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**FASTTRACK CONGRESS**
*Arrhythmias*

# Catheter ablation vs. thoracoscopic surgical ablation in long-standing persistent atrial fibrillation: CASA-AF randomized controlled trial

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**Aims** Long-standing persistent atrial fibrillation (LSPAF) is challenging to treat with suboptimal catheter ablation (CA) outcomes. Thoracoscopic surgical ablation (SA) has shown promising efficacy in atrial fibrillation (AF). This multicentre randomized controlled trial tested whether SA was superior to CA as the first interventional strategy in *de novo* LSPAF.

**Methods and results** We randomized 120 LSPAF patients to SA or CA. All patients underwent predetermined lesion sets and implantable loop recorder insertion. Primary outcome was single procedure freedom from AF/atrial tachycardia (AT) ≥30 s without anti-arrhythmic drugs at 12 months. Secondary outcomes included clinical success (≥75% reduction in AF/AT burden); procedure-related serious adverse events; changes in patients' symptoms and quality-of-life scores; and cost-effectiveness. At 12 months, freedom from AF/AT was recorded in 26% (14/54) of patients in SA vs. 28% (17/60) in the CA group [OR 1.128, 95% CI (0.46–2.83), $P = 0.83$]. Reduction in AF/AT burden ≥75% was recorded in 67% (36/54) vs. 77% (46/60) [OR 1.13, 95% CI (0.67–4.08), $P = 0.3$] in SA and CA groups, respectively. Procedure-related serious adverse events within 30 days of intervention were reported in 15% (8/55) of patients in SA vs. 10% (6/60) in CA, $P = 0.46$. One death was reported after SA. Improvements in AF symptoms were greater following CA. Over 12 months, SA was more expensive and provided fewer quality-adjusted life-years (QALYs) compared with CA (0.78 vs. 0.85, $P = 0.02$).

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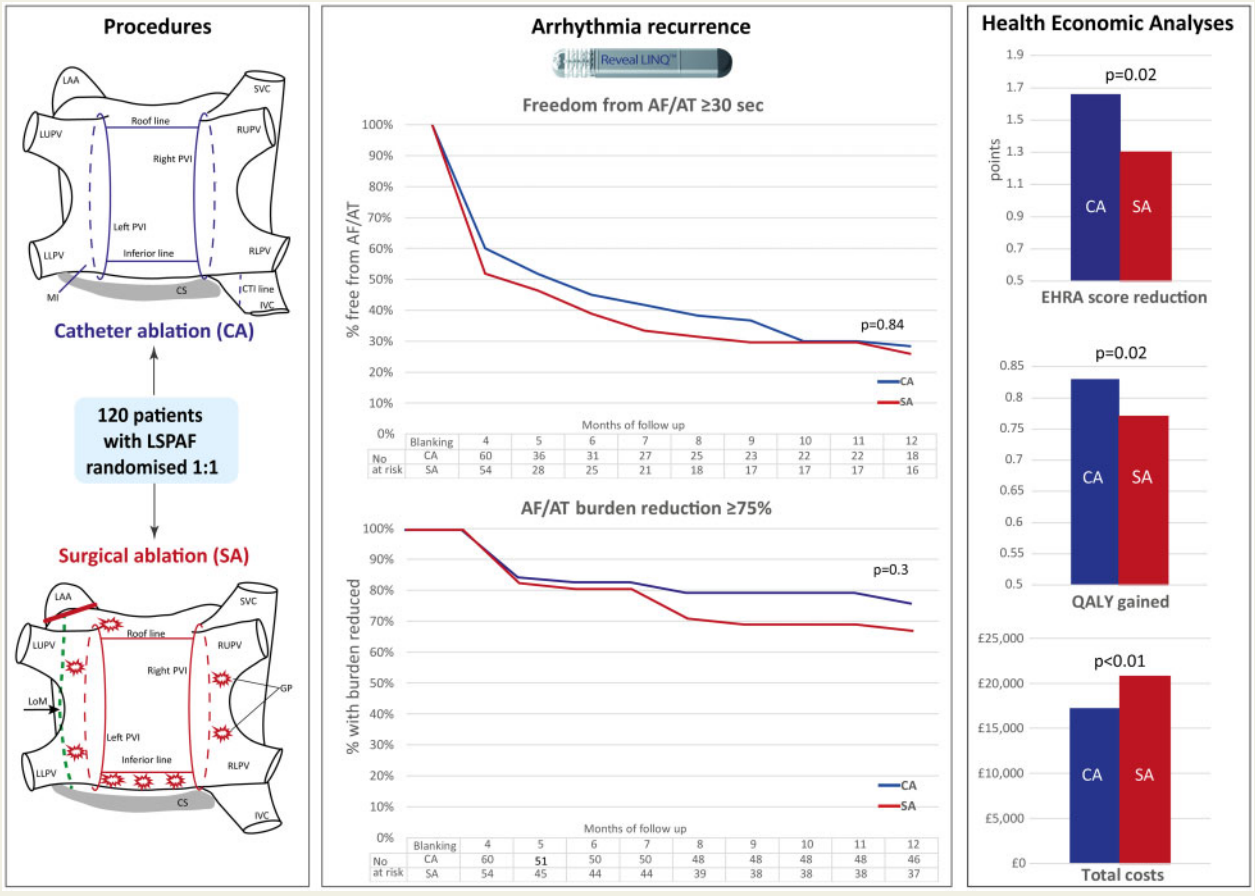
**Conclusion** Single procedure thoracoscopic SA is not superior to CA in treating LSPAF. Catheter ablation provided greater improvements in symptoms and accrued significantly more QALYs during follow-up than SA.

**Clinical Trial Registration** ISRCTN18250790 and ClinicalTrials.gov: NCT02755688

## Graphical Abstract



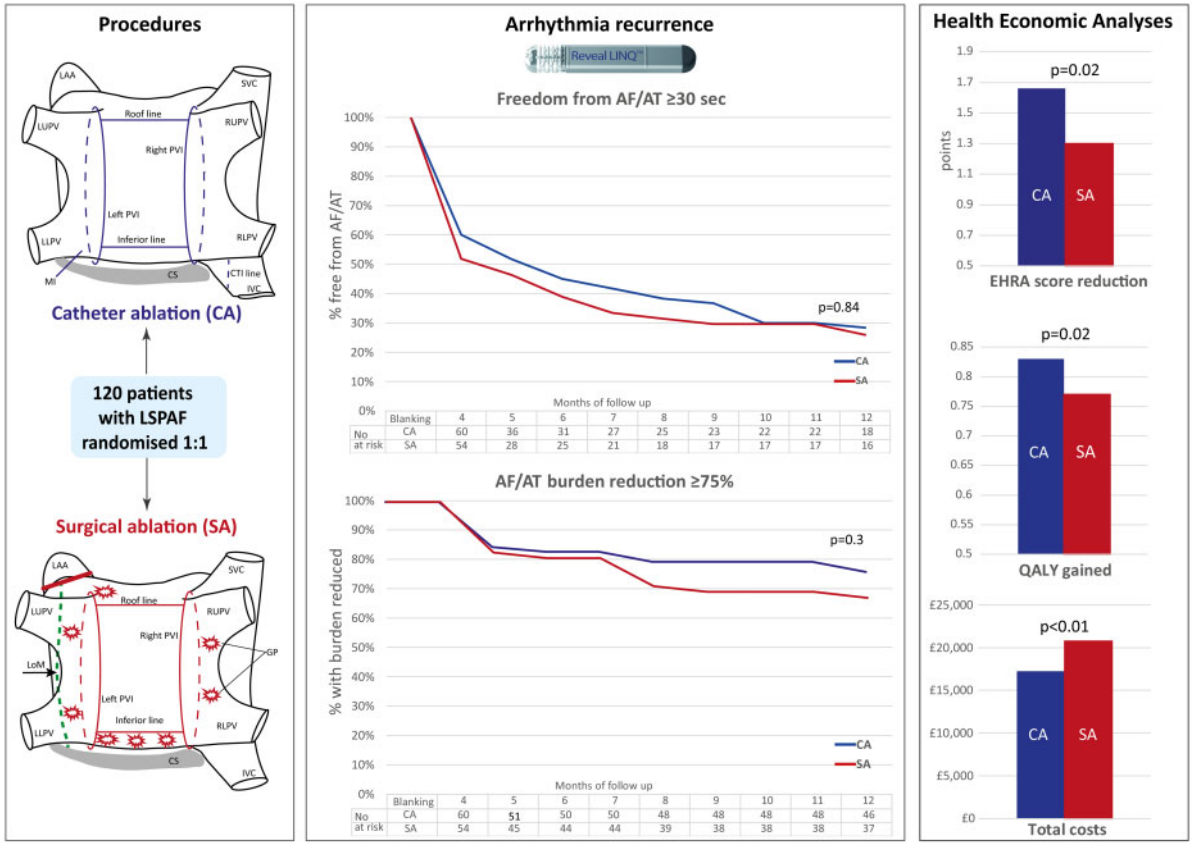

**Keywords** Arrhythmia • Electrophysiology • Atrial fibrillation • Catheter ablation • Epicardial PVI • Implantable loop recorder

# Introduction

Worldwide, atrial fibrillation (AF) affects 1–2% of the population and its prevalence is increasing.[1] Atrial fibrillation is associated with lower quality of life, increased morbidity and mortality, and a large number of hospital admissions.[2,3] Management of AF requires considerable health resources estimated at 2% of the NHS budget in the UK.[3,4]

Atrial fibrillation management consists of stroke prevention with anticoagulants and ventricular rate control with pharmacological agents. For rhythm control, catheter ablation (CA) is superior to anti-arrhythmic drugs (AAD) and is routinely offered to patients with symptomatic AF.[3,5,6] Catheter ablation can reliably maintain sinus rhythm (SR) in 60–80% of patients with paroxysmal AF[3] and is almost as effective (≈60%) in early persistent AF.[7] However, long-standing persistent AF (LSPAF), defined as continuous AF greater than 12 months, represents the most advanced end of the disease spectrum and CA outcomes in this setting are suboptimal, often requiring multiple CA procedures to establish normal heart rhythm.[8,9]

Thoracoscopic surgical ablation (SA) was proposed to be more effective due to the direct application of transmural and contiguous lesions as well as the ability to ablate ganglionic plexi (GP) and exclude the left atrial appendage (LAA). Previous non-randomized




**Take home figure** *Left:* Schematic representation of lesion placement in catheter and surgical ablation. Most lesions were performed by radiofrequency ablation (thin red or blue lines) but left atrial appendage (LAA) was occluded with a clip (thick red line) and the Ligament of Marshall (LoM) was dissected (dashed green line). *Middle:* Kaplan–Meier survival plots illustrating freedom from AF/AT (left) and clinical success (right) of both treatments. *Right:* Graphical representation of symptoms improvement (EHRA score reduction), QALY gained and the total costs associated with both treatments at 12 months.

studies in LSPAF utilizing intermittent cardiac rhythm monitoring reported encouraging results.[10,11] Continuous cardiac rhythm monitoring is essential to accurately assess AF recurrences as well as estimate AF burden reduction, an important marker of clinical success.[12–14]

In this randomized controlled trial (RCT), we sought to determine whether thoracoscopic SA was superior to CA as a first-line procedure in *de novo* LSPAF patients, refractory or intolerant to at least one AAD (Class 1 or 3). We compared the effectiveness, safety, impact on quality of life, and cost-effectiveness of these two treatments.

# Methods

## Trial design

CASA-AF is a prospective, multicentre, RCT conducted at 4 high-volume UK centres. The trial was approved by the UK NRES ethical review board (15/SC/0023) and conforms to the Declaration of Helsinki. The published protocol was in accordance with the Interventional Trials (SPIRIT) 2013 statement.[15,16] The conduct of the study was overseen by two independent bodies, the Data Monitoring and the Trial Steering Committees.

## Study participants

Adults with symptomatic LSPAF, EHRA symptom score >2, left ventricular ejection fraction ≥40%, referred for treatment and suitable for both procedures were eligible. Exclusion criteria included valvular heart disease (severity greater than mild) and previous cardiothoracic surgery (including surgical AF interventions). Detailed inclusion and exclusion criteria are provided in the Supplementary material (*Table* A1). All participants provided written informed consent.

### Treatment allocation

Patients were randomly assigned to treatment groups by computer-generated sequence in a 1:1 ratio using minimization. The system used the study site, participant's sex, and the diameter of the left atrium (<50 and ≥50 mm) as stratifying variables. Treatment allocation was concealed and heart rhythm assessors, the trial statistician and the health economist were blinded to treatment arms. Double blinding in this study was not possible due to the marked differences in the procedural techniques.

## Study procedures

### Procedures

Procedure details and pre- and post-ablation patient management have been previously published in the trial protocol.[16] In SA, radiofrequency

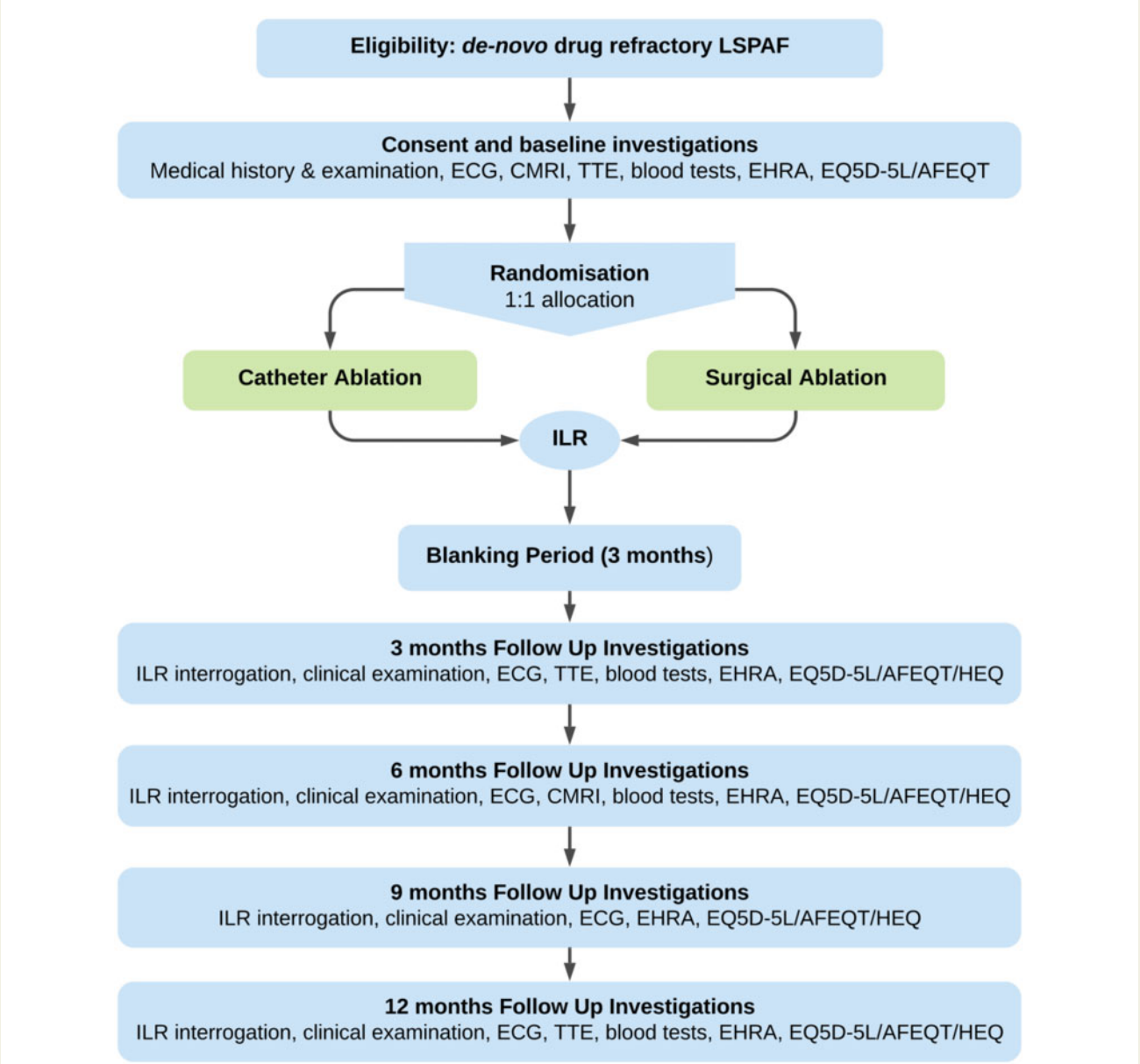



**Figure 1** Schematic representation of CASA-AF study design. AAD, anti-arrhythmic drugs; AF, atrial fibrillation; AFEQT, AF Effect on QualiTy-of-life questionnaire; AT, atrial tachycardia; CMRI, cardiac magnetic resonance imaging; ECG, electrocardiogram; EHRA, European Heart Rhythm Association score for AF; EQ-5D-5L, quality of life questionnaire; HEQ, health economic questionnaire; IL, implantable loop recorder; TTE, trans thoracic echocardiogram.

ablation was performed under direct vision starting with pulmonary vein isolation (PVI), then GP ablation, followed by linear roof and inferior line ablation to create a posterior wall box lesion. The LAA was then excluded using the AtriClip® LAA excluder system (AtriCure). (*Take home figure*, Left panel).

We mandated the presence of a cardiac electrophysiologist to ensure conduction block testing for all lesions.[17] Cardiac surgeons had to be experienced in video-assisted thoracoscopic AF surgery with a minimum of 20 procedures performed as the primary operator.

In CA, trans-septal puncture was followed by point-by-point radiofrequency ablation including PVI, roof and inferior line to create a posterior wall box lesion. A lateral mitral isthmus and cavotricuspid isthmus line completed the lesion set (*Take home figure*, Left panel).

Conduction testing to confirm bi-directional block for all lesions was done in the usual manner in both treatment arms with additional ablation where necessary. In both groups, an implantable loop recorder (ILR) was implanted at the end of the procedure.

### Follow-up schedule

Study assessments and frequency of follow-up visits are detailed in *Figure 1*. AAD therapy (flecainide, procainamide, amiodarone, or sotalol) was terminated before the end of the blanking period (3 months). Recurrence of symptomatic AF during the blanking period was treated with DC cardioversion with or without AADs. Patients were offered percutaneous CA if AF/atrial tachycardia (AT) recurred outside the blanking period.

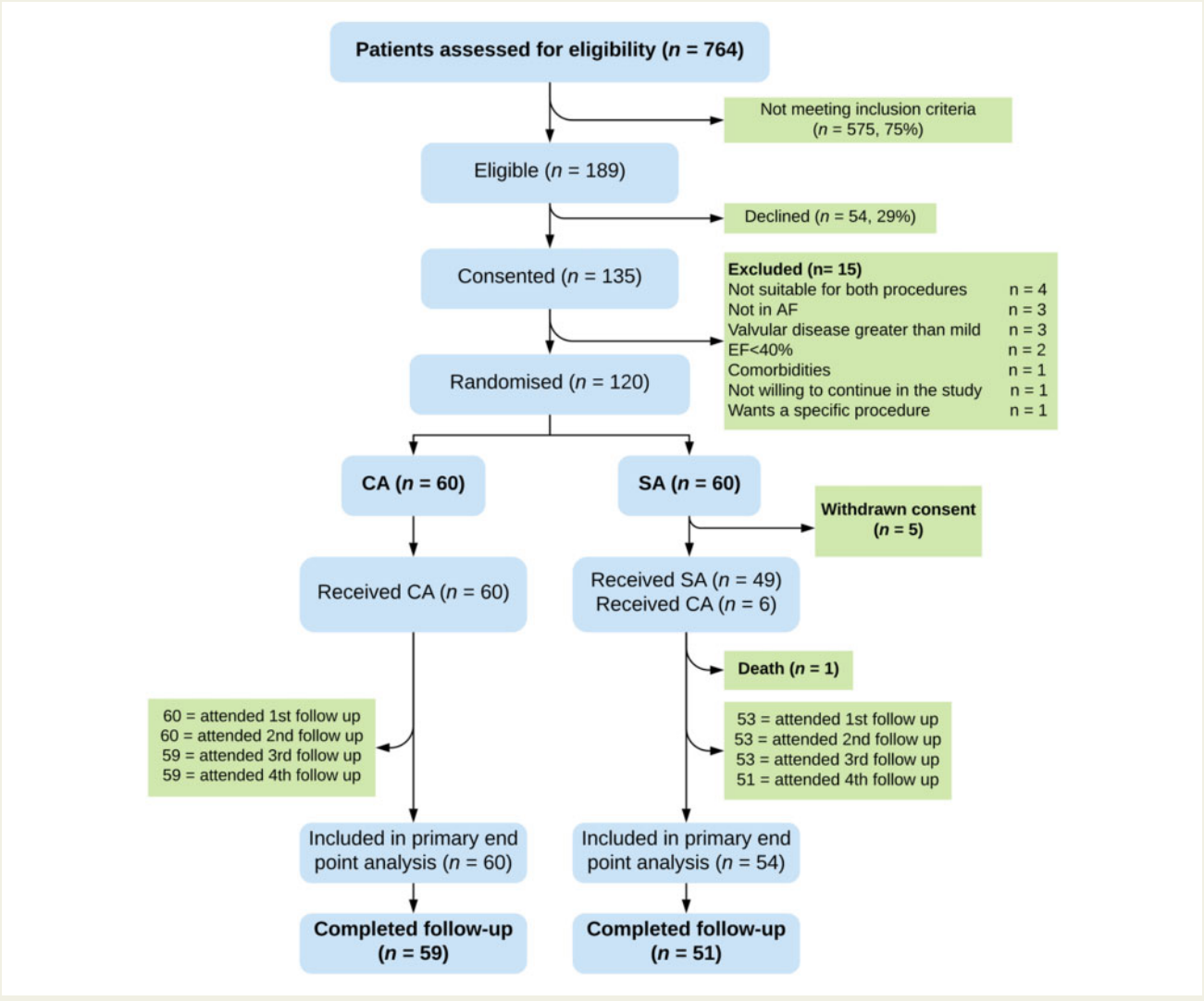



**Figure 2** CONSORT diagram.

### Implantable loop recorder

Continuous cardiac monitoring was provided by a Reveal LINQ ILR (Medtronic, Minneapolis, MN) with two aggressive AF/AT detection algorithms.[18] A blinded senior cardiac physiologist regularly analysed data to produce monthly heart rhythm assessments. Further details of the ILR analysis, programming and data quality control can be found in the Supplementary material Sections 5–7.

## Study endpoints

The primary outcome was freedom from AF/AT ≥30 s after a single ablation procedure, without AADs during the 12 months follow-up, excluding blanking period.

Secondary outcomes included a safety endpoint (intervention-related serious adverse event, defined as permanent injury or death, one that requires unplanned intervention for treatment, or one that prolongs or requires unplanned hospitalization for >48 h), clinical success rate (reduction of AF/AT burden ≥75%), changes in symptoms [European Heart Rhythm Association (EHRA) overall score] and quality-of-life scores [Atrial Fibrillation Effect on QualiTy-of-life Questionnaire (AFEQT); EQ-5D-5L UK cross-walk index score],[19] and within-trial health economic assessment using quality-adjusted life-years (QALYs) and healthcare costs (UK £2019) accrued over the 12 months of follow-up.

Independent reviews of heart rhythm and safety endpoints were conducted by committees blinded to treatment allocation.

## Statistical analysis

The sample size calculations were based on the effect size estimates available in the literature and from our own pilot study (see Supplementary material Section 3). Intention to treat analyses were performed on complete cases. Sensitivity analyses were used to explore the impact of missing data, non-compliance, and withdrawals. R statistical software version 4.0.0 was used to analyse data. Sample size ($n = 120$, 10% attrition rate included) was calculated to allow 90% power and 5% significance level to detect a clinically important difference in the primary outcome. The primary outcome of the trial was the proportion of treated participants, free from AF/AT episodes lasting ≥30 s within 12 months after a single procedure and without AADs. Arrhythmia-free patients were identified through monthly ILR data assessments from the end of the blanking

period to the end of the 12 months follow-up (Supplementary material Section 4). Burden of AF/AT reduced ≥75% of the time every month was a marker of clinical success of the procedure. Chi-squared test and logistic regression were used for comparison between the trial arms. Freedom from AF/AT and burden reduction were also analysed using Kaplan–Meier survival curves.

Continuous data were analysed by either Student's *t*-test or Mann–Whitney test and presented as mean (±standard deviation-SD), mean (95% confidence interval) or median (interquartile range-IQR) depending upon distribution of obtained data. A $P < 0.05$ is considered significant.

# Results

## Patients

Patient recruitment took place between September 2015 and June 2018. Of 120 patients randomized (SA = 60, CA = 60), five patients withdrew consent post-randomisation in the SA arm and were excluded from analyses (modified intent to treat principle). Study treatment was received by 115 patients of whom 110 completed all follow-up. Patient flow is shown in *Figure 2*.

Patients had a mean age of 62.3 (±9.6) years, were predominantly male (74%), with mean left atrial diameter 44.7 (±6) mm and in continuous AF for a median (IQR) of 22 (16–31) months.

Baseline characteristics are shown in *Table 1*.

## Procedures

The procedural characteristics are shown in *Table 2*. Median duration of SA was significantly longer (265 min; IQR: 220–310) than CA (219 min; IQR: 192–261), $P = 0.002$. Pulmonary vein isolation (all PVs) during SA was faster than in CA, with a median ablation time of 3.8 (2.6–5.9) vs. 31 (25.5–38.6) min ($P < 0.001$). Median length of hospital stay was longer for SA than for CA [6 (5–7) vs. 2 (2–2) days, $P < 0.001$]. Further details are provided in Supplementary material (*Table A2*).

All 60 patients randomized to CA underwent ablation, compared with 55 in the SA arm, due to withdrawals post-randomization. In the SA group, six patients crossed over to CA due to lung or cardiac adhesions precluding access for SA and two patients had incomplete lesion sets due to adverse anatomical features: one patient did not have the left pulmonary vein (PV) isolated nor the LAA excluded, and the other did not have LAA exclusion.

## Primary and secondary endpoints

### Primary endpoint

Freedom from AF/AT ≥30 s was recorded in 26% (14/54) of patients in SA and 28% (17/60) in the CA group following a single procedure and without AADs [OR 1.128, 95% CI (0.46–2.82), $P = 0.84$] (*Take home figure*, Middle panel)

One patient did not have ILR data due to non-compliance; we used their quarterly 12-lead ECGs to establish freedom from AF/AT. One patient died after SA, so they were excluded from these analyses.

Sensitivity analyses including a per-protocol and multiple imputation techniques for missing data did not change the results of the comparisons.

### Secondary endpoints

Single procedure clinical success was achieved in 66% (36/54) of patients in the SA arm compared with 77% (46/60) in the CA arm [OR 1.64, 95% CI (0.67–4.84), $P = 0.3$] (*Take home figure*, Middle panel). Of those that did not achieve clinical success, 18% (10/54) in the SA and 15% (9/60) in the CA arm, had redo CA procedures [OR 1.29, 95% CI (0.48–3.46), $P = 0.31$].

Procedure-related serious adverse events within 30 days of the intervention (*Table 3*) occurred in 15% (8/55) of patients in the SA arm compared with 10% (6/60) in the CA arm ($P = 0.46$). Over the 12-month follow-up period procedure-related serious adverse events (Supplementay material *Table A4*) were recorded in 18% (10/55) of participants after SA, compared with 15% (9/60) after CA arm ($P = 0.65$). Procedure-related adverse events rate over the 12-month follow-up period (Supplementary material *Table A5*) was greater in the SA than the CA arm: 40% (22/55) vs. 15% (9/60) [OR 3.78, 95% CI (1.55–9.21), $P = 0.003$]. One death in the SA arm occurred 3 weeks post-procedure due to sepsis complicated by multi-organ failure and bleeding oesophageal and gastric ulcers.

Improvements in patient-reported symptom and quality-of-life measures were seen from the first 3 months after ablation and sustained to the end of follow-up in both groups (*Figure 3*). However, the differences in mean EHRA, AFEQT, and EQ-5D-5L scores at 12 months were significantly worse for SA than CA: 0.916 ($P = 0.02$), -6.74 ($P = 0.05$), and -0.079 ($P = 0.02$), respectively (Supplementary material *Table A6*). Over the 12-month follow-up, SA was associated with significantly lower QALYs than CA (0.78 vs. 0.85, $P = 0.02$) and higher costs which translated to an incremental net benefit of £4918 (95% CI: £1101–8735) for CA vs. SA at a conservative cost-effectiveness threshold of £20 000 per QALY (Supplementary material *Table A6*).

# Discussion

This is the first RCT to compare thoracoscopic SA with CA as the index procedure in LSPAF patients with rigorous follow-up using continuous cardiac monitoring and comprehensive analysis of symptoms, quality of life, and cost-effectiveness. The main finding was that SA conferred no benefit over CA in terms of freedom from AF/AT, AF burden reduction or in procedure-related serious adverse events. Catheter ablation was associated with greater symptom and quality-of-life improvement measured by disease-specific (AFEQT, EHRA) and generic health outcomes measures (EQ-5D-5L), was less costly, and hence more cost-effective than SA.

The underlying substrate in paroxysmal AF responds well to PVI which can be achieved by CA with excellent results.[3] In contrast, the LSPAF substrate is more advanced due to complex neurohormonal remodelling resulting in LA dilation and myocardial fibrosis which renders this arrhythmia difficult to treat with CA.[3] Unsurprisingly, LSPAF is an area where there is a paucity of data and a genuine unmet need for optimal treatment.

Our study is unique as the role of thoracoscopic SA as an index intervention in LSPAF has not been previously investigated in an RCT. Current guidelines recommend SA as a potential therapeutic option for symptomatic AF when CA has failed (IIaB) or for symptomatic drug-refractory persistent or LSPAF (IIaC).[3]

**Table 1 Baseline characteristics of CASA-AF study participants**

| Characteristics | All ($n$ = 120) | CA ($n$ = 60) | SA ($n$ = 60) |
|---|---|---|---|
| Age (years), mean (SD) | 62.3 (9.6) | 60.8 (10.1) | 63.8 (8.9) |
| Male sex, *n* (%) | 89 (74.2) | 45 (75) | 44 (73.3) |
| BMI (kg/m$^2$), median (IQR) | 30.2 (27–32.8) | 30.6 (27.6–33.3) | 29.7 (26.1–32.8) |
| Townsend deprivation index, median (IQR) | -0.4 (-2.2–1.4) | -0.7 (-2.5–0.6) | -0.1 (-2–1.8) |
| IMD score, median (IQR) | 12.7 (7.7–22.3) | 11.1 (5.5–21.5) | 14 (8.7–22.6) |
| Ethnicity, *n* (%) | | | |
| White | 112 (93) | 57 (95) | 55 (92) |
| Asian | 1 (1) | 0 (0) | 1 (2) |
| Black[a] | 3 (3) | 1 (2) | 2 (3) |
| Middle-eastern | 1 (1) | 1 (2) | 0 (0) |
| Systolic blood pressure (mmHg), mean (SD) | 127.9 (16.7) | 126.6 (16.3) | 129.1 (17.2) |
| Diastolic blood pressure (mmHg), mean (SD) | 79.8 (12) | 81.5 (13.1) | 78 (10.6) |
| Ejection fraction (%), mean (SD) | 56.9 (8.9) | 55.2 (8.9) | 58.8 (8.7) |
| Left atrial diameter (mm), mean (SD) | 44.6 (5.9) | 44.6 (6) | 44.7 (5.8) |
| Diagnosis of persistent AF to procedure (months), median (IQR) | 22 (16–31) | 19.5 (15–29.2) | 25 (19–35.5) |
| Medical history, *n* (%) | | | |
| Hypertension | 56 (46.7) | 23 (38.3) | 33 (55) |
| Diabetes | 9 (7.5) | 4 (6.7) | 5 (8.3) |
| Coronary artery disease | 13 (10.8) | 7 (11.7) | 6 (10) |
| Stroke, TIA or thromboembolism | 5 (4.2) | 1 (1.7) | 4 (6.7) |
| $CHA_2DS_2VASc$ score, *n* (%) | | | |
| 0 | 34 (28.3) | 21 (35) | 13 (21.7) |
| 1 | 34 (28.3) | 18 (30) | 16 (26.7) |
| 2 | 27 (22.5) | 11 (18.3) | 16 (26.7) |
| ≥3 | 25 (20.8) | 10 (16.7) | 15 (25) |
| HASBLED score, *n* (%) | | | |
| 0 | 23 (19.2) | 12 (20) | 11 (8.3) |
| 1 | 49 (40.8) | 30 (50) | 19 (31.7) |
| 2 | 39 (32.5) | 15 (25) | 24 (40) |
| ≥3 | 9 (7.5) | 3 (5) | 6 (10) |

AF, atrial fibrillation; BMI, body mass index; CA, catheter ablation; $CHA_2DS_2VASc$, congestive heart failure, high blood pressure, Age 75, Diabetes, previous Stroke or clot, Vascular disease, Age 65–74, Sex; HASBLED, hypertension; Abnormal liver/renal function, Stroke history, Bleeding history or predisposition, Labile INR (international normalized ratio), Elderly, Drug/alcohol usage; IMD, indices of multiple deprivation; IQR, interquartile range; SA, surgical ablation; SD, standard deviation; TIA, transient ischaemic attack.
[a]Including African-Caribbean.

**Table 2 Comparison of procedural characteristics in patients who had catheter ablation ($n$ = 60) or surgical ablation ($n$ = 49)**

| | CA, $N$ = 60 | SA, $N$ = 49* | Mann–Whitney test ($P$-value) |
|---|---|---|---|
| Total procedure time (min) | 219 (191.5–261.2) | 265 (220–310) | 0.002 |
| Fluoroscopy time (min) | 17 (11–24) | — | — |
| Total ablation time (min) | 67 (53–79) | 15 (13–22) | <0.001 |
| Radiation dose (cGycm$^2$) | 1121 (594.5–1844.5) | — | — |
| Length of stay (days) | 2 (2–2) | 6 (5–7) | <0.001 |

Data are presented as median (IQR).
CA, catheter ablation; IQR, interquartile range; SA, surgical ablation.
*Data from six patients who crossed over from SA to CA group are not included in this table.

**Table 3 Procedure-related serious adverse events within 30 days of the ablation**

| Serious adverse event | Catheter ablation ($n = 60$) | Surgical ablation ($n = 55$) |
|---|---|---|
| Anaphylactic shock | | 1 (2) |
| Chest infection | 4 (7) | 2 (4) |
| Congestive heart failure | 1 (2) | 1 (2) |
| Death | | 1 (2) |
| Gastric ileus | 1 (2) | |
| Hemi-diaphragmatic paralysis | | 1 (2) |
| Hemi-diaphragmatic paresis | | 1 (2) |
| Infection | 1 (2) | |
| Pacemaker insertion | | 1 (2) |
| Pain at wound site | | 1 (2) |
| Pleural effusion | | 1 (2) |
| Pseudo-aneurysm of femoral artery | 1 (2) | |

Data are presented as total number of patients with the event, *n* (%). There were 8 events in the CA arm (6 patients) and 10 in the SA arm (8 patients).

Early standalone thoracoscopic SA studies showed promising arrhythmia-free outcomes with subsequent RCTs supporting this finding albeit in mixed AF populations.[17,20–22] The FAST study, reported significantly greater AF-free survival at 12 months without AADs in the SA group compared with CA (65.6% vs. 36.5%; $P = 0.002$), although the adverse event rate was considerably higher (34% vs. 16%).[19] However, two-thirds of patients in this study had prior unsuccessful CA and 67% had paroxysmal AF. Further limitations of this study include lesion set heterogeneity, inconsistent verification of conduction block and intermittent 7-day ambulatory ECG monitoring. Similarly, Pokushalov *et al.*[21] undertook an RCT with 64 patients who had previously failed initial CA. This was a mixed AF population and at 12 months, SA was associated with better AF-free survival compared with CA (81% vs. 47%; $P = 0.004$) based on continuous cardiac monitoring. Adiyaman *et al.*[22] reported a small non-inferiority RCT in predominantly paroxysmal AF (74%) patients with continuous cardiac monitoring over 2 years of follow-up. SA was less effective in this study as 29% of patients were free from arrhythmia compared with 56% in CA group (log-rank $P = 0.059$), and 20% of SA patients had a major complication with none in the CA group.

Our earlier non-randomized pilot study focused on finding the optimal index intervention to treat LSPAF. The results suggested SA may be superior to CA at 1 year as 73% vs. 32% of patients were free from AF/AT, using intermittent 7-day ambulatory ECG monitoring.[10] We subsequently designed the CASA-AF RCT to definitively answer which technique was more effective as a first-line invasive strategy in LSPAF. We chose continuous cardiac monitoring to provide a comprehensive assessment of heart rhythm.[14] In addition, we examined the effects of the two treatments on symptoms, quality of life, and health economic outcomes.

All patients had *de novo* LSPAF with a median time from persistent AF diagnosis to ablation of just under 2 years. The CA freedom from AF/AT outcome in this trial is in line with previous reports.[9] However, the SA outcomes were poorer than in previous studies, which most probably relates to a combination of baseline study population characteristics and intensity of follow-up with ILR in our study.[22] Other fundamental differences are that previous studies included a high proportion of patients with paroxysmal AF who are known to respond well to treatment, and secondly, SA was conducted following initial failed CA. In essence, these were reverse staged hybrid procedures which extended or completed previous lesion sets, and the reported efficacy of SA in these studies was in fact the combined efficacy of two ablation procedures. Furthermore, we know that the use of continuous cardiac monitoring with ILR is more representative of the true rate of AF recurrence than intermittent monitoring methods, especially in asymptomatic patients.[23] In fact, intermittent monitoring may overestimate the success rate of ablation procedures compared with continuous monitoring.[12,13] Finally, the evolution of CA techniques, including contact force catheters, high-density multielectrode mapping, and lesion prediction algorithms, has provided incremental benefits in durability of lesion sets thereby reducing the potential benefit of application of RF under direct vision to the myocardial tissues as performed in SA.[24–26]

## Clinical outcomes

The primary endpoint we chose was based on the definition of AF ablation success from the 2012/2017 consensus document on AF ablation.[27] From the clinical perspective, it is extremely stringent as patients may derive significant symptomatic relief from AF burden reduction, be deemed a clinical success, but fail the study endpoint. The clinical improvement, measured in this study by ≥75% reduction of AF/AT burden, with just one procedure and without AADs, was very encouraging for both procedures at around 70%. Given that these patients were highly symptomatic and in continuous AF for 2 years, this reduction in AF burden provided significant clinical benefit as demonstrated by the improvement from baseline in quality-of-life measures. The AF burden reduction may be a better indicator of positive clinical outcomes and therefore the use of continuous cardiac monitoring to accurately assess the burden of arrhythmia pre- and post-ablation is desirable.

## Safety outcomes

In comparison to other trials, our procedure-related complication rates were low.[20–22] However, one death occurred following SA and although there were no differences in serious adverse events within 30 days or 1 year between the groups, the overall adverse events rates during the 12-month follow-up were higher in the SA arm (Supplementary material *Table A5*).

## Quality of life and health economics outcomes

This study is the first to report change in symptoms, change in quality of life, and health economic outcomes for SA and CA. Our quality-of-life assessment was rigorous using three validated tools including AF specific and generic measures. We found consistent improvements in all measures from baseline to 12 months in both groups but the mean difference in scores at 12 months for all three measures

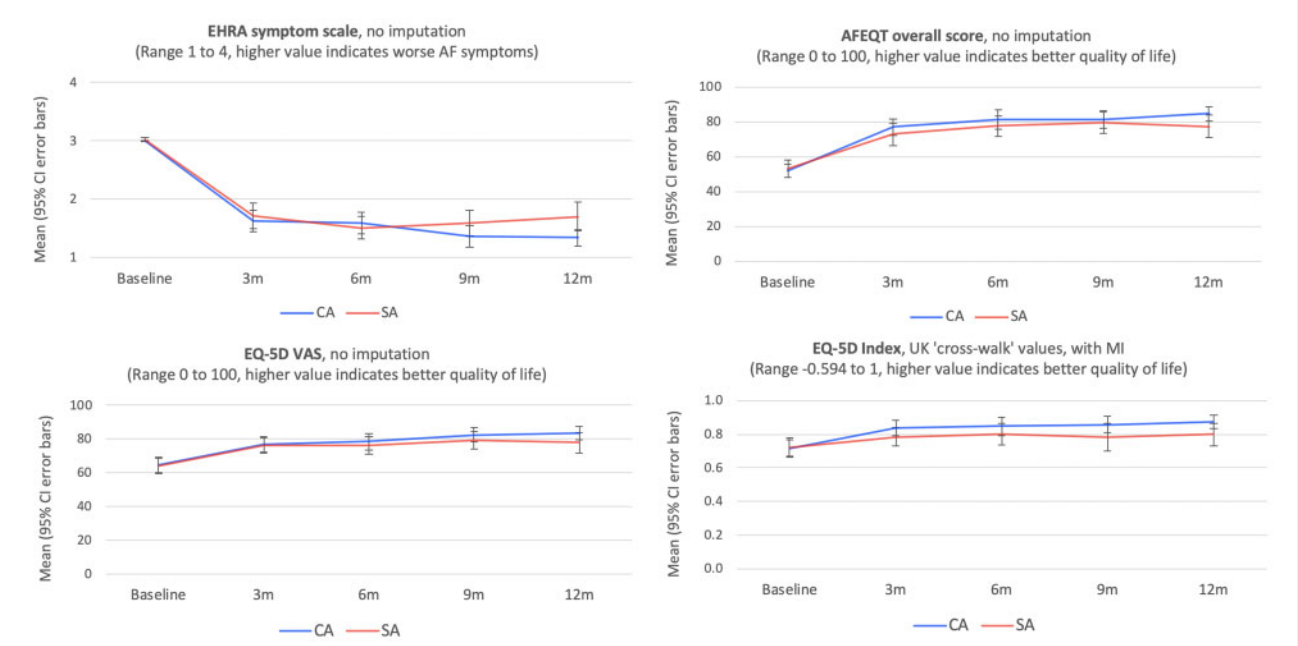



**Figure 3** Changes in symptoms and health-related quality of life over time. AFEQT, AF Effect on QualiTy-of-life; CA, catheter ablation; EHRA, European Heart Rhythm Association score for AF; EQ-5D-5L VAS, quality of life questionnaire's visual analogue scales; SA, surgical ablation.

were in favour of CA. This benefit in quality of life for CA may reflect the relatively more invasive nature of SA and the higher rate of late complications. Furthermore, over the 12 months of follow-up, CA was associated with a modest but statistically significant gain of 0.069 QALYs and NHS cost saving of £3534 per patient compared with SA. This translates to an incremental net benefit of £4918 for CA vs. SA at a conservative cost-effectiveness threshold of £20 000 per QALY. The estimated probability that CA was less costly and hence more cost-effective than SA was 98.9%.

## Limitations

The main limitation of this study is that the interventions were performed in four highly specialized centres in the UK, which may have an impact on the generalizability of results. Secondly, the study was not double-blinded, as it was not possible given the very different access sites, invasiveness and operators required for the two procedures. Finally, thoracoscopic AF ablation which includes LAA exclusion may confer benefits in terms of reduced stroke and bleeding risks, which was not specifically addressed here.

# Conclusion

In this multi-centre RCT, we found that thoracoscopic SA is not superior to CA in establishing and maintaining normal SR in patients with LSPAF. Catheter ablation was associated with greater improvements in symptoms and quality of life and was more cost-effective than SA. We therefore recommend CA as the first-line interventional therapy for patients' symptomatic LSPAF refractory to drug therapy.

# Supplementary material

Supplementary material is available at *European Heart Journal* online.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