NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of radiofrequency catheter ablation for atrial fibrillation

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 May 2005.

Procedure names

- Radiofrequency catheter ablation for atrial fibrillation.
- Percutaneous radiofrequency catheter ablation for atrial fibrillation.

Specialty societies

- British Cardiovascular Intervention Society.
- British Pacing and Electrophysiology Group.
- British Cardiac Society.
- Society of Cardiothoracic Surgeons, Great Britain and Ireland.

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.

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 treatment 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 impulses to travel between the chambers of the heart.

Alternative methods of creating lesions in the atria by ablation have been developed, using energy sources such as radiofrequency, microwave, cryotherapy and ultrasound.

What the procedure involves

Radiofrequency catheter ablation is a minimally invasive procedure that is usually carried out under sedation. A catheter is inserted into the femoral vein and threaded up into the heart, using fluoroscopy to ensure correct positioning. An attachment at the tip of the catheter sends out radiofrequency energy, producing heat that damages the targeted area of heart muscle. Electrophysiology testing may be done before the procedure to identify and map the source of the abnormal electrical signals. Advanced imaging and mapping techniques that do not require fluoroscopy have also been developed for use in this procedure.

Several different strategies may be used, including linear ablation in the left or right atrium and ablation of focal triggers of atrial fibrillation.

Efficacy

In a small randomised controlled trial 21% (3/14) of patients treated with radiofrequency catheter ablation had recurrence of atrial fibrillation at 12 months, compared with 60% (9/15) of patients treated with medication ($p = 0.02$).

In a non-randomised comparative study of 1171 patients, 78% of patients treated with radiofrequency catheter ablation were estimated to be free of atrial fibrillation at 3 years, compared with 37% of patients treated with medication ($p < 0.001$). Patients receiving radiofrequency catheter ablation had a significantly reduced risk of death compared with those receiving medication.

A large survey reported that 76% (6644/8745) of patients had resolution of symptoms of atrial fibrillation after a median follow-up of 12 months (this proportion ranged from 22 to 91% among different centres).

The Specialist Advisors noted the lack of long-term data and the difficulty of objectively assessing the success of this procedure.

Safety

In a non-randomised comparative study 8% (46/589) of patients treated with radiofrequency catheter ablation had adverse events during follow-up compared with 19% (98/582) of patients treated with medication. Adverse events included congestive heart failure (32/589), transient ischaemic attack (8/589), myocardial infarction (7/582) and ischaemic stroke (4/589).

A comparable complication rate (6%) was reported in a large survey of 8745 patients who had undergone catheter ablation for atrial fibrillation. The most significant complications reported in this study were 4 (0.05%) cases of early deaths, 20 (0.28%) strokes, 47 (0.66%) transient ischaemic attacks and 107 (1.22%) episodes of cardiac tamponade.

These two studies also reported that 2 and 3.9% of patients respectively (12/589 and 340/8745) developed a atypical flutter of new onset after undergoing catheter ablation.

The Specialist Advisors listed the potential adverse events as stroke, cardiac tamponade and pulmonary vein stenosis.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to radiofrequency catheter ablation for atrial fibrillation. The search strategy is described in Appendix A. The following selection criteria 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.

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. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with atrial fibrillation.
Intervention/test	Radiofrequency catheter ablation.
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 eight studies; including one randomised controlled trial, a non-randomised controlled study and six studies treated as case-series in this overview. One of these case-series is a report of a survey from 181 centres undertaking catheter ablation. Information on the source of energy was available for only4918 patients (53%) and of these patients 89% received radiofrequency catheter ablation.

Existing reviews on this procedure

A Health Technology Assessment review on radiofrequency catheter ablation for cardiac arrhythmias was published by the Canadian Coordinating Office for Health Technology Assessment in 2002. Nine relevant studies were identified and the review concluded that catheter ablation for most cardiac arrhythmias is associated with good procedureal success rates but there remains insufficient evidence to draw specific conclusions about its long term clinical efficacy.

Table 1 Summary of key efficacy and safety findings on radiofrequency catheter ablation for atrial fibrillation

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein

Study details	Key efficacy findings	Key safety findings	Comments
Krittayaphong R (2003)[2] Randomised controlled trial Thailand 30 patients • 50% (15/30) RFA • 50% (15/30) antiarrhythmia medication (amiodarone) Mean age (years): • RFA = 55.3 • Medication = 48.6, p = 0.17 Mean duration of AF (months): • RFA = 62.9 • Medication = 48.2, p = 0.51 Inclusion criteria: age 15 to 75 years; symptomatic paroxysmal or persistent AF for more than 6 months; refractory to at least 1 antiarrhythmic medication; never been given amiodarone Exclusion criteria: transient AF or treatable cause of AF; bleeding disorders; thyroid disorders; previous stroke; severe underlying illness that limited life expectancy to less than 1 year; psychiatric disorder; valvular heart disease; unwilling to participate in research Follow-up = 12 months	RFA procedure could not be performed in one patient due to failure of transeptal puncture. Recurrence of AF at 1 year: • RFA = 21.4% (3/14) • Medication = 60% (9/15), p = 0.02 Frequency of symptoms in RFA group decreased from mean 42.8 ± 22.6 attacks per month at baseline to 0.9 ± 2.8 attacks per month at 1 year after procedure, p < 0.001 Reduction in frequency of symptoms in medication group was not statistically significant There were no significant changes in the general health score (SF-36) at 6 and 12 months in the medication group compared with baseline The general health score in the RFA group was significantly higher at 6 and 12 months (p = 0.007). The physical functioning score was also significantly improved	**Complications of RFA procedure** • Stroke = 7.1% (1/14) • Groin haematoma = 7.1% (1/14) **Adverse effects of medication** • Gastrointestinal side effects (mainly nausea) = 40% (6/15) • Corneal microdeposit = 13.3% (2/15) • Hypothyroidism = 13.3% (2/15) • Abnormal liver function test = 13.3% (2/15) • Hyperthyroidism = 6.7% (1/15) • Sinus node dysfunction = 6.7% (1/15)	Method of randomisation not described. Pulmonary vein isolation and linear ablation of right atrium. An electroanatomic mapping system was used. A maintenance dose of amiodarone was given to patients in the RFA group for 3 months after the procedure.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Pappone C (2003)[3] Non-randomised controlled study Italy 1998–2001 1171 patients • 50% (589/1171) RFA • 50% (582/1171) antiarrhythmic medications Mean age (years): • RFA = 65 • Medication = 65, p = 0.99 Mean duration of AF (years): • RFA = 5.5 • Medication = 3.6, p < 0.001 Inclusion criteria: symptomatic AF Exclusion criteria: contraindication to anticoagulation; New York Heart Association functional class IV; myocardial infarction or cardiac surgery within the past 3 months; sick sinus syndrome or atrioventricular conduction disturbances without an artificial pacemaker; ventricular tachyarrhythmias; thyroid dysfunction; unsuccessful cardioversion to sinus rhythm by drugs and/or electroshock Median follow-up = 900 days (range 161 - 1508)	Patients in sinus rhythm at discharge: • RFA = 100% (589/589) • Medication = 100% (582/582) Authors note that 19.5% (115/589) of patients receiving RFA were prescribed a previously ineffective antiarrhythmic before discharge because of AF episodes and/or the need for electrical cardioversion at the end of the procedure. Reduction in risk of death for ablated patients = 54% (p < 0.001) Percentage of AF-free patients at 3 years (Kaplan-Meier estimates): • RFA = 78% • Medication = 37%, p < 0.001 Physical and mental quality of life scores (SF-36) at 1 year were higher for ablated patients than for those treated medically. Scores for ablated patients reached the levels of the general population	**Complications of RFA procedure** • Cardiac tamponade = 0.7% (4/589) • Stroke = 0% (0/589) • PV stenosis = 0% (0/589) **Adverse events during follow-up** Total adverse events: • RFA = 8% (46/589) [54 events] • Medication = 19% (98/582) [117 events] Congestive heart failure: • RFA = 5.4% (32/589) • Medication = 9.8% (57/582) Myocardial infarction: • RFA = 1.2% (7/589) • Medication = 1.4% (8/582) Peripheral embolism: • RFA = 0.2% (1/589) • Medication = 0.5% (3/582) Transient ischaemic attack: • RFA = 1.4% (8/589) • Medication = 4.6% (27/582) Ischaemic stroke: • RFA = 0.7% (4/589) • Medication = 2.6% (15/582) Haemorrhagic stroke: • RFA = 0.3% (2/589) • Medication = 1.2% (7/582) Total deaths: • RFA = 6.4% (38/589) • Medication = 14.3% (83/582) Deaths due to cardiovascular causes: • RFA = 3.1% (18/589) • Medication = 10.1% (59/582) 2% (12/589) ofablated patients developed atypical atrial flutter.	No randomisation, consecutive patients. The decision to undergo catheter ablation or medical treatment was made by the patient or the electrophysiologist. Circumferential pulmonary vein ablation. The ablation group had significantly longer arrhythmia duration, greater number of arrhythmics used and more frequent hospitalisations than the medical group. Nonfluoroscopic electrogeometric mapping system used. AF recurrence was defined as a symptomatic episode lasting more than 10 minutes and confirmed by ECG. Quality of life was assessed for 109 consecutive ablated and 102 medically treated patients. 2% (19/1171) patients were lost to follow-up. Maintenance of sinus rhythm was associated with reductions in morbidity and mortality in both groups.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Cappato R (2005)[4] Worldwide survey (181 centres) 1995–2002 9370 patients (11762 procedures) Age range: 16 - 86 years Inclusion criteria (proportion of centres): drug refractory AF (93%); paroxysmal AF (100%); persistent AF (53%); permanent AF (20%) Exclusion criteria (proportion of centres): upper limit of left atrial size between 50 and 60 mm of maximal transverse diameter (46%); a lower limit of left ventricular ejection fraction between 30% and 35% (65%); prior heart surgery (64%). Median follow-up = 12 months (range 1 - 98)	Freedom from AF in the absence of antiarrhythmic drugs = 52.0% (4550/8745) (range among centres = 14.5 - 76.5%) Freedom from AF in the presence of formerly ineffective antiarrhythmic drugs = 23.9% (2094/8745) (range among centres = 8.8 - 50.3%) Resolution of symptoms with or without drugs = 76.0% (6644/8745) (range among centres = 22.3 - 91.0%)	**Complications** • Total major complications = 6.0% (524/8745) • Periprocedural death = 0.05% (4/8745) [including 2 cases of massive cerebral thromboembolism] • Cardiac tamponade = 1.2% (107/8745) • Sepsis, abscess or endocarditis = 0.01% (1/8745) • Pneumothorax = 0.02% (2/8745) • Haemothorax = 0.2% (14/8745) • Permanent diaphragmatic paralysis = 0.1% (10/8745) • Femoral pseudoaneurysm = 0.5% (47/8745) • Arteriovenous fistulae = 0.4% (37/8745) • Valve damage = 0.01% (1/8745) • Aortic dissection = 0.03% (3/8745) • Stroke = 0.2% (20/8745) • Transient ischaemic attack = 0.5% (47/8745) • PV stenosis = 1.3% (117/8745) • Atypical atrial flutter of new onset = 3.9% (340/8745)	Questionnaires were sent to 777 centres and relevant data were received from 181 (23%). Median number of procedures per centre = 37.5 (range 1 - 600) Techniques used differed between and within centres. They included right atrial compartmentalisation, focal ablation and pulmonary vein isolation. Responding centres were uniformly distributed in all continents. Inclusion and exclusion criteria varied between centres. Energy source used was known for 4649 patients: 89% received radiofrequency, 5% cryotherapy, 2% ultrasound, 2% laser; 2% other forms of energy. Complete data for assessment of efficacy were available for 93% (8745/9370) of patients. 24.3% (2122/8745) required two procedures and 3.1% (267/8745) required three procedures. The success rate increased as the number of procedures performed per centre increased.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Bourke J (2005)[5] Case series UK 1999–2002 100 patients Mean age = 52 years (range 23 - 73) Mean duration of AF = 53 months (range 6 - 180) Inclusion criteria: Symptomatic paroxysmal or persistent AF Exclusion criteria: structural heart disease; transient or systemic causes of AF such as thyroid dysfunction, systemic inflammation or biochemical derangement; arrhythmia caused by alcohol excess Follow-up = 6 months	Sinus rhythm immediately after procedure = 77% (77/100) Sinus rhythm and asymptomatic at 6 months = 55% (55/100) Symptomatic paroxysmal or persistent AF at 6 months = 45% (45/100) Sinus rhythm and asymptomatic at 6 months without drugs = 17% (17/100) Sinus rhythm at 6 months, with or without drugs: • paroxysmal AF = 73% (26/36) • persistent AF = 45% (29/64), p = 0.01	**Complications** • Cardiac tamponade = 6% (6/100) • Coronary artery embolus = 2% (2/100) • Acute left upper pulmonary vein ostium spasm = 2% (2/100) • Groin haematoma = 2% (2/100) • Complete heart block = 1% (1/100) • Sedation related hypotension = 1% (1/100) • Upper GI haemorrhage = 1% (1/100) • Symptomatic PV stenosis = 0% (0/100)	Consecutive patients Study includes the first 100 patients to undergo pulmonary vein catheter ablation at the hospital. Typically, AF symptoms had not been controlled by trials of two antiarrhythmic drugs before patients were considered for RFA. Focal pulmonary vein ablation. No losses to follow-up. The occurrence of asymptomatic AF in patients free from arrhythmia symptoms was excluded using a 48 hour Holter recording. No patient underwent a repeat ablation procedure during the 6-month follow-up. Study centre had a policy of continuing antiarrhythmic treatment indefinitely in patients with persistent AF before ablation. Additional mapping aids were used for the last 38 patients.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Jaïs P (2004)[6] Non-randomised comparative study (comparing different patterns of ablation) France 2001–2002 200 patients: • 50% (100/200) PV isolation and cavotricuspid and mitral isthmus ablation • 50% (100/200) PV isolation and cavotricuspid ablation without mitral isthmus ablation Mean age (years): • PV isolation with mitral isthmus ablation = 55 ± 10 • PV isolation without mitral isthmus ablation = 52 ± 10 Mean duration of AF (years): • PV isolation with mitral isthmus ablation = 6 ± 6 • PV isolation without mitral isthmus ablation = 7 ± 6 Inclusion criteria: symptomatic, drug-refractory paroxysmal AF. Follow-up = 12 months	Mitral isthmus block achieved in 92% (92/100) of patients Recurrence of atrial arrhythmia immediately after procedure: • PV isolation with mitral isthmus ablation = 32% (32/100) • PV isolation without mitral isthmus ablation = 49% (49/100), p = 0.02 Freedom from AF without antiarrhythmic drugs at 12 months: • PV isolation with mitral isthmus ablation = 87% (87/100) • PV isolation without mitral isthmus ablation = 69% (69/100), p = 0.002	**Complications with PV isolation and mitral isthmus ablation** • Cardiac tamponade = 4% (4/100) No significant PV stenosis or thromboembolic complications were observed acutely or at 1 year	Consecutive patients. Patients were hospitalised for 2 days at 1,3,6 and 12 months follow-up for assessment including transthoracic echocardiography, Holter recordings, stress testing and CT scan of PVs at 1 year. 23% (46/200) of patients had structural heart disease at study entry. The power was reduced for the last 25 patients receiving mitral isthmus ablation to reduce the risk of cardiac tamponade.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Verma A (2005)[7] Case series USA 2002–2003 700 patients (42 with left atrial scarring) Mean age (years): • Left atrial scar = 59 ± 13 • No left atrial scar = 53 ± 13 Mean duration of AF (years): • Left atrial scar = 7.0 ± 4.9 • No left atrial scar = 6.1 ± 5.4 Paroxysmal AF: • Left atrial scar = 26% (11/42) • No left atrial scar = 40% (263/658) Inclusion criteria: symptomatic AF (paroxysmal, persistent or permanent) refractory to two or more antiarrhythmic drugs Exclusion criteria: Repeat PV antrum isolation procedure; history of any previous catheter ablation; previous cardiac surgery Mean follow-up = 15.8 ± 7.8 months	Late recurrence of AF (beyond 2 months): • Overall = 21.7% (152/700) • Left atrial scar = 57% (24/42) • No left atrial scar = 19% (128/658), p = 0.003 75% (114/152) of patients with recurrence had nonparoxysmal AF, compared with 57% (312/548) of patients without recurrence, p = 0.047 Only the presence of left atrial scar was a significant independent risk factor for AF recurrence in multivariate model: hazard ratio = 3.4 (95% CI, 1.3-9.4)	Not reported	Consecutive patients. The aim of the study was to assess the impact of left atrial scarring on the outcome: 6% (42/700) patients had left atrial scarring. Intracardiac echocardiography was used to guide the catheter. All 4 PVS and the superior vena cava were isolated in every patient. Electroanatomic mapping was used for some patients. 44% (309/700) of patients had structural heart disease at study entry.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Saad E (2003)[8] Case series USA and Italy 608 patients Mean age = 51.3 years Inclusion criteria: drug-refractory symptomatic AF Follow-up = 12 months	Not reported	**Complications** • Severe PV narrowing = 3.4% (21/608) • Moderate PV narrowing = 4.4% (27/608) • Mild PV narrowing = 7.7% (47/608) • Cerebrovascular accidents = 0.7% (4/608) • Cardiac tamponade = 0.5% (3/608) • Haematoma = 0.5% (3/608) 8.8% (22/249) of patients showed increasing PV narrowing over time	Consecutive patients. Different ablation strategies were used. Electroanatomic mapping was used for 71 patients. CT scan at 3 months follow-up to screen for PV stenosis. All patients with mild or moderate PV stenosis were asymptomatic. 38% (8/21) of patients with severe PV stenosis were asymptomatic. Incidence of PV stenosis was significantly lower when intracardiac echocardiography was used.

Abbreviations used: AF = atrial fibrillation, RFA = radiofrequency ablation, PV = pulmonary vein			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Arentz T (2003)[9] Case series Germany 47 patients Mean age = 55 ± 10 years Inclusion criteria: highly symptomatic paroxysmal (> 2 episodes per week) or persistent (> 4 weeks) AF resistant to more than 3 antiarrhythmic drugs Follow-up = 2 years	Recurrence of AF within 4 weeks = 55% (26/47) Stable sinus rhythm without antiarrhythmic drugs at 2 years • Overall = 51% (24/47) • Patients with paroxysmal AF = 61% (22/36) • Patients with persistent AF = 18% (2/11) Freedom from AF in presence of previously ineffective antiarrhythmic drug therapy at 2 years = 26% (12/47)	Complete occlusion of pulmonary vein = 8.5% (4/47) Significant narrowing of pulmonary vein = 19.2% (9/47) Only three of the 13 patients with pulmonary vein stenosis complained of moderate dyspnoea on exertion. The remaining 10 patients did not report any symptoms The risk of pulmonary vein stenosis was 8% (3/37) with an ostial ablation site and 45% (10/22) with a distal ablation site in smaller vessels ($p < 0.01$)	Patient selection not described. RFA of focal triggers inside the pulmonary veins and/or ostial pulmonary vein isolation. All patients were scheduled to undergo transoesophageal Doppler-echo and angio MRI 2 years after the initial procedure. These were repeated 3-6 months after the 2 year follow-up for all patients with pulmonary vein stenosis. Transoesophageal Doppler-echo was performed in 94% (43/47) of patients and MRI in 83% (39/47) of patients. 8 patients had structural heart disease at study entry. Stenotic veins had a significantly smaller diameter than nonstenotic veins (10.4 mm versus 13.0 mm, $p < 0.05$). The total delivered power and the total ablation time per pulmonary vein were not correlated with the risk of stenosis.

Validity and generalisability of the studies

- One study included only patients with paroxysmal atrial fibrillation.[6] The remaining studies either included patients with persistent or permanent atrial fibrillation or they did not specify what type of atrial fibrillation was included.

- Some studies excluded patients with structural heart disease.

- The techniques varied both within and between studies, in terms of patterns of ablation and energy levels used. These differences are likely to have had an impact on the safety and efficacy of the procedure.

- Some studies specified that electroanatomic mapping was used for some or all of the cases. [2,3,5,7,8]

- The large survey included some patients who had received catheter ablation using different kinds of energy source, but the majority of procedures used radiofrequency.[4] The inclusion and exclusion criteria also varied between centres contributing to this survey.

- Different outcome measures were used. The randomised controlled trial reported only subjective outcome measures.[2]

Specialist Advisors' opinions

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

- For patients for whom drug therapy has failed, appropriate comparators would be the surgical maze procedure or catheter ablation of the atrioventricular node and pacemaker implantation.

- There is some uncertainty about the role of this procedure as first-line therapy (as an alternative to drugs).

- Techniques have evolved and this is likely to have an impact on the safety and efficacy of the procedure.

- There is a small but significant rate of serious complications.

- This procedure is technically difficult and there is a long learning curve.

- In order to achieve long-term maintenance of sinus rhythm some patients may need to undergo a second or third procedure.

- This procedure has the potential to make a major impact on the NHS, in terms of numbers of patients eligible for treatment and use of resources.

Issues for consideration by IPAC

IPAC has previously considered radiofrequency ablation, microwave ablation and cryoablation in association with other cardiac surgery (IPG 121, IPG 122 and IPG 123).

References

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

2 Krittayaphong R, Bhuripanyo K, Pooranawattanakul S, et al., A randomized clinical trial of the efficacy of radiofrequency catheter ablation and amiodarone in the treatment of symptomatic atrial fibrillation. *Journal of the Medical Association of Thailand* 2003; 86: S8–S16.

3 Pappone C, Rosanio S, Augello G, et al. Mortality, morbidity, and quality of life after circumferential pulmonary vein ablation for atrial fibrillation. *Journal of the American College of Cardiology* 2003; 42: 185–97.

4 Cappato R, Calkins H, Chen S-A, et al. Worldwide survey on the methods, efficacy, and safety of catheter ablation for human atrial fibrillation. *Circulation* 2005; 111: 1100–5.

5 Bourke JP, Dunuwille A, O'Donnell D, et al. Pulmonary vein ablation for idiopathic atrial fibrillation: six month outcome of first procedure in 100 consecutive patients. *Heart* 2005; 91: 51–7.

6 Jaïs P, Hocini M, Hsu L-F, et al Technique and results of linear ablation at the mitral isthmus. *Circulation* 2004; 110: 2996–3002.

7 Arentz T, Jander N, von Rosenthal J, et al. Incidence of pulmonary vein stenosis 2 years after radiofrequency catheter ablation of refractory atrial fibrillation. *European Heart Journal* 2003; 24: 963–9.

8 Verna A, Wazni O, Marrouche N, et al. Pre-existent left atrial scarring in patients undergoing pulmonary vein antrum isolation. *Journal of the American College of Cardiology* 2005; 45: 285–92.

9 Saad EB, Rossillo A, Saad CP, et al. Pulmonary vein stenosis after radiofrequency ablation of atrial fibrillation. *Circulation* 2003; 108: 3102–7.

Appendix A: Additional papers on radiofrequency catheter ablation for atrial fibrillation not included in the summary tables

The following table outlines studies that are considered potentially relevant to the overview but were not included in the main data extraction table and is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Comments	Direction of conclusions
Callans F, Gerstenfeld E, Dixit S, et al. Efficacy of repeat pulmonary vein isolation procedures in patients with recurrent atrial fibrillation. *Journal of Cardiovascular Electrophysiology* 2004; 15: 1050–5.	74 patients. Mean follow-up = 9 months.	Case series. Repeat procedures.	AF cure or 90% reduction in AF episodes = 86% (64/74) after repeat PV isolation.
Dagres N, Clague JR, Kottkamp H, et al. Impact of radiofrequency catheter ablation of accessory pathways on the frequency of atrial fibrillation during long-term follow-up. *European Heart Journal* 2001; 22: 423–7.	116 patients. Mean follow-up = 24 months.	Case series. Patients with manifest or concealed accessory pathways.	Recurrent AF = 20% (18``/91) Older age was the only significant predictor of AF recurrence.
Deisenhofer I, Schneider M, Bohlen-Knauf M, et al. Circumferential mapping and electric isolation of pulmonary veins in patients with atrial fibrillation. *American Journal of Cardiology* 2003; 91: 159–63.	75 patients. Mean follow-up = 230 days.	Case series.	At 1 month, 48% (36/53) sinus rhythm. 40% repeat ablation. PV stenosis = 17% (13/75) Pericardial effusion = 5% (4/75).
Hsu L-F, Jais P, Hocini M, et al. Incidence and prevention of cardiac tamponade complicating ablation for atrial fibrillation. *PACE* 2005; 28: S106–9.	348 procedures	Case series. Incidence and prevention of cardiac tamponade.	3% cardiac tamponade during linear ablation. RF power was subsequently reduced and tamponade occurred in 1% of patients.
Jais P, Shah D, Haissaguerre M, et al. Efficacy and safety of septal and left-atrial linear ablation for atrial fibrillation. *American Journal of Cardiology* 1999; 84: 139R–146R.	54 patients. Mean follow-up = 19 months.	Case series.	Sinus rhythm = 68.5% (37/54) Pericardial effusion = 9% (5/54)
Kottkamp H, Tanner H, Kobza R, et al. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions. *Journal of the American College of Cardiology* 2004; 44: 869–77.	100 patients. 12 month follow-up.	Case series.	Freedom from AF = 88% (measured on 24h ECG) and 74% (7 day ECG).
Macle L, Jais P, Weerasooriya R, et al. Irrigated-tip catheter ablation of pulmonary veins for treatment of atrial fibrillation. *Journal of Cardiovascular Electrophysiology* 2002; 13: 1067–73.	136 patients. Mean follow-up = 9 months.	Case series.	Moderate PV stenosis = 0.7% After 9 month follow-up, 81% freedom from AF including 66% not taking antiarrhythmic drugs. Reablation = 49%
Oral H, Chugh A, Lemola K, et al. Noninducibility of atrial fibrillation as an end point of left atrial circumferential ablation for paroxysmal atrial fibrillation. *Circulation* 2004; 110: 2797–801.	100 patients. 6 month follow-up.	Case series.	Sinus rhythm and AF not inducible = 40% (40/100) After repeat treatment, 90% (27/30) patients had noninducible AF.
Oral H, Chugh A, Scharf C, et al. Incremental value of isolating the right inferior pulmonary vein during pulmonary vein isolation procedures in patients with paroxysmal atrial fibrillation. *Pacing & Clinical Electrophysiology* 2004; 27: 480–4.	176 patients. Mean follow-up = 15 months.	Case series. Effect of isolating 4 rather than 3 PVs.	Freedom from AF = 58% with 3 PVs isolated, compared to 73% when all 4 PVs were isolated (p = 0.07).

Article title	Number of patients/ follow-up	Comments	Direction of conclusions
Pappone C, Oral H, Santinelli V, et al. Atrio-esophageal fistula as a complication of percutaneous transcatheter ablation of atrial fibrillation. *Circulation* 2004; 109: 2724–6.	2 patients.	2 case reports.	2 cases of atrio-oesophageal fistula after circumferential PV ablation in different centres. 1 patient died, 1 survived after surgery.
Pappone C, Oreto G, Rosanio S, et al. Atrial electroanatomic remodelling after circumferential radiofrequency pulmonary vein ablation. *Circulation* 2001; 104: 2539–44.	251 patients. 10 month follow-up.	Case series. Use of electroanatomic guidance.	Overall freedom from AF = 80% (201/251) [85% for paroxysmal AF, 68% for permanent AF]
Saad E, Marrouche N, Saad C, et al. Pulmonary vein stenosis after catheter ablation of atrial fibrillation: emergence of a new clinical syndrome. *Annals of Internal Medicine* 2003; 138: 634–8.	335 patients. 12 month follow-up.	Case series. Clinical course and symptoms associated with PV stenosis.	Severe PV stenosis = 5% 56% of patients with severe PV stenosis had symptoms, which included shortness of breath, cough and haemoptysis.
Scharf C, Oral H, Chugh A, et al. Acute effects of left atrial radiofrequency ablation on atrial fibrillation. *Journal of Cardiovascular Electrophysiology* 2004; 15: 515–21.	144 patients.	Case series.	Conversion to atrial tachycardia = 4% Conversion to atrial flutter = 4%.
Schwartzman D, Bazaz R, Nosbisch J. Catheter ablation to suppress atrial fibrillation: evolution of technique at a single center. *Journal of Interventional Cardiac Electrophysiology* 2003; 9: 295–300.	112 patients.	Cohort study, comparing different patterns of ablation.	Noninducibility of AF = 47% (focal ablation), 69% (individual vein encircling), 87% (vestibule encircling).
Sporton SC, Earley MJ, Nathan AW, et al. Electroanatomic versus fluoroscopic mapping for catheter ablation procedures: a prospective randomized study. *Journal of Cardiovascular Electrophysiology* 2004; 15: 310–5.	102 patients.	Randomised controlled trial, comparing electroanatomic imaging with conventional fluoroscopic mapping.	Success was similar using either technique.
Stabile G, Bertaglia E, Senatore G, et al. Feasibility of pulmonary vein ostia radiofrequency ablation in patients with atrial fibrillation: a multicenter study (CACAF pilot study). *Pacing & Clinical Electrophysiology* 2003; 26: 284–7.	69 patients. Mean follow-up = 9 months.	Case series.	Freedom from AF = 84%. Major complications = 4% (pericardial effusion, transient ischaemic attack, tamponade).
Thomas SP, Boyd AC, Aggarwal G, et al. Percutaneous pulmonary vein isolation for treatment of atrial fibrillation. *Internal Medicine Journal* 2004; 34: 453–7.	74 patients. Follow-up = 6 months.	Case series.	At 6 months, sinus rhythm = 73% (54/74) [52% for permanent AF, 81% for paroxysmal AF, p = 0.01] 3% cardiac tamponade 4% moderate PV stenosis
Vasamreddy C, Lickfett L, Jayam V, et al. Predictors of recurrence following catheter ablation of atrial fibrillation using an irrigated-tip catheter. *Journal of Cardiovascular Electrophysiology* 2004; 15: 692–7.	75 patients. Mean follow-up = 10 months.	Case series.	Freedom from AF = 52% Improved AF = 13% No benefit = 35% Pericardial tamponade = 3% Stroke = 3% Best results in patients aged < 50 years with paroxysmal AF.
Wu R, Brinker J, Yuh D, et al. Circular mapping catheter entrapment in the mitral valve apparatus: a previously unrecognised complication of focal atrial fibrillation ablation. *Journal of Cardiovascular Electrophysiology* 2002; 13: 819–21.	1 patient.	Case report.	Entrapment of circular mapping catheter within mitral valve apparatus.
Yu W-C, Hsu T-L, Tai C-T, et al. Acquired pulmonary vein stenosis after radiofrequency catheter ablation of paroxysmal atrial fibrillation. *Journal of Cardiovascular Electrophysiology* 2001; 12: 887–92.	102 patients. Follow-up = up to 16 months	Case series.	PV stenosis = 33% (34/102) 3 patients with stenosis of both upper PVs had mild dyspnoea on exertion, only 1 had mild increase of pulmonary pressure.

Appendix B: Literature search for radiofrequency catheter ablation for atrial fibrillation

Action	Version searched (if applicable)	Date searched
The Cochrane Library	The Cochrane Library 2005 Issue 1	9/03/2005
CRD Databases		9/03/2005
Embase	1980 to 2005 Week 10	
Medline	1966 to February Week 4 2005	9/03/2005
Premedline	March 08, 2005	9/03/2005
CINAHL		9/03/2005
Current Contents (limit to current year only)		9/03/2005
National Research Register	2005 Issue 1	9/03/2005
Controlled Trials Registry		9/03/2005

Medline Search

1. catheter ablation/
2. (catheter adj5 ablat$).tw.
3. or/1-2
4. radiofrequen$.tw.
5. electrosurgery/
6. 4 or 5
7. 3 and 6
8. atrial fibrillation/
9. atrial fibrillation.tw.
10. 8 or 9
11. 7 and 10
12. limit 11 to humans
13. limit 12 to english language
14. limit 13 to yr=1990 - 2005