Clinical Commissioning Policy Proposition
Catheter ablation for paroxysmal and persistent atrial fibrillation 1903

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether the clinical commissioning policy will be funded will be made by NHS England following a decision by the Clinical Priorities Advisory Group.

Version control

Version number	Summary of amends	Initials	Date
V1.3	Incorporate Post Panel Comments	SA	16th October 2019
V1.4	Incorporate Panel gateway 2 comments	SA	12th December 2019
V1.5	Post stakeholder testing	SA	4th June 2020

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Commissioning Position

Summary

A final decision as to whether catheter ablation for paroxysmal and persistent atrial fibrillation will be routinely commissioned will made by NHS England following a recommendation from the Clinical Priorities Advisory Group. The proposal is: catheter ablation is recommended to be available as a treatment option through routine commissioning for paroxysmal and persistent atrial fibrillation within the criteria set out in this document.

Executive Summary

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain language summary

About atrial fibrillation

Atrial fibrillation (AF) is the most common arrhythmia (heart rhythm disorder). Some people with AF may have no symptoms at all whilst other people can have symptoms that come and go and yet others have constant symptoms. Symptoms of AF include shortness of breath, chest pain, feeling dizzy or a feeling of the heart beating rapidly (known as palpitations) and lethargy. AF significantly increases the risk of a stroke. AF-related strokes are more disabling and can prove fatal, more so than any other type of stroke. A blood clot can form in the heart when the heart is not beating in normal regular rhythm. If a clot breaks away from the heart and travels to the brain this may cause a stroke. AF can also cause heart failure in some people if their heart rate remains too fast for a long time.

About current treatments

People with AF can be offered a range of medicines, known as anti-arrhythmic drugs, to try to restore and maintain a normal heart rhythm or to slow the heart rate down. These medicines may not always be successful or tolerated by people. In such cases, a procedure known as catheter ablation can be considered.

Ablation is the targeted destruction of the tissue within the heart that causes the arrhythmia (heart rhythm disorder). Ablation procedures are carried out in people that have non-permanent atrial fibrillation when medicines are not working or tolerated. Percutaneous left atrial catheter ablation is an ablation procedure that is carried out under sedation or a general anaesthetic. A small skin cut

is made in the groin and thin tubes, known as catheters, are inserted into the femoral vein. These catheters are advanced into the upper chambers, the atria, of the heart under X-ray guidance. Certain parts of the left atrium are targeted with an energy source to isolate the areas that cause AF.

About proposed treatments

Catheter ablation is currently available on the NHS and there is evidence that supports its use in reducing the symptoms of AF. It is not clear how many times this procedure should be repeated if the symptoms return.

What we have decided

NHS England has carefully reviewed the evidence to treat paroxysmal and persistent atrial fibrillation with catheter ablation. We have concluded that there is enough evidence to continue to make the treatment available at this time.

Committee discussion

The Clinical Priorities Advisory Group are asked to consider the evidence and the policy proposition. See the committee papers (link) for full details of the evidence.

The condition

Atrial fibrillation (AF) is the most common cardiac arrhythmia. It has an estimated prevalence of 3% in persons over 20 years old and approximately 1.4 million people in England have AF (Adderley et al 2019). AF is caused by uncoordinated electrical activity, often arising from specific arrhythmogenic foci, within the walls of the atria and prevents effective atrial contraction. Uncoordinated electrical activity within the atria causes the irregular, and sometimes rapid, contraction of the ventricles that result in a reduction in cardiac output.

People with AF may be asymptomatic or have a range of symptoms, including: palpitations, dizziness, shortness of breath, chest pain, reduced exercise capacity and significantly impaired quality of life. The presence of AF also increases the risk of stroke. AF can be classified according to its duration:

- paroxysmal AF: starts and stops spontaneously, in most cases within 48 hours
- persistent AF: starts spontaneously but lasts longer than 7 days or is terminated by cardioversion
- permanent AF

Current treatments

First-line treatment for AF is pharmacological using anti-arrhythmic medications. These medications are classified according to their effect on heart rhythm (rhythm control) or heart rate (rate control). In an emergency setting, people with AF may require electrical cardioversion to restore a normal heart rhythm but this is not related to the long-term management of AF.

Whilst anti-arrhythmic medications can be used successfully, they are not always tolerated or effective and ablation procedures can be considered in certain situations. Percutaneous left atrial catheter ablation is a minimally invasive procedure that can be offered to people with symptomatic paroxysmal or persistent atrial fibrillation as an alternative to anti-arrhythmic medications. It is aimed at targeting and disrupting the conduction of abnormal electrical activity throughout the atria. Catheter ablation is not recommended as a treatment for patients with permanent AF.

The procedure is performed with sedation or under general anaesthesia. A small skin incision is made in the groin and catheters and electrodes are inserted into the femoral vein. The catheters and electrodes are moved towards the heart under fluoroscopic guidance and enter the right

atrium and puncture the inter-atrial septum to enter the left atrium. Areas within the left atrium that are likely to trigger the initiation of AF are identified and targeted with an energy source to cause localised irreversible damage to prevent and stop the initiation and therefore the symptoms of AF. The duration of the procedure is usually between 2 and 4 hours.

Alternative forms of ablation include surgical ablation. This is a similar procedure to catheter ablation but is performed via a mini-thoracotomy or thoracoscopic procedure and requires the use of a general anaesthetic.

Catheter ablation is an effective treatment for symptomatic AF in suitable people. In people with paroxysmal AF, approximately 80% obtain symptomatic improvement after ablation, the majority of whom will be able to discontinue anti-arrhythmic medications. In people with persistent AF, approximately 50% will obtain symptomatic improvement in the short- to medium-term. Between 33% and 50% of all people undergoing catheter ablation for AF will require at least one further procedure, however, there is uncertainty around the additional benefit of multiple repeat procedures.

The National Institute for Health and Care Excellence (NICE) has published guidance on the management of AF (CG180, NICE 2015) with recommendations on the usage of catheter ablation. NICE also has Interventional Procedure Guidance (IPG) on the use of two forms of catheter ablation (NICE IPG 427 and NICE IPG 563). NHS England has a Service Specification (A09/S/b) on electrophysiology and ablation services which includes AF ablation.

Proposed treatments

This policy updates the previous policy with more recent evidence and sets out the criteria for the use of percutaneous left atrial catheter ablation for patients with symptomatic paroxysmal or persistent AF.

Epidemiology and Needs Assessment

AF is an increasingly common arrythmia but is frequently asymptomatic. So, it is difficult to identify, suggesting prevalence is under-estimated. The cardiac dysfunction in AF gives rise to symptoms like breathlessness and palpitations. The risk of stroke among people with AF is also elevated, because of an increased predisposition to clots in the left atrium which can then embolise in the cerebrovascular circulation. The risk of stroke among people with AF varies depending on other risk factors. Estimating the risk of stroke is an important part of individual patient management as it determines the potential benefits anticoagulation.

Current prevalence estimates of AF for England are developed from primary care registers. These registers do not unfortunately identify the types of atrial fibrillation, or the degree of symptom control. So, it gives little information about the numbers of individuals meeting definitions of persistent or paroxysmal arrythmia. No epidemiological estimates have been identified for the proportion of individuals on primary care registers that meet the proposed policy inclusion criteria.

One approach to filling this gap in knowledge about the populations potentially able to benefit from catheter ablation is to examine patterns of service use. In practice, population intervention rates vary enormously between CCG populations, from barely detectable (<6 per million crude population) to more than 200/million (https://nicor6.nicor.org.uk/CRM/device.nsf/AF). Further, the number of cases of AF ablation have grown steadily over the last decade, suggesting that potential demand for the procedure is far from fully met. Ablation rates therefore seem more likely to reflect service capacity than population need. It is not obvious therefore how establishing an estimate reliable enough for planning can be developed without new data collection.

Data from the 2016/17 National Audit of Cardiac Rhythm management Devices and Ablation shows that approximately 9,000 ablations are performed for AF each year in England and Wales. This figure is growing by approximately 6% per year. Data comparing the UK with Western Europe

show that the UK performs less than half the number of ablations per million population compared to these countries, therefore, it is anticipated that the growth in ablation procedures will continue.

Evidence summary

NHS England has concluded that there is sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication.

Summary of Results: Paroxysmal Atrial Fibrillation

One Health Technology Appraisal (HTA), one systematic review (SR) and three randomised controlled trials (RCTs) fulfilling the PICO criteria for clinical effectiveness and safety were identified for inclusion. One Health Technology Appraisal (HTA) (Skelly et al 2015) and three more recently published randomised controlled trials (RCTs) (Marrouche et al 2018, Nielsen et al 2017, and Bertaglia et al 2017) were found assessing the effectiveness of catheter ablation compared with medical treatment.

One systematic review (SR) (Phan et al 2016) and one more recently published RCT (Jan et al 2018) were found comparing catheter ablation with surgical ablation. One UK based study of the cost effectiveness of catheter ablation in comparison to medical therapy (Reynold et al 2014) was found. No studies eligible for inclusion were found investigating the cost effectiveness of catheter ablation versus surgical ablation.

1. Clinical Effectiveness

Catheter ablation (CA) versus medical therapy (MT) (rhythm and/or rate control) in the treatment of paroxysmal AF

- **All-cause mortality:** Skelly et al (2015) reported no difference in all-cause mortality between the intervention groups within 30 days based on pooled results from three RCTs (n=570) [CA 0% to 0.7% versus medical therapy 0%]; however, no test of statistical significance was reported. There was also no difference between the two study arms at up to 12 months [three RCTs (n=333) CA 0% to 1% versus MT 0% to 3.6%)] and at 24 months [two RCTs (n=408) CA 1.4% versus MT 2.8%] p value not reported for both.
- **Freedom from arrhythmia recurrence:** The HTA by Skelly et al (2015) reported a statistically significant difference in favour of CA for freedom from arrhythmia recurrence at 12 months based on pooled results from four RCTs [CA n=226/286 (79%) versus MT n=64/245 (26.1%); risk ratio (RR) 3.06 (95% CI 2.35 to 3.90); p<0.05]. They also report results for 24 to 48 months based on three RCTs [CA n=226/311 (72.6%) versus MT n=178/308 (57.8%); RR 1.24 (95% CI 1.11 to 1.47) in favour of CA; p<0.05]. Freedom from any AF was also reported by Nielsen et al (2017) after a five-year follow-up [CA n=126/146 (86%) versus MT n=105/148 (71%); RR=0.82 (95% CI 0.73 to 0.93) in favour of CA, p=0.001] and symptomatic AF; [CA n=137/146 (94%) versus MT n=126/148 (85%); RR 0.91 (95% CI 0.84 to 0.98); p=0.015].
- **Freedom for AF burden:** Neilson et al (2017) (n=294) reported a significantly lower AF burden in the CA group compared with medical therapy (anti-arrhythmic drugs) at five-year follow-up. 85% and 95% percentiles[1] for the CA group were 0% and 56% respectively versus 7% and 97% respectively for the antiarrhythmic drugs (AADs) group; p=0.003. Corresponding percentiles for symptomatic AF were also significantly lower for CA: 0%, 7% (CA) versus 0%, 11% (AADs); p=0.02.
- **Maintenance of sinus rhythm:** Bertaglia et al (2017) (n=92) did not find any difference in the maintenance of sinus rhythm after a 12-year follow-up between patients who had undergone CA and those on AADs [n=22/42 (51.2%) versus n=22/50 (44%) respectively; p=0.402].
- **Improvement in LVEF (patients with HF):** Marrouche et al (2018) reported on the median LVEF changes in paroxysmal AF (PAF) patients with HF (LVEF of 35% or less). At 60 months

[1] The 95th percentile implies that 95% of the time, the burden is below this amount: so, the remaining 5% of the time, the burden is above that amount and 85th percentile implies that 85% of the time, the burden is below this amount: so, the remaining 15% of the time, the burden is above that amount.

median LVEF increases were: CA (n=14) 7% [interquartile range (IQR) 5% to 16%) versus MT (n=11) 8% (IQR -1% to 23%]; however, the difference was not statistically significant (p=0.81).

- **Cardiac hospitalisation or re-admission:** Skelly et al (2015) reported that, at 12 to 24 months following CA, patients had fewer cardiac hospitalisations or re-admissions than those on MT based on results from two RCTs. One RCT (n=67) reported at 12 months CA 9.4% versus MT 54.3% and the other (n=294) at 24 months CA 0% versus MT 1.4%. However, results were not pooled and no tests of statistical significance were reported.
- **Repeat ablation rates:** Skelly et al (2015) reported that based on data from three RCTs (n=184), the frequency of repeat ablation following RFA ranged from 0% to 43% within 12 months of CA. The results were not pooled. They report that over follow-up periods of longer than 12 months to 48 months, frequency of repeat ablation varied across four trials including 619 patients, this ranged from 12.5% to 49.2% with a pooled risk of 24.2% (95% CI 12.6 to 41.5).
- **Composite of death or hospitalisation for worsening heart failure:** Marrouche et al (2018) (n=118[2]) reported that, at a median follow up of 37.6 months, composite of death or hospitalisation for worsening heart failure (HF) was numerically but not statistically significantly in favour of CA [CA n=17/54 (31.5%) versus MT n=34/64 (53.1%); hazard ratio (HR) 0.60 (95% CI 0.34 to 1.08)], no p value was reported.
- **Quality of life:** Nielsen et al (2017) (n=294) reported no difference in quality of life scores after a five-year follow-up between the CA and MT study groups; SF-36[3] physical component scores were: CA 51 (interquartile range (IQR) 44 to 56) versus MT 52 (IQR 46 to 55), p=0.88; SF-36 mental component scores were CA 54 (IQR 47 to 57) versus MT 54 (IQR 49 to 56), p=0.94; there was no difference between groups in each of the eight scales from the SF-36 questionnaire (p>0.15 for all); no further details were provided. For the Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA) score[4], no difference was observed between groups in the ASTA index (mean 0.56± SD 0.71 (CA) vs 0.61±SD 0.63 (MT), p=0.18).
- Skelly et al (2015) reported no statistical differences between treatment groups for the SF-36 MCS scores at 12 months based on two RCTs (n=406); this held true whether the analysis was done using the difference in mean scores at follow-up 2.26 (95% CI -2.12 to 7.40) or using the difference in change from baseline scores 1.88 (95% CI -0.47 to 4.50). For PCS, catheter ablation was favoured over medical therapy when the pooled estimate was calculated using differences in mean follow-up scores (overall effect 2.85; 95% CI 0.93 to 4.82), however when the analysis was based on the change from baseline the effect was no longer statistically significant (overall effect 2.88; 95% CI 0.18 to 5.25). No p values were reported.
- The authors also reported no difference in both quality of life measures at 24 months for mean MCS scores [one RCT (n=294), CA: 51.1 ± SD 9.2 versus MT 50.9 ± SD 8.0] and mean PCS scores [one RCT (n=294), CA: 50.0 ± SD 8.8 versus MT 47.9 ± SD 8.9] and 48 months for mean MCS scores [one RCT (n=198) RFA: 52.9 ± SD 9 versus MT 51.9 ± SD 9] and mean PCS scores [one RCT (n=198) RFA: 52.3 ± SD 9 versus MT 52.6 ± SD 8]. No other details were reported.

Catheter ablation (CA) versus surgical ablation (SA) in the treatment of paroxysmal AF

- **Freedom from AF or any arrhythmia:** The RCT by Jan et al (2018) reported on the incidence of AF or any arrhythmia at mean follow-up of 30.5 months; [SA n=8/24 (33.4%) versus CA n=17/26 (65.4%); odds ratio (OR) 3.78 (95% CI 1.17 to 12.19); p=0.048]. This is in line with results from the SR by Phan et al (2016) which reported that surgical ablation is better at preventing AF (or any arrhythmia) than CA at up to 12 months follow-up; [SA (n=133) 82% versus CA (n=136) 62.5%; RR 1.35 (95% CI 1.01 to 1.79); p=0.04].

[2] Patients with paroxysmal AF.
[3] The SF-36 questionnaire is a 36-item, patient-reported survey of patient health, it consists of eight scaled scores, which are the weighted sums of the questions in their section.
[4] The ASTA questionnaire scores eight symptoms of arrhythmia.

- **Re-intervention rates:** Jan et al (2018) (n=50) reported re-intervention rates at mean follow-up of 30.5 months in SA versus CA as n=4/24 (16.7%) versus n=9/26 (34.6%) respectively; however, no tests of statistical significance were reported.

2. Safety

Catheter ablation versus medical therapy (rhythm and/or rate control) in the treatment of paroxysmal AF

- **Stroke occurrence:** Skelly et al (2015) reported no difference in stroke occurrence within 30 days based on pooled results from three RCTs (n=481) [CA 0% to 0.7% versus medical therapy 0%; no test of statistical significance reported] and beyond 30 days based on two RCTs [CA n=0/98 (0%) versus MT n=0/96 (0%), p=NS]. No transient ischaemic attacks (TIAs) were reported at 12 or 48 months; however, one RCT (n=294) reported 0.7% in both the CA (1/146) and MT (1/148) groups. No p values were reported.

- **Major bleeding:** Skelly et al (2015) reported on major bleeding at one month from one RCT (n=67) although no tests of statistical significance was reported; [2/32 (6.3%) CA versus 1/35 (1.9%) MT].

- **Other complications:** Skelly et al (2015) reported on other complications attributable to CA such as cardiac tamponade within 24 months (n=512) [pooled risk from four RCTs of 1.7% (95% CI 0.8 to 3.6)], pericardial effusion within 48 months (n=519) [pooled risk from three RCTs 0.6% (95% CI 0.2 to 1.8)], pulmonary vein stenosis at 12 months [pooled risk based on two studies (n=122) was 1.6% (95% CI 0.4 to 6.3) and pooled risk based on two studies (n=283) with 24-month follow-up was 0.7% (95% CI 0.2 to 2.8). Other ablation-related harms reported in the HTA included perforation at the trans-septal puncture (one RCT n=194, 0.5%), myopericarditis (two RCTs n=333, 0% to 1.7%) and haematoma at catheter insertion site (2 RCTs n=276, 1.6% to 2.2%). The authors also reported drug intolerance requiring discontinuation based on one RCT (n=99) in 23.2% of patients in the MT arm and 0% in the CA arm.

Catheter ablation versus surgical ablation (SA) in the treatment of paroxysmal AF

- **Peri-procedural complication rates:** The RCT by Jan et al (2018) (n=50) reported peri-procedural complication rates of CA n=3/24 (12.5%) CA versus SA n=0/26 (0%) but no test of statistical significance was reported.

3. Cost effectiveness

Catheter ablation versus medical therapy (rhythm and/or rate control)

- Reynolds et al (2014) reported an ICER of £21,957 per QALY gained, with the use of cryoballoon ablation versus antiarrhythmic drugs (AADs). The authors concluded that, beyond a threshold of £22,000 per QALY gained, ablation becomes the more cost-effective intervention, with probabilities of 86% and 97.2% of being cost effective at thresholds of £30,000 and £40,000 per QALY gained, respectively.

4. Conclusion

One Health Technology Appraisal (HTA), one systematic review (SR) and three randomised controlled trials (RCTs) fulfilling the PICO criteria for clinical effectiveness and safety were identified for inclusion.

There was moderate quality evidence for the effectiveness of CA compared with medical therapy, in patients with paroxysmal AF and very limited data compared with surgical ablation. Compared with medical therapy, CA appeared to improve AF freedom, which could be sustained at five years. However, there were no benefits in terms of all-cause mortality (beyond 30 days), quality of life or LVEF (in PAF patients with HF). These results should be interpreted with caution because of the limitations of the data included in the HTA by Skelly et al (2015). There was substantial

heterogeneity across included studies, which were mostly small, and a formal assessment of publication bias was not conducted. There was wide variability across studies and only one trial was considered to be good quality. Other important limitations of the evidence base include unclear randomisation concealment and lack of assessor blinding. These factors make it difficult to draw firm conclusions from the results of this review. Results from the RCT by Marrouche et al (2018) were based on a small number of patients with PAF in the study (n=118). In addition, physicians were not blinded in any of the studies although the assessors were mostly blinded. The long-term follow-up studies also involved significant loss of patients to follow up and crossover from medical therapy to ablation.

Surgical ablation appears to be more effective at maintaining AF freedom and reducing recurrent of any form of atrial arrhythmias included symptomatic AF. However, peri-procedural complication rates appear higher with surgical ablation. These results should be interpreted with caution because they are based on limited data from one indirect comparison and two very small direct comparison studies included in one of the systematic reviews identified.

There was moderate quality evidence for the cost effectiveness of cryoballoon ablation compared with medical therapy, with a UK NHS perspective. Cryoballoon ablation was cost effective beyond a threshold of £22,000 per QALY gained. This result should be treated with caution because the RCT data used for the efficacy assessment in the calculation may have exaggerated the benefit of cryoballoon ablation. The study was also funded by the equipment manufacturer.

The published data on the effectiveness, safety and cost effectiveness of CA in paroxysmal AF, especially long-term data are fraught with limitations which make any conclusive interpretation difficult. No conclusions regarding which patients may benefit most, or regarding which patients may not benefit from CA, are possible with current evidence. Further long-term studies are required to establish whether preservation of sinus rhythm by CA or AADs therapy in AF has any impact on long-term outcome measured as survival and freedom from stroke and heart failure.

Summary of Results: Persistent Atrial Fibrillation

Two systematic reviews (SR) and one recently published randomised controlled trial (RCT), fulfilling the PICO criteria for clinical effectiveness and safety, were identified for inclusion. One systematic review (Berger et al 2019) compared catheter ablation (CA) with minimally invasive surgical ablation in patients with AF. The second systematic review (Chen et al 2018) compared CA with medical therapy (rhythm and/or rate control) in AF patients, whilst the RCT (Marrouche et al 2018), published after the search date of the systematic review, compared CA with medical therapy in AF patients with heart failure (HF).

One systematic review (Neyt et al 2013) of published cost effectiveness studies fulfilling the PICO criteria for cost effectiveness was found.

1. Clinical effectiveness

Catheter ablation versus medical therapy (rhythm and/or rate control)

- **All-cause mortality:** Three out of eight RCTs in one SR (n=559). No significant difference between CA and medical therapy (risk ratio[5] (RR) 0.47, [95%CI 0.22 to 1.02]; p=0.05) (Chen et al 2018).
- **AF Freedom rates:** Three out of eight RCTs (n=262) in one SR (Chen et al 2018). Pooled results found a significant improvement after CA compared with medical therapy (rhythm control) (RR 2.08, [95%CI 1.67 to 2.58]; p<0.00001). Pooled results, from another three out of eight RCTs included in Chen et al (2018) with 338 patients (mean follow-up six to 24 months) who were completely off anti-arrhythmic drugs (AADs) after CA, also showed a significant benefit in favour of CA (RR 1.82, [95%CI 1.33 to 2.49]; p=0.0002).

[5] Risk ratio or relative risk is the ratio of the probability of an outcome in an exposed group to the probability of an outcome in an unexposed group.

- **Need for cardioversion:** Three out of eight RCTs (n=394) in one SR (Chen et al 2018) reported rates of p cardioversion after the blanking period[6]. Pooled results showed that, compared to AADs, CA significantly reduced the number of participants needing cardioversion (RR 0.59, [95%CI 0.46 to 0.76]; p < 0.0001). Number needed to treat (NNT) with CA to prevent one case of cardioversion was 4.2.
- **Hospitalisation:** Two out of eight RCTs (n=349) in one SR (Chen et al 2018), showed a significant reduction in hospitalisation after CA compared with AADs (RR 0.54, [95%CI 0.39 to 0.74]; p=0.0002). NNT with CA to prevent one hospitalisation was 6.7.
- **Improvement in LVEF:** One RCT of HF patients with persistent AF (n=63); four out of eight RCTs in one SR (n=205). At 60 months, median left ventricular ejection fraction (LVEF) increased by 10% (interquartile range (IQR) 1 to 20) in 37 HF patients with persistent AF after CA versus -2.5% (IQR -7 to 5) in 26 patients on medical therapy; p=0.004 (Marrouche et al 2018). Pooled data from 4 RCTs (n=205) showed a significant increase in LVEF in patients treated with CA compared with medical therapy (mean difference (MD) 7.72, [95%CI 4.78 to 10.67]; p< 0.00001) (Chen et al 2018).
- **Composite of death or hospitalisation for worsening HF:** 1 RCT (n=245). At a median follow up of 37.6 months, the outcome was reported in 34/125 (27.2%) patients after CA versus 48/120 (40.0%) after medical therapy (hazard ratio (HR) 0.64 [95% CI 0.41 to 0.99], p value not reported) (Marrouche et al 2018).
- **Six-minute walk distance (6MWD):** Three out of eight RCTs in one SR (n=150) found no significant difference between CA and medical rate control (MD = 19.17, [95%CI −11.43 to 49.76]; p= 0.22) (Chen et al 2018).
- **Minnesota Living with Heart Failure Questionnaire (MLHFQ):** Three out of eight RCTs in one SR (n=140). A pooled analysis detected a significant reduction in MLHFQ score, indicating improved quality of life after CA versus medical rate control (MD 11.13, [95% CI 2.52 to 19.75]; p=0.01) (Chen et al 2018).

Catheter ablation versus minimally invasive surgical ablation

- **Freedom from AF:** Berger et al (2019) reported rate of AF freedom at 12 months after surgical ablation (SA) versus CA, based on two direct comparison RCTs (n= 67). These studies showed numerically but not statistically significantly higher AF freedom after SA versus CA (odds ratio (OR) 2.58, [95%CI 0.83 to 8.03], p value not reported).
- Berger et al (2019) also conducted an indirect comparison between CA and SA with and without AADs. AF freedom was higher after SA than after CA. This effect was further enhanced when AADs use was permitted during follow-up. In 7,502 CA patients from 41 studies versus 339 SA (5 studies), without AADs, 51% [95% CI 46 to 56%] CA patients versus 69% [95% CI 64 to 74%] SA patients were free from AF at 12 months; p value not reported. AF freedom rates on AADs were higher with both treatments. In 3,133 CA patients (29 studies) versus 196 SA patients (3 studies) 58% [95% CI 54 to 63%] of CA patients versus 71% [95% CI 64 to 74%] of SA patients were free from AF at 12 months; p value not reported.

2. Safety

Catheter ablation versus medical therapy (rhythm and/or rate control)

- **Ablation or drug-related complication rates:** Eight RCTs in one SR (n=809) (Chen et al 2018). Pooled results from four (n=604) out of eight RCTs showed no significant difference between CA and medical rhythm control with AADs (RR 1.95, [95%CI 0.52 to 7.25]; p=0.32).

Catheter ablation versus minimally invasive surgical ablation

[6] In the period immediately after AF ablation, early recurrences of atrial arrhythmias (ERAA) are common and may not necessarily imply long-term ablation failure. Therefore, guidelines recommended implementation of a “blanking period” post-ablation during which AF or OAT recurrences need not be counted against long term ablation success.

- **Overall death and procedure-related death**: One SR reported no difference between CA and surgical ablation (SA) in both outcomes. After CA, mortality was 1.1% (38/3264) and procedure-related death 0.1% (3/3052); after SA, the outcomes were 1.1% (5/464) and 0% (o/464) respectively (Berger et al 2019).
- **Bleeding:** Combined major and minor bleeding rates were 7.7% (21/272) and 1.7% (124/7515) in the CA and SA groups respectively (Berger et al 2019).
- **Other adverse events:** Number of RCTs and patients evaluated were not specifically reported. Generally, adverse events after CA were infrequent. The commonest complications were any bleeding (1.7%), pericarditis (1.4% - 54/3981) and pacemaker implantation (0.9% - 3/345); thromboembolic events occurred in 0.7% (53/7169) of patients. After SA, pneumothorax occurred in 6.1% (31/509) of patients, 2.7% (8/301) required pacemaker implantation, 1.6% (8/489) were converted to sternotomy and thromboembolic events occurred in 1.4% (8/557). Overall, irreversible adverse events occurred more frequently after SA than after CA (Berger et al 2019).

3. Cost effectiveness

Catheter ablation versus medical therapy (AADs or rate control)

- One SR of health economic studies (Neyt et al 2013) reported data from two studies of persistent AF patients. For first line ablation compared with second line rate control, reported ICERs depended on patients' ages and $CHADS_2$ scores and were between $60,804 USD (£46,837)/QALY (age 65 years; $CHADS_2$ score 1) and $80,615 (£62,100) (age 75 years; $CHADS_2$ score 3).

- For second line ablation compared with second line rate control, reported ICERs were: $73,947 USD (£56,961)/QALY (age 65 years; $CHADS_2$ score 1) to $96,846 (£74,600) (age 75 years; $CHADS_2$ score 3).

4. Conclusion

Moderate quality evidence was found for the effectiveness of CA compared with medical therapy, in patients with persistent AF, and very limited data comparing CA with surgical ablation.

Compared with medical therapy, CA appeared to improve AF freedom, reduce hospitalisation and the need for cardioversion. However, there are no benefits in terms of all-cause mortality. In AF patients with heart failure, CA appears to significantly improve LVEF and hospitalisation for worsening HF. There was no significant difference in ablation or drug-related complications.

Compared with surgical ablation the quality of evidence was weak, but surgical ablation appears to be more effective than CA at establishing and maintaining sinus rhythm, albeit at the expense of higher bleeding rates. There was however no difference between CA and surgical ablation in overall and procedure-related death.

There are no good quality studies on the cost effectiveness of CA compared with surgical ablation or medical treatment in patients with persistent AF. The available studies are of very limited quality and not from a perspective that can be easily extrapolated to the UK healthcare system.

The published data on the effectiveness, safety and cost effectiveness of CA in persistent AF is limited as most studies have been conducted in mixed AF patients (paroxysmal AF, permanent AF and persistent AF), without ensuring adequate matching for all subtypes and without consistently reporting the results separately. Further assessments in large-scale RCTs investigating CA versus medical therapy or surgical ablation specifically in persistent AF, are warranted.

Implementation

All patients being considered for AF ablation should have documented evidence of formal shared decision making using a tool approved by NHS England & Improvement. In addition, patients should have completed a PROMS form using a tool approved by NHS England & Improvement.

Inclusion criteria

Paroxysmal and Persistent AF

- Age 18 years and over with no previous history of congenital heart disease. For children and adults with pre-existing congenital heart disease, cardiologists should refer to existing guidance on the management of congenital heart disease, as this is outside the scope of this policy. This includes patients with percutaneous ASD closure devices who should only have an ablation in specialist Level 1 adult congenital heart disease centres who are experienced in dealing with such patients.
- All patients must have a BMI of 40 or less and those with a BMI between 35 and 40 must have undergone a period of intensive weight management with loss of at least 10% of initial body weight.
- Patients being considered for AF ablation should undergo a frailty assessment using a scoring system such as the Rockwood Clinical Frailty Scale (CFS). For patients considered to have more than mild frailty, a comprehensive geriatric assessment (CGA) is required to determine whether such patients can be optimised and be suitable for the procedure. A multidisciplinary team involved with the CGA should inform this decision making.

Paroxysmal AF only

- Paroxysmal AF is defined as at least two episodes of symptomatic atrial fibrillation (defined as Class 2b or worse of the modified EHRA classification (Wynn et al 2014)) in the previous 6 months lasting a minimum of 60 minutes in total or necessitating admission to hospital *and* terminating spontaneously within seven days.
- Ongoing symptoms despite a minimum of 3 months antiarrhythmic drug therapy. Antiarrhythmic drugs for this purpose are defined as beta-blockers, rate-limiting calcium channel blockers, Vaughan Williams Class I or Class III agents.

Persistent AF only

- Persistent atrial fibrillation (AF), is defined[7] as two or more episodes of symptomatic atrial fibrillation (defined as Class 2b or worse of the modified EHRA classification (Wynn et al 2014)) in the previous 24 months which are each sustained beyond 7 days, or last less than 7 days but necessitate pharmacological or electrical cardioversion.
- Symptoms must have been improved by cardioversion and there must be a clear temporal link between recurrence of symptoms and return of atrial fibrillation.
- Patients should remain symptomatic and have evidence of attempted rate control with up to two agents (beta-blockers, rate-limiting calcium channel blockers or digoxin) for at least 3 months.
- Left atrial diameter <55 mm or absolute left atrial volume <80ml.

Re-do criteria

- Redo procedures should only be considered in patients with ongoing symptomatic episodes of atrial fibrillation or atrial tachycardia.
- Patients with paroxysmal AF should have had no more than 2 previous ablations in the last 5 years for AF or atrial tachycardia[8].
- Patients with persistent AF should not have had more than 2 previous ablations for AF or atrial tachycardia.

[7] European Society of Cardiology.

[8] Report Following Formal Consensus Method for Establishing the Inclusion and Exclusion Criteria for Treating Atrial Fibrillation Using Left Atrial Ablation Procedure (UIN 1903).

- Under exceptional circumstances a further ablation procedure can be considered but this needs to be reviewed and agreed by an expert external to the centre.

Exclusion criteria

Paroxysmal and Persistent AF

- Life expectancy ≤ 5 years as with the inclusion of re-do procedures, the benefit is not likely to be fully achieved for 2 years.
- Planned cardiovascular intervention.
- Contraindication to anticoagulation therapy or heparin (in the absence of LAA occlusion device).
- AF secondary to a transient or correctable abnormality, including electrolyte imbalance, trauma, recent surgery, infection, toxin ingestion, and endocrinopathy (including hypo- and hyperthyroidism).
- Significant and permanent liver failure.
- Acute coronary syndrome, cardiac surgery, angioplasty, or cerebrovascular accident within 3 months prior to treatment.
- Intra-atrial thrombus, tumour, or other abnormality precluding catheter insertion.
- Uncontrolled hypertension.

Paroxysmal AF only

- NYHA class IV when not in AF.

Persistent AF only

- NYHA class IV
- Hypertrophic cardiomyopathy.
- Duration of AF greater than 2 years.
- Significant mitral valve disease, defined as severe mitral stenosis or regurgitation (as defined by ESC guidelines (Baumgartner et al (2017)) or a mechanical mitral valve replacement

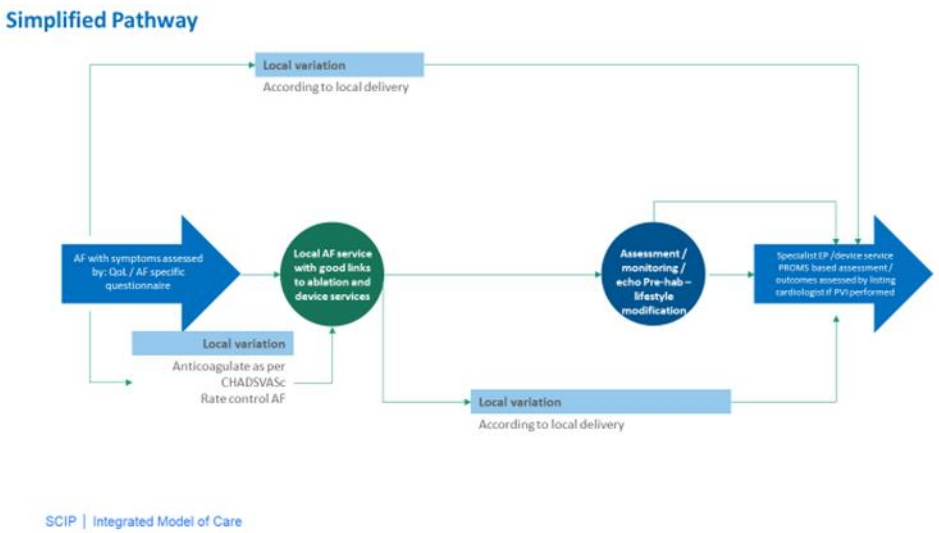

Figure 1. This is the draft model pathway in current development with the NHS England Specialised Cardiac Improvement Programme (Abbreviations: AF – atrial fibrillation; EP – electrophysiology; PROMS – patient reported outcome measures; SDM - shared decision making; CHADSVASc - CHA_2DS_2-VASc Score for Atrial Fibrillation Stroke Risk

Governance Arrangements

Treatment will be commissioned from a limited number of centres and each centre will be expected to demonstrate minimum numbers of procedures (as defined in the Service Specification A09/S/b). It is anticipated that sites will produce information leaflets (clinical indications, clinical benefits, complications, need for follow up, current evidence base and its limitations) for patients about percutaneous left atrial catheter ablation. They will also have the ability to undertake formal shared decision making (using NHS England approved tools); inform and provide information on PROMS and issue questionnaires (using NHE England approved tools). Alternatively, ablation sites will have information available via their website.

Subsequent to the acute period (0-7days), follow-up will likely be in the centre which undertook the procedure. It is anticipated that patients will be seen at least once thereafter. Annual monitoring by the main treatment centre will take place until the RCTs report in 2023 and the policy is reviewed.

A National Registry set up by the National Institute for Cardiovascular Outcomes Research (NICOR) already exists to record procedural outcomes with percutaneous left atrial catheter ablation Submission of data to this database will be mandatory for all procedures undertaken. Linkage with other databases for follow-up and with the Medical Research Information Service is encouraged.

The use of percutaneous left atrial catheter ablation will subject to the NHS England clinical decision support system. A suspected problem (‘adverse incident’) with the medical device should be reported using the Yellow Card Scheme as soon as possible at the following link: https://www.gov.uk/report-problem-medicine-medical-device.

Mechanism for funding

Funding and commissioning will be managed through the relevant local NHS England Specialised Commissioning Team. Due to the need for specialist equipment and facilities and the limited number of trained healthcare professionals (doctors and cardiac physiologists), electrophysiology (EP) and ablation services are provided in specialised cardiac centres as defined within the Manual of Prescribed services (2018). Specialised Centres for Cardiac electrophysiology and ablation are annotated as 13B under Identification Rules (IR) for specialised cardiac services.

Audit requirements

Every case of catheter ablation should be submitted to NICOR (National Institute for Cardiovascular Outcomes Research). Centres should undertake an annual audit of their catheter ablation programme, reporting efficacy and safety outcomes within the clinical governance structure of their hospital and network. They should benchmark themselves against existing and developing regional, national and international data. Audits should cover referral, patient selection, procedure indications, method of anaesthesia, duration of hospital stay, type of procedure performed, peri-procedural complications. Complications (including time of occurrence) to be monitored would include (strokes, TIAs, embolic events, bleeding, vascular access complications, pericardial effusion, pericardial tamponade +/- pericardiocentesis, phrenic injury, atrio-oesophageal fistula, pulmonary vein stenosis, heart block, all cause / cardiovascular / procedure related deaths).

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. This includes PROM data outcome which will be used to review the policy in future as necessary. If a review is needed due to a new evidence base then a new Preliminary Policy Proposition needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Anti-arrhythmic drugs	This is a group of medicines that are used to either slow the heartrate or change an abnormal heart rhythm to a normal rhythm.
Atrial fibrillation	This is a heart condition that causes an irregular heartbeat. It results from loss of coordinated contraction of the two atria – the upper receiving chambers of the heart.
Atrium	The heart is divided into four chambers that are connected by heart valves. The upper two chambers are called atria. The atria are separated into the left atrium and the right atrium by an interatrial septum.
Femoral vein	The femoral vein is located in the upper thigh and pelvic region of the body. It is used to gain access to the heart in catheter ablation.
Percutaneous	Performed through the skin.
Catheter ablation	A minimally invasive procedure that can be offered to people with symptomatic paroxysmal or persistent atrial fibrillation as an alternative to anti-arrhythmic medications. It is aimed at targeting and disrupting the conduction of abnormal electrical activity throughout the atria.

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