



Australian Government
Department of Health and Ageing



Australia and New Zealand Horizon Scanning Network

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Horizon Scanning Technology Prioritising Summary

Minimally invasive surgical treatment of atrial fibrillation

August 2008



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**

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ISBN

Publications Approval Number:

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from departments in all states and territories, the Australia and New Zealand governments; and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID S000081

NAME OF TECHNOLOGY MINIMALLY INVASIVE SURGICAL TREATMENT OF ATRIAL FIBRILLATION

PURPOSE AND TARGET GROUP PATIENTS REQUIRING TREATMENT FOR ATRIAL FIBRILLATION

STAGE OF DEVELOPMENT (IN AUSTRALIA)

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- Yes
- No
- Not applicable

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
United States	✓		
Japan	✓		
United Kingdom	✓		

IMPACT SUMMARY

Currently, most patients with atrial fibrillation (AF) are treated intraoperatively during open heart surgery for mitral valve repair or coronary artery bypass grafting. The development of a minimally invasive surgical treatment for AF potentially offers patients with lone AF the benefits of surgery without subjecting them to the risks associated with open heart surgery. At the time of writing, this technique is not practised within the Australian healthcare system.

BACKGROUND

AF is a form of cardiac arrhythmia (irregular heart rhythm). Under normal circumstances, electrical pulses from the sinus node, the heart's pacemaker, cause the two upper chambers of the heart (atria) to contract. The pulse then travels to the atrioventricular node, which causes the two lower chambers of the heart (ventricles) to contract. However, in individuals with AF, a problem within the sinus node causes the atria to twitch or quiver rather than contract. This in turn distorts the electrical message sent to the atrioventricular node and causes the ventricles to contract out of rhythm.

AF can be classified as a first-detected episode or recurrent atrial fibrillation. Recurrent AF can be subclassified as paroxysmal (self-terminating, usually <24 hours), persistent (sustained >7 days) or permanent. In some patients, AF causes symptomatic tachycardia (abnormally fast heart rate), reduced cardiac output and tachycardia-induced cardiomyopathy (weakness of the heart muscle), which can eventually lead to heart failure (Gillinov and Saltman 2008). AF is associated with increased mortality and morbidity, particularly in patients requiring mitral valve repair or coronary artery bypass grafting. AF is an independent predictor of patient mortality, with studies reporting a 1.5-fold to 2.0-fold increase in total and cardiovascular mortality (Benjamin et al 1998; Kannel et al 1998). In addition, individuals with AF are at a higher risk for stroke. Despite continuing efforts to understand the pathophysiology of AF, its electrophysiologic causes remain unknown. However, research has shown that the pulmonary veins and posterior left atrium are critical anatomic sites for the treatment of AF (Gillinov and Saltman 2008).

Various treatment options are available to restore sinus rhythm, including pharmacological therapy, electrical cardioversion, pacing and surgical ablation. To date, research has shown that anti-arrhythmic drugs have a 40% to 60% success rate of maintaining sinus rhythm after one year, and this is marred by various complications. The documented problems related to the use of anti-arrhythmic drugs include aggravation of arrhythmia (Podrid 1999). In addition, the anti-coagulative drugs used to reduce the incidence of ischaemic stroke are associated with an increased risk of bleeding. Meanwhile, electrical cardioversion is usually most effective only in patients with recent-onset AF, and the long-term effectiveness of this treatment option is in doubt (Fuster 2007).

Surgical treatment is the most effective long-term treatment for AF. The Cox-Maze procedure, which is the current standard surgical treatment requiring open heart surgery, involves creating a maze of small incisions along both the right and left atria. These incisions heal and create scar tissue, which inhibits the re-entry of the irregular electrical impulses that cause AF. Despite the effectiveness of the Cox-Maze procedure, it is not widely used because it requires open heart surgery via median sternotomy, cardiopulmonary bypass and aortic cross-clamping (Matsutani et al 2008). Efforts to simplify the Maze procedure include the utilisation of various energy sources, such as radiofrequency and microwave energy, to create the heart lesions. Nevertheless, open chest techniques requiring cardiopulmonary bypass are considered too invasive for patients whose sole indication is AF.

In an effort to simplify the procedure and reduce the associated risks, minimally invasive surgical procedures have been proposed which can be performed on a beating heart (Gillinov and Saltman 2008). The first report of a minimally invasive procedure was published in 2003, and since then three main techniques have been developed to provide less invasive AF treatment: (1) robotics, (2) thoracoscopy and (3) minithoracotomy. Several novel procedures have been trialled, from a totally thoracoscopic approach utilising a linear flexible microwave/radiofrequency unipolar device for ablation of pulmonary veins (Pruitt et al 2007) to bilateral thoracoscopic pulmonary vein isolation with left atrial appendage excision (Wolf et al 2005). In addition to decreased patient morbidity, minimally invasive techniques may benefit patients in whom warfarin, heparin or anti-arrhythmic medications are contraindicated (Wolf 2007).

CLINICAL NEED AND BURDEN OF DISEASE

AF is the most common form of sustained cardiac arrhythmia and its incidence has been shown to increase with age (Medi et al 2007). It is estimated that 8% of individuals over 80 years of age are affected, with the Framingham Study indicating that the age-adjusted incidence of AF has increased significantly (12.6%, $p=0.014$) from the 1960s to 2000 (Miyasaka et al 2006)

Research has revealed that AF is present in up to 50% of patients undergoing mitral valve surgery and in 1% to 6% of patients undergoing coronary artery bypass grafting or aortic valve surgery. In patients with mitral valve dysfunction, AF is an indicator of advanced cardiovascular disease as it is associated with higher New York Heart Association functional class, more severe left ventricular dysfunction and a greater left atrial size (Saltman 2008). In most of these patients, intraoperative treatment of AF is usually recommended. It is important to note that the number of patients presenting in operating theaters with coronary or valvular disease in combination with AF is relatively low. Therefore, intraoperative treatment of AF at present only addresses a small proportion of the affected population.

DIFFUSION

At the time of writing, there is no indication that minimally invasive techniques for the treatment of AF are being utilised within Australia and New Zealand. It is likely that minimally invasive procedures would greatly benefit patients suffering from lone AF where the risks of open surgery with cardiopulmonary bypass and induced cardiac arrest cannot be justified. The diffusion of these minimally invasive procedures is expected to be rapid if they are proven effective.

COMPARATORS

The main comparator to minimally invasive AF treatment is the Cox-Maze III procedure.

SAFETY AND EFFECTIVENESS ISSUES

Three case series studies (level IV intervention evidence) were selected for inclusion in this prioritising summary. Results are presented as mean \pm standard deviation unless stated otherwise.

Pruitt et al (2007) examined the effectiveness of a thoracoscopic box lesion approach for the treatment of drug-resistant lone AF in 100 patients (66 male, 34 female) with an average age of 60.9 ± 9.8 years (range 37 to 81 years). The mean duration of AF was 72.4 ± 79.5 months, with 64% of patients having paroxysmal, 11 % having persistent and 25% having permanent AF. The procedure utilised a linear flexible unipolar device (Flex 10® AFx Microwave Ablation System, Guidant Corporation, Santa Clara, CA, USA) to create a box lesion around all four pulmonary veins. In addition, the left atrial appendage was closed with an endostapler in 85% of patients.

Edgerton et al (2007) studied the feasibility of minimally invasive pulmonary vein isolation and partial autonomic denervation of the left atrium for the treatment of AF in 83 patients (61 male, 22 female). The procedure was performed via thoracotomy, but there was no mention of left atrial appendage excision. Mean patient age was 60 years (range 38 to 80), while duration of AF was >12 months in 90.1% (73/83), 6 to 12 months in 6.3% (5/83) and <6 months in 3.7% (3/83). The authors noted that 80.7% (67/83) of patients were on anti-arrhythmic drugs at the time of operation and 25.3% (21/83) had undergone previous catheter ablation.

Wolf et al (2005) investigated video-assisted bilateral pulmonary vein isolation in 27 AF patients (22 male, 5 female). All patients had unsuccessful drug therapy or were intolerant to anti-arrhythmic drugs or warfarin. Pulmonary vein isolation was achieved thoracoscopically via blunt dissection and the use of a bipolar radiofrequency clamp and radiofrequency generator system. The left atrial appendage was excised by stapling with an EZ 45 stapler (Ethicon, Inc., Cincinnati, OH, USA).

A) SAFETY

In the 100 patients treated by Pruitt et al (2007), there was one case of cerebral vascular accident (1%), two cases of reoperation for bleeding (2%) and seven cases of diaphragmatic dysfunction (7%) over a mean follow-up length of 23.1 months. No incidences of myocardial infarction or port-site infection occurred. There were no hospital deaths; however three late deaths (3%) were reported. Of the 88 patients who survived and did not experience procedure failure, two experienced a transient ischaemic attack (2.3%), two suffered a cerebral vascular accident (2.3%) and one had complications related to anticoagulant medication.

After 6 month post-treatment, Edgerton et al (2007) reported complications in 3.6% of patients (3/83): one case of clotted haemothorax, one incidence of renal insufficiency and one transient case of decreased movement and sensation in the arm and shoulder. One patient died due to tearing of the left atrial appendage base (1.2%).

Wolf et al (2005) reported that none of the 27 patients required blood products either intraoperatively or during hospitalisation and that no deaths occurred. Four patients (14.8%) experienced complications during the follow-up period (mean: 173.6 days). Three of these patients suffered minor complications, namely right pneumothorax, right forearm phlebitis and suspected pericarditis. The fourth patient was readmitted three weeks after treatment for shortness of breath and suspected AF. This patient was readmitted again at 3.5 months post-treatment with exacerbation of congestive heart failure and atrial flutter. However, the authors noted that this patient was morbidly obese and had a 2-year history of persistent AF, hypertension and angina. These factors may have contributed to the observed complications.

B) EFFECTIVENESS

Pruitt et al. (2007) noted that three patients (3%) required pacemaker implantation and the procedure failed in 9 patients (9%) (underwent the Cox-Maze procedure). At discharge, Pruitt et al (2007) reported that 59% (59/100 patients) of patients had normal sinus rhythm. At the last follow-up (36 months), 42% (37/88 patients) had normal sinus rhythm as verified by electrocardiography (ECG). When the results were presented for each follow-up interval: 0 to 12 months, 12 to 24 months, 24 to 36 months, and >36 months, the proportion of patients with normal sinus rhythm were 83.3% (5/6), 42.5% (17/23), 30.3% (10/33) and 55.6% (5/9), respectively. The persistence of AF in paroxysmal and permanent AF patients at last follow-up was similar.

Edgerton et al (2007) reported that 91.8% (56/61) of patients who underwent ECG testing had sinus rhythm at 6 months post-treatment. Meanwhile, of the 57 patients with long-term Holter monitors (6 months), 73.7% (42/57) had no detectable AF (defined as episodes lasting longer than 15 seconds). In contrast to the observations of Pruitt et al (2007), Edgerton and colleagues (2007) noted that patients with paroxysmal AF achieved better results relative to persistent/long-standing persistent AF (82.1% [32/39] versus 55.6% [10/18]), but no statistical tests were conducted. Overall, 77% of patients who underwent ECG testing and 63.2% of patients who had long-term monitors did not require the use of anti-arrhythmic drugs at 6 months post-treatment.

Wolf et al (2005) reported that no conversions to sternotomy or thoracotomy were necessary. The authors stated that over 3 months of postoperative data were available for 85.2% (23/27) of patients. Twelve-lead ECG or outpatient telemetry monitoring revealed that 91.3% (21/23) of patients were free of AF (with no symptoms). The study protocol necessitated that patients receive anti-arrhythmic drugs for approximately 3 months post-treatment, and were then weaned off these drugs as tolerated. Overall, 65.2% (15/23) of patients evaluated beyond 3 months were successfully weaned off anti-arrhythmic drugs, while 26.1% (6/23) were off anti-arrhythmic drugs at the 3-month follow-up. The remaining two patients continued with pharmacological treatment (8.7%).

Both Pruitt et al (2007) and Edgerton et al (2007) recorded subjective measures of effectiveness, such as patient satisfaction and perception of the procedure. Pruitt et al (2007) reported that 52.3% (46/88) of patients were pleased with their outcome and 55.7% (49/88) felt that the operation was beneficial. Despite this, 76.1% (67/88) of

patients reported continued occurrence of AF palpitations. When asked to compare their health to that of the previous year, 62.5% (55/88) reported they were 'much' or 'somewhat' better, 28.3% (6/88) felt about the same while 9.1% (8/88) felt 'much' or 'somewhat' worse. No account was given for the remaining 19 patients.

Edgerton et al (2007) asked 56 patients to predict their rhythm at the 6-month ECG follow-up. The authors noted that 86% (48/56) of patients felt that they were in sinus rhythm, 13% (7/56) felt that they had AF and 2% (1/56) could not ascertain their rhythm. Of the patients who felt they were in sinus rhythm, 85% were correct, while 100% of patients who felt they had AF were correct.

COST IMPACT

The cost of minimally invasive AF treatment procedures is highly variable, owing to the fact that there is no standardised protocol and the type of equipment utilised varies across centres. No cost-effectiveness studies examining minimally invasive surgical treatment for lone AF patients have been conducted to date.

The study by Lamotte et al (2007) utilised a Markov model to predict the cost-effectiveness of four AF intervention options: high-intensity focused ultrasound (HIFU)-assisted surgical ablation, Cox-Maze procedure, and percutaneous ablation compared with pharmacological treatment.¹ The study concluded that all interventional treatments had good incremental cost-effectiveness ratios compared to pharmacological treatment. Both HIFU ablation and Cox-Maze conducted concomitantly with coronary artery bypass grafting were highly cost-effective (GB£4005 to GB£7448 per quality-adjusted life-year gained [QALYG] and GB£1341 to GB£3471 per QALYG, respectively). Percutaneous ablation as a subsequent procedure to coronary artery bypass grafting was also cost-effective (GB£7041 to GB£17,372 per QALYG), but to a lesser extent.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

No issues were identified from the retrieved material.

SUMMARY OF FINDINGS

The included studies comprised case series and reported mixed results with regard to the effectiveness of minimally invasive AF treatments. Two studies of a total of 110 patients presented encouraging results, with over 90% of patients attaining sinus rhythm between 3 and 6 months after treatment. In contrast, a third study of 100 patients achieved notably lower success rates. However, the latter study differed from the other two in the procedure utilised to treat AF. The results imply that surgical ablation with microwave

¹ The model assumes that both HIFU and Cox-Maze were conducted concomitantly with coronary artery bypass grafting. Percutaneous ablation was considered a subsequent treatment after coronary bypass.

energy to create a box lesion around all four pulmonary veins may be less effective than pulmonary vein isolation and denervation. In particular, the use of microwave energy may not provide sufficient electrical isolation of the pulmonary veins to achieve long-term AF resolution.

All three studies reported mostly minor complications with only one incidence of hospital mortality occurring. However, without a comparative study, it is difficult to know whether the risk of more serious complications, which occurred in a small minority of patients, is higher compared to patients treated with other therapies.

HEALTHPACT ACTION

Despite the promising results of some studies, minimally invasive treatment of AF is still in the early stages of development. There is no consensus regarding ablation strategy during these procedures, and most studies do not utilise consistent measures of effectiveness. In order to elucidate the effectiveness of various minimally invasive procedures (as well as the ablative methods used), guidelines have been published to facilitate reporting of outcomes in the surgical treatment of AF (Shemin et al 2007).

Based on the limited evidence available and the likelihood that long-term outcomes will not be available for several years, minimally invasive surgical AF treatments will be archived.

NUMBER OF STUDIES INCLUDED

Total number of studies 3
Level IV intervention evidence

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SEARCH CRITERIA TO BE USED
Minimally invasive atrial fibrillation
Atrial Fibrillation/surgery*