Title: Left Atrial Appendage Occlusion: Clinical Benefit

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Research question:

1. What is the evidence for the clinical effectiveness of left atrial appendage (LAA) occlusion to reduce the risk of stroke?

2. Are there patient populations in which LAA occlusion would not offer a benefit and reduce the risk of stroke?

3. Is there any evidence for adverse events associated with the use of devices for LAA occlusion?

Methods:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 1, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2003 and March 2008, and are limited to English language publications only. Filters were applied to limit the retrieval to systematic reviews, clinical studies, and guidelines. Internet links are provided, where applicable. The summary of findings was prepared from the abstracts of the relevant information.

Results:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews and meta-analyses are presented first. These are followed by randomized controlled trials, observational studies and evidence-based guidelines.
One randomized controlled trial, seven observational studies and one evidence-based guideline were identified from the literature search results. No relevant health technology assessments, systematic reviews, or meta-analyses were identified. Recent review articles are included in the Appendix.

**Overall summary of findings:**

A report published in 2003 described the design of the Left Atrial Appendage Occlusion Study (LAAOS) that will enroll 2500 patients randomized to receive LAA occlusion or no LAA occlusion.\(^2\) The purpose of this study will be to assess the effects of LAA occlusion on long-term stroke prevention and patients will be followed for 5 years.\(^2\) Before examining the long-term outcomes of LAA occlusion, it was necessary to determine the safety, feasibility, and rate of successful occlusion.\(^2\) A pilot study of the LAAOS RCT was published in 2005, and sutures or stapling were used to occlude the LAA during coronary bypass grafting surgery.\(^1\) Complete LAA occlusion was verified in 45% of sutured cases and in 72% of stapled cases. At the end of the follow-up period, 2.6% of patients in the treatment group experienced thromboembolic events. The authors concluded that it is safe to perform LAA during CABG and that larger trials would be needed to determine if LAA occlusion is effective in preventing stroke.\(^1\)

Two observational studies investigated the benefits of surgical LAA occlusion.\(^6,7\) Schneider et al. examined six patients with transesophageal echocardiography (TEE) 23-159 days after surgery to verify the complete closure of the LAA.\(^6\) This examination revealed complete LAA closure in one patient. Although all patients in the study group remained on anticoagulant therapy, one patient had a stroke four weeks after surgery. The authors suggested that incomplete occlusion may increase the risk of stroke and therefore TEE is necessary to ensure that the LAA is completely occluded.\(^6\) Garcia-Fernandez et al. assessed whether LAA occlusion is associated with risk of embolism.\(^7\) Retrospectively, 205 patients were identified who had mitral valve replacement and 58 of these patients underwent LAA occlusion. During the time from surgery to echocardiography study, 27 patients had an embolism.\(^7\) A predictor of the occurrence of an embolism was the absence of LAA occlusion (odds ratio 6.7), however an incomplete occlusion was associated with an increased risk of embolism (odds ratio 11.9).\(^7\)

Three observational studies investigated the feasibility and clinical effectiveness of the percutaneous left atrial appendage transcatheter occlusion system (PLAATO).\(^3,5,9\) Patients in all three studies had a contraindication to anticoagulants and possessed at least one risk factor for stroke.\(^3,5,9\) Omran et al. examined nine patients by echocardiography prior to, during, <48h, 3 months, 6 months and 1 year after LAA occlusion.\(^9\) There were no thrombotic complications observed in any of the patients during follow up.\(^9\) Ostermayer et al. presented the results of two prospective, multi-center observational studies involving 111 patients.\(^5\) The PLAATO device was successfully implanted in 108 of 111 patients. During the average follow-up period of 9.8 months, two patients experienced a stroke.\(^5\) El-Chami et al. investigated the long term clinical outcomes of 11 patients who received the PLAATO device.\(^3\) After three years one patient had experienced a stroke. These findings indicated a stroke risk of 3% per year in this population which is comparable to that observed in similar patients receiving warfarin therapy.\(^3\) All three studies suggested that the PLAATO device is a feasible method for LAA occlusion and is of an acceptable level of risk in patients with atrial fibrillation and a contraindication to anticoagulants.\(^3,5,9\)

Sick et al. studied the feasibility of percutaneous implantation of the WATCHMAN system for LAA occlusion.\(^4\) The device was implanted in 66 patients, and after 45 days of follow-up, 93% of patients showed a complete occlusion of the LAA. No strokes were observed among patients
during the follow-up period even though more than 90% of patients had stopped taking anticoagulant therapy. The authors suggested that the WATCHMEN system is safe and feasible.\textsuperscript{4}

Meier et al. investigated the use of the Amplatzer atrial septal occluder for percutaneous LAA occlusion in 16 patients with atrial fibrillation.\textsuperscript{8} The LAA was completely occluded in all patients and no embolic events or other adverse events were observed during the follow-up period of 5 patient-years. The Amplatzer technique may be a safe alternative to the PLAATO technique for LAA occlusion and can be done with local anesthesia with a venous puncture.\textsuperscript{8}

The Interventional Procedure Guidance from the National Institute for Health and Clinical Evidence (NICE) suggested that the current evidence available is insufficient to recommend percutaneous LAA occlusion without special arrangements.\textsuperscript{10} They recommended that the procedure only be used when standard therapy is unsuitable.\textsuperscript{10}

Overall, it appears that LAA occlusion may be safe and effective at reducing the risk of stroke, however, more research is needed. The PLAATO, WATCHMEN and Amplatzer devices may all be feasible percutaneous methods for LAA occlusion, but more large scale studies are needed to verify both safety and effectiveness in stroke prevention.\textsuperscript{3-5,8,9} LAA occlusion appears to be beneficial for patients who are unable to tolerate anticoagulant therapy.\textsuperscript{3,5,9} There does not appear to be any evidence of adverse events related to the use of percutaneous methods of LAA occlusion\textsuperscript{3-5,8,9} while surgical occlusion of the LAA may actually increase the risk of stroke if occlusion is incomplete.\textsuperscript{6,7}
References summarized:

**Health technology assessments**
No literature identified

**Systematic reviews and meta-analyses**
No literature identified

**Randomized controlled trials**


**Observational studies**


Guidelines and recommendations


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Appendix – Further information:

Horizon scanning report


Case reports


Review articles


