothorax, major bleeding, and the need for pacemaker. In the CA group, 1 patient died at 1 month of subarachnoid hemorrhage.

Conclusion—In atrial fibrillation patients with dilated left atrium and hypertension or failed prior atrial fibrillation CA, SA is superior to CA in achieving freedom from left atrial arrhythmias after 12 months of follow-up, although the procedural adverse event rate is significantly higher for SA than for CA.

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Key Words: ablation ■ atrial fibrillation ■ surgery

C atheter ablation (CA) has become an established invasive procedure in patients with atrial fibrillation (AF) refractory to antiarrhythmic drugs (AADs).[1–4] The efficacy of CA may vary considerably, depending on the strategy and technology used and the stage of the electroanatomic disease.[1–7] For paroxysmal AF, >70% single-procedure efficacy is considered achievable, whereas for (longstanding) persistent AF, additional target ablation and multiple procedures are needed to achieve a reasonable result. For any AF ablation procedure, pulmonary vein (PV) isolation (PVI) is considered a mandatory cornerstone.[2,3]

Clinical Perspective on p ●●●

Until the rise of CA, the Cox maze surgery was the only invasive treatment for AF. Although highly effective, it was technically challenging, entailing complete open heart surgery by dedicated surgeons in selected populations.[8–10] In 2006, Wolf et al[11] described a video-assisted thoracoscopic surgical ablation (SA) consisting of PVI from the epicardial side with a bipolar radiofrequency (RF) clamp, ablation of ganglia over the left atrial (LA) surface, and excision of the LA appendage. Initial efficacy of this minimally invasive surgery has been reported to be >90% in selected populations.[11–15]

With 2 invasive percutaneous options available, there is growing debate on the relative position of CA and SA, although no direct comparative trials have been performed. In the 2010 European Society of Cardiology guidelines,[2] CA in AF patients refractory to AAD has received a Class 2A or 2B

(Level of Evidence A/C) indication, depending on paroxysmal or (longstanding) persistent AF, whereas SA has a Class 2B (Level of Evidence C) indication only after failure of CA. To the best of our knowledge, the present study is the first prospective randomized clinical trial to provide a head-to-head comparison of CA and SA in a well-described population of AF patients.

Methods

A prospective randomized clinical trial was designed to compare CA and SA in a well-described population of patients with AF. The study was performed at St. Antonius Hospital in Nieuwegein, the Netherlands, and the Hospital Clinic in Barcelona, Spain. The protocol was in accordance with the Helsinki Declaration and was approved by the ethics committee of both hospitals and the Dutch central trial registration organization VCMO/CCMO. The trial was registered at www.clinicaltrials.gov (No. NCT00662701). Enrollment started in July 2007 and was stopped in June 2010; the last follow-up was completed in July 2011.

Protocol

Consecutive patients with drug-refractory AF referred for invasive treatment were screened for eligibility. Patients who met all criteria and were willing to participate were enrolled and randomized after providing written informed consent. The randomization process was performed and balanced in blocks of 6 patients at each individual site by drawing a preprinted randomization letter in a sealed envelope. The main randomization list was kept in a sealed envelope and was not opened until the last patient had been randomized. The inclusion criteria were documented, symptomatic paroxysmal and/or persistent AF for at least 12 months that was refractory to or intolerant of at least 1 AAD, age between 30 and 70 years, and mentally able and willing to give informed consent. Because SA is still considered to be tertiary treatment for only selected patients,[2,3] the study included patients who were considered less amenable to CA[16] on the basis of LA diameter of 40 to 44 mm with hypertension, LA diameter ≥45 mm, or failure of a prior CA for AF. Patients were excluded if they had longstanding AF >1 year, cardiac CA or a surgical cardiac procedure in the last 3 months, previous stroke or transient ischemic attack, LA thrombus, LA size >65 mm, left ventricular ejection fraction <45%, mitral or aortic valve regurgitation above grade 2, moderate to severe mitral or aortic stenosis, active infection or sepsis, pregnancy, unstable angina, myocardial infarction within the previous 3 months, AF secondary to electrolyte imbalance, thyroid disease, other reversible or noncardiovascular causes for AF, history of blood-clotting abnormalities, known sensitivity to heparin or warfarin, life expectancy of <12 months, involvement in another clinical study involving an investigational drug or device, pleural adhesions, prior thoracotomy, prior cardiac surgery, and elevated hemidiaphragm.

A preprocedural 7-day Holter was performed to establish preexisting type and burden of AF. A baseline physical examination, echocardiogram, and computed tomography/magnetic resonance imaging scan were done to exclude significant structural cardiac disease and to establish PV anatomy. In addition, a quality-of-life questionnaire was taken. During follow-up, patients were seen at the outpatient clinic at 3, 6, and 12 months. At each visit, patients were questioned for any adverse events and the existence of palpitations. A routine 12-lead ECG was taken at each visit. A blanking period of 3 months was allowed, after which AADs were discontinued. Amiodarone was encouraged to be discontinued at discharge but no later than 3 months. At 6 and 12 months, a 7-day Holter was performed to document the presence of arrhythmias. At 6 months, a follow-up computed tomography/magnetic resonance imaging scan was done to determine PV stenosis.

Procedure

After randomization and preprocedural diagnostic tests, patients were scheduled for CA or SA. The CA procedure consisted of a wide-area linear antrum ablation with documented PV isolation with decapolar circular mapping catheter as the end point.[2,3,17] Local anesthesia was achieved with lidocaine, and during the ablation, patients were given conscious sedation with diazepam combined with fentanyl at the discretion of the operator. Transseptal access was achieved by standard Brockenbrough method. At St. Antonius Hospital, a standard 4-mm single-tip RF catheter (Biosense-Webster) was used with a maximum power of 35 W, temperature of 55°C, and applications of 1 minute combined with the 3-dimensional NavX navigation (St. Jude Medical). No additional lines were performed, regardless of the type of AF. At the Hospital Clinic, a 3.5-mm irrigated-tip RF catheter (Biosense-Webster) was used in combination with 3-dimensional CARTO navigation (Biosense-Webster). Application duration per position was based on impedance changes and voltage reduction. An additional LA line could be made at the discretion of the operator. Roofline block was demonstrated during LA appendage pacing by continuous double potentials and activation around the PVs with a caudocranial pattern along the posterior wall,[18] whereas the mitral isthmus line[19] was made empirically without a critical definition for bidirectional block. Before the procedure, vitamin K antagonists were discontinued to lower the international normalized ratio to between 2.0 and 2.5 (St. Antonius Hospital) or to <2.0 with 3 days of bridging low-molecular-weight heparin (Hospital Clinic). During the procedure, intravenous heparin was given to reach an activated clotting time of >250 seconds.

In the SA group, patients were treated with video-assisted thoracoscopy under general anesthesia, according to the (modified) minimally invasive surgery protocol described by Wolf et al[11] and Edgerton et al.[12] In brief, PVI was performed from the epicardial side with a bipolar RF ablation clamp (AtriCure). At least 2 overlapping applications around each of the ipsilateral veins were made, and isolation was confirmed by the absence of PV potentials and exit block during pacing. In Barcelona, an additional application was made in the interatrial Waterston groove in the right side to isolate the ganglionic plexi from the atria. On the left side, the ligament of Marshal was cut, but no additional ablation of ganglionic plexi was pursued. At St. Antonius Hospital, in addition to PVI, the bilateral epicardial ganglia were found by high-frequency stimulation and ablated, as confirmed by the absence of a vagal response after ablation. Additional lines[15] could be made to the aortic trigone or at the LA roof or by making a posterior box lesion, all at the discretion of the operator. Sensing and pacing maneuvers verified isolation of the posterior box. The trigone line and roofline were made on an anatomic basis with aid of the Cool Rail (AtriCure) without determining conduction block. In all SA patients, the LA appendage was removed by stapling and then cutting the blind end of the appendage. All patients in the CA and SA groups were treated under either aspirin or vitamin K antagonist treatment, depending on the CHADS2 score. The international normalized ratio during the procedure was targeted to be <2.5 but >2.0 for patients with persistent AF. In both the CA and SA groups, all patients were treated with vitamin K antagonists in the first 3 months after the procedure, which were continued at the discretion of the treating cardiologist on the basis of freedom from AF and CHADS2 score. In the CA group, bridging therapy with low-molecular-weight heparin was done until the international normalized ratio was >2.0.

In both treatment groups, electric or chemical cardioversion was allowed during the treatment within the 3-month blanking period as needed to regain sinus rhythm, as a part of good clinical practice. Any cardioversion outside the blanking period during the 12-month follow-up was regarded as a failure for the efficacy end point.

End Points

The primary efficacy end point of the trial was freedom from any LA arrhythmia lasting >30 seconds during the 12-month follow-up without the use of AADs in accordance with the generally accepted consensus document of 2007.[2,3] A secondary efficacy end point was freedom from LA arrhythmia with AADs. The primary safety end point was the rate of significant adverse events (SAEs), including, among others, death, stroke, transient ischemic attack, major bleeding requiring surgery or blood transfusion or >2.0 points hemoglo-
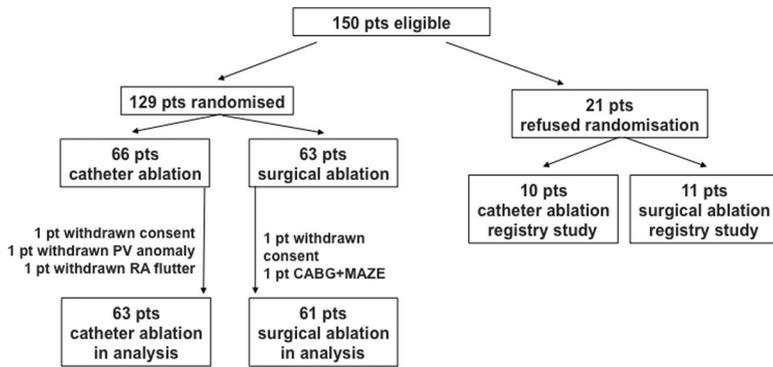
Figure 1. Patient (pt) inclusion and randomization. CABG indicates coronary artery bypass graft; PV, pulmonary vein; and RA, right atrium.

bin decrease, cardiac tamponade and/or perforation, significant/ symptomatic PV stenosis >70%, pericarditis, acute coronary syndrome, myocardial infarction, diaphragmatic paresis/paralysis, persistent air leak, pneumothorax, empyema, superficial wound infections, pneumonia, and conversion to complete thoracotomy. Safety end points were also analyzed as the adverse event rate periprocedurally and during the 12-month follow-up.

Statistical Analysis

The primary efficacy analysis was based on an intention-to-treat analysis of all randomized patients who underwent their procedure. With an estimated success rate of 60% for ablation and 85% for surgery, 120 patients should have been enrolled, allowing for 5% dropout, for a power of 80% with a 1-sided Fisher exact test with a significance level of 0.025 (NCSS-PASS statistics software, www.ncss.com). The proportion of patients free from AF and other secondary LA arrhythmias at all serial ECGs and both 6- and 12-month 7-day Holter recording was calculated. Follow-up was complete for all patients, justifying the use of binary end points. Two-by-two tables with 2-sided Pearson χ^2 test and the Yates continuity correction were used to analyze the main outcome. The prespecified subgroup analyses and post hoc subgroup analyses (by center, previous ablation or LA dilatation, AF type, and preprocedural Holter result) are presented as a Forest plot depicting odds ratios with 95% confidence intervals. Tests on heterogeneity of treatment effects across the levels of the subgroups were performed. The analysis of the safety end points was descriptive by calculating rates, whereas for the overall figure, the Fischer exact test was used. All statistical analyses were performed with R, version 2.13 (www.r-project.org).

Results

Of the 150 patients eligible for inclusion, 21 refused randomization and formed a separate registry. Figure 1 provides an overview of the patient distribution. A total of 129 patients were randomized, 66 to CA and 63 to SA. In the CA group, 3 patients were withdrawn before the procedure and were excluded from analysis because of withdrawal of consent, change in diagnosis to typical right atrial flutter, and PV anatomy congenital anomaly. In the SA group, 2 patients were withdrawn and excluded from the analysis before the procedure because of withdrawal of consent and change to coronary artery bypass graft plus maze surgery. Finally, 63 patients in the CA group and 61 patients in the SA group were included in the analysis, 59 patients from St. Antonius Hospital and 64 patients from Hospital Clinic. The baseline characteristics of the population are presented in Table 1. The mean age was 56±8 years; 101 were male and 23 were female. The AF type was paroxysmal in 67% and persistent in 33%, of which 8% was continuous persistent AF of <1 year. The time since first diagnosis of AF was ≈7 years. The

CHADS2 score was 0 in 60%, 1 in 30%, and >1 in 10%. Of the included patients, 67% had a prior unsuccessful CA as the inclusion criterion, and 33% had LA dilatation >40 mm as the primary inclusion criterion. The baseline 7-day Holter recording showed no AF in 48%, paroxysmal AF in 20%, and continuous AF in 32%. In the SA group, patients had slightly more paroxysmal AF, both as the initial diagnosis and in the preprocedural Holter recording, with a lower CHADS2 score and slightly more prior failed ablation as inclusion criteria.

Table 1.   Baseline Characteristics of Patients

	CA N=63	SA N=61
Male	55 (87.3%)	45 (73.8%)
Age, yr	56.0±7.2	56.1±8.0
BMI, Kg/m^2	28.6±3.5	27.8±4.6
Prior MI	2 (3.2%)	0
LVEF	55.5±8.2%	57.7±6.8%
LA diameter, mm	43.2±4.8	42.5±6.5%
Prior failed CA	38 (60.3%)	45 (73.8%)
LA diameter 40–45 mm and hypertension	15 (23.8%)	8 (13.1%)
LA diameter ≥45 mm	10 (15.9%)	8 (13.1%)
AF type:		
PAF	37 (58.8%)	45 (73.8%)
PersAF	26 (41.2%)	16 (26.2%)
Years since diagnosis	6.8±5.3	7.4±6.3
Pre-procedure Holter:		
No AF	23 (40.4%)	29 (55.8%)
Paroxysmal AF	10 (17.5%)	12 (23.1%)
Continuous AF	24 (42.1%)	11 (21.2%)
Prior AAD use:		
1	28.3%	16.3%
2	41.5%	35.7%
3	15.1%	32.7%
≥4	15.1%	16.3%
Amiodarone	26 (41.3%)	30 (29.2%)
CHADS2-score:		
0	35 (58.3%)	38 (63.3%)
1	17 (28.3%)	17 (28.3%)
≥2	8 (13.4%)	4 (6.7%)

Table 2. Procedural Characteristics of CA and SA

	CA N=63	SA N=61
Total procedure time, min	163±55	188±59 (P=0.0177)
Flurorscopy time, min	27±11	. . .
PVI	62 (98.2%)	60 (98.3%)
PV reablated redo pts:		
1	1 (2.6%)	. . .
2	9 (23.7%)	. . .
3	3 (7.9%)	. . .
4	25 (65.8%	45 (100%)
LAA excision	. . .	60 (98.3%)
LA lines:		
Roof	30 (47.6%)	17 (27.9%)
Mitral isthmus	15 (23.8%)	. . .
Trigone		10 (16.4%)
Posterior box	. . .	10 (16.4%)
No. additional lines:		
1	17 (27.4%)	9 (14.8%)
2	14 (22.6%)	2 (3.3%)
3	. . .	8 (13.1%)
RF energy PVI	33±20 min	8.9±2.8 applications

Table 3. Efficacy Endpoints for CA and SA

Freedom of LA Arrhythmia	CA N=63	SA N=61	P-Value
Overall, 12 mo	23 (36.5%)	40 (65.6%)	P=0.0022
Overall, 12 mo allowing AAD	27 (42.9%)	48 (78.7%)	P<0.0001
Overall, 6 mo	28 (44.4%)	41 (67.2%)	P=0.0178
PAF group	13/37 (35.1%)	31/45 (68.9%)	P=0.0047
PersAF group	9/25 (36%)	9/16 (56%)	P=0.3411
Prior failed CA	14/38 (36.8%)	30/44 (68.2%)	P=0.0089
LA dilation/ hypertension	9/25 (36.0%)	10/17 (58.8%)	P=0.3411
Nieuwegein	10/30 (33.3%)	18/29 (62.1%)	P=0.0513
Barcelona	13/33 (39.4%)	22/31 (70.9%)	P=0.0336

Procedure

Table 2 shows the procedural information for the CA and SA groups. The mean procedure, fluoroscopy, and RF times in the CA ablation group were 163±55, 27±11, and 33±20 minutes, respectively. There was no significant difference in procedure and fluoroscopy times between the 2 centers. Mean SA procedure time was longer at 188±59 minutes (P=0.0177) without the need for fluoroscopy and 8.9±2.8 bipolar RF clamp applications. In all SA patients, PVI was the cornerstone of ablation, followed by ganglia ablation and LA appendage excision in the SA group. In the group with failed prior CA, all patients were found to have ≥1 PV with intact PV-LA conduction before reisolation, which were then subsequently reisolated (Table 2). In the CA group, only at the Hospital Clinic were additional lines made at the LA roof in 30 patients (47.6%), mitral annulus in 15 patients (27.4%), or both in 14 patients (22.6%). In the SA group, all PVs were always surgically ablated regardless of whether there was LA-PV conduction. In addition, various combinations of additional lines were created only at St. Antonius Hospital in 19 patients (31%). In 1 patient in both the CA and SA groups, the ablation protocol could not be performed or completed because of complications.

Efficacy of CA and SA

Table 3 lists the outcomes of CA and SA during the 12-month follow-up. No patients were lost to follow-up. At 6 months, freedom from LA arrhythmia lasting >30 seconds without AADs was seen in 44.4% in the CA group versus 67.2% in the SA group (P=0.0178). During continuation of follow-up, the difference in effect increased, further favoring SA. The primary efficacy end point of freedom from any LA arrhythmia of >30 seconds in the absence of AADs after 12 months

was 36.5% in the CA group and 65.6% in the SA group (P=0.0022). Thus, to increase the efficacy for freedom from LA arrhythmia by performing SA instead of CA, the number needed to treat was 3.4 (95% confidence interval, 2.3–8.7). Another 12 patients also remained free from LA arrhythmias but were not considered a success for the primary end point because they were not free from AADs during follow-up. Allowing for AAD use, CA efficacy was 42.9% and SA efficacy was 78.7% (P<0.0001). Regarding the timing of the 40 CA failures, 7 patients (17.5%) failed before the scheduled 6-month visit, 7 (17.5%) between the 6- and 12-month visits, 3 (7.5%) at the 12-month visit, and 23 (57.5%), the majority, at or around the 6-month visit. Of the 21 SA failures, 3 (14.3%) occurred before 6 months, 2 (9.5%) between the 6- and 12-month visits, 0 at the 12-month visit, and 16 (76%) at or around the 6-month visit.

Figure 2 shows the Forest plot for the subgroup analysis. The treatment effect was consistent for the 2 sites, with CA efficacy of 33.3% at St. Antonius and 39.4% at the Hospital Clinic and SA efficacy of 62.1% at St. Antonius and 70.9% at the Hospital Clinic. The use of an irrigated RF catheter or the creation of additional lines did not significantly affect the efficacy in this population. The superior efficacy of SA showed a specifically favorable trend toward paroxysmal AF patients and previously unsuccessful CA patients. All tests on heterogeneity of treatment effects performed across the levels
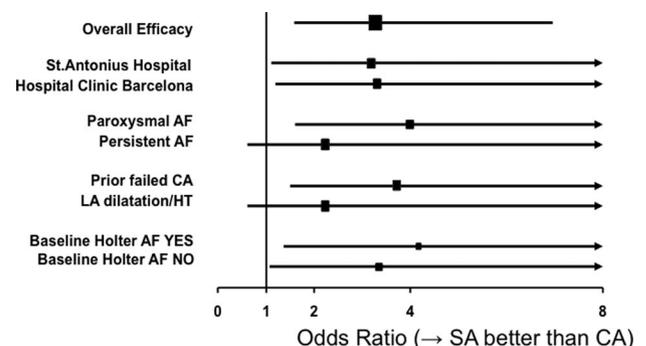

Figure 2. Forest plot of subgroup analysis for surgical ablation (SA) vs catheter ablation (CA) efficacy. AF indicates atrial fibrillation; LA, left atrium; and HT, heart transplantation.

Table 4.   Procedural Adverse Events of CA and SA

Adverse Events	CA N=63	SA N=61	P-Value
Pericardial effusion/tamponade	1	1	
TIA/Stroke	1	1	
Pneumothorax	...	6	
Hematothorax	...	1	
Rib fracture	...	1	
Sternotomy for bleeding	...	1	
Pneumonia	...	1	
Death	...	...	
PM implant	...	2	
Total	2 (3.2%)	14 (23.0%)	P=0.001
Minor			
Groin hematoma/bleed	4 (6.3%)	...	

of the subgroups showed consistency of results with a significance level of >0.2.

Safety of CA and SA

Tables 4 and 5 list all adverse events, significant and minor, both periprocedurally and during the 12-month follow-up. The primary safety end point of all SAEs during 12-month follow-up was 34.4% in the SA group versus 15.9% in the CA group (P=0.027). The procedural adverse event rate was similar at both sites but significantly higher for SA with 23.0% (14 SAEs in 14 patients) than for CA with 3.2% (2 SAEs in 2 patients; P=0.001). The number needed to treat to prevent a procedural adverse event by performing CA instead of SA was therefore 5.05 (95% confidence interval, 3.3–42.5). The median duration of hospitalization was 2.0 days for CA versus 5.5 days for SA (P<0.001). In the SA group, 1 patient required conversion to median sternotomy for bleeding. One patient required a pacemaker implantation for sinus node dysfunction, whereas another had a pacemaker for bradycardia and nonsustained polymorphic VT. In 1 patient, the SA procedure could not be completed because of obesity and severe pulmonary hypertension, leading to severely prolonged hospitalization. Other complications included

Table 5.   Adverse Events During 12-mo Follow-Up of CA and SA

Adverse Events	CA N=63	SA N=61	P-Value
Stroke	1	...	
TIA	1	...	
Pneumonia	2	2	
Hydrothorax	...	2	
Heart failure by AF	2	...	
SAB causing death	1	...	
Pericarditis	...	1	
Fever unknown origin	...	1	
Ileus	1	1	
PV stenosis >70%	...	...	
Total	8 (12.6%)	7 (11.5%)	P=1.0
Minor			
Groin hematoma/bleed	2 (3.2%)	...	

pneumothorax (n=6), hematothorax (n=1), stroke (n=1), tamponade (n=1), and rib fracture (n=1). Most of the pneumothorax cases were managed conservatively without the need for drainage or prolongation of hospitalization. In 1 patient in the CA group, PVI was not performed because of pericardial effusion after transseptal puncture with spontaneous recovery. All other patients could be treated successfully without the need for conversion to a (minimally invasive) surgical approach. In the CA group, 1 patient had a transient ischemic attack with complete convalescence; in terms of minor adverse events, 4 patients (6.6%) had a groin hematoma without a drop in hemoglobin level or need for treatment.

During the 12-month follow-up, 8 SAEs (12.7%) occurred in the CA group versus 7 (11.5%) in the SA group (P=1.0; Table 5). Of note, 1 patient in the CA group died after 1 month of subarachnoid hemorrhage while on vitamin K antagonists. In the CA group, stroke (n=1) and transient ischemic attack (n=1) were also observed, as well as heart failure caused by AF with a high ventricular rate (n=2). In the SA group, 2 late cases of hydrothorax, one that required draining, were notable. No significant (>70%) or symptomatic PV stenosis was observed on 6-month computed tomography/magnetic resonance imaging in either group. Heterogeneity testing did not show differences in effect according to site with P>0.2.

Discussion

To the best of our knowledge, this is the first randomized clinical trial to directly compare CA and SA for the treatment of AF. The reported efficacy for CA varies widely, although freedom from AF of >70% is considered acceptable.[2,3] Minimally invasive SA single-center success rates have been reported to be between 75% and 92% in selected populations.[11–15] In our study, in a population of patients with failed prior CA and/or dilated atria and hypertension,[15] SA was found to be superior to CA in achieving freedom from LA arrhythmia after a 12-month follow-up, albeit at the cost of a higher adverse event rate.

Procedural Effects of SA and CA

In the present study, we evaluated the strategy of endocardial CA versus epicardial SA; the latter strategy turned out to be significantly more efficacious. Several factors may play a role in explaining this difference. A total of 69% of our population consisted of patients with AF recurrence after a failed prior procedure, which could signify a predisposition to CA failure. Moreover, in the redo patients in the CA arm, only PVs still showing LA-PV conduction were reablated, whereas in the SA arm, all PVs were always ablated. Although the difference in effect was consistent in patients with and without a prior procedure, the study was not powered to establish the significance of this factor. There was also no apparent difference between using irrigated-tip and non–irrigated-tip ablation for CA or the specific study center where treatment was performed. The efficacy difference may result from superior transmurality of the epicardial bipolar RF lesion creation in SA, resulting in more antral PVI and permanent conduction block. We did not perform a repeated electrophys-

iology study to determine whether chronic PVI was indeed achieved in either treatment group.

Some studies have shown beneficial effects of adding LA ablation lines to PVI, specifically in patients with persistent AF.[2,3,6,7,18,19] At both study sites, the cornerstone of CA was electrically confirmed PVI by wide-area ablation in the antrum. In 49% of patients, an additional LA ablation line was performed, which did not seem to affect the efficacy regardless of the underlying type of AF. The patients in the SA group tended to have a diagnosis of paroxysmal AF slightly more often, whereas baseline Holter also showed no AF or paroxysmal AF more often. Because in more advanced stages of AF additional targets such as lines or ablation with complex fractionated atrial electrograms seem mandatory,[6,7] patients in the CA group may have been undertreated compared with patients in the SA group. The present trial was not designed to study such detailed differences.

Another factor may be the difference in the extent of the lesion set of CA compared with SA. SA not only results in PVI but also targets the epicardial ganglia and comprises LA appendage excision. Several studies have demonstrated the role of these ganglia in AF initiation and maintenance, whereas ablation of ganglia alone could lead to cure of AF.[20–22] So far, no randomized clinical trials have quantified the added effect of surgical ganglia ablation to achieve freedom from AF. Elimination of LA appendage ectopy may also facilitate in obtaining freedom from AF,[23] which may have contributed to the higher efficacy of SA observed. In the SA, 31% of patients had various additional LA ablation lines at the LA roof, aortic trigone, mitral isthmus, or box lesion around the PVs. This did not appear to affect the efficacy of SA at 12 months; if anything, efficacy tended to be a little lower in patients with such lines. Of note, part of these lines were made on an anatomic basis without verifying that conduction block had indeed been established. Whether additional lesions during either CA or SA would be beneficial for specific patient populations remains to be determined[24,25]; this study was not designed or powered to answer that question.

In both the CA and SA arms, the final efficacy was considerably lower than expected during the design of the trial in 2007. The estimates of efficacy were based on historical data in the literature on CA and SA. It was obviously not possible to predict the final mix of included patients for parameters such as failed prior ablation, persistent AF, and LA diameter. In the CA group, >40% of patients finally had nonparoxysmal AF and may have been undertreated by PVI alone. In addition, 67% had already failed a prior CA, which may be a more serious predisposition to failure than anticipated. Most historical data on the efficacy of CA and SA before the consensus statement of 2007[3] are based on heterogeneous criteria of success and less thorough rhythm follow-up than performed in this trial. As is becoming more apparent in current publications, longer duration of arrhythmia follow-up may reveal lower efficacies of invasive procedures than previously reported. This is also true for SA; in many of the initial publications in selected small populations, rhythm follow-up was usually <12 months, and arrhythmia detection was less frequent and shorter than 7 days.

Safety of SA and CA

CA is considered least invasive because it involves access to the heart through a small femoral puncture hole under local anesthesia. SA is considered minimally invasive when performed through video-assisted thoracoscopic surgery, mainly distinguishing it from complete open chest Cox maze surgery. The procedure requires general anesthesia, sequential deflation of both lungs, and transthoracic access to the heart involving several collateral structures. CA for AF has been performed in increasing numbers since 1998, and several large registries have focused on safety. The update of the worldwide survey for AF ablation[4] showed major adverse events in 741 of 10.781 patients (4.54%). The adverse event rate of 3.2% of CA in the present trial seems in line with the published data. The events reported with CA seemed more transient and did not require any intervention, perhaps because all operators were highly skilled at both high-volume AF ablation centers. The adverse events seemed to center around (anti-) coagulation, with bleeding on the one hand and transient ischemic attack, stroke, and subarachnoid hemorrhage leading to death on the other hand. New anticoagulation drugs are becoming available that may provide an answer to this well-known dilemma.[26,27]

There are no large registries for minimally invasive SA that provide good insight into safety. Several smaller series have been promising in this respect.[11–15] However, the procedural SA adverse event rate of 23.0% was clearly higher than that of CA. These SA complications tended to result mostly from direct mechanical injury during the procedure. About half required additional interventions and/or prolonged hospitalization, and most resolved without leaving permanent damage. The inability to complete the SA in a patient with substantial comorbidity highlights the importance of patient selection for this elective surgical procedure. Obviously, as minimally SA techniques and tools improve and the volume and experience of operators increase, such complications may diminish over time. Although some of the SAEs, both procedural and during follow-up, may not have been directly linked to the procedure itself, it is clear that cardiologists and their patients should consider the higher event rate, before deciding on a more invasive surgical procedure for AF, even though the efficacy may be superior.

Limitations

Arrhythmia follow-up was performed with intermittent ECG, 7-day Holter, and sometimes event recording, which may underestimate absolute arrhythmia recurrence. Most patients in our study had undergone a prior unsuccessful CA as inclusion criterion. This may make the conclusion less applicable to patients with the inclusion criterion of dilated LA or to the general AF population. In the population studied, 67% had paroxysmal AF and 33% had continuous persistent AF <1 year. Although we did not observe a significant effect of AF type on efficacy, the study may have been underpowered for this factor. In the patients who had AF during the CA or SA procedure, PV ablation was simply repeated without prior measurement of actual PV-LA conduction. In both the CA and SA groups, there were differences between the sites in several of the practical procedural details. Although the efficacy of CA and

SA was consistent and similar at the sites, the trial was not powered to study the effect of such differences.

Conclusion

In AF patients with a dilated LA and hypertension or failed prior LA CA, minimally invasive SA is superior to CA in achieving freedom from LA arrhythmias after 1 year of follow-up. The procedural adverse event rate, however, is significantly higher for SA than for CA. These findings may guide physicians and patients when considering invasive AF treatment options.

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Disclosures

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CLINICAL PERSPECTIVE

Catheter ablation (CA) and minimally invasive surgical ablation (SA) have become accepted therapy for antiarrhythmia drug–refractory atrial fibrillation (AF). This study describes the first randomized clinical trial comparing the efficacy and safety of CA and SA during 12 months of follow-up. One hundred twenty-four patients with antiarrhythmia drug–refractory atrial fibrillation with left atrial dilatation and hypertension (42 patients, 33%) or failed prior CA (82 patients, 67%) were randomized to CA (63 patients) or SA (61 patients). CA consisted of linear antral pulmonary vein isolation and optional additional lines. SA consisted of bipolar radiofrequency isolation of the bilateral pulmonary vein, ganglionated plexi ablation, and left atrial appendage excision with optional additional lines. Follow-up at 6 and 12 months was performed by ECG and 7-day Holter recording. The primary end point, freedom from left atrial arrhythmia >30 seconds without antiarrhythmia drugs after 12 months, was 36.5% for CA and 65.6% for SA ($P=0.0022$). There was no difference in effect for subgroups, which was also consistent at both sites. The primary safety end point of significant adverse events during the 12-month follow-up was significantly higher for SA than for CA (n=21 [34.4%] versus n=101 [5.9%]; $P=0.027$), driven mainly by procedural complications such as pneumothorax and bleeding. In the CA group, 1 patient died at 1 month of subarachnoid hemorrhage while on vitamin K antagonists. The results indicate that in atrial fibrillation patients with dilated left atrial and hypertension or failed prior CA, SA is superior in achieving freedom from left atrial arrhythmias after 12 months of follow-up at the cost of a higher procedural serious adverse event rate. These findings may guide physicians and patients in choosing between these invasive treatments for atrial fibrillation.

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