NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

Closing the left atrial appendage of the heart to prevent stroke in people with non-valvular atrial fibrillation using keyhole surgery

Atrial fibrillation (AF) is the irregular and rapid beating of the upper two chambers of the heart (the atria). Typical symptoms can include palpitations, dizziness, shortness of breath and fatigue. In people with AF, blood clots often form in the left atrial appendage, which is a small sac off the left atrium. These clots can travel in the blood to the brain, where they may block the blood flow, causing a stroke. In this procedure, the mouth of the left atrial appendage is closed to prevent the migration of blood clots. This is carried out through small incisions in the chest, and using a video camera to help guide the procedure.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make 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 December 2010.

Procedure name

- Thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

Specialty societies

- Society for Cardiothoracic Surgery in Great Britain and Ireland.

Description

Indications and current treatment

Atrial fibrillation (AF) 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.

Patients with AF may be asymptomatic or they may have symptoms including fatigue, chest pain, palpitations, dizziness and shortness of breath. 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. Evidence suggests that most thrombi develop in the left atrial appendage (LAA), a small sacculation of the left atrium located between the left upper pulmonary vein and the left ventricle.

Atrial fibrillation is associated with increased risk of death and of embolic stroke from atrial thrombus. The risk of thromboembolic events in patients with AF (of non-rheumatic origin) is assessed by the $CHADS_2$ score which is based on the presence or absence of congestive heart failure, hypertension, age over 75, diabetes mellitus and previous stroke or transient ischaemic attack (TIA). In patients with low risk of thromboembolism ($CHADS_2$ score 0 to 1) aspirin may be used. Patients with more than one risk factor are considered to be at a high risk of thromboembolic stroke ($CHADS_2$ score > 1) and are generally treated with anticoagulation therapy, most commonly warfarin. However, warfarin is associated with haemorrhagic complications, and is contraindicated in some patients. These patients may require alternative therapy to reduce the risk of stroke. Obliteration of the LAA can be through a percutaneous, open or thoracoscopic approach.

What the procedure involves

Thoracoscopic exclusion of the LAA is usually performed with the patient under general anaesthesia. Transoesophageal echocardiography (TOE) guidance is used to confirm absence of LAA thrombus before the procedure is performed. It is usually performed alongside other procedures such as thoracoscopic epicardial radiofrequency or microwave ablation.

Incisions are made in order to introduce the thoracoscopic instruments. An endobronchial tube is sometimes used to reduce the volume of the left lung. The pericardium is opened anterior or posterior to the phrenic nerve, and the atrial appendage is excluded (usually using staples but a specially designed clip is being developed) in order to prevent blood clots from forming in the LAA. A chest drain may be left in one of the port holes until the lung is fully expanded and postoperative TOE may be used to confirm exclusion of the LAA.

Patients are usually discharged on oral antiplatelet or anticoagulant agents.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism. Searches were conducted of the following databases, covering the period from their commencement to 25 November 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection 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 were 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, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with atrial fibrillation.
Intervention/test	Thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism.
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 approximately 238 patients from 6 case series[1,2,3,4,5,6].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Blackshear JL (2003)[1]

Case series
USA
Recruitment period: not reported
Study population: patients with non-rheumatic chronic or intermittent AF
n = 15
Mean age: 67 years
Sex: 73.3% male
Patients with a prior history of thromboembolism: 11

Patient selection criteria: at least one clinical risk factor for stroke (prior thromboembolism, hypertension, age > 75 years, left ventricular dysfunction, or diabetes mellitus) and either an absolute contraindication to warfarin or documentation of prior LAA thrombosis despite adequate oral anticoagulation

Technique: general anaesthesia, TOE to confirm absence of LAA thrombus at time of surgery, thoracoscopic left appendage totally obliterated with a loop snare or stapler with no cardiac invasion

Maximum follow-up: 60 months
Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 15

Incidence of thromboembolic events (mean follow-up of 42 months)
1 patient (aged 79 years) with prior stroke, congestive heart failure, severe left ventricular dysfunction, and multiple subdural haematomas, suffered a fatal stroke 55 months after the procedure.
1 patient with a history of multiple prior strokes had a small non-disabling stroke during hospitalisation for pneumonia 3 months after the procedure.
<table>
<tr><th>Outcome</th><th>Rate per patient-year (95% CI)</th></tr>
<tr><td>Overall rate of stroke</td><td>4.0% (1.0 to 16)</td></tr>
<tr><td>Rate of fatal stroke</td><td>2.0% (0.3 to 13)</td></tr>
<tr><td>Rate of death or stroke</td><td>6.0% (2.0 to 19)</td></tr>
<tr><td>Rate of stroke in 11 patients with history of thromboembolism</td><td>5.2% (1.3 to 21)</td></tr>
<tr><td>Rate of stroke in 4 patients without history of thromboembolism</td><td>0%</td></tr>
</table>
</td>
<td>Postoperative complications:
• 1 patient with bleeding from torn accessory LAA, necessitating urgent thoracotomy.
• 1 patient with hypertrophic non-obstructive cardiomyopathy had refractory pump failure requiring prolonged intensive care unit stay.
• 1 patient had atelactasis.
• 1 patient had prolonged air leak.
• 1 patient required investigation and treatment of genitourinary bleeding.
• 1 patient had chronic pleuritic pain.
Death unrelated to the procedure:
1 patient died after coronary bypass grafting 34 months after the procedure.
Another patient with chronic hepatitis C, variceal and small intestinal blood loss, and prior systemic embolism, died from hepatic failure.</td>
<td>Follow-up issues:
• Contact by telephone at 6-month intervals.

Study design issues:
• Patients selected from 2 medical centres.

Study population issues:
• 1 patient took sustained warfarin during follow-up.
• 12 patients had history of hypertension and 11 had bleeding diatheses including 5 with prior intracranial haemorrhage and 1 with prior meningioma surgery.

Other issues:
• Authors also provided the previously published rate of stroke in patients treated with aspirin (from the Stroke Prevention in Atrial Fibrillation studies) (13% [95% CI 0.9 to 19]) but this was not statistically significant compared with the rate in those with a history of thromboembolism or without a history of thromboembolism (when significance is accepted at the 0.05 level).</td>
</tr>
</table>

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Pruitt CJ (2007)[2] **Case series** USA Recruitment period: 2003–6 Study population: patients with drug-resistant symptomatic paroxysmal, persistent or permanent AF n = **100 (LAA exclusion attempted in 86)** Mean age: 60.9 years Sex: 66% male Mean duration of AF: 72.4 months Left atrial dimension: ≤4.5 cm in 42%, 4.6–5.9 cm in 53% and ≥6.0 cm in 5% Patient selection criteria: not reported Technique: thoracoscopic radiofrequency epicardial ablation (off-pump) followed by thoracoscopic LAA closure with Endostapler (Ethicon, Somerville, NJ, USA) with no-knife stapling cartridge Maximum follow-up: **39.8 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **88 (of which only 85 were treated with LAA closure)** LAA excision was unsuccessful in 1 patient (reason not reported). ***Incidence of thromboembolic events (mean follow-up of 23.1 months)*** Of the 88 patients available for follow-up, 2.3% (2/88) experienced a TIA and 2.3% (2/88) had a CVA. ***Operative characteristics*** Mean duration of the procedure was 181.5 minutes. **Outcomes related to epicardial ablation:** ***Use of medication*** At last follow-up, 11.4% (10/88) were on amiodarone and 54.5% (46/88) were on warfarin. ***Sinus rhythm (on ECG)*** 42.0% (37/88) of patients were in normal sinus rhythm at last follow-up (mean 23.1 months). Of those with 0–12 months follow-up, 83.3% (5/6; 95% CI 35.9 to 99.6) were in normal sinus rhythm; of those with 12–24 months follow-up, 42.5% (17/40; 95% CI 27.0 to 59.1); of those with 24–36 months 30.3% (10/33; 95% CI 15.6 to 48.7); of those with more than 36 months 55.6% (5/9).	***Intraoperative complications***3% (3/100) of patients required a mini-thoracotomy intraoperatively to control bleeding. ***Postoperative complications*** 2% (2/100) required reoperation for bleeding. 7% (7/100) had diaphragmatic dysfunction (only 1 was symptomatic). 3% (3/100) required a permanent pacemaker. Postoperatively, no patients had myocardial infarction but 1 patient had CVA. ***Late complications*** 3% (3/100) of patients died (cause of death and timing not reported). Of the 88 survivors, 2.3% (2/88) had a complication from anticoagulation (time of occurrence and details not reported).	**Follow-up issues**: • No patients lost to follow-up. **Study design issues**: • Retrospective using patients' hospital records, but follow-up questionnaires and telephone interviews were completed by patients, family members or the patients' physician. • Study includes 100 patients but LAA exclusion was only attempted in 86 (it was not attempted in the other 14 because of anatomical reasons). Of these 100 patients, 9 required Cox-Maze because epicardial ablation was unsuccessful at treating symptoms so were not included in follow-up. **Study population issues**: • AF was paroxysmal in 64 patients, persistent in 11 and permanent in 25.

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Cui Y-Q (2010)[3] **Case series** China Recruitment period: 2006–8 Study population: patients with paroxysmal, persistent or long-standing persistent AF refractory to medication n = **81 (71 treated with LAA exclusion)** Mean age: 57.6 years Sex: 58.6% male Duration of AF: 5.9 years Patient selection criteria: less than 70 years old, failed catheter ablation, history of stroke or embolism, LAA thrombus Exclusion criteria: left atrial dimension greater than 70 mm, left ventricular fraction less than 30% on ultrasonic cardiography, previous cardiac surgery, severe pleural adhesions Technique: video-assisted minimally invasive bilateral pulmonary vein antrum isolation (with bipolar radiofrequency ablation), LAA occlusion using EZ-45G Endostapler (Johnson and Johnson Medical, Inc, Arlington, Texas) and division of ligament of Marshall; aspirin or warfarin was given postoperatively based on the patient's $CHADS_2$ score until sinus rhythm was present Maximum follow-up: **19 months** Conflict of interest/source of funding: none	Number of patients analysed: **81 (71 treated with LAA exclusion)** ***Incidence of thromboembolic events (mean follow-up of 12.7 months)*** Postoperative stroke rate in the group was 1.2% (exact figures not reported; assumed to be 1 out of 81 patients) Of the 10 patients who did not have LAA obliteration, none had CVA during the mean follow-up of 12.7 months. ***Operative characteristics*** Mean blood loss during the procedure was 81 ml and mean duration of the procedure was 2.5 hours. **Outcomes related to epicardial ablation (n = 81):** ***Use of medication*** 12.3% (10/81) of patients stopped taking amiodarone at 1 month and 85.2% (69/81) stopped taking it at 3 months. ***Sinus rhythm (on ECG)*** Follow-up / In normal sinus rhythm Discharge: 72.5% (58/81) 6 months: 78.5% (62/79) 12 months: 79.6% (39/49) 18 months: 88.9% (8/9)	***Complications*** • 1 patient died of cerebral infarction 1 month after the procedure. • 1 patient had acute cardiac dysfunction from subendocardial infarction and recovered within 12 days. • 2.5% (2/81) of patients had wound exudation. The following events are likely to be related to the pulmonary vein isolation: 1 patient was converted to sternotomy after being shown to have bleeding during right inferior pulmonary vein dissection. 1 patient had reintubation because of hypoxemia in the intensive care unit.	**Follow-up issues**: • Transthoracic ultrasonic cardiography at 1, 3, 6, 12 months. • 1 patient was lost to follow-up after discharge (reason not reported). **Study design issues**: • Study included 81 patients but the first 10 did not have LAA obliteration because the centre did not have the right endoscopic cutters. • Cardioversion was performed in 18 patients during follow-up and before discharge. **Study population issues**: • AF was paroxysmal in 49 patients, persistent in 17 and long-standing persistent in 15. • 3 patients had LAA removed before ablation because preoperative TOE and CT scanning showed abnormal density in the LAA. Only one of these had confirmed thrombus after LAA excision but the other had thickened trabeculae. • Preoperative characteristics: 14.8% (12/81) of patients had had a stroke or arterial embolism, 4.9% (4/81) had catheter ablation, 28.4% (23/81) of patients were taking warfarin, 85.2% (69/81) aspirin, 23.5% (19/81) were smokers, 38.2% (31/81) had hypertension, 4.9% (4/81) had diabetes, and 2.5% (2/81) had a permanent pacemaker implanted.

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Yilmaz A (2010)[4] **Case series** Netherlands Recruitment period: 2007–not reported Study population: paroxysmal or persistent AF refractory to medication n = **30** Mean age: 55.6 years Sex: 77% male Mean duration of AF: 79.0 months Mean left atrial diameter: 42.1 mm Patient selection criteria: between 18 and 80 years of age with at least moderate heart function Exclusion criteria: previous cardiac or lung surgery, AF for more than 10 years, left atrium larger than 70 mm Technique: thoracoscopic pulmonary vein isolation with RF energy followed by amputation of LAA with PDS endoloop (Ethicon, Amersfoort, Netherlands) in first procedures and with Autosuture Endo Gia stapler (Tyco Healthcare Group, North Haven, Connecticut, USA) in later procedures; all patients had oral anticoagulation for at least 3 months after surgery Maximum follow-up: **19 months** Conflict of interest/source of funding: not reported	Number of patients analysed: **30** ***Incidence of thromboembolic events*** There were no CVAs or TIAs over a mean follow-up of 11.6 months (and no patients received a pacemaker). **Outcomes related to epicardial ablation:** ***Use of medication*** For patients with a successful procedure, freedom from antiarrhythmic drugs was 65%, freedom from warfarin was 48% and freedom from both was 26%. In the first 15 patients with longer follow-up, these figures were 73%, 55% and 36%. ***Sinus rhythm (on ECG)*** With the exception of the first 3 months (considered a blanking period), 77% had no 'single' registration of AF during follow-up. All patients who had previously failed percutaneous left-sided catheter ablation were free from AF at mean 9.8 months follow-up. Freedom from AF was 84%, 75% and 33% for paroxysmal, persistent and permanent AF, respectively (p > 0.05).	***Complications*** 2 patients required thoracostomy drain for residual pneumothorax from inadequate removal of the drains (not from pulmonary lesion). 1 patient required conversion to median sternotomy because of severe pleural adhesions. Another required conversion to median sternotomy because of bleeding from the right lower pulmonary vein (this is likely to be related to the pulmonary vein isolation procedure).	**Follow-up issues**: • Referring cardiologist was sent questionnaire for follow-up. ECG at 1 week, 3 weeks, 3 months, 6 months and 12 months. **Study design issues**: • Retrospective; data taken from clinical and out-patient files. **Study population issues**: • AF was paroxysmal in 63% (19/30), persistent in 27% (8/30), and longstanding persistent in 10% (3/30) (it was permanent in 10% [3/30]). • 3 had diminished left ventricular function with estimated left ventricular fraction of 30–40%. • 18 had previously had percutaneous catheter ablation for AF (all but one of these had paroxysmal AF).

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Wudel JH (2008)[5] **Case series** USA Recruitment period: 2004–5 Study population: patients with symptomatic, intermittent paroxysmal or persistent AF refractory to medication n = **22** Mean age: 63 years Sex: 68.2% male Mean duration of AF: 45.2 years Mean ejection fraction: 0.548 mm Mean left atrial size: 34.7 mm Patient selection criteria: either unsuccessful to antiarrhythmic drug therapy, intolerant to anticoagulants, unsuccessful catheter-based ablation or any combination of these Exclusion criteria: greater than mild mitral regurgitation, severe systolic dysfunction, untreated coronary disease, morbid obesity or significantly large left atrium Technique: thoracoscopic epicardial bipolar radiofrequency ablation, removal of ligament of Marshall, thoracoscopic LAA exclusion with Thoracic Endoscopic Linear Cutter EZ45G (Ethicon Endo-Surgery, Inc, Cincinnati, OH) with staples; anticoagulation and antiarrhythmic drugs were stopped if the referring cardiologist felt it necessary Maximum follow-up: **27 months (all at least 1 year)** Conflict of interest/source of funding: not reported	Number of patients analysed: **21** LAA excision was not attempted in 1 patient because of adhesions secondary to a previous catheter ablation. ***Incidence of thromboembolic events (mean follow-up of 18.1 months)*** There were no occurrences of stroke in the follow-up period. ***Operative characteristics*** Mean duration of the procedure was 182 minutes. **Outcomes related to epicardial ablation (n = 22):** ***Use of medication and AF symptoms*** At the end of follow-up, 91% (20/22) were free of symptoms without antiarrhythmic therapy for at least 6 months at the last follow-up (2 had less symptoms but remained on antiarrhythmic therapy). 91% (20/22) were no longer on warfarin at the conclusion of the study period (2 patients continued on warfarin secondary to symptomatic AF). ***Sinus rhythm*** Holter monitoring in the 20 patients without symptoms at follow-up showed all were in sinus rhythm with no AF or atrial flutter (but 2 had 4 beats each of paroxysmal atrial tachycardia).	***Perioperative complications*** 1 patient required outpatient skin incision revision. 1 patient had a pulmonary embolism requiring rehospitalisation.	**Follow-up issues**: • 1 patient refused Holter monitoring despite being asymptomatic and being on no medication so was excluded from the analysis. • Outpatient clinic scheduled 3 months after procedure and the patient was then followed by the referring physician for 6 months. **Study design issues**: • Retrospective. **Study population issues**: • AF was paroxysmal in 14 patients and persistent in 8. • Preoperative characteristics: 95.5% (21/22) of patients had previous unsuccessful antiarrhythmic drug therapy, 36% (8/22) had previous cardioversion, 27.4% (6/22) were unable to take warfarin, 31.8% (7/22) had previous catheter ablation, 13.6% (3/22) had preoperative pacemaker; dilated cardiomyopathy, previous cardiac surgery, coronary artery disease, previous TIA/CVA and idiopathic hypertrophic subaortic stenosis occurred in 4.5% (1/22) each and 86.4% (19/22) had hypertension.

Abbreviations used: AF, atrial fibrillation; CI, confidence interval; CT, computer tomography; CVA, cardiovascular accident; ECG, electrocardiogram; LAA, left atrial appendage; TIA, transient ischaemic attack; TOE, transoesophageal echocardiography

Study details	Key efficacy findings	Key safety findings	Comments
Salenger R (2004)[6] **Case series** USA Recruitment period: 2004–5 Study population: patients with persistent or paroxysmal AF n = **14** Mean age: 60 years Sex: 64.2% male Mean duration of AF: 74 months Patient selection criteria: not reported Technique: thoracoscopic epicardial microwave ablation and LAA exclusion with endoscopic stapler (Endo-GIA, Ethicon, New Brunswick, NJ, USA) amiodarone, preoperative antiarrhythmic drugs and oral anticoagulation were continued until 3 months after the procedure (the later 2 were discontinued after sinus rhythm was documented on 2 consecutive visits at least 3 months apart) Maximum follow-up: **12 months** Conflict of interest/source of funding: not reported	Outcomes were related to sinus rhythm which is not the aim of LAA exclusion. LAA excision was only successful in 64% (9/14) of patients. **Outcomes related to epicardial ablation:** ***Sinus rhythm*** 71% (10/14) of patients were in sinus rhythm at discharge, 100% (14/14) at 6 months follow-up and 67% at 12 months. (Exact figures not reported but calculated by analyst; unable to determine patient numbers for those in sinus rhythm at 12 months – 67% may be incorrect).	***Complications*** 2 patients required conversion to an open procedure to control bleeding from the LAA (one was from a retraction injury and the other a torque injury). 1 patient had pneumonia and discharge home was delayed 17 days after the procedure. 1 patient had a pulmonary embolism and discharge home was delayed 14 days after the procedure (not clear from study when this occurred; appears to be postoperatively). 1 patient received a permanent pacemaker 9 months after the procedure because of sick sinus syndrome.	**Follow-up issues**: ECG follow-up scheduled at 1, 3, 6, 9, and 12 months. **Study design issues**: • Retrospective • 5 patients did not have LAA excision because of technical difficulties with either the stapler or the positioning of the appendage. **Study population issues**: • AF was paroxysmal in 10 patients and persistent in 3. • 50% of the patients had unsuccessful chemical and/or electrical cardioversion.

Efficacy

Thoracoscopic exclusion of the LAA alone

A case series of 15 patients treated with thoracoscopic exclusion of the LAA alone reported an overall rate of stroke to be 4% (95% confidence interval [CI] 1.0 to 16) per patient-year over a mean follow-up of 42 months. One patient with prior stroke, congestive heart failure, severe left ventricular dysfunction and multiple subdural haematomas suffered a fatal stroke 55 months after the procedure. Another patient with a history of multiple strokes suffered from a small non-disabling stroke during hospitalisation for pneumonia 3 months after the procedure[1].

Thoracoscopic exclusion of the LAA with epicardial ablation

A case series of 100 patients treated with thoracoscopic epicardial radiofrequency ablation (86 with attempted thoracoscopic LAA exclusion) reported that of 88 patients available for follow-up, 2% (2/88) experienced a TIA and 2% (2/88) experienced a cardiovascular accident (CVA) over a mean follow-up of 23.1 months[2].

A case series of 81 patients treated with thoracoscopic epicardial radiofrequency ablation (of which 71 also had thoracoscopic LAA exclusion) reported a postoperative stroke rate of 1% over a mean follow-up of 12.7 months (exact figures not reported but this is likely to be 1 patient)[3].

A case series of 30 patients treated with thoracoscopic epicardial radiofrequency ablation and thoracoscopic LAA exclusion reported no CVAs or TIAs over a mean follow-up of 11.6 months[4].

A case series of 22 patients treated with thoracoscopic epicardial radiofrequency ablation and thoracoscopic LAA exclusion reported no occurrences of stroke over a mean follow-up of 18.1 months[5].

Safety

Death

The case series of 100 patients (86 with attempted thoracoscopic LAA exclusion) reported that 3% (3/100) of patients died (cause of death and whether the patients had thoracoscopic LAA exclusion were not reported; timing of death was not reported but it was described as a late complication)[2].

The case series of 81 patients reported that 1 patient died of cerebral infarction 1 month after the procedure[3].

Conversion to or requirement for open surgery

The case series of 15 patients reported postoperative requirement for thoracotomy because of bleeding in 1 patient[1].

The case series of 100 patients (86 with attempted thoracoscopic LAA exclusion) reported intraoperative conversion to minithoracotomy to control bleeding in 3% (3/100) of patients[2].

The case series of 30 patients reported that 7% (2/30) of patients required thoracostomy drain because of residual pneumothorax from inadequate removal of the drains (not from a pulmonary lesion); and 1 patient required conversion to median sternotomy because of severe pleural adhesions[4].

The case series of 14 patients reported that 14% (2/14) of patients required conversion to an open procedure to control bleeding from the LAA[6].

Other

The case series of 15 patients reported the following postoperative adverse events in 1 patient each: refractory pump failure requiring prolonged intensive care unit stay in a patient with hypertrophic non-obstructive cardiomyopathy, atelactasis, prolonged air leak, investigation and treatment of genitourinary bleeding, and chronic pleuritic pain[1].

The case series of 100 patients (86 with attempted thoracoscopic LAA exclusion) reported the following postoperative adverse events: CVA in 1% (1/100) of patients, reoperation for bleeding in 2% (2/100), diaphragmatic dysfunction in 7% (7/100; only 1 was symptomatic), requirement for a permanent pacemaker in 3% (3/100). A late complication from anticoagulation occurred in 2% (2/88) of patients followed up (time of occurrence and details not reported)[2].

The case series of 81 patients reported wound exudation in 2% (2/81) of patients and acute cardiac dysfunction from subendocardial infarction (recovery within 12 days) in 1 patient[3].

The case series of 14 patients reported the following adverse events in 1 patient each: pulmonary embolism resulting in discharge 14 days after the procedure and pneumonia resulting in discharge 17 days after the procedure[6].

Validity and generalisability of the studies

- The evidence includes studies with small numbers of patients and with a maximum of 60 months of follow-up. In order to show whether thoracoscopic exclusion of the LAA prevents thromboembolic events, studies including larger patient numbers with longer follow-up are required.

- All but 1 study reported on the use of LAA exclusion alongside other procedures, usually thoracoscopic epicardial radiofrequency or microwave ablation. Although a number of the studies reported on the occurrence of thromboembolism after the procedure, the main outcome of these studies was the effect of the procedures on the symptoms of atrial fibrillation such as maintaining a normal sinus rhythm. Some studies were excluded if they did not report on occurrence of thromboembolic events.
- Most studies used a staple to exclude the LAA. A clip has been designed specifically for this procedure (Atriclip Cosgrove-Gillinov Left Atrial Appendage Occlusion System or Gillnov clip) but evidence on the use of this device in humans has not yet been published. The FDA have not yet approved the use of the clip, but it has received a CE mark.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism. NICE interventional procedures guidance 349 (2010). Available from www.nice.org.uk/guidance/IPG349
- Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation. NICE interventional procedures guidance 294 (2009). Available from www.nice.org.uk/guidance/IPG294
- Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation. NICE interventional procedures guidance 286 (2009). Available from www.nice.org.uk/guidance/IPG286
- High-intensity focused ultrasound for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 184 (2006). This guidance is currently under review and is expected to be updated in 2009. For more information, see www.nice.org.uk/guidance/IPG184

- Percutaneous radiofrequency catheter ablation for atrial fibrillation. NICE interventional procedures guidance 168 (2006). Available from www.nice.org.uk/guidance/IPG168
- Radiofrequency ablation for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 121 (2005). Available from http://www.nice.org.uk/guidance/IPG121
- Microwave ablation for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 122 (2005). Available from www.nice.org.uk/guidance/IPG122
- Cryoablation for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 123 (2005). Available from www.nice.org.uk/guidance/IPG123

Clinical guidelines

- The management of atrial fibrillation. NICE clinical guideline 36 (2006). Available from www.nice.org.uk/guidance/CG36

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr Steven Hunter, Mr Jonathan Hyde, Mr Simon Kendall, Society for Cardiothoracic Surgery in Great Britain and Ireland

- Currently, this procedure is used by only a small number of clinicians. One adviser stated that he performs this in all patients who are in atrial fibrillation through a median sternotomy and thoracoscopically.
- One Adviser considers this procedure standard practice as part of video-assisted thoracoscopic ablation for a very small number of surgeons in the UK. The other Advisers commented that it is not a commonly used procedure.
- The only comparator may be the percutaneous version of this procedure which uses a device to occlude the LAA.
- Anecdotal adverse events include incomplete occlusion with residual appendage, neuralgia from the thoracoscopic port sites, bleeding and tearing of the appendage (repaired through small thoracotomy), and the usual risk with general anaesthesia. Additional theoretical events include massive bleeding and death, lung damage and inadvertent cardiac damage.
- Key efficacy outcomes include total occlusion of the LAA with endothelialisation and a demonstrable absence of residual appendage (on echocardiography); and prevention of sequelae of thrombus (such as stroke or TIA).
- One Adviser commented that there are concerns that stapling the LAA does not occlude the whole appendage because the shape of the stapling device

does not allow staples at the base of the appendage. A specially designed occlusion device can be used that allows staples to be placed at the base. One Adviser stated that they used this regularly.

- Experience in video-assisted thoracoscopic surgery is required such as formal training in thoracic surgery (including proctoring) and cardiac surgical experience in open chest LAA ablation. Also, they should be proficient in LAA occlusion via sternotomy.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

- See 'Validity and generalisability of the studies' section about appropriateness of the evidence.

References

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3. Cui Y, Li Y, Gao F et al. (2010) Video-assisted minimally invasive surgery for lone atrial fibrillation: A clinical report of 81 cases. Journal of Thoracic and Cardiovascular Surgery 139:326–32.

4. Yilmaz A, Geuzebroek GS, Van Putte BP et al. (2010) Completely thoracoscopic pulmonary vein isolation with ganglionic plexus ablation and left atrial appendage amputation for treatment of atrial fibrillation. European Journal of Cardio-thoracic Surgery 38:356–60.

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6. Salenger R, Lahey SJ, and Saltman AE. (2004) The completely endoscopic treatment of atrial fibrillation: Report on the first 14 patients with early results. Heart Surgery Forum 7:446–50.

Appendix A: Additional papers on thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Balkhy HH, Chapman PD, and Arnsdorf SE. (2004) Minimally invasive atrial fibrillation ablation combined with a new technique for thoracoscopic stapling of the left atrial appendage: case report. Heart Surgery Forum 7:353–5.	Case report n = 1 Follow-up = 6 months	Microwave ablation and LAA exclusion with a new computer-mediated flexible thoracoscopic stapling system. Patient had significant clinical improvement in symptoms.	Outcomes related to sinus rhythm.
Edgerton JR, Brinkman WT, Weaver T et al. (2010) Pulmonary vein isolation and autonomic denervation for the management of paroxysmal atrial fibrillation by a minimally invasive surgical approach. Journal of Thoracic & Cardiovascular Surgery 140:823–8.	Case series n = 52 (LAA exclusion in 88% [44/50] of patients) Follow-up = 12 months	Antiarrhythmic drugs stopped in 33 of 37 patients and warfarin in 30 of 37 patients in whom ablation was successful at 12 months.	Outcomes related to sinus rhythm.
Johnson WD, Ganjoo AK, Stone CD et al. (2000) The left atrial appendage: our most lethal human attachment! Surgical implications. European Journal of Cardio-thoracic Surgery 17:718–22.	Case series n = 7 Follow-up = not reported	1 patient with diffuse vascular disease had a stroke occurred several weeks after surgery (TOE showed no thrombus in atrium). The other patients have been free from stroke while off Coumadin.	Patients included in Blackshear JL (2003) in table 2.
Pruitt JC, Lazzara RR, Dworkin GH et al. (1330) Totally endoscopic ablation of lone atrial fibrillation: initial clinical experience. Annals of Thoracic Surgery 81:1325–30.	Case series n = 46 Mean follow-up = 7.6 months	Patient on amiodarone decreased from 79.5% (35/44) at discharge to 25% (11/44) at follow-up; propafenone decreased from 9.1% (9/44) to 4.5% (2/44) and Coumadin from 100% to 50% (22/44). There was one late death (cause unknown). 2 patients had diaphragmatic dysfunction.	Patients included in Pruitt et al. (2007) in table 2.
Puskas J, Lin E, Bailey D et al. (2007) Thoracoscopic Radiofrequency Pulmonary Vein Isolation and Atrial Appendage Occlusion. Annals of Thoracic Surgery 83:1870–2.	Case report n = 1 Follow-up = 6 months	One episode of AF 1 week later but no further episodes over 6 months.	Outcomes related to sinus rhythm.

Sirak J, Jones D, Sun B et al. (2008) Toward a Definitive, Totally Thoracoscopic Procedure for Atrial Fibrillation. Annals of Thoracic Surgery 86:1960–4.	Case series n = 32 Mean follow-up = 6 months	Outcomes related to sinus rhythm. 15 of 23 followed up longer than 3 months were successfully weaned off antiarrhythmic drugs and 6 were being weaned off at 3 months. 21 of 24 patients with 6 month follow-up are in sinus rhythm with no antiarrhythmic medications.	Outcomes related to sinus rhythm.
Wolf RK, Schneeberger EW, Osterday R et al. (2005) Video-assisted bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. Journal of Thoracic and Cardiovascular Surgery 130:797–802.	Case series n = 27 Mean follow-up = 6 months	Outcomes related to sinus rhythm. 4 complications: 3 were quickly resolved (right pneumothorax resolved with no treatment, right forearm phlebitis, suspected pericarditis resolved with steroids) but one patient had dyspnea and AF 3 weeks after treatment treated with antiarrhythmia.	Outcomes related to sinus rhythm.
Yilmaz A, Van Putte BP, and Van Boven WJ. (2008) Completely thoracoscopic bilateral pulmonary vein isolation and left atrial appendage exclusion for atrial fibrillation. Journal of Thoracic and Cardiovascular Surgery 136:521–2.	Case series n = 9 Mean follow-up = 284 days	Outcomes related to sinus rhythm. Warfarin was stopped after 6 months in all but one patient with history of CVA. 2 had unilateral paralysis of the diaphragm (no further details provided) but no further complications.	Outcomes related to sinus rhythm (and patients may be included in Yilmaz 2010 in table 2).

Appendix B: Related NICE guidance for thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

Guidance	Recommendations
Interventional procedures	**Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism. NICE interventional procedures guidance 349 (2010).** 1.1 Current evidence suggests that percutaneous occlusion of the left atrial appendage (LAA) is efficacious in reducing the risk of thromboembolic complications associated with non-valvular atrial fibrillation (AF). With regard to safety, there is a risk of life-threatening complications from the procedure, but the incidence of these is low. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 Patient selection should be carried out by a multidisciplinary team including a cardiologist and other appropriate clinicians experienced in the management of patients with AF at risk of stroke. Patients should be considered for alternative treatments to reduce the risk of thromboembolism associated with AF, and should be informed about these alternatives. 1.3 Percutaneous occlusion of the LAA is a technically challenging procedure which should only be carried out by clinicians with specific training and appropriate experience in the procedure. 1.4 This procedure should be carried out only in units with on-site cardiac surgery. 1.5 Any device-related adverse events resulting from the procedure should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA). **Percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation. NICE interventional procedures guidance 294 (2009).** 1.1 Current evidence on the safety and efficacy of percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for atrial fibrillation (AF) is inadequate in quantity. Therefore this procedure should only be used with special arrangements for clinical governance and consent. 1.2 Clinicians wishing to undertake percutaneous (non-thoracoscopic) epicardial catheter radiofrequency ablation for

	AF should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG294publicinfo). 1.3 Patient selection and treatment should be carried out only by a team specialising in the treatment of cardiac arrhythmias that includes experts in electrophysiology and ablation. 1.4 The procedure should only be carried out by interventional cardiologists with specific training in electrophysiology, and in accessing the pericardial space and performing complex ablation procedures. 1.5 The procedure should only be carried out in units with arrangements for emergency cardiac surgical support in case of complications. 1.6 The NHS Information Centre for health and social care runs the UK Central Cardiac Audit Database, and clinicians should enter details about all patients undergoing percutaneous (non thoracoscopic) epicardial catheter radiofrequency ablation for AF onto this database (www.ccad.org.uk). 1.7 Clinicians are encouraged to enter patients into research studies that aim to provide more information about patient selection, the use of this procedure as an adjunct to other procedures, freedom from AF in the long term and relief of associated symptoms, and the safety profile of the procedure. NICE may review the procedure on publication of further evidence. **Thoracoscopic epicardial radiofrequency ablation for atrial fibrillation. NICE interventional procedures guidance 286 (2009).** 1.1 There is evidence of efficacy for thoracoscopic epicardial radiofrequency ablation for atrial fibrillation (AF) in the short term and in small numbers of patients. The assessment of cardiac rhythm during follow-up varied between studies, and some patients were concomitantly treated with anti-arrhythmic medication. Evidence on safety shows a low incidence of serious complications but this is also based on a limited number of patients. Therefore the procedure should only be used with special arrangements for clinical governance, consent and audit or research. 1.2 Clinicians wishing to undertake thoracoscopic epicardial radiofrequency ablation for AF should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy, and provide them with clear

	written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG286publicinfo). 1.3 Patient selection for thoracoscopic epicardial radiofrequency ablation for AF should involve a multidisciplinary team including a cardiologist and a cardiac surgeon, both with training and experience in the use of intraoperative electrophysiology. 1.4 The procedure should only be carried out by surgeons with specific training and experience in both thoracoscopic surgery and radiofrequency ablation. 1.5 The NHS Information Centre for Health and Social Care runs the UK Central Cardiac Audit Database (CCAD), and is developing a database for this procedure. Clinicians should collect data on the procedure and submit them to the database when it becomes available (www.ccad.org.uk). 1.6 NICE encourages further comparative research into the treatment and management of AF, with clearly defined outcomes. NICE may review this procedure on publication of further evidence. **High-intensity focused ultrasound for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 184 (2006). [THIS GUIDANCE IS UNDER REVIEW]** 1.1 Current evidence on the safety and efficacy of high-intensity focused ultrasound (HIFU) for atrial fibrillation in association with other cardiac surgery is insufficient for this procedure to be used without special arrangements for consent and for audit or research. 1.2 Clinicians wishing to undertake HIFU for atrial fibrillation in association with other cardiac surgery should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, use of the Institute's Information for the public is recommended (available from www.nice.org.uk/IPG184publicinfo). • Audit and review clinical outcomes of all patients undergoing HIFU for atrial fibrillation in association with other cardiac surgery. 1.3 Patient selection and follow-up should be carried out by a multidisciplinary team. Cardiac surgeons undertaking this procedure should have specific training in the use of high-intensity focused ultrasound equipment. 1.4 Publication of safety and efficacy outcomes will be useful. The Institute may review the procedure upon publication of further evidence. **Percutaneous radiofrequency catheter ablation for atrial fibrillation. NICE interventional procedures guidance 168**

	(2006). 1.1 Current evidence on the safety and efficacy of percutaneous radiofrequency ablation for atrial fibrillation appears adequate to support the use of this procedure in appropriately selected patients (see section 2.1.4) provided that normal arrangements are in place for audit and clinical governance. 1.2 Clinicians should ensure that patients fully understand the potential complications, the likelihood of success and the risk of recurrent atrial fibrillation associated with this procedure. In addition, use of the Institute's Information for the public is recommended (available from www.nice.org.uk/IPG168publicinfo). 1.3 This procedure should only be performed in specialist units and with arrangements for cardiac surgical support in the event of complications. 1.4 This procedure should only be performed by cardiologists with extensive experience of other types of ablation procedures. 1.5 The Department of Health runs the UK Central Cardiac Audit Database (UKCCAD), and clinicians are encouraged to enter all patients undergoing percutaneous radiofrequency ablation for atrial fibrillation onto this database (www.ccad.org.uk). **Radiofrequency ablation for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 121 (2005).** 1.1 Current evidence on the safety and efficacy of radiofrequency ablation (RFA) for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection and follow-up should be carried out by a multidisciplinary team. Cardiac surgeons wishing to use this procedure should have specific training in the use of radiofrequency equipment. **Microwave ablation for atrial fibrillation in association with other cardiac surgery. NICE interventional procedures guidance 122 (2005).** 1.1 Current evidence on the safety and efficacy of microwave ablation for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection and follow-up should be carried out by a multidisciplinary team. Cardiac surgeons wishing to use this procedure should have specific training in the use of microwave energy equipment. **Cryoablation for atrial fibrillation in association with other**

	cardiac surgery. NICE interventional procedures guidance 123 (2005). 1.1 Current evidence on the safety and efficacy of cryoablation for atrial fibrillation in association with other cardiac surgery appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Patient selection and follow-up should be carried out by a multidisciplinary team. Cardiac surgeons wishing to use this procedure should have specific training in the use of cryoablation equipment.
Clinical guidelines	**The management of atrial fibrillation. NICE clinical guideline 36 (2006)** 1.4.2.2 In patients with permanent AF where antithrombotic therapy is given to prevent strokes and/or thromboembolism (see section 1.8.6): • adjusted-dose warfarin should be given as the most effective treatment • adjusted-dose warfarin should reach a target INR of 2.5 (range 2.0 to 3.0) • where warfarin is not appropriate, aspirin should be given at 75 to 300 mg/day • where warfarin is appropriate, aspirin should not be coadministered with warfarin purely as thromboprophylaxis, as it provides no additional benefit.

Appendix C: Literature search for thoracoscopic exclusion of the left atrial appendage (with or without other cardiac surgery) in atrial fibrillation for the prevention of thromboembolism

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	25/11/2010	November 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	25/11/2010	-
HTA database (CRD website)	25/11/2010	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	25/11/2010	November 2010
MEDLINE (Ovid)	25/11/2010	1950 to November Week 3 2010
MEDLINE In-Process (Ovid)	25/11/2010	November 24, 2010
EMBASE (Ovid)	25/11/2010	1980 to 2010 Week 46
CINAHL (NLH Search 2.0)	25/11/2010	-
Zetoc	25/11/2010	-
BLIC (Dialog DataStar)	08/06/2010	-

Trial sources searched on 10/06/2010 and 25/11/2010

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 04/06/2010 – 10/06/2010

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Atrial Fibrillation/
2	(atr* adj3 fibrill*).tw.
3	AF.tw.
4	Thromboembolism/
5	thromboembol*.tw.
6	Stroke/
7	stroke*.tw.
8	Atrial Appendage/
9	left atrial append*.tw.
10	LAA.tw.
11	or/1-10
12	Video-Assisted Surgery/
13	Thoracoscopy/
14	Thoracoscopes/
15	thoracoscop*.tw.
16	(thoracoscop* adj3 (exclu* or obliter* or eliminate*)).tw.
17	(surg* adj3 (staple* or clip*)).tw.
18	gillinov.tw.
19	or/12-18
20	11 and 19
21	Animals/ not Humans/
22	20 not 21