TITLE: Left Atrial Appendage Occlusion: Economic Impact and Existing HTA Recommendations

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CONTEXT AND POLICY ISSUES:

Atrial fibrillation (AF) is the irregular, rapid beating of the atria of the heart and is the most common cardiac arrhythmia. Patients with AF have an elevated risk of stroke, which is a leading cause of death and disability among patients with the condition. The elevated risk of stroke in AF relates to a predisposition to inefficient blood flow. Stagnation of blood flow in the left atrium can lead to thrombus formation, which increases the risk of embolic stroke. The left atrial appendage (LAA) is a small, long tubular structure branching from the left atrial cavity. Because of its anatomy, the efficiency of blood flow in the LAA is reduced. In patients with AF, over 90% of atrial thrombi originate in the LAA.

A number of drugs are in use or clinical trials for stroke prevention in atrial fibrillation, including anticoagulants, antiplatelet agents, thrombin inhibitors and Factor Xa inhibitors. The anticoagulant warfarin is often used for stroke prevention in patients with AF at high-risk for stroke who have no contraindications. Warfarin has consistently been shown to reduce the risk of stroke in patients with AF by over 60% compared to no treatment, and by 30% to 40% compared to low-dose aspirin. However, warfarin use has some disadvantages including numerous food and drug interactions, the need for frequent monitoring, and the risk of bleeding complications. Because of this, alternative therapies for stroke prevention have been sought.

One alternative that has been explored is the occlusion of the LAA to prevent thrombi escape. As surgical occlusion or removal of the LAA is invasive and limited to patients undergoing open-heart surgery, devices for percutaneous occlusion of the LAA have been developed. The first such device developed as an alternative to surgical occlusion was the percutaneous left atrial appendage transcatheter occlusion (PLAATO) system, which showed a reduction in stroke rate in clinical trials but was discontinued due to economic reasons. The Watchman device is a newer device available for LAA occlusion and was evaluated in a large prospective, randomized controlled trial (PROTECT-AF) which demonstrated its non-inferiority to chronic warfarin for stroke prevention in AF patients. Though not yet licensed by Health Canada, patients unable to
take warfarin can get the Watchman through a compassionate use process. Another device, the Amplatzer Septal Occluder (ASO), has been used for LAA occlusion and is licensed for use in Canada but was not designed for this purpose.\(^4\)

This report examines the evidence of the cost-effectiveness of percutaneous occlusion of the LAA in patients with AF who are at elevated risk for stroke.

**RESEARCH QUESTIONS:**

1. What is the cost-effectiveness of percutaneous occlusion of the left atrial appendage for patients with non-valvular atrial fibrillation at elevated risk for stroke?

2. What are the evidence-based recommendations that considered cost-effectiveness of percutaneous occlusion of the left atrial appendage for patients with non-valvular atrial fibrillation at elevated risk for stroke?

**METHODS:**

A limited literature search was conducted on key health technology assessment resources, including Ovid MEDLINE (1950 to August Week 3 2010), PubMed, The Cochrane Library (Issue 8, 2010), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language, with no time limit for articles’ publication dates. No filters were applied to limit the retrieval by study type.

**SUMMARY OF FINDINGS:**

One publication\(^3\) was identified that included a cost analysis of LAA occlusion for stroke prevention. No relevant guidelines were identified.

**Economic evaluations**

In 2010, the North East Treatment Advisory Group performed a cost analysis of the use of the Watchman device for LAA occlusion and stroke prevention compared to low-dose aspirin.\(^3\) Costing was performed from the perspective of the National Health Service (NHS), but was not specific to patients with AF. Costs were calculated in pounds (£), but it was unclear what year was used for costing.

Using figures for the United Kingdom (UK) health care system, the estimated cost of implanting a Watchman device without complications was £11,380. This estimate was derived from a device cost of £5,280 (including value added tax), procedure cost of £5,951 (based on NHS payment-by-results billing codes) and the cost of post-procedural drugs.

Using a calculated number needed to treat (NNT) of 100, based on a meta-analysis of antithrombotic therapy for stroke prevention\(^9\) and results of the PROTECT-AF trial,\(^8\) the estimated cost to prevent one stroke compared to aspirin alone was £1.14 million annually. An NNT of 100 indicates that, compared to treatment with aspirin alone, 100 patients would be required to receive the device to prevent one ischemic stroke. Assuming a 10-year survival
period, the authors calculated a cost of £114,000 per stroke prevented. The average lifetime cost of a stroke was estimated to be £18,000, with the lifetime cost of a severe stroke, which tends to have higher levels of residual disability, estimated at £50,000, less than one-half of the Watchman procedure cost.

Because the cost estimates are dependent on expected survival rates and residual disability following a stroke, the authors state that it is difficult to determine whether a Watchman device for stroke prevention meets the conventional criteria for cost-effectiveness. The authors concluded that the benefits of stroke reduction by a Watchman device may be greater in patients with a high baseline risk. Given the demographics of their patient population, with an annual risk of ischemic stroke of 4%, the authors concluded that the majority of patients would derive no benefit from the Watchman device.

This study is limited by the underlying assumptions of the analysis, particularly the assumption of a 10-year survival period, which may be optimistic given a predominantly male patient population with a mean age of 72. Furthermore, estimates of stroke risk were not specifically based on patients with non-valvular AF. The analysis is sensitive to both the survival rate and the estimated cost of a stroke, which depends on residual disability, but no sensitivity analysis was done. Adverse event rates were not considered, though they may affect treatment costs, nor were pre- and post-operative appointment costs. The cost analysis was carried out relative to low-dose aspirin, not warfarin which may be the preferred treatment for patients with higher risk of stroke. Aspirin is generally indicated for patients with low to moderate risk of stroke. Finally, cost analysis was done based on costs in the UK and may not be generalizable to the Canadian health care system.

Limitations

One cost analysis was identified, comparing the Watchman device for LAA occlusion plus low-dose aspirin to low-dose aspirin alone for stroke prevention. This analysis was based on estimates from the UK and may not generalize to a Canadian context. The available analysis was done comparing one particular device for LAA occlusion (Watchman) and one drug regimen (low-dose aspirin) and, therefore, may not be generalizable to other occlusion devices, such as PLAATO or ASO devices, or other drugs, such as warfarin.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

One UK-based cost analysis was identified. This analysis indicated that the Watchman device for stroke prevention by LAA occlusion was more costly per stroke prevented than low-dose aspirin. However due to the limitations of this analysis and the lack of additional economic evidence, it is difficult to draw firm conclusions on the cost-effectiveness of LAA occlusion for stroke prevention in patients with non-valvular AF.

No evidence-based guidelines or recommendations that considered cost-effectiveness were identified, nor were any cost-effectiveness evaluations.
REFERENCES:


