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Keywords
Left atrial appendage, occlusion, closure, percutaneous, UK

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Demand for Left Atrial Appendage Occlusion in the UK
The Sentinel Stroke National Audit Programme (SSNAP) is a national quality improvement project that has recorded stroke data for most of the UK since 2012. In its most recent 2019 annual report (Table 1), it found that over a third of patients with known AF were not on oral anticoagulation therapy prior to their stroke presentation (n=1,566, 36.7%). Although this proportion has declined significantly compared with previous years – 61.6% in 2014 – it is still high enough to cause concern. Given that the majority of patients with AF and stroke were aged ≥70 years (68.9%) and suffered from hypertension (54.9%), it is unlikely that low perceived stroke risk was the main reason for the lack of anticoagulation among these patients. Although the exact reasons remain unclear, the report did highlight that many of these patients were not anticoagulated due to contraindications (n=421, 26.8%). This figure would chime with the observation from primary care’s Quality Outcomes Framework data that about 6% of the overall AF cohort in the UK are deemed to have contraindications to anticoagulation, although this was lower than the estimated 12% from the US. Furthermore, the SSNAP data showed that 2,705 strokes occurred in AF patients who were already receiving anticoagulation therapy (12.3% of the total cohort).

A UK population-based cohort study of 11,481 patients with AF who were treated with a DOAC between January 2012 and December 2016 found that almost a third of patients had discontinued DOAC treatment within 1 year. The majority of these patients (60.4%) had a gap of at least 30 days without stroke protection before eventually reinitiating treatment with a vitamin K antagonist or DOAC. However, a significant percentage (n=813, 7.1%) still remained without anticoagulation following this period. Similar discontinuation rates were reported in other non-UK cohorts. Overall, these data demonstrate that there is a clear demand for LAA occlusion therapy

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It was our practice that all procedures were performed jointly by a consultant electrophysiologist and an interventional cardiologist under transoesophageal echocardiogram guidance. Post-procedural dual antiplatelet therapy.

The procedure appeared to result in a reduction of stroke rates compared with historical cohorts with a corresponding risk profile. In those who did have a stroke despite LAA occlusion, none were disabling, and all patients made a full recovery. This finding supports the notion that LAA occlusion may be associated with a Rockwood frailty score of ≥6 or a life expectancy of less than 3 years were deemed unsuitable for LAA occlusion. All procedures undertaken were to be recorded on a national registry to allow prospective evaluation of long-term outcomes. The plan was to perform 400 cases in the first year at the same 10 centres that were part of the CtE process, increasing to 1,200 a year over 5 years with the approval of additional centres following another round of selection in summer 2019. At the time of writing this review (February 2020), no more centres have been commissioned. Recently, the Scottish Health Technologies Group released a report advising that NHS Scotland should offer LAA occlusion to similar patients.20 Figure 1 shows a timeline of the LAA occlusion service delivery in the UK.

Access to Left Atrial Appendage Occlusion

BROADLY SPEAKING, THE ELIGIBILITY AND FUNDING CRITERIA FOR LAA OCCLUSION IN THE UK RESEMBLE THAT OF FRANCE, THE US, AUSTRALIA, POLAND AND CANADA.24-26 The fundamental difference, however, is in the restriction in the number of centres commissioned to provide LAA occlusion in the UK set at 10 as this puts a significant constraint on the provision of this service at a population level. In Germany, provision of LAA occlusion is dependent on individual insurance providers and is not subject to restrictions. In New Zealand, there are severe restrictions imposed on LAA occlusion in the public sector, but patients with anticoagulation-resistant strokes and a high risk of bleeding may be covered by private health insurance.27

Data on Left Atrial Appendage Occlusion

The final report of the CtE registry was produced in early 2019 and included 525 patients with AF who underwent LAA occlusion.21 Virtually all cases were performed under general anaesthetic (99.4%) and with intraoperative transoesophageal echocardiographic imaging (99.5%). Median fluoroscopy time and procedural duration in minutes were 10 (inter quartile range [IQR] 7–15) and 75 (IQR 57–110), respectively. Overall procedural success was 89% with a periprocedural mortality risk of 1%. Median length of stay was one night with 22.4% of patients requiring an extended admission (≥2 days). No differences in outcomes were seen between the various devices used. Risk of ischaemic stroke during follow-up was significantly reduced compared with that predicted from validated risk scoring systems, affirming the role of LAA occlusion in patients with AF who have contraindications to anticoagulation therapy. Furthermore, subsequent linkage of 460 patients with two UK datasets (Hospital Episode Statistics and Office of National Statistics) produced comparable data with the registry, adding confidence to the results.27

Based on our experience at a large tertiary centre in the UK, LAA occlusion can be performed with a high procedural success rate (82/83, 98.8%) in patients with contraindications to anticoagulation therapy.24 The procedure appeared to result in a reduction of stroke rates compared with historical cohorts with a corresponding risk profile. In those who did have a stroke despite LAA occlusion, none were disabling, and all patients made a full recovery. This finding supports the notion that LAA occlusion may be associated with fewer AF-related strokes, as well as lesser severity of strokes when they do occur.29-32 It was our practice that all procedures were performed jointly by a consultant electrophysiologist and interventional cardiologist under transoesophageal echocardiogram and fluoroscopic guidance. Post-procedural dual antiplatelet therapy was mandated for 6 weeks, followed thereafter by single antiplatelet therapy up to 6 months. Most patients in our centre

Table 1: Summary of SSNAP 2019 Annual Report

| Patient Variables | Prevalence |
|-------------------|------------|
| Total patients with strokes: | n=22,068 |
| • Known AF | 26.8% |
| • Contraindicated | 9.9% |
| Median age (IQR) | 77 years (66–85) |
| Prior comorbidities: | n=4,271 |
| • Hypertension | 54.9% |
| • Stroke or TIA | 26.0% |
| • Diabetes | 22.4% |
| • Congestive heart failure | 4.9% |
| Anticoagulation status: | 19.4% |
| • Prescribed | 63.3% |
| • Not prescribed | 26.8% |
| Newly diagnosed AF | 5.6% |

IQR = interquartile range; SSNAP = Sentinel Stroke National Audit Programme; TIA = transient ischaemic attack. Source: Sentinel Stroke National Audit Programme (SSNAP), 2020.20 Adapted with permission from SSNAP.
were kept in for overnight monitoring and discharged the following day, with a mean length of hospital stay of one day. More recently, Williams et al. demonstrated that LAA occlusion can be performed safely as a day-case procedure with very low rates of complications and readmissions.33

A retrospective registry by Betts et al. reported on outcomes from 371 patients with AF who underwent percutaneous LAA occlusion at eight centres in the UK prior to the period when the CtE registry was active.34 The follow-up period was over 24 months. Overall procedural success was 92.5% with an annual relative risk reduction based on predicted risk profiles for ischaemic stroke, thromboembolic events and major bleeding of 90.1%, 87.2% and 92.9%, respectively. The number of LAA occlusions undertaken at each centre varied significantly with a median of 40 cases (IQR 5–145). This suggests that some centres in the UK performed very few procedures during the study period, a factor which has been shown to be associated with worse outcomes.35

The UK-specific data appear broadly in agreement with that from international registries (Table 2).21,23–33 The relatively high periprocedural mortality rates reported in the CtE registry and study by Williams et al. was also observed by Tzikas et al. and may be related to an initial learning curve with the procedure.21,33,37 Overall, a direct comparison of complication rates across studies may be inaccurate due to confounders related to differences in the inclusion criteria and baseline risk factors. With this in mind, the periprocedural mortality rates found in the aforementioned studies were greater than in the Registry on WATCHMAN Outcomes in Real-Life Utilization (EWOLUTION) study (NCT01972282).38 Worse primary outcomes observed in the real-life registries compared with randomised trials may be explained by recruitment of patients with a higher risk of stroke, along with greater prevalence of comorbidities causing contraindication to oral anticoagulation.25,36

Despite evidence to support the role of LAA occlusion in patients with AF who have contraindications to anticoagulation therapy, there are several factors to be considered. About half of the cases in the UK were performed using the Amplatzer Amulet device (Abbott). However, results from RCTs are currently only available for the Watchman device (Boston Scientific).35,36 Furthermore, these trials excluded patients who were considered unsuitable for anticoagulation, thereby further limiting generalisability of their results to patients receiving LAA occlusion.

In general, the use of an epicardial approach for LAA occlusion remains poorly explored. Nonetheless, this offers an interesting prospect as the relatively high periprocedural complication rates may potentially be balanced by the absence of an intracardiac device, thereby negating the need for even short-term anticoagulation and the risk of device-related thrombus.39,40 Currently, the majority of the data on LAA occlusion are derived from real-world registries that may be subject to selection and reporting bias. There are limited studies directly comparing LAA occlusion to placebo and additional well-designed RCTs are needed. There are two ongoing RCTs that may provide some insight on the matter – Prevention of Stroke by Left Atrial Appendage Closure in Atrial Fibrillation Patients After Intracerebral Hemorrhage (STROKECLOSE, NCT02830152) and Assessment of the WATCHMAN™ Device in Patients Unsuitable for Oral Anticoagulation (ASAP-TOO; NCT02928497) but results are not expected for several years. It has also been suggested that LAA occlusion may be feasible in patients with proven LAA thrombus although this needs further evaluation.42

Cost Efficacy of Left Atrial Appendage Occlusion

In a publicly funded healthcare system, such as the NHS, the cost-effectiveness of LAA occlusion is an important consideration. Using recent estimates, the cost of each procedure was about £11,600.43 This represented an increase of 78% compared with the lifetime cost of medical therapy with antplatelets alone. However, when the higher initial cost of the procedure is balanced against a reduction in medical and social care expenditure from lower stroke rates, it is forecasted to be cost neutral over a 15-year period. When compared with the cost of medical therapy with anticoagulants, LAA occlusion was found to achieve cost parity between 4.9 years versus dabigatran and 8.4 years versus warfarin.44 The study by Panikker et al. estimated that LAA occlusion may save up to £7,194 at 10 years compared with other therapies. As such, the predicted remaining lifespan of individuals is an important factor when assessing their suitability for LAA occlusion. Similar cost benefits have also been demonstrated in studies in the US.45–47

In the current UK setting – and many other parts of the world – the majority of patients with AF are seen in primary care. This includes many patients who may be deemed unsuitable for anticoagulation by GPs. However, given the new policy changes and the unavailability of LAA occlusion until recently, many clinicians may not be aware that there exists an alternative for such patients. Estimates from NHS England predict that referral networks may require more than 5 years to become established and eventually only 10% of LAA occlusion-eligible patients will be considered for this treatment.42

Table 2: Cost Efficacy of Left Atrial Appendage Occlusion

| Year | Description |
|------|-------------|
| 2011 | NICE guidance recommends LAAO in certain patients with AF |
| 2012 | Draft NHS policy reveals future plans to restrict LAAO therapy |
| 2014 | Limited funding by NHS England for LAAO in 10 specialised sites using the process of CtE |
| 2016 | CtE evaluation completed |
| 2016 | Service delivery of LAAO in the NHS ceased |
| 2018 | Decision by NHS England to continue commissioning of LAAO for selected patients |

CtE = commissioning through evaluation; LAAO = left atrial appendage occlusion; NHS = National Health Service; NICE = National Institute for Health and Care Excellence.
Table 2: Comparison of Left Atrial Appendage Occlusion in the UK Compared with Rest of the World

| Study population | Mean follow-up, months (SD) | CHADS2 score, mean (SD) | CHA2DS2-VASc score, mean (SD) | HAS-BLED score, mean (SD) | Mean age, years (SD) | Male (%) | Female (%) | Device implanted (%) | Discharge anti-thrombotic regimen (%) | Procedural success (%) | Major procedural complications (%) |
|------------------|----------------------------|-------------------------|-------------------------------|---------------------------|-----------------------|---------------------|-------------|----------------------|-------------------------------------|------------------------|-----------------------------------|
| UK               |                            |                         |                               |                           |                       |                     |             |                      |                                     |                        |                                    |
| Betts et al. 2017† (n=371) | 72.9 (8.3) | 38.1 | 2.6 | 3.7 (1.1) | 72.9 (8.3) | 88.9 | 91.0 | 63.0 | Watchman | 10.8 | 0.25 | 0.95 |
| CTE registry, 2019‡ (n=525) | 74.5 (8.0) | 7.7 | 50.4 | 0.7 | 74.5 (8.0) | 68.7 | 92.5 | 34.7 | Amplatzer Cardiac Plug | 50.1 | 0.25 | 0.76 |
| Williams et al. 2018§ (n=117) | 75.6 (NA) | 41.0 | 0 | 0 | 75.6 (NA) | 67.7 | 92.5 | 2.3 | Amplatzer Amulet | 39.1 | 0.25 | 0.76 |
| PROTECT AF, 2019¶ (n=463)¹ | 71.7 (8.8) | 6.0 | 0 | 0 | 71.7 (8.8) | 0 | 92.5 | 0 | Others | 0 | 0 | 0 |
| PREVAIL, 2014¶ (n=269)* | 74.0 (7.4) | 0 | 0 | 0 | 74.0 (7.4) | 67.7 | 92.5 | 0 | Not specified | 0 | 0 | 0 |
| Tzikas et al. 2016∥ (n=1,047) | 75.0 (8.0) | 91.0 | 100 | 69.0 | 75.0 (8.0) | 75.0 (8.0) | 92.5 | 0 | Procedural success (%) | 92.5 | 0.76 | 0.76 |
| Mean follow-up, months (SD) | 24.7 (16.1) | NA | NA | 2.6 (1.2) | 24.7 (16.1) | 18.0 (10.0) | 0 | 0 | AC contraindicated | 6.0 | 0 | 0 |
| Male (%) | 88.9 | 68.7 | 66.7 | 4.2 (1.6) | 88.9 | 0 | 0 | 0 | AC not contraindicated | 0 | 0 | 0 |
| Female (%) | 91.0 | NA | NA | 4.3 (1.5) | 91.0 | 11.8 (5.8) | 100 | 0 | AC contraindicated | 0 | 0 | 0 |
| Study population Any indication* | 75.6 (NA) | 2.2 (NA) | NA | 3.34 (1.17) | 75.6 (NA) | 2.2 (NA) | 3.5 | 3.34 | AC not contraindicated | 0 | 0 | 0 |
| AC contraindicatedAC contraindicatedAC not contraindicated | NA | NA | NA | NA | NA | NA | NA | NA | AC contraindicated | NA | AA |
| Mean age, years (SD) | 70.4 | 70.4 | 70.4 | 3.7 (1.1) | 70.4 | 67.7 | 67.7 | 0.76 | Any indication* | 0.76 | 0.76 |
| Male (%) | 68.7 | 66.7 | 66.7 | 3.7 (1.1) | 68.7 | 66.7 | 66.7 | 0.76 | AC contraindicated | 0.76 | 0.76 |
| Female (%) | 31.3 | 33.3 | 33.3 | 7.1 (0.9) | 31.3 | 33.3 | 33.3 | 0 | AC not contraindicated | 0 | 0 |

1. LAA occlusion group only, includes absolute and relative contraindication for AC, resistant stroke, intolerance to OAC and lifestyle choice.
2. Includes absolute and relative contraindication for AC, resistant stroke, and drug interaction.
3. Definition differs; slightly between trials, lestimates from CTE report; AC = anticoagulation; APT = antiplatelet therapy; CIE = Commissioning through Evaluation; CV = cardiovascular; DAPT = dual antiplatelet therapy; LAA occlusion = left atrial appendage occlusion; NA = not available; OAC = oral anticoagulation; RoW = rest of world; SE = systemic embolism; TIA = transient ischaemic attack.

Conclusion

Percutaneous LAA occlusion appears to be a viable option in patients with AF who have contraindications to anticoagulation therapy, which comprise 5-6% of the total AF population. Availability of this therapy is at present significantly restricted in the UK compared with many countries in western Europe and the US.

Clinical Perspective

- Percutaneous LAA occlusion is associated with a significant reduction in thromboembolic risk among patients with AF who have contraindications to anticoagulation therapy.
- Patients with AF who have high thromboembolic risk and are unable to tolerate anticoagulation, including those with anticoagulation-resistant strokes should be referred to a specialist for consideration of percutaneous LAA occlusion.
- The procedure is associated with a high initial cost that appears to be subsequently balanced against a reduction in medical and social care expenditure from lower stroke rates over a 10-15-year period.

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