NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of cryoablation for atrial fibrillation as an associated procedure with other cardiac surgery

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in July 2004.

Procedure name

- Cryoablation for atrial fibrillation as an associated procedure with other cardiac surgery.

Specialty society

- Society of Cardiothoracic Surgeons in Great Britain and Ireland.
- British Pacing and Electrophysiology Group.

Description

Indications

Atrial fibrillation.

Atrial fibrillation is the irregular and rapid beating of the upper two chambers of the heart (the atria). It may be classified as paroxysmal, persistent or permanent. It is the most common type of arrhythmia, affecting approximately 0.5% of the adult population[1]. The incidence increases markedly with age. Patients with atrial fibrillation may be asymptomatic or they may have symptoms including palpitations, dizziness and breathlessness. They also have an increased risk of stroke, as a result of blood clots forming in the left atrium and then embolising to the brain.

Although atrial fibrillation may occur in the absence of other heart disease, it is particularly common in patients with mitral valve disease. Patients with a history of atrial fibrillation for longer than a year are less likely to be restored to normal sinus rhythm after mitral valve surgery alone than patients with intermittent atrial fibrillation or those who have had atrial fibrillation for less than a year.

Current treatment and alternatives

Conservative treatments include medications to control the heart rhythm and rate, electrical cardioversion and anticoagulants to prevent blood clots forming. A surgical approach known as the Cox maze procedure was developed to treat atrial fibrillation. This is usually performed at the same time as open heart surgery for another indication, such as mitral valve disease. Multiple strategically placed incisions are made in both atria to isolate and stop the abnormal electrical impulses. All the incisions are then sutured and a 'maze' of scar tissue subsequently forms at the incision sites, which blocks the electrical impulses from travelling through the atrium. A single pathway is left intact for the impulse to travel between the chambers of the heart.

What the procedure involves

Cryoablation of the atria can be performed via a catheter introduced through a femoral vein but surgical cryoablation for atrial fibrillation is typically carried out in patients undergoing concomitant open-heart surgery, including mitral valve replacement or repair. Cryoablation is sometimes used during the Cox maze surgical procedure to replace some of the incisions but it has been used more recently to recreate the whole standard lesion set of the traditional Cox maze surgery**.** Ablation may be carried out on both atria or on the left atrium only.

Cardiac surgery is usually performed through a median sternotomy. The patient is connected to a cardiopulmonary bypass machine and an incision is made to enter the left atrium. Cryoablation may be performed before or after the concomitant cardiac surgical procedure. A cryoprobe is used to freeze tissue along a pattern of lines in the left atrium. Following freezing, the damaged tissue forms scars that disrupt the transmission of the electrical impulses. The procedure may then be repeated in the right atrium. The ablation can be performed from within or outside the atrium.

Cryoablation is faster than the traditional Cox maze procedure.

Efficacy

One non-randomised trial compared patients treated with mitral valve surgery and cryoablation with patients having mitral valve surgery and the conventional surgical maze procedure. 85% (94/110) of patients treated with cryoablation were in sinus rhythm at discharge, compared with 86% (95/110) of patients treated with the conventional maze surgery ($p = 0.84$). The survival rate at 3 years was 92% for the cryotherapy group and 98% for the conventional maze group ($p = 0.32$). Two non-randomised trials compared patients having cryoablation and heart valve surgery with patients having heart valve surgery only. In the cryoablation groups 100% (36/36) and 78% (25/32) of patients were in sinus rhythm immediately after surgery, compared with 33% (5/15) and 22% (4/18) of patients in the control groups. In one of these studies, 90% (26/29) of patients treated with cryoablation were in sinus rhythm at 9 months, compared with 25% (4/16) of patients in the control group ($p < 0.0005$). In the other study, 78% (28/36) of patients treated with cryoablation and 20% (3/15) of patients in the control group were in sinus rhythm at 6 months ($p < 0.05$).

The Specialist Advisors did not raise any specific concerns regarding the efficacy of the procedure.

Safety

Because the cryoablation is performed with concomitant cardiac surgery, it is sometimes difficult to differentiate those complications that are specifically related to the cryoablation procedure.

Three studies reported the rate of in-hospital mortality, which ranged from 0% (0/28) to 3% (3/95). Four studies reported that between 3% (1/32) and 14% (4/28) of patients required a pacemaker to be implanted. Other complications that were reported less commonly included reoperation, delayed cardiac tamponade, mediastinitis, low cardiac output, intra-aortic balloon pump, dialysis, and transient ischaemic attack.

The Specialist Advisors noted that heart block damage to the circumflex coronary artery, intraoperative myocardial infarction, and oesophageal injury were potential adverse effects of the procedure.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to intraoperative cryoablation for atrial fibrillation as an associated procedure with other cardiac surgery. Searches were conducted via the following databases, covering the period from their commencement to July 2004: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and Science Citation Index. Trial registries and the Internet were also searched. No language restriction was applied to the searches.

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study.
Patient	Patients with atrial fibrillation and requiring concomitant cardiac surgery.
Intervention/test	Intraoperative cryoablation of the atria.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on three non-randomised controlled trials and three case series studies. One non-randomised controlled trial comparing intraoperative cryoablation with conventional maze surgery was identified.[2] Two non-randomised controlled trials comparing patients given heart valve surgery with cryoablation and patients given heart valve surgery only are summarised in Table 2.[3,4] Three case series, including a total of 163 patients, are also described.[5,6,7]

Table 2 Summary of key efficacy and safety findings on intraoperative cryoablation for atrial fibrillation with concomitant cardiac surgery

Study Details	Key efficacy findings	Key safety findings	Comments
Nakajima H (2002)[2] Non-randomised controlled trial 1992 – 2001 Japan 220 patients: • 50% (110/220) mitral valve surgery and cryoablation • 50% (110/220) mitral valve surgery and conventional maze procedure. Mean age: • Cryoablation group = 60 years • Conventional maze group = 58 years. Mean follow-up: • Cryoablation group = 18.8 months • Conventional maze group = 64.1 months.	Mean cardiopulmonary bypass time : • cryoablation = 186 minutes • conventional maze = 214 minutes, p = 0.001 Sinus rhythm at discharge: • cryoablation = 85.4% (94/110) • conventional maze = 86.4% (95/110), p = 0.84 Perioperative recurrence of AF: • cryoablation = 54% (59/110) • conventional maze = 60% (66/110), p = 0.34 Actuarial survival rate at 3 years: • cryoablation = 91.7% • conventional maze = 98.0%, p = 0.32 Actuarial freedom from stroke at 3 years: • cryoablation = 99.0% • conventional maze = 99.0%, p = 0.68 Event-free survival (freedom from cardiac death, thromboembolism, reoperation, and anticoagulation-related haemorrhage) at 3 years: • cryoablation = 88.5% • conventional maze = 96.2%, p = 0.31 Actuarial freedom from recurrence of sustained AF at 3 years: • cryoablation = 99.0% • conventional maze = 90.4%, p = 0.11	**Complications** Reexploration for bleeding: • cryoablation = 2% (2/110) • conventional maze = 5% (5/110), p = 0.25 Delayed cardiac tamponade: • cryoablation = 2% (2/110) • conventional maze = 0% (0/110), p = 0.15 High dose of inotropes needed postoperatively: • cryoablation = 0% (0/110) • conventional maze = 5% (5/110), p = 0.02 Acute renal failure: • cryoablation = 0% (0/110) • conventional maze = 3% (3/110), p = 0.08 Tracheotomy: • cryoablation = 0% (0/110) • conventional maze = 1% (1/110), p = 0.31 Mediastinitis: • cryoablation = 1% (1/110) • conventional maze = 0% (0/110), p = 0.31	No randomisation. The choice of procedure depended on the period when the operation was performed. 110 pairs of patients were matched on age, preoperative duration of AF > 10 years, preoperative dimension of left atrium > 70 mm, history of previous cardiac surgery, and concomitant aortic valve operation. Only hospital survivors were included in the study. The incidences of preoperative history of stroke and associated coronary artery disease were significantly higher in the cryoablation group. The follow-up was significantly longer for patients in the conventional maze surgery group. Cryoablation probe CCS-200 (Cooper Surgical, Shelton, USA).

Study Details	Key efficacy findings	Key safety findings	Comments
Gaita F (2000)[3] Non-randomised controlled trial Italy 50 patients: • 64% (32/50) heart valve surgery and cryoablation • 36% (18/50) heart valve surgery alone. Mean age: • Cryoablation group = 62 years • Surgery only group = 68 years. Follow-up: 12 months Indications: chronic AF in patients undergoing heart valve surgery for mitral or aortic valve disease, or both. Mean duration of AF: • Cryoablation group = 6.1 years • Surgery only group = 6.9 years.	Sinus rhythm immediately after surgery: • cryoablation = 78% (25/32) • surgery only = 22% (4/18), p < 0.001 Sinus rhythm at discharge: • cryoablation = 74% (23/31) • surgery only = 12% (2/17), p value not stated Sinus rhythm at 9 months (with or without additional radiofrequency ablation or antiarrhythmia drug treatment): • cryoablation = 90% (26/29) • surgery only = 25% (4/16), p < 0.0005 Sinus rhythm at 9 months in patients without additional treatment: • cryoablation = 69% (20/29) • surgery only = 12% (2/16), p < 0.002 Survival at 12 months: • cryoablation = 87% (20/23) • surgery only = 94% (16/17), p value not stated	**Complications** In-hospital mortality: • cryoablation = 3% (1/32) • surgery only = 6% (1/18), p = NS Reoperation for periprosthetic leakage: • cryoablation = 3% (1/32) • surgery only = 0% (0/18), p = NS High dose of inotropes needed postoperatively: • cryoablation = 9% (3/32) • surgery only = 11% (2/18) Pacemaker implantation: • cryoablation = 3% (1/32) • surgery only = 0% (0/18), p = NS	No randomisation. The controls were patients who refused cryoablation. Controls were matched for age, AF duration, and heart valve disease. Ablation of left atrium only. Losses to follow-up at 12 months = 25% (8/32) in cryoablation group. One patient in the cryoablation group was subsequently treated with a single application of radiofrequency energy. Some patients remained on antiarrhythmic drugs throughout the follow-up period. Dual-probe cryosurgical system (Frigitronics, Cooper Surgical, Shelton, USA).

Study Details	Key efficacy findings	Key safety findings	Comments
Sueda T (1997)[4] Non-randomised controlled trial Japan 51 patients: • 71% (36/51) heart valve surgery and cryoablation • 29% (15/51) heart valve surgery alone. Mean age: • Cryoablation group = 61 years • Surgery only group = 55 years. Mean follow-up: 18 months (range 2 to 51 months) Indications: mitral valve disease and chronic atrial fibrillation Mean duration of AF: • Cryoablation group = 7.8 years • Surgery only group = 8.2 years	Sinus rhythm immediately after surgery: • cryoablation = 100% (36/36) • surgery only = 33% (5/15) Sinus rhythm at 1 month: • cryoablation = 86% (31/36) • surgery only = 27% (4/15), $p < 0.05$ Sinus rhythm at 6 months (with or without additional cardioversion or antiarrhythmia drug treatment): • cryoablation = 78% (28/36) • surgery only = 20% (3/15), $p < 0.05$	**Complications** No serious complications were reported.	No randomisation. The controls were patients who were treated before the ablation procedure was introduced in the study centre.

Study Details	Key efficacy findings	Key safety findings	Comments
Manasse E (2003)[5] Prospective cohort study Italy 1998 – 2002 95 patients Mean age = 61 years Median follow-up = 36 months (range 6 to 54 months) Concomitant surgical procedures: mitral valve surgery (n = 83), aortic valve surgery (n = 8), tricuspid valve surgery (n = 2), coronary bypass (n = 1), none (n = 1) Indications: Continuous atrial fibrillation > 6 months, not susceptible to cardioversion (permanent atrial fibrillation) or atrial fibrillation > 6 months but transiently cardiovertible or < 6 months in presence of severely disabling symptoms (persistent atrial fibrillation) Average duration of atrial fibrillation: Permanent = 65 months, persistent = 34 months	Sinus rhythm at discharge = 70.5% (67/95) Sinus rhythm at follow-up = 81.4% (70/86)	**In-hospital complications** Mortality = 3.2% (3/95) Major cardiac reoperation = 3.2% (3/95) Revision for bleeding = 2.1% (2/95) Pacemaker implantation = 4.2% (4/95) Low cardiac output = 8.4% (8/95) Intra-aortic balloon pump = 1.1% (1/95) Dialysis = 1.1% (1/95) Transient ischaemic attack = 1.1% (1/95) **Complications during follow-up** Mortality = 6.3% (6/95) Major cardiac reoperation = 5.2% (5/95) Pacemaker implantation = 2.1% (2/95) Overall crude mortality = 9.4% (9/95)	Consecutive patients. Ablation of left atrium only. Electrical or pharmacological conversion was always attempted before discharge if atrial fibrillation or atrial flutter were present. Referring doctor was advised to withdraw antiarrhythmic therapy after 3 to 6 months, in the absence of atrial fibrillation or atrial flutter recurrence. There was one operative death due to a tear of the left atrial wall, resulting from the cryoprobe being retracted before thawing was complete. A significantly higher mortality was seen in patients who remained with atrial fibrillation, compared with those who converted to sinus rhythm either definitely or temporarily. Authors state that the proportion of patients with peri-valvular leak was approximately the same as in the non-cryo surgery population at the same centre. Dual-probe cryosurgical system (Frigitronics, Cooper Surgical, Shelton, USA).

Study Details	Key efficacy findings	Key safety findings	Comments
Yamauchi S (2002)[6] Case series Japan 40 patients Mean age = 60 years (range 44 to 76 years) Follow-up: 1 month Concomitant surgical procedures: mitral valve surgery (n = 36), tricuspid annuloplasty (n = 11), aortic valve replacement (n = 4), intracardiac repair (n = 3) Indications: atrial fibrillation and cardiac disease, including mitral valve disease, and atrial septal defect Average duration of atrial fibrillation = 8 years (range 0.4 to 20 years)	Sinus rhythm immediately after surgery = 78% (31/40)	**Complications** Pacemaker implantation = 8% (3/40)	Selection of patients not described. Epicardial mapping was used to determine the optimal sites for cryoablation.

Study Details	Key efficacy findings	Key safety findings	Comments
Doll N (2003)[7] Case series 2002 – 2003 Germany 28 patients Mean age = 60 years (range 30 to 76 years) Follow-up: 6 months Concomitant surgical procedures: mitral valve surgery (n = 13), other cardiac surgery (n = 14), none (n = 1) Indications: chronic atrial fibrillation (82%), symptomatic paroxysmal atrial fibrillation (18%) Average duration of atrial fibrillation = 6.8 years (range 1 to 40 years)	Mean cardiopulmonary bypass time = 112 minutes. Sinus rhythm immediately after surgery = 96% (27/28). Sinus rhythm at discharge = 82% (23/28). Atrial fibrillation in early postoperative period = 50% (14/28). Postoperative electrical cardioversion = 32% (9/28).	**Complications** Pacemaker implantation = 14% (4/28) No hospital mortality.	Patient selection not described Ablation of left atrium only. 71% (20/28) patients had a right anterolateral minithoracotomy with femoral access cardiopulmonary bypass, 29% (8/28) patients had a median sternotomy. SurgiFrost cryoablation device (CryoCath, Irvine, USA).

Validity and generalisability of the studies

- There are many aspects of the cryoblation procedure that varied within and among studies, including the pattern of ablation lesions and the type of probe. This needs to be taken into consideration when the safety and efficacy are compared among studies.

- Patients were treated with concomitant heart surgery and some of the reported complications would have been due to this surgery rather than to the cryoablation procedure.

- One study used a minithoracotomy approach for the majority of patients.[5] This may have a different safety profile from the median sternotomy approach that is traditionally used for the procedure.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

- Cryotherapy is one of several energy sources that can be used to treat atrial fibrillation.

Issues for consideration by IPAC

None other than those described above.

References

1 Grubb NR and Furniss S. Radiofrequency ablation for atrial fibrillation. *British Medical Journal* 2001; 322: 777–80.

2 Nakajima H, Kobayashi J, Bando K, et al. The effect of cryo-maze procedure on early and intermediate term outcome in mitral valve disease: case matched study. *Circulation* 2002; 106: I46 – I50.

3 Gaita F, Gallotti R, Calò L, et al. Limited posterior left atrial cryoablation in patients with chronic atrial fibrillation undergoing valvular heart surgery. *Journal of the American College of Cardiology* 2000; 36: 159–66.

4 Sueda T, Nagata H, Orihashi K, et al. Efficacy of a simple left atrial procedure for chronic atrial fibrillation in mitral valve operations. *The Annals of Thoracic Surgery* 1997; 63: 1070–5.

5 Manasse E, Gaita F, Ghiselli S, et al. Cryoablation of the left posterior atrial wall: 95 patients and 3 years of mean follow-up. *European Journal of Cardio-Thoracic Surgery* 2003; 24: 731–40.

6 Yamauchi S, Ogasawara H, Saji Y, et al. Efficacy of intraoperative mapping to optimise the surgical ablation of atrial fibrillation in cardiac surgery. *The Annals of Thoracic Surgery* 2002; 74: 450–7.

7 Doll N, Kiaii BB, Fabricius AM, et al. Intraoperative left atrial ablation (for atrial fibrillation) using a new argon cryocatheter: early clinical experience. *The Annals of Thoracic Surgery* 2003; 76: 1711–5.

Appendix A: Additional papers on cryoablation for atrial fibrillation as an associated procedure with other cardiac surgery not included in the summary tables

Article title	Number of patients/ follow-up	Comments	Direction of conclusions
Chen MC, Chang JP, Guo GBF, et al. Atrial size reduction as a predictor of the success of radiofrequency maze procedure for chronic atrial fibrillation in patients undergoing valvular surgery. *Journal of Cardiovascular Electrophysiology* 2001; 12: 867–74.	119 patients. 24 month follow-up.	Radiofrequency and cryoablation used to create lesions.	Sinus rhythm: Maze II ablation pattern = 73%, Maze III ablation pattern = 81% control = 11%
Gaita F, Gallotti R, Riccardi R, et al. Follow-up of three different patterns of cryolesions limited to posterior left atrium in patients with chronic atrial fibrillation and valvular disease. *Pacing & Clinical Electrophysiology* 2000; 23: 599.	36 patients. 6 month follow-up.	Conference abstract. 3 different patterns of cryolesions.	No complications. No statistically significant differences among patients in 3 groups.
Lee JW, Choo SJ, Kim KI, et al. Atrial fibrillation surgery simplified with cryoablation to improve left atrial function. The Annals of Thoracic Surgery 2003; 76: 1711–5.	83 patients. 6 months follow-up.	Standard Maze surgery combined with cryoablation.	No perioperative mortality. Sinus rhythm restored earlier in cryoablation group.
Morishita A, Harada M, Watanabe M. How to spread out the satisfactory exposure: placement technique in right-sided maze procedure. *Journal of Cardiovascular Surgery* 2000; 41: 575–7.	12 patients.	Case series.	Sinus rhythm = 92%.

Appendix B: Literature search for cryoablation for atrial fibrillation as an associated procedure with other cardiac surgery

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in EMBASE, Current Contents, PreMedline and all EMB databases.

For all other databases a simple search strategy using the key words in the title was employed.

1. exp Atrial Fibrillation/
2. intraoperative.mp.
3. exp Thoracic Surgery/
4. cryotherapy.mp. [mp=ti, ab, sh, tn, ot, dm, mf, rw]
5. cryoablation.mp. [mp=ti, ab, sh, tn, ot, dm, mf, rw]
6. 4 or 5
7. 1 and 6