Radiofrequency Catheter Ablation for Cardiac Arrhythmias: A Clinical and Economic Review

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No conflicts disclosed by Hussein Z. Noorani, Raymond Yee, Deborah Marshall, Stuart Connolly, Graham Nichol and Bernie O’Brien.
HIGHLIGHTS

What is already known about this topic?

- Catheter ablation is a treatment for patients with heart rhythm disturbances (cardiac arrhythmias) called tachycardias. Tachycardias cause symptoms that degrade the quality of life of individuals and are a life-long medical problem. Some of them are common medical problems (such as atrial fibrillation) and may begin at a young age with the potential for life-long morbidity. Certain tachycardias can be life threatening. Drug therapy to control these tachycardias is often ineffective or causes intolerable side effects.

- There are several tachycardias that differ in their causes and mechanisms so that general statements about the overall clinical efficacy and cost-effectiveness of catheter ablation therapy for the various tachycardias cannot be made.

- Presently, catheter ablation delivered by radiofrequency energy (RFA) is the predominant procedure used for the treatment of tachycardias and may be curative or palliative.

Assessment Objectives

To evaluate the:

1. evidence for the clinical efficacy of RFA through a review of research studies; and
2. cost-effectiveness of RFA through a review of economic evaluations.

What this assessment adds:

- This is the first synthesis of research studies and economic evaluations of RFA in Canada.

- For the following conditions, RFA is associated with a high procedural success rate and a low rate of complications within two years of follow-up:
  a. Paroxysmal supraventricular tachycardia (PSVT) secondary to an accessory pathway (Wolff-Parkinson-White syndrome, pre-excitation syndrome and variants)
  b. PSVT secondary to atrioventricular node re-entry
  c. Atrial flutter
  d. Focal and re-entrant atrial tachycardias

- Limited evidence also demonstrates that elimination of these tachycardias improves symptoms and/or quality of life.

- For the following conditions, catheter ablation is still within the research domain and technological advances are being introduced to better deal with these tachycardias. Data concerning short and long-term clinical success, recurrence, and complication rates may be available within the next five years:
  a. Atrial fibrillation: including focal or linear catheter ablation or pulmonary vein isolation procedures
  b. Ventricular tachycardia (VT) in the setting of structural heart disease

- In adult patients with either symptomatic PSVT or VT patients with implantable defibrillators who experience frequent recurrences, RFA is both more effective and less costly than drug therapy options. For these patients, RFA costs within US $21,000 (C $33,000) per quality-adjusted-life-year gained.

- For all the different types of ablation procedures, there is a paucity of high quality outcome studies comparing ablation with alternative therapies.
EXECUTIVE SUMMARY

The Issue
Catheter ablation is a procedure intended for the treatment of patients with particular heart rhythm disturbances (cardiac arrhythmias) called tachycardias. These tachycardias cause disabling symptoms and a few are potentially life threatening. Tachycardias can be treated with antiarrhythmic drugs, but drug therapy is frequently ineffective or causes intolerable side effects. Catheter ablation delivered by radiofrequency energy (RFA) is at present the predominant procedure used for the treatment of tachycardias and may be curative or palliative. RFA has been available within Canada for over a decade but access to these procedures remains limited, waits may be long, and there are marked geographic disparities in availability. The demand for RFA is increasing as it is now moving and developing to address the more common arrhythmias such as atrial fibrillation, thus further contributing to limited access and long waits for these procedures in Canada.

As a general guideline, ablation is clearly indicated either where a tachycardia is refractory to drug therapy, the patient is intolerant of drugs or non-compliant, or the drugs are contraindicated because of existing comorbid conditions. However, catheter ablation is often recommended to patients as first line therapy for a variety of tachycardias because it represents curative therapy.

Objectives
The objectives of this report are (1) to evaluate the evidence for the clinical efficacy of RFA through a systematic review of research studies, and (2) to evaluate the cost-effectiveness of RFA through a systematic review of economic evaluations. The purpose of this review is to inform decision-makers about the current evidence-base of catheter ablation for cardiac arrhythmias and of the future implications and technological advances of the procedure. This report is a collaborative project with the Canadian Cardiovascular Society.

Clinical Review
Methods: Published literature was identified between January 1985 and November 2001 by searching electronic bibliographic databases using the DIALOG® system. The focus of this review was on adult patients. Two reviewers conducted independent screening reviews of all citation titles and abstracts retrieved. Relevant studies and reports were retrieved, reviewed and classified by subject under six categories based on tachycardia type: pre-excitation syndromes (of which the Wolff-Parkinson-White (WPW) syndrome is the most common); atrioventricular node re-entrant tachycardia (AVNRT); atrial flutter; other atrial tachycardias; atrial fibrillation (AF); and ventricular tachycardia (VT).

Results: Of the 968 abstracts/citation titles identified through the literature search strategy, 111 primary research studies (11%) met the inclusion criteria. These consisted of 18 studies on the pre-excitation syndromes, 22 studies on AVNRT with one study also reporting on the pre-excitation syndromes, 16 studies on atrial flutter, nine studies related to other atrial tachycardias, 29 studies in general on AF, and 18 studies on VT. These studies were primarily single-centre cohort reports. Only ten of these studies (9%) were RCTs.
RFA of paroxysmal supraventricular tachycardia (pre-excitation syndromes, AV node re-entry), atrial flutter and focal atrial tachycardias are all procedures associated with high procedural success rates (>75%) that are sustained during a follow-up period of one to two years. Complication rates in most of these studies are reported to be close to five per cent. Limited evidence also demonstrates that elimination of these tachycardias improves symptoms and/or quality of life. The clinical benefits of atrial flutter ablation are diminished in patients with concomitant AF. Clinical efficacy data for RFA of AF, and VT secondary to underlying structural heart disease, are less conclusive than those of the above tachycardias.

**Economic Review**

**Methods:** Appropriate economic terms were substituted for clinical terms for the literature search strategy. Two reviewers using a standard worksheet and common definitions of terms extracted data. Studies were classified as model-based or trial-based. Studies that considered only costs or quality of life or provided insufficient data to be able to calculate an incremental cost-effectiveness ratio were not considered within the primary analysis, but were summarized and discussed within this review.

**Results:** Of the 192 abstracts/citation titles identified, 21 (11%) were included in this review: three cost-effectiveness studies, 12 cost studies, and six studies considering quality of life and cost, or quality of life only. These studies focused on different and specific patient groups with select target disorders. In adult patients with either symptomatic paroxysmal supraventricular tachycardias or VT patients with implantable cardioverter defibrillators who experience frequent recurrences, RFA dominates drug therapy options with a cost-effectiveness ratio within US $21,000 (C $33,000) per quality-adjusted-life-year. Specifically, in adult patients with WPW syndrome, the range of cost-effectiveness for RFA varies depending on baseline risk, but seems to dominate other options of drug therapy, surgical therapy, observation, or lie within the above cost-effectiveness ratio. RFA is not cost-effective in the treatment of asymptomatic WPW syndrome adult patients of any age.

**Conclusions**

Catheter ablation for most cardiac arrhythmias is associated with good procedural success rates but there remains insufficient evidence to draw specific conclusions about its long-term clinical efficacy and cost-effectiveness. RFA is considered primarily as an adjunct procedure to pacemaker implantation for AF, and to antiarrhythmic drugs and implantable cardioverter defibrillator therapy for VT.

For all the different types of ablation procedures, there is a paucity of high quality outcome studies comparing ablation with alternative therapies. There exist no Canadian guidelines for catheter ablation but current practices do not appear to vary markedly from the guidelines or recommendations made by international specialty societies. If future evidence from controlled trials, especially in patients with AF and atrial flutter, demonstrates more conclusive benefits of ablation as technique and experience advance, utilization could climb significantly.
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1 INTRODUCTION

Catheter ablation is a procedure intended to treat patients with particular heart rhythm disturbances called tachycardias. These tachycardias cause disabling symptoms and a few are potentially life threatening. Tachycardias can be treated with antiarrhythmic drugs, but drug therapy is frequently ineffective or causes intolerable side effects. Surgical treatments of some types of tachycardias became available in the early 1970’s. Catheter ablation was introduced in the 1980’s as a less traumatic and less expensive means of curing or eliminating tachycardia symptoms and its use is now widespread. Access to these procedures in Canada remains limited at present, waits may be long, and there are marked geographic disparities in availability.

The purpose of this review is to inform decision-makers about the current evidence base of catheter ablation for cardiac arrhythmias and of the future implications and technological advances of the procedure. This report is a collaborative project with the Canadian Cardiovascular Society.

1.1 Background

The term tachycardia literally means “rapid heart” and refers to the group of heart rhythm disturbances or “cardiac arrhythmias” in which the heart beats too quickly. A tachycardia develops when an area of the heart tissue is abnormal or its electrical properties are abnormal. The tissue that is the root cause of the tachycardia is commonly referred to as the “arrhythmia substrate”. Tachycardias are sub-divided into two general classes: supraventricular tachycardias and ventricular tachycardias. The classes of tachycardias and those for which RFA has been used as a treatment modality or is currently under investigation are listed below.

<table>
<thead>
<tr>
<th>A. Supraventricular Tachycardias (SVT)</th>
<th>B. Ventricular Tachycardias (VT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paroxysmal Supraventricular Tachycardia (PSVT)</td>
<td>Sustained Monomorphic VT</td>
</tr>
<tr>
<td>1. Accessory pathway-mediated Orthodromic, antidromic &amp; pre-excited tachycardias (Wolff-Parkinson White (WPW) syndrome)</td>
<td>Primary (No Structural Heart Disease)</td>
</tr>
<tr>
<td>2. AV nodal re-entrant tachycardia (AVNRT)</td>
<td>1. Idiopathic right ventricular outflow tract tachycardia</td>
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<tr>
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<td>2. AV nodal re-entrant tachycardia (AVNRT)</td>
<td></td>
</tr>
<tr>
<td>Atrial tachycardias</td>
<td>Secondary (Structural Heart Disease)</td>
</tr>
<tr>
<td>1. Atrial flutter-isthmus dependent clockwise &amp; counterclockwise</td>
<td>1. Intramyocardial VT</td>
</tr>
<tr>
<td>2. Other re-entrant atrial tachycardias (e.g. scar related)</td>
<td>2. Bundle Branch VT (Fascicular)</td>
</tr>
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<td>3. Focal &amp; automatic (ectopic) atrial tachycardias</td>
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<tr>
<td>4. Sinus node re-entrant tachycardia</td>
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<td>5. Inappropriate sinus tachycardia</td>
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<tr>
<td>Junctional ectopic tachycardia</td>
<td>Polymorphic VT*</td>
</tr>
<tr>
<td>Multifocal atrial tachycardia*</td>
<td>Ventricular fibrillation (VF)*</td>
</tr>
<tr>
<td>Atrial fibrillation (AF)</td>
<td></td>
</tr>
</tbody>
</table>

*Not considered amenable to RFA at present
Tachycardias are a diverse group of rhythm disorders that differ greatly in their mechanism, aetiology, and prevalence in the general population. Some, such as the pre-excitation syndromes (commonly referred to as the WPW syndrome) and AVNRT are due to abnormal tissue present at birth (congenital or developmental in origin) and may have a genetic basis. Others, such as VT and AF, occur primarily in individuals with long-standing high blood pressure, heart valve abnormalities, heart attacks or any other heart disease that damages or scars heart tissue (structural heart disease). Some tachycardias result from heart surgery but may not appear until many years after the surgery. Some, such as atrial flutter and AF may have more than one cause while some other tachycardias are of uncertain aetiology. A concise explanation of the various mechanisms that underlie the tachycardias is beyond the scope of this review but it is important to recognize that the arrhythmia mechanism has a bearing upon the clinical efficacy of catheter ablation.

Accurate data regarding the incidence and prevalence of the various tachycardias in the population are limited. One early report conservatively estimated that SVT afflicts nearly one per cent of adults. AF is the most common tachycardia and is responsible for approximately 30 per cent of hospitalizations for arrhythmias in the U.S. The annual incidence ranges from under one per cent in individuals under 50 years of age to nine per cent in those over 80 years old. Studies indicate that 25 per cent of AF patients have underlying problems with coronary artery disease and AF, and nearly one-third of patients undergoing coronary artery bypass surgery will develop AF post-operatively. In young healthy individuals, AVNRT is the most common problem followed by WPW syndrome and its variants.

Tachycardias cause significant morbidity and degrade quality of life (QOL). The rapid heart racing gives rise to complaints of palpitations, shortness of breath, fatigue and functional limitations, weakness, poor exercise tolerance or chest pain. These symptoms arise because heart racing compromises the normal heart’s ability to pump blood to all the bodily organs efficiently (including the brain, kidneys, heart and liver). This potentially can lead to heart failure, heart attacks, or compromises in kidney function. Decreases in brain blood flow can lead to strokes in older patients, dizziness or blackouts possibly causing other physical injury. Individuals may make repeated visits to the emergency department for acute treatment to terminate each attack. For a few patients, the cause is self-limited or is easily cured by treatment of the underlying medical disorder, thereby eliminating any future problems of tachycardia. Unfortunately, most patients remain at risk for attacks throughout their lives. Therefore, antiarrhythmic drug therapy to suppress attacks is life-long unless a permanent cure takes effect. Regardless of the treatment modality, chronic therapy is intended primarily to improve symptoms and QOL since premature death is of primary concern in only a few conditions.

SVTs are generally benign rhythm disturbances that rarely cause premature death. A few patients suffer from incessant forms of SVT that can lead to tachycardia-induced cardiomyopathy, a serious deterioration in myocardial contraction that leads to heart failure, and if not corrected, death. Where the tachycardia is eliminated early enough, recovery of heart function may be complete. It is estimated that one in 1,000 patients with WPW syndrome possess a potentially lethal form that is difficult to detect without electrophysiology (EP) studies. Sudden death can occur. Finally, most VT occurs in individuals with structural heart disease and is a potentially life-threatening arrhythmia.
The first step in management is to identify the type of the responsible tachycardia by recording it during an attack. However, this may not be possible despite repeated attempts due to the infrequency or short duration of attacks. Chronic treatment is often initiated in the absence of a definitive diagnosis. The usual first-line of therapy is empiric antiarrhythmic drugs (drugs are tried by “trial and error”), sometimes in drug combinations, until an effective regimen is found. Frequently, drugs are ineffective, cause intolerable side effects or can even cause serious and life-threatening adverse reactions. Drug adverse-effects erode patient compliance and reduce QOL and long-term therapy has financial costs. If empiric-drug therapy is unsuccessful, the patient may be referred to a specialist for further investigations and management. The primary alternative to drug therapy is catheter ablation after an EP study to determine the exact tachycardia diagnosis.

1.2 Technology Overview

1.2.1 Catheter ablation

Ablation means, “to remove” and the aim of cardiac ablation is either to eliminate the arrhythmia substrate or the ability for that tachycardia to produce disabling symptoms. Thus, ablation may be a curative or palliative procedure. Cardiac tissue was first ablated by surgically cutting, burning, or freezing the arrhythmia substrate and was most popular during the 1970s and 1980s. The desire to avoid operative morbidity and mortality led to the development of catheter ablation but surgical ablation remains an acceptable alternative where catheter ablation fails. Catheter ablation is known by different names in various parts of the world.

An EP study is performed prior to catheter ablation to determine the type(s) of tachycardia(s) and the location(s) of the arrhythmia substrate(s). They are usually performed during the same session with at least one trained cardiac electrophysiologist and registered nurse in attendance. Many facilities also have a second electrophysiologist and nurse or registered technologist present during ablation procedures. Multi-electrode catheters are inserted into the upper leg, neck, or shoulder veins and guided by fluoroscopy to the heart. Pacing techniques are used to induce the tachycardia and the signals from specific locations in the heart are recorded. Drugs are sometimes infused to facilitate tachycardia induction. EP-study measurements determine final diagnosis and the best approach to catheter ablation.

EP studies usually require only a small amount of sedative medication for adults. However, ablation procedures can be lengthy and cause some discomfort so intravenous/conscious sedation or general anaesthesia may be administered by trained nursing staff or an anaesthesiologist. An ablation catheter is inserted and detailed mapping is performed to precisely locate the best ablation site(s). The catheter is connected to the ablation energy generator and ablation energy is applied, often multiple times, to destroy the arrhythmia substrate while minimizing damage to healthy surrounding myocardium. Testing is repeated to determine if the ablation was immediately successful before proceeding to ablate other sites. At the end of the ablation procedure and after a suitable waiting period, the physician will perform a final EP study to verify procedural success before removing the catheters. The total procedure time for an average catheter-ablation procedure varies widely but is in the order of three to five hours with difficult cases taking as long as seven hours.
Because tachycardias can differ greatly in arrhythmia substrate type and location, catheter ablation techniques have been adapted to meet the specific challenges posed by each particular tachycardia. Thus, it is more appropriate to consider catheter ablation as a family of related procedures based upon a common principle rather than simply as a single procedure directed at different parts of the heart. Catheter ablation is most successful and safe for tachycardias arising from a single, discrete arrhythmia substrate that the catheters and energy delivered can readily reach.

When catheter ablation was first introduced in the early 1980s, high voltage electrical shocks were used. This was replaced in the mid-1980s by safer radiofrequency (“cautery”) energy and it remains the predominant energy delivered in catheter ablation. Radiofrequency energy destroys myocardial tissue by resistive heating (similar to toaster elements) at the electrode-tissue interface and creates a small-volume superficial “burn”. While radiofrequency catheter ablation (RFA) has been a good technique for some tachycardias, it has limitations. To create deeper and larger burns, the catheter tip can be cooled by simultaneous irrigation with saline. Other energy forms that are being investigated for use in difficult tachycardias such as AF and VT include laser, ultrasound, and microwave energy. Finally, cryothermal energy (“freezing”) is also being tested because it permits freezing of target tissue while leaving a stronger healing scar. Computer-based mapping techniques have also been developed to more easily and accurately identify ablation sites and better ablation catheter designs may make ablation easier and safer. Therefore, while RFA of some tachycardias may currently be associated with disappointing success and complication rates, investigational approaches such as alternative energy sources, mapping techniques and catheter technologies may improve its safety and clinical efficacy.

1.2.2 Catheter ablation procedure

While clinical practice varies among individual centres, it is common practice to admit patients on the day of the procedure and discharge patients with uncomplicated ablation procedures on the same or following day. It is recommended that patients visit their referring physician within the first seven to 10 days post-procedure. Patient follow-up after an ablation procedure varies among many ablation centres with geographic distance and referring physician experience and expertise being important factors.

EP studies and catheter ablation are invasive interventional cardiac procedures that must be performed in a hospital, in a specialized procedure room such as a cardiac catheterization laboratory. Essential equipment for catheter ablation includes a variable-pulse digital fluoroscopy unit, specialized computer-based signal processing and recording systems to acquire and digitally store study information, and an ablation energy generator. Computer-based simultaneous multiple-point mapping systems are increasingly seen as an essential component for addressing the challenging types of tachycardia. Equipment within the room to ensure patient safety includes an external defibrillator unit, standard cardiopulmonary resuscitation equipment, and non-invasive physiologic monitoring equipment (heart rate, blood pressure, respiration, oxygen saturation). Oxygen, suctioning equipment, pericardiocentesis trays and echocardiography must be readily available. Anaesthesia equipment and drugs also need to be available for those patients requiring general anaesthesia. Many centres share the use of both a cardiac catheterization laboratory and staff expertise; however, where justified by case volume
and complexity, centres of excellence have developed EP laboratories dedicated solely for ablation procedures with dedicated staff.

The specific indications for catheter ablation will be discussed with each specific tachycardia in the following sections below. As a general guideline, ablation is clearly indicated either where a tachycardia is refractory to drug therapy, the patient is intolerant of drugs or non-compliant, or the drugs are contraindicated because of existing comorbid conditions. However, catheter ablation is often recommended to patients as first line therapy for a variety of tachycardias because it represents curative therapy.

1.2.3 General limitations and complications of catheter ablation

There are limitations and complications that are common to all catheter ablation procedures, while some depend upon the specific tachycardias and will be discussed in the appropriate sections below. In general, successful catheter ablation outcome depends on an adequate diagnostic EP study with correct diagnosis and identification of the arrhythmia substrate. This is not always possible for some tachycardias. The number and size of the tissue that needs to be ablated, and the depth of the tissue within the heart wall, also determine the likelihood of success for some tachycardias.

EP studies are associated with a low complication rate.\textsuperscript{11,12} Peripheral vessels can be damaged with resulting impairment of circulation. Other risks include pneumothorax, thrombophlebitis, transient bundle branch block or AV block, myocardial perforation with or without cardiac tamponade and induction of VF. Myocardial perforation can occur during catheter ablation with the potential for major haemorrhage or cardiac tamponade. Ablation in the left atrium or ventricle requires a transeptal or retrograde aortic approach that involves a risk of systemic thrombemboli or myocardial infarction. Some tachycardias are difficult and take many hours to map and ablate and X-ray exposure can be lengthy. There is concern regarding the long-term effects in patients that undergo such protracted, difficult ablation procedures.\textsuperscript{13}
2 OBJECTIVES

The objectives of this report are:

(1) to evaluate the evidence for clinical efficacy of RFA through a systematic review of research studies; and

(2) to evaluate the cost-effectiveness of RFA through a systematic review of economic evaluations.
3 CLINICAL EFFICACY REVIEW

3.1 Methods

3.1.1 Literature search strategy

Published literature was identified by searching electronic bibliographic databases using the DIALOG® system on January 25, 2001 (Appendix 1). The year 1985 was chosen as the beginning date for the literature search for the clinical and economic reviews given the introduction of catheter ablation into clinical practice in the mid-1980s. A “one-search” was performed on MEDLINE®, HealthSTAR, EMBASE®, BIOSIS Previews®, PASCAL, and SciSearch®. The Cochrane Library on CD-ROM, 1999 Issue 4, was also searched. An update search on these databases was performed on November 5, 2001. The websites of health technology assessment (HTA) agencies, near HTA agencies, and other specialized databases, such as trial registries and the databases of the National Health Service Center for Reviews and Dissemination, were searched. These searches were supplemented by the bibliographies of selected papers and documents in the CCOHTA library collection.

Two primary search strategies were developed according to the study objectives: one for the clinical review, and one for the economic review (Appendix 1). Below are the specifics of the methodology pertaining to the clinical review. The specific methods adopted for the review of economic studies are described in section four of this report.

3.1.2 Selection of abstracts and retrieval of full-text articles

Two reviewers conducted independent screening reviews of all citation titles and abstracts retrieved. The reviewers read citation abstracts (or titles only, if the abstract was not available) to make inclusion decisions for subsequent full-text review.

The primary inclusion criterion for this review was that the primary study report clinical outcomes pertaining to RFA for cardiac arrhythmias. No language restrictions were placed on the selection of abstracts and the inclusion of articles for this report. Publications as a letter or abstract only, or duplicate publications of the same study results were excluded for this review.

The focus of this review was on adult patients given that the number of children who warrant ablation procedures due to malignant cardiac arrhythmias is very small. The paediatric patient population also has an entirely different substrate for arrhythmias in the majority of cases, and the most common arrhythmias in this age group are different from those in the adult group.

Case reports and small cohort studies involving less than 10 patients were excluded from further review. Clinical outcome data from trials were reviewed, including primary endpoints such as acute procedural success rates as well as recurrence and complication rates over the follow-up period of the study. Secondary endpoints reviewed included functional capacity and QOL. It was expected that the vast majority of published catheter ablation studies involving adult patients would be limited to non-randomized cohort studies reporting clinical efficacy and safety data. A few randomized controlled trials (RCTs) were expected which compared clinical outcomes of catheter ablation with other forms of therapy.
Relevant studies and reports were retrieved, reviewed, and classified by subject under six categories based on the arrhythmia type conducive to ablation: pre-excitation syndromes-accessory pathway ablation; AVNRT-slow AV node pathway ablation; isthmus dependent atrial flutter ablation; ablation of other atrial tachycardias (including sinus tachycardias); ablation of AF (AV node ablation; AV node modification; linear ablation; focal & pulmonary vein ablation); and VT ablation.

3.2 Results

Nine hundred and sixty-eight abstracts/citation titles were identified through the literature search strategy. Of these citations, 111 primary research studies (11%) met the inclusion criteria. These consisted of 18 studies on the pre-excitation syndromes, 22 studies on AVNRT with one study also reporting on the pre-excitation syndromes, 16 studies on atrial flutter, nine studies related to other atrial tachycardias, 29 studies in general on AF, and 18 studies on VT. These studies were primarily single-centre cohort reports. Only 10 of these studies (9%) were RCTs. Further study specifics are provided under each of the following sections.

3.2.1 Pre-excitation syndromes-accessory pathway ablation

a) Clinical overview

The pre-excitation syndromes, of which WPW syndrome is the most recognizable, are a group of congenital disorders caused by the presence of one or more accessory pathways. Accessory pathways are abnormal electrical connections between atrial/AV junctional and ventricular tissue crossing the AV annulus and this anatomic location makes them susceptible to catheter ablation. The prevalence of this abnormality in the population has been estimated to be in the range of 1-15%, with new cases arising at a rate of 0.004% per year.14

Many individuals with pre-excitation syndromes have no clinical tachycardia and are identified during routine medical examination. It has been estimated that up to 50% of cases may develop recurrent symptomatic tachycardia episodes. These tachycardias vary in frequency, duration, symptom severity, and the degree to which they impact on QOL. The most common tachycardias are AVRT (orthodromic and antidromic) and AF. Rarely, patients may present with sudden death. The mechanism relates to rapid conduction over the accessory pathway during AF with the development of VF.15 There are markers that identify patients who are at risk but these may require EP studies. Antiarrhythmic drugs are often prescribed to symptomatic patients and can reduce or eliminate attacks in a varying proportion of patients. However, drug treatment is usually life-long since tachycardia attacks generally do not decrease (and commonly increase) with age.

b) Evidence

Tachycardias caused by the presence of accessory pathways were among the first arrhythmias to be treated by RFA. Eighteen primary outcome studies were identified for ablation of accessory pathways.16-33

Thirteen of these studies (72%) reported sufficient outcomes data for purposes of tabulation and were considered within the primary analysis (Appendix 2, Table 1).16-28 Of these thirteen studies, one study was a U.S. based multi-centre clinical trial,26 one study reported the results of a survey
of catheter ablative procedures in 164 institutions within the United States,\textsuperscript{16} and the remaining 11 studies being single-centre cohort studies. These studies were representative of five countries including one Canadian study. Five (of 13) studies were specific to WPW syndrome.

Of the remaining studies from the 18 that were located, two studies (11\%) examined the effect of successful accessory pathway ablation on QOL (one of these studies was a randomized comparison with drug therapy, and the other being a prospective cohort).\textsuperscript{31,32} The remaining three studies provided insufficient outcomes data for purposes of tabulation and thus were not considered within the primary analysis.\textsuperscript{29,30,33}

**Success, recurrence and/or complication rates**

Reports published over the past decade have enrolled symptomatic patients who have been drug refractory or drug-intolerant. Patients may have multiple accessory pathways but most centres have expressed catheter ablation success rates in terms of the number of patients, ranging from 40 to 2,527 patients (Appendix 2, Table 1). These studies have reported procedural success rates ranging from 87-99\% in patients (Table 1). The multi-centre study by Calkins et al. (1999), for example, showed an overall success rate of 95\%, with right sided and postero-septal pathway locations having the lowest success rates (90\% and 88\%, respectively).\textsuperscript{26} These results confirm the earlier findings of the North American Society of Pacing and Electrophysiology Registry (1992)\textsuperscript{16} and the study of Kay et al (1993).\textsuperscript{28}

The failure rate of RFA in patients with multiple accessory pathways has been observed to be higher and procedures are of a significantly longer duration.\textsuperscript{27} The study by Chen et al (1994) showed that ablation efficacy was similar for elderly (>65 years) and younger patients.\textsuperscript{25} RFA success rate has been observed to be dependent on the experience of the electrophysiologist in performing catheter ablation procedures.\textsuperscript{29} Calkins et al. (1999) also found that the volume of ablation procedures performed by the study institution was a predictor of success rate.\textsuperscript{26}

Ten (of 13) studies reported recurrence rates of accessory pathways (Table 1) of 0-11\% with a follow-up period of 3-24 months. There are several reasons for recurrence after apparent success. Schlüter et al. (1997), for example, reported the findings at repeat ablation in 54 of 1,280 patients (4\%) who had recurrence of symptoms after a first ablation procedure.\textsuperscript{23} “True” recurrence occurred in nine patients (0.7\%) manifesting a previously “dormant” accessory pathway not detected during the first procedure. Most of these recurrences were successfully ablated at a second, and rarely, a third session.\textsuperscript{23}

The complication rate reported from twelve studies was 0-11\% (Table 1). The multi-centre study by Calkins et al. (1999) reported the 11\% complication rate but only 3\% were major complications (requiring intervention) for the entire study population which included three separate study groups: patients undergoing accessory pathway ablation, AV node slow pathway ablation for AVNRT, and complete AV node ablation for AF.\textsuperscript{26} Complication risk is dependent upon accessory pathway location and the ablation approach. AV node injury causing AV block is a significant risk with septal pathways. Myocardial perforation, myocardial infarction, and stroke are important complications with left-sided pathways.
**Quality of life**

Two studies have examined the effect of successful accessory pathway ablation on QOL. In a prospective, randomized trial by Lau et al. (1995) involving 55 patients with accessory pathway-related tachycardias, successfully ablated patients showed improved QOL scores and exercise capacity when tested three months after ablation. Improvements in total QOL scores were observed before and at 3 months after ablation in these patients for “General Health Questionnaire” (20 vs. 17, p<0.02), “Somatic Symptoms Inventory” (73 vs. 76, p<0.02), and “Sickness Impact Profile” (26 vs. 11, p<0.001). This improvement in QOL was progressive and sustained over a one-year period. In contrast, patients who had failed ablation attempts and patients on drug therapy showed no change in either parameter. This study, however, showed a marked imbalance in the number of patients recruited in each treatment arm (46 patients in the RFA arm, and nine patients on drug therapy), which raises issues concerning the adequacy of randomization. However, these findings are similar to that reported by Bubien et al. (1996) examining, in general, QOL pre-and post-ablation in a diverse group of patients (n=229 patients) with various tachycardias. The study population consisted of 46 patients with WPW syndrome; patients with accessory pathways showed marked improvement in almost all of the short form (SF)-36 QOL subscales (33% overall improvement at six months compared to baseline), and perceived ability to perform daily activities at one month post-ablation and these improvements persisted to six months.

**Asymptomatic patients**

There exists some divergence of opinion concerning the advisability of catheter ablation for asymptomatic individuals with overt pre-excitation. These individuals have a low but finite risk (estimated at <1 per 1000 patient-years) of sudden death due to rapid conduction over the accessory pathway and ventricular response during AF even though they have no clinical tachycardia problem when identified. These high-risk individuals are identifiable by specific EP markers. There are no studies specifically examining ablation in this group of patients, and previously cited cohort studies have not identified these patients for sub-group analysis. Some centres routinely recommend catheter ablation to eliminate even the remote possibility of sudden death. Other centres, on the other hand, consider the risks of catheter ablation to outweigh its limited benefit in this sub-group of patients and offer catheter ablation selectively, depending on circumstances such as occupation, high-risk physical or recreational activity, and patient preference.

c) **Summary**

Data on catheter ablation of accessory pathways in symptomatic patients is based on findings from non-randomized studies primarily involving clinical experiences from single-centres. Acute procedural success rates range from 87-99% with reported recurrence rates of 0-11% and complications of 0-11% over a follow-up period of three to 24 months. Higher failure rates of RFA are observed in patients with multiple accessory pathways. Results from two studies with relatively small-sample sizes, including one RCT, demonstrate that successful ablation is associated with some improvements in QOL and functional capacity.
3.2.2 AVNRT-AV node pathway ablation

a) Clinical overview
AVNRT is the most common sustained atrial arrhythmia, other than AF. AVNRT is now known to be due to an imbalance in the electrical properties of the two main sets of atrial fibers providing input into the AV node. This tachycardia can thus be eliminated by ablating either the anterior (fast pathway) or posterior (slow pathway) fibers.

b) Evidence
Twenty-two studies reported outcomes for RFA of AVNRT. Four studies were comparisons of ablation of the slow pathway to ablation of the fast pathway: one RCT and three single-centre cohort studies. An additional 10 studies were specific to slow-pathway ablation; all were single-centre cohort studies representing five countries.

Of the remaining studies of the 22 that were located, five cohort studies involved both types of ablation procedures. An additional three non-randomized studies (one study has been discussed in the previous section on ablation for accessory pathways) have examined the effect of ablation for control of AVNRT on QOL.

Success, recurrence and/or complication rates
Although ablation of both the slow and fast pathways has been evaluated, the four studies comparing both approaches report a higher success rate (68-100% vs. 46-94%) for slow pathway ablation (Table 2). Two studies, including one RCT from Langberg et al. (1993), also report a lower complication rate (0-4% vs. 5-6%). The most significant complication is the development of complete AV block requiring a permanent pacemaker which occurs in 1% of patients. While these studies report that AVNRT can be ablated with a high procedural success and modest complication rates, there are no data from RCTs that specifically address whether this should be done.

Quality of life
Three non-randomized QOL studies have been performed which evaluated patients before and after catheter ablation for AVNRT. The single-centre study performed at a Kaiser Permanente Medical Care Program in Northern California evaluated 273 symptomatic patients (mean age 55 years, majority being women) undergoing RFA for AVNRT. Study patients reported a significant reduction in overall symptom scores after RFA from 5.8 to 3.1 per patient (p<0.001). The number of moderate to severe symptoms declined to an even greater extent. Urgent care visits decreased from 4.6 in the year before the procedure to 0.4 in the year after the procedure (p<0.05).

Bubien et al. (1996) have also observed improvements in Arrhythmia Symptom scores (ranging from 17-28 points) in 59 patients with AVNRT. Both of these studies, however, suffer from significant design limitations. Patients undergoing a major procedure have a high psychological incentive to feel better. In the Larson study, for example, patient recall was used for pre-treatment QOL assessment and it may have been flawed. Patients were often referred when symptoms were prevalent and regression to the mean is often a major factor associated with improvement after referral for a major procedure. Given these limitations, one cannot reliably conclude from this study that ablation for AVNRT is superior to drug therapy. One of the
primary reasons for the absence of any RCT is that very few patients, once referred to a centre that performs these procedures, are likely to be willing to be randomized.

Finally, there was a prospective non-randomized study by Bathina et al. (1998) comparing QOL outcomes (SF-36 and Health Transition scores) for 79 patients with PSVT, 40 of whom chose drug therapy and 39 chose RFA. Patients were followed for 12 months without crossover. The mechanism of tachycardia could only be ascertained in the RFA patients and was AVNRT in 66%, accessory pathway-related in 26% and atrial tachycardia in 8%. RFA eliminated symptoms in 74% of patients versus 33% treated by drugs. Improvement in SF-36 scores was observed in both the RFA and drug therapy group. However, RFA improved QOL in more general health categories than drug therapy: at follow-up, ablation was associated with significant improvements in bodily pain (p<0.005), general health (p<0.05), vitality (p<0.05), and role emotion (p<0.05) compared with medication. Younger patients (<50 years) showed a greater improvement in QOL scores than older patients.

c) Summary
Overall success rates for AV node pathway RFA of AVNRT, based primarily on the results from cohort studies, are reported to be 46-100%. Ablation of the slow pathway has a higher success (68-100% vs. 46-94%) and lower complication rate (0-4% vs. 5-6%) compared to ablation of the fast pathway. Evidence from three non-randomized QOL studies, which evaluated patients before and after AV node pathway ablation, report a decline in symptoms and/or frequency of urgent visits by study patients following ablation.

3.2.3 Isthmus dependent atrial flutter ablation

a) Clinical overview
Classic atrial flutter exhibits characteristic features on the electrocardiogram. Detailed mapping studies have determined that this is a re-entrant tachycardia with a re-entrant circuit confined to the right atrium. The arrhythmia substrate responsible for the tachycardia is slow conduction in a narrow band of tissue between the inferior vena cava, tricuspid annulus and coronary sinus ostium called the cavo-tricuspid isthmus. There are common and uncommon subtypes that differ only in the direction of the activation wavefront.

In some patients, atrial flutter is the sole arrhythmia and there is no obvious underlying cause such as structural heart disease. In many other patients, AF and flutter co-exist or atrial flutter develops after treatment of AF by antiarrhythmic drugs. Many such patients have a past history of myocardial infarction, valvular heart disease, previous heart surgery or hypertension. Patients present with rapid palpitations that persist for hours to days and this chronic rhythm problem is often resistant to most antiarrhythmic drugs. Persistent tachycardia can result in congestive heart failure. Catheter ablation procedures were developed following recognition that the critical part of the re-entrant circuit was located in the accessible cavo-tricuspid isthmus.

b) Evidence
Sixteen studies reported outcomes for RFA of atrial flutter. Eleven studies were of ablation for lone atrial flutter, three of which also examined its effects on QOL (Table 3). The remaining five studies were of ablation for atrial flutter and AF. Of these, 14 studies were
single-centre cohort series and two studies were randomized comparisons with antiarrhythmic drug therapy (one study on atrial flutter, and a second study for atrial flutter and AF).

**Success, recurrence and/or complication rates**

For patients whose sole arrhythmia is atrial flutter, catheter ablation has been reported to be curative. In the randomized study by Natale et al. (2000), 61 patients with frequent atrial flutter episodes (at least two attacks in four months) were randomly allocated to receive antiarrhythmic drug therapy or ablation. After a mean follow-up of 21±11 months, fewer drug-treated patients were still in sinus rhythm (36% vs. 80%, p<0.01), more drug-treated patients had documented AF episodes (53% vs. 29%, p<0.05) and more drug-treated patients had been rehospitalized at least once (63% vs. 22%, p<0.01) (Table 3).

Larger cohort series involving (\geq 100) patients with drug refractory atrial flutter confirm the high procedural success (83-100%) using conventional radiofrequency energy (Table 3). However, clinical recurrence has been reported to be as high as 15.5% (n=31) in one study involving 200 patients. The majority of the study population (26 of 31 patients) in this cohort series underwent a second or third ablation procedure with no further recurrences of flutter. Of particular interest was the development of AF on follow-up in 11 patients (5.5%) without a prior history of the arrhythmia. In the failed cases, radiofrequency energy can be delivered while irrigating the ablation catheter with saline to cool the tip and achieve deeper burns. Jaïs et al. (1998), for example, used this technique in 13 (of 170) patients with atrial flutter who failed conventional RFA. Almost all of the study patients showed return of some isthmus conduction and the majority were cured by a second ablation procedure when the isthmus was completely transected. Twelve (92%) of these saline irrigated ablation procedures were successful with no complications, with an overall success rate of 99.5% for catheter ablation using any method.

**Quality of life**

Three small studies have also looked at the effect of ablation upon QOL and activity levels. In the randomized study by Natale et al. (2000) reported above, ablated patients showed improvement in both ‘sense of well-being’ (from 2.0±0.3 to 3.8±0.5, p<0.01) and daily-life functioning (from 2.3±0.4 to 3.6±0.6, p<0.01) compared to drug-treated patients, based on scores from a 16-item “Quality of Life Enjoyment and Satisfaction Questionnaire”. Lee et al. (1999) have also studied the effect of atrial flutter ablation on QOL and health care utilization. The study included 100 consecutive drug refractory patients, 27 of whom also had documented AF. Atrial flutter ablation was successful in about 97% of cases although atrial flutter recurred in 6% (Table 3). AF occurred during follow-up in 56% of patients with a prior history of AF, but in only 12% of those without prior AF. Patients with and without prior AF shared similar QOL scores at baseline but improvements in symptoms scores, QOL, and activities of daily living at six months were of smaller magnitude in patients with concomitant AF. Antiarrhythmic drug prescription, hospitalization and visits to the emergency department were all significantly decreased following RFA. The study by Anselme et al. (1999), also involving 100 patients, reported as above a similar trend in QOL scores. Both of the latter studies share the methodologic limitations of small sample size, non-randomized single cohort design, and a short follow-up assessment period.
**Atrial flutter and AF**

The results of RFA for patients with mixed atrial flutter and fibrillation are more difficult to evaluate because the relationship between atrial flutter and AF is complex and incompletely understood. In some patients, atrial flutter may trigger AF while the reverse may be true in others. Atrial flutter may only be seen when AF is treated with antiarrhythmic agents. Thus, the effects of ablating the atrial flutter substrate would depend upon the relationship in any given patient and it is not surprising that studies have provided inconclusive results.

Five cohort studies reported that patients undergoing atrial flutter ablation are much more likely to have symptomatic AF episodes on follow-up if they have structural heart disease, a prior history of AF, or inducible AF during the ablation procedure. Paydak et al. (1998), for example, showed that patients with both left ventricular dysfunction and prior history of AF were three times more likely to experience problems with AF after atrial flutter ablation. On the other hand, Reithmann et al. (2000) reported that patients developing atrial flutter after treatment of AF with amiodarone have a much greater likelihood of eliminating both of these arrhythmias by atrial flutter ablation than patients who have both atrial flutter and AF without drugs (20% vs. 76%). Clearly more studies are needed to establish the role of flutter isthmus ablation in patients with concomitant atrial flutter and AF.

c) **Summary**

Evidence from one small-randomized study demonstrates that elimination of the arrhythmia substrate results in reduced symptoms, lower rate of complications and rehospitalization, and improved QOL compared to drug-therapy with a mean follow-up of close to two years. Evidence from cohort series report overall acute procedural success rates of up to 83-100% where atrial flutter is the sole arrhythmia but up to 15% of patients may experience a clinical recurrence. The clinical benefits of flutter ablation are diminished in patients with concomitant AF.

**3.2.4 Ablation of other atrial tachycardias (including sinus tachycardias)**

a) **Clinical overview**

Tachycardias originating from atrial tissue are rare and constitute a small proportion of the arrhythmias ablated. They can originate from within the sinus node (“normal pacemaker complex”) or from tissue remote from the sinus node. Atrial tachycardias are divided into those due to an automatic focus (a single cluster of malfunctioning cells that fire rapidly) and those that are the result of a re-entrant circuit that may be so small as to be indistinguishable from an automatic focus. Therefore, tachycardias that appear to arise from a very small spot in the atria are referred to as focal atrial tachycardias. Atrial flutter is a specific type of atrial tachycardia and has already been discussed in the previous section. An important group of re-entrant atrial tachycardias are those seen late following heart surgery where the surgical scar acts as a barrier around which there may be re-entry of electrical activity. Finally there is something called inappropriate sinus tachycardia which is poorly understood. Mostly young, otherwise healthy females have elevated resting and ambulatory heart rates associated with symptoms of fatigue, palpitations, light-headedness and other systemic complaints.

Atrial tachycardias cause symptoms by virtue of the rapid heart racing which can be very difficult to manage and many are refractory to antiarrhythmic agents. Some become incessant and can lead to heart failure (tachycardia-induced cardiomyopathy).
The main difficulty limiting ablation efficacy in atrial tachycardias is the ability to induce the tachycardia and map the site in the EP laboratory. Newer computer-assisted mapping equipment may improve success rates but they are at present expensive and require significant advanced training.

b) Evidence

Only nine single-centre cohort studies pertaining to ablation of various drug-refractory atrial tachycardias were identified for this report (Table 4). Of these, three studies were of ablation for intra-atrial re-entrant tachycardia,\textsuperscript{74-76} two studies for sinus node re-entry,\textsuperscript{77,78} two studies primarily reporting on focal atrial tachycardia,\textsuperscript{79,80} and the remaining two studies reporting on outcomes for the various tachycardias.\textsuperscript{81,82} Although the total reported experience involves very small numbers, the success rate has been high (73-100%) with a low complication rate. No large multi-centre RCT’s concerning atrial tachycardias have been performed and there are few data pertaining to the effects on QOL.

Two cohort studies reported results of RFA for inappropriate sinus tachycardia.\textsuperscript{77,78} Lee et al. (1995) used intra-cardiac ultrasound to guide RFA in 16 patients.\textsuperscript{78} Complete ablation was the goal in four patients and all were successful but upon follow-up (20.5±0.3 months), two patients required a permanent pacemaker for symptomatic bradycardias and one patient developed a new ectopic atrial tachycardia. Of 12 patients undergoing modification, all were acutely successful but two had recurrences after seven months. Hemi-diaphragm paralysis presumably due to phrenic-nerve injury was a complication in one patient.\textsuperscript{78}

c) Summary

The success rate of RFA for atrial tachycardias, based on very small cohort reports, has been reported to be within 73-100%. It is, however, difficult to comment on its clinical efficacy given the rarity of atrial tachycardias and limited experience with this procedure. No RCT’s concerning atrial tachycardias have been performed and there are few data pertaining to the effects of ablation on QOL. Inappropriate sinus tachycardia is a rare but poorly understood condition. RFA likely can achieve reasonable procedural success but long-term clinical efficacy is uncertain. Sinus node ablation for this condition remains an experimental therapy.

3.2.5 Atrial fibrillation

a) Clinical overview

AF is the most common serious heart-rhythm disorder which affects about 3% of the Canadian population.\textsuperscript{83} The incidence of AF increases markedly with age. AF causes symptoms because electrical impulses conducting through the AV node cause a rapid and irregular ventricular rate. Treatment strategies for AF include reducing the risk of stroke by means of anti-thrombotic therapy and controlling symptoms related to rapid and irregular heart rate. Currently, drug therapy constitutes the first-line therapy for AF patients.\textsuperscript{83} Two basic strategies are used for controlling the symptoms of AF. One is to return the heart rhythm to normal by means of antiarrhythmic drugs in combination with electrical cardioversion and keep it in normal rhythm by drug therapy. The other strategy for symptom control accepts the rhythm to be AF but controls the ventricular rate.\textsuperscript{83} The standard approach is to control the ventricular rate using drugs like digoxin, beta-blockers, and calcium antagonists.\textsuperscript{83} In nearly 50% of patients drug
therapy is ineffective at maintaining sinus rhythm. Drugs also cause intolerable side effects. Currently, patients are considered for one of several catheter-ablation approaches only after failed drug therapy to prevent AF recurrences, control of the ventricular rate is not possible with drugs, or when the patient continues to have significant symptoms.

b) Evidence
Twenty-nine studies have reported outcomes of ablation for AF. Specifically, 15 studies report on AV node ablation for rate control in AF, five studies on AV node modification, three studies on linear AF, and six studies on focal AF and pulmonary vein ablation. The study specifics are provided under each of the following sections.

**AV node ablation for rate control in AF**
The first ablation procedure established for arrhythmia control was complete ablation of the AV node to eliminate the rapid and irregular ventricular rate. AV node ablation is a palliative treatment that isolates the AF to the atrial tissue but does not eliminate it. Implantation of a permanent rate-responsive pacemaker is required concomitantly, although it can be inserted several weeks before the ablation procedure. AV node ablation and pacemaker implantation is performed both in patients with chronic and intermittent (paroxysmal) AF. In both of these clinical situations, the rationale and procedure for AV node ablation is the same although the type of pacemaker used is different. In chronic AF, a single-chamber ventricular pacemaker is used and in patients with intermittent AF one can use either a ventricular pacemaker or a dual-chamber pacemaker with the ability to switch automatically from dual to single-chamber pacing modes as the patient goes in and out of AF.

Of the 15 studies on AV nodal ablation, ten reported outcomes for chronic AF, including two RCTs and eight cohort studies (Table 5). An additional two randomized studies report on clinical outcomes for intermittent AF, and three studies report on the safety profile of AV node ablation.

**Studies of AV node ablation for chronic AF:** Three cohort studies have established that AV node ablation and pacemaker implantation can provide a reasonable level of control of the ventricular rate in patients who have chronic AF. What is the appropriate role of this procedure? Five uncontrolled follow-up studies have reported improved indices (palpitation, exercise tolerance, fatigue) of QOL, or improved cardiac performance and exercise capacity after AV node ablation for chronic AF. For example, Kay et al. (1988) compared patients before and after AV node ablation and reported improvement in the McMaster Health Index from 0.69 to 0.92 (p=0.002). These studies indicate that patients who undergo this procedure have improved symptoms but they do not tell us whether AV node ablation is superior to alternative therapies without ablation.

Two RCTs performed by the same investigative group, have compared AV node ablation to alternative therapeutic approaches. In the first study, Brignole et al. (1994) randomized 23 patients to receive AV node ablation plus pacemaker therapy, or pacemaker therapy alone. After 15 days there were significantly greater reductions in palpitations (-92% vs. -37%), rest dyspnea (-79% vs. -40%), effort dyspnea (-65% vs. -30%), and exercise intolerance (-54% vs. -17%) in patients receiving RFA. The patients not receiving ablation therapy then underwent
ablation. Compared to before ablation, this patient subgroup experienced 15% increase in exercise duration during standard exercise-stress testing at three months of follow-up. These investigators then performed a second larger study (1998), in 66 patients with chronic AF who had congestive heart failure and heart rate greater than 90 beats per minute. The follow-up period was 12 months and the primary outcome endpoints were validated measures of QOL. Patients undergoing RFA had significantly lower scores for palpitations (-78%) and effort dyspnea (-22%). After adjustment for baseline values, these patients also experienced reductions in exercise intolerance (-20%), easy fatigue (-17%), and chest discomfort (-50%). In the drug-therapy group, 10 patients went on to RFA because of worsening of their symptoms (four patients before the completion of the study and six patients immediately after the 12-month visit). Cardiac performance evaluated by means of standard echocardiography and exercise testing did not differ significantly between the two groups and remained stable over time.

Summary: Ablation of the AV node with pacemaker implantation, based on evidence from two RCTs, provides benefit over pacemaker therapy alone or conventional antiarrhythmic drug therapy for controlling the ventricular rate and improving symptoms in a select group of patients with chronic AF. These findings, however, are limited by the relatively small study sample recruited in these trials and by the fact that both of these trials were unblinded and performed by the same group of investigators.

Randomized studies of AV node ablation for intermittent AF: AV node ablation and pacemaker implantation for intermittent AF patients has important differences when compared to chronic AF patients. Conventional drug therapy includes both drugs that tend to maintain normal sinus rhythm as well as control the ventricular rate in AF. The type of pacemaker used after AV node ablation is also potentially different. Patients with intermittent AF tend to be healthier and have less severe heart disease than those with chronic AF. Thus, it is important to assess the clinical outcome of AV node ablation in this group separately.

Marshall et al. (1999) randomized 60 patients with frequent AF (at least monthly) or with intolerable drug side effects. Patients were randomized to a continuation of drug therapy, or to either a dual-chamber or a single-chamber pacemaker. The primary outcome measures were assessments of QOL. After 18 months of follow-up, patients with dual chamber pacing and AV node ablation had significantly improved scores compared to patients receiving drug therapy for: overall symptoms were 41% better (p<0.01), palpitations were 58% better (p=0.0001), and breathlessness was 37% better (p<0.05). Several patients were unable to tolerate the single-chamber ventricular pacing and they were crossed over to dual chamber pacing. Of those who tolerated single chamber pacing, scores for palpitations were significantly better (p<0.05) than with drug therapy.

Brignole et al. (1997) compared AV node ablation and dual chamber pacing to drug therapy in an RCT involving 43 patients. Twenty-two patients were randomized to AV node ablation and pacemaker, but only 21 patients had a successful ablation. Patients with ablation had statistically significantly lower scores in the ‘Living with Heart Failure’ questionnaire (-51%, p=0.0006), palpitations (-71%, p<0.0001), and exercise intolerance (-46%, p=0.001).
Summary: These two small RCTs provide limited evidence that ablation plus implantation of a pacemaker is more beneficial than drug therapy in selected patients with intermittent AF who have not responded well to usual drug regimens. Is ablation of the AV node and pacemaker implantation the treatment of choice for the management of symptoms of AF? Current data does not allow one to fully address this issue. The RCTs available include a highly selected cohort of patients who remained symptomatic in spite of reasonable attempts at drug therapy. These studies do not address the typical patient with AF who has a relatively low level of symptoms on standard drug therapy for AF. It is possible that these patients would also benefit from ablation and pacemaker implantation but no studies have been designed to address this issue.

The safety of AV node ablation: Two uncontrolled studies have suggested that patients undergoing AV node ablation and pacemaker implantation face an increased risk of death, especially sudden death, both early and later after AV node ablation. Life-threatening ventricular arrhythmias and procedural deaths have been anecdotally reported. There have also been reports of a higher than expected mortality rate late after ablation. There are two potential mechanisms for an increased risk of sudden death after AV node ablation; pacemaker failure and VF, perhaps secondary to QT prolongation.

The problem with uncontrolled follow-up studies is that it is impossible to distinguish whether the observed mortality after AV node ablation is related to pre-existing heart disease or to the procedure itself. Two studies address this issue to some extent. Gasparini et al. (2000) reported a large cohort follow-up study from 12 Italian hospitals (585 patients). There were a total of 40 cardiac deaths (23 non sudden and 17 cardiac sudden deaths). There was a higher risk of sudden death for patients with left ventricular ejection fraction below 45% and with coronary artery disease. There were 133 patients who had ‘lone’ AF (without underlying identifiable structural heart disease) in whom there were no sudden deaths during a mean follow-up of just over three years. Ozcan et al. (2001) have reported the follow-up of 350 patients undergoing AV node ablation for AF and compared them to age and sex-matched control patients. During a mean follow-up of 36 months, 78 patients died. After correcting for a baseline history of previous myocardial infarction or congestive heart failure and for treatment with cardiac drugs, the observed survival was similar to the control group. None of 26 patients with lone AF died during follow-up. The observed survival rates amongst the whole group of patients who underwent ablation were also similar to that of 229 control patients with AF who received antiarrhythmic drug therapy rather than AV node ablation.

Summary: The above cohort follow-up studies suggest that mortality following AV node ablation is not related to the procedure itself but to the patient’s underlying heart disease. While a small increased risk of sudden death cannot be excluded by these cohort reports, it is reasonable to suggest that AV node ablation has at least an acceptable three-year safety profile.

AV Node Modification: Five published studies, including two RCTs, have indicated that it is possible to partially interrupt AV nodal conduction without causing complete AV block, thus avoiding a permanent pacemaker (Table 6). This approach grew from experience with slow pathway ablation for AVNRT. Stabile et al. (1998) compared the fast and slow pathway RFA in patients with chronic AF in a prospective randomized crossover trial involving 33 patients. They discovered that both types of ablation resulted in slowing of the mean ventricular rate with
the fast pathway ablation having a significantly lower rate than the posterior approach (80±19 beats per minute vs. 111±16 beats/minute, p<0.001). There was, however, a significant risk of developing complete AV block with the anterior approach (6%). In four (of eight) patients, this risk of AV block was higher if the posterior approach was first attempted followed by an anterior approach (33% incidence of AV block by the stepwise approach, p=0.09). The slowing of ventricular rate during AF after ablation of the posterior approach (slow pathway) has also been observed in a cohort study by Tebbenjohanns et al. (1995) with a one-year follow-up period.

No trials were identified for this report that compared AV nodal modification to pharmacological rate control. One RCT compared AV node ablation and pacemaker implantation to AV node modification without pacemaker in patients with medically refractory AF. In this trial of 60 patients both methods were associated with improvements in QOL over a six-month follow-up period (on a QOL scale of 0-very good to 4-very bad; mean score of ‘3’ before and mean score of ‘1’ after AV node ablation vs. mean score of ‘3’ before and mean score of ‘2’ after AV node modification). Compared to those patients having AV node modification, in addition to greater improvement in general QOL, patients undergoing complete AV node ablation had reduced frequency of major symptoms and of symptoms during an attack of AF.

Summary: The available data indicate that it is possible to achieve the reduction in the ventricular rate by means of AV nodal modification without need for a pacemaker. Data from one RCT, however, indicates that results of this approach are inferior to complete AV node ablation and pacemaker implantation. Therefore, AV nodal modification is currently not an established treatment.

Linear AF Ablation: Surgical procedures have been developed to cure AF by cutting or freezing the atrial wall at specific critical sites. Electrophysiologists have tried to duplicate the success of surgeons without the attendant surgical morbidity.

To date, there have been only three small, published cohort studies enrolling drug-refractory paroxysmal AF patients (Table 7). These studies report modest success (28-57%) in eliminating or reducing the frequency of AF recurrence but safety and technical difficulties have been major causes for concern. Complication rates ranged from 4-50%, including some potentially life-threatening adverse events such as stroke and hemo-pericardium. These have been difficult procedures with reported mean-procedure times of nearly 10 hours and radiation exposure of more than three hours reported in one study. These results reflect the early learning experience of investigators and the difficulties involved in making long continuous ablation lines using existing ablation equipment. Determining the optimal location of these ablation lines has also been an important issue. Linear ablation for AF remains an experimental procedure requiring substantial technical refinements before any firm conclusions can be drawn about its safety and clinical efficacy.

Focal AF and Pulmonary Vein Ablation: Until recently, scientists believed that AF was due to a diffuse disease process and that AF ablation required extensive ablation of atrial tissue, such as in linear ablation. Investigators mapping AF and performing linear ablation procedures began reporting cases wherein a single small atrial focus firing at rapid rates seemed to initiate AF and ablating this spot stopped it completely. This led to the hypothesis that, at least in some patients,
AF may have a focal mechanism and a “focal AF ablation” approach might be effective. Early reported success with this approach has forced a complete reassessment of the fundamental nature and pathophysiology underlying AF. It remains unknown which proportion of AF patients have a focal mechanism and would be candidates for focal AF ablation nor how this patient group can be identified.

The largest published studies on focal ablation of AF have emanated from Bordeaux, France and Taipei, Taiwan (Table 8). The largest cohort reported by the French investigators involved 225 patients with drug-refractory AF. All patients had very frequent AF episodes (daily) and many were selected because they manifested frequent ectopy on electrocardiogram monitoring. Unfortunately, this study was short on important details. Pulmonary vein foci were identified in 96% of patients with many having multiple foci. The number of patients requiring more than one ablation procedure was not specified but they reported an overall success rate of 70% in their cohort. Success rate was dependent upon the number of identified foci (93% for patients with single focus, 73% for two foci and 55% for three or more foci). An important observation was that nearly one half of AF recurrences were due to recovery of an ablated focus. New foci not previously recognized accounted for the remainder. The most concerning risk of ablation within the pulmonary vein is the possible development of pulmonary vein stenosis. A reduction in vein diameter ≥50% was observed in nine patients (4%) but only two patients (0.9%) had symptoms and required intervention to correct the hemodynamic problem.

Qualitatively similar results have been reported by the Taipei group in two studies involving 42 and 79 patients, respectively. In the first report, 57 of 61 foci were successfully ablated. After 8±2 months of follow-up, 88% remained free of symptomatic AF and the remaining 12% were successfully treated with previously ineffective antiarrhythmic drugs. Only one patient had a minor complication and no pulmonary vein stenosis was reported. In the second report, 116 foci (89% in the pulmonary veins) were identified and 95% were ablated. After 6±2 months of follow-up, 86% of patients were free of AF without the need for antiarrhythmic drugs. They performed trans-esophageal echocardiogram after ablation in a subset of their patients and found evidence of pulmonary vein stenosis in 42% although none had significant symptoms.

A common finding of these early reports is that there is a strong predilection for AF foci to be located in the pulmonary veins, particularly the left and right upper vessels. Over the four years since their initial description, AF ablation approach and methodology has changed significantly. Initially, only sites that were clearly triggers for AF were ablated. Later, sites of frequent atrial ectopy were targeted because they appeared to correlate with the sites of AF initiation. Most recently, investigators have identified electrical signals coming from within pulmonary veins of these AF patients. Early results suggest that eliminating these potentials or isolating the pulmonary veins so that these electrical signals cannot reach the heart tissue might eliminate AF attacks. Haissaguerre et al. (2000) described their experience in an additional 90 patients with 197 foci (97% in the pulmonary veins). Forty-nine patients (54%) required more than one ablation session because of new pulmonary-vein potentials. Overall success after 8±5 months was 71% with an additional 13% of cases completely controlled for after addition of antiarrhythmic drug therapy. There was an inverse relationship between the number of sites with pulmonary-vein potentials and clinical success (1 focus = 93%; 2 foci = 73%; ≥3 foci = 55%). Successful ablations were correlated with complete elimination of identified pulmonary-vein
potentials (90% vs. 55%, p=0.002). Pulmonary vein stenosis was seen in 4% of cases and was associated with symptoms in two patients.\textsuperscript{11} Interventions needed to correct the complication were not reported. Mapping of pulmonary veins to identify these pulmonary-vein potentials and ablate them can be a difficult and time-consuming process. In these investigators’ experienced hands, the total procedure time for patients with single foci was close to three hours but was over five hours in patients with multiple foci.\textsuperscript{11} Alternative catheter technology and ablation energy (cryothermy, ultrasound) sources may help increase the probability of ablation success with reduced procedure duration and radiation exposure.

**Summary:** Focal AF ablation and pulmonary vein ablation approaches are under active research. Ablation of AF foci remote from the pulmonary veins carries the same efficacy and safety rates as RFA for atrial tachycardia. Pulmonary vein ablation is evolving rapidly but published cohort studies to date are limited to a few investigative centres and reported follow-up is too short to ascertain long-term efficacy. Appropriate patient selection, ablation methodology, and procedural target sites and endpoints have yet to be clearly defined and long-term outcome data are not available. The reports in this review suggest encouraging short-term clinical success rates of 62-88%. Pulmonary vein ablation must be considered an experimental procedure which requires further investigation using randomized-study design in larger populations of patients.

### 3.2.6 Ventricular tachycardia

**a) Clinical overview**

VT arising from the ventricular chambers most commonly occurs in patients with underlying structural heart disease (previous myocardial infarction or dilated cardiomyopathy) causing scar tissue to develop. In this setting, VT is a potentially life-threatening disorder that may precipitate hypotension, syncope, or death. There are several different types of VTs but only monomorphic VT is currently amenable to catheter ablation because the VT follows a predictable single path that can be mapped. Because of the extensive scarring, patients commonly have more than one monomorphic VT, each with its own re-entrant path within scar tissue of the heart muscle (intramyocardial) and it may not be possible to identify and ablate all the sites. Monomorphic VT may be quite hemodynamically and electrically stable so that some patients are able to walk into an emergency department to seek medical attention. Others may present with rapid palpitations accompanied by blackout or collapse and need emergency treatment and electrical cardioversion. Patients with VT secondary to heart disease are at increased risk of sudden cardiac arrhythmic death. Antiarrhythmic drug therapy guided by EP studies is recommended in patients with hemodynamically well-tolerated sustained monomorphic VT but those presenting with hypotension or hemodynamic collapse should be offered an implantable cardioverter defibrillator (ICD). Catheter ablation is indicated in ICD patients who have received recurrent shocks because of many spontaneous VT episodes.

Uncommonly, healthy individuals without heart disease can develop VT (idiopathic). Unlike other VT’s, this tachycardia is benign with a good prognosis similar to the SVTs. The focus can readily be identified and ablated in drug refractory or intolerant individuals.
b) Evidence

Eighteen single-centre cohort studies met the study inclusion criteria of ablation for VT. Of these, thirteen studies reported on VT secondary to structural heart disease (Table 9), and five studies for primary VT (no structural heart disease) (Table 10).

**VT secondary to structural heart disease**

Studies on ablation for secondary VT have reported success rates in the range of 37-86% with complications in up to 16% of patients (study patients ranging from 10 to 146). In addition to an absence of randomized trials with other therapeutic approaches, patients in these studies represent a highly selected subset of patients with frequently, troublesome drug-refractory VT causing severe symptoms or discharges from their ICD. Most study patients had ischemic heart disease and many had more than one VT morphology. The limited success reflects difficulties in attaining adequate VT maps, manipulating the ablation catheter precisely to the target sites and creating sufficiently large enough ablation lesions. Newer computer-based mapping systems have helped improve the accuracy, completeness, and duration of the mapping process. Alternative ablation technologies that can create larger deeper lesions (cryothermy, saline irrigated tip RFA, microwave, and ultrasound) may also improve efficacy.

Patients with structural heart disease can rarely develop a special form of VT involving the specialized conduction tissue or fascicles of the ventricles (bundle branch or fascicular VT). The fascicles have characteristic locations in the ventricles regardless of the patient, making mapping and ablation easier. Fascicular VT may be stubbornly resistant to antiarrhythmic drugs. Where it is the sole clinical problem, catheter ablation can eliminate this arrhythmia. Because of its rarity, there are no studies of substantial size examining the efficacy and safety of catheter ablation for fascicular VT. The two small cohort studies reviewed for this report were published in 1993 and 1995 with 28 and 16 patients undergoing ablation, respectively. Both studies reported 100% procedural success in ablating the responsible fascicle. In the report by Blanck et al. (1993), complications were seen when direct-current shock ablation was used but none after switching to RFA energy. The primary complication was AV conduction abnormalities prompting implantation of permanent pacemakers in four study patients. A complication rate of 6% from ablation was seen in another reported study. Late deaths were reported in both studies but could not be directly attributed to the ablation procedure. These patients have compromised left ventricular function and are at significant risk for other ventricular arrhythmias and sudden cardiac death.

**Primary VT**

An uncommon form of monomorphic VT can occur in young patients without structural heart disease (repetitive or idiopathic monomorphic VT). This type of VT is not associated with an increased risk of premature death and the primary reason for treatment is to reduce symptoms. The tachycardias may respond to beta-blockers or calcium-channel blockers or even intravenous adenosine but patients are often resistant or intolerant of drugs. Like SVTs, these tachycardias may increase in frequency or duration over the course of time and become more resistant to antiarrhythmic drugs. The tachycardia focus is usually in the right ventricular outflow tract or the left ventricular apical septum although other ventricular locations are possible. Because this arrhythmia has a well-defined focus of small size, it is amenable to mapping and ablation. Owing to the relative rarity of this entity, no comparative trials have been undertaken against other
therapeutic approaches. Only five single-centre cohort studies were identified for this report (Table 10). These published reports were of small sample size and involved 12-28 patients. Reported procedural success ranged from 78-100% with these studies reporting less than 10% risk of complications that can include myocardial perforation with cardiac tamponade and stroke.

c) Summary:
VT in the setting of structural heart disease is potentially life threatening. Catheter ablation in this case is considered only as an adjunct to therapy with antiarrhythmic drugs and ICDs in patients who have very frequent attacks. Evidence from small-sample cohort studies on ablation for secondary VT have reported success rates in the range of 37-86% with complications in up to 16% of patients. In addition to an absence of randomized trials with other therapeutic approaches, patients in these studies represent a highly selected subset of patients with frequently, troublesome drug-refractory VT causing severe symptoms or discharges from their ICD. Only five single-centre cohort studies were identified for this report for primary VT. These published reports were of small sample size and involved 12-28 patients. For patients without structural heart disease, reported procedural success for VT ablation range from 78-100%, with cohort studies reporting less than 10% risk of complications that can include myocardial perforation with cardiac tamponade and stroke. Owing to the relative rarity of this entity, no comparative trials have been undertaken against other therapeutic approaches and thus this is currently not an established procedure.

3.3 Conclusions
Catheter ablation is a therapeutic modality that has evolved to meet the challenges posed by the different tachycardias. The procedure continues to adopt newer technologies in order to address the most difficult of tachycardias. Ablation of PSVT (pre-excitation syndromes, AV nodal re-entry), atrial flutter and focal atrial tachycardias are all procedures associated with high procedural success rates (>75%) that are sustained during a follow-up period of one to two years. Limited evidence also demonstrates that elimination of these tachycardias improves symptoms and/or quality of life. Catheter ablation of AF (focal, pulmonary vein or linear ablation) and VT secondary to underlying structural heart disease are presently considered as experimental procedures as there remains insufficient published data to draw conclusions about their clinical efficacy and safety profile. For all the different types of ablation procedures, there is a paucity of high quality outcome studies comparing ablation with alternative therapeutic approaches and this provides opportunity for future research.
4 REVIEW OF ECONOMIC EVALUATIONS

4.1 Methods
The literature search strategy for this section is outlined in Appendix 1. Appropriate economic terms were substituted for clinical terms under the “trials filter” for the clinical review.

We excluded studies that 1) considered only interventions other than ablation, 2) were abstracts from conference proceedings, and 3) considered only children. Studies that considered only costs or QOL or provided insufficient data to be able to calculate an incremental cost-effectiveness ratio were not considered within the primary analysis. We summarized these studies in a standardized tabular format and briefly discussed them below.

Data were extracted by two reviewers using a standard worksheet and common definitions of terms. Items were reviewed, and differences were resolved by consensus. Studies were classified as model-based or trial-based. Since the range of interventions considered, patient populations, and methods used were highly variable, these studies were summarised qualitatively but not pooled quantitatively.

4.2 Results
Of the 192 abstracts/citation titles, the literature search identified 61 studies for review (32%). Of these, four considered other interventions only (ICDs, electrophysiologic studies, and cardiac pacemakers),133-136 seven were abstracts from conference proceedings,137-143 one was in Spanish and summarised another paper already included in the analysis,144 one was in Italian and summarised another paper already included in the analysis,145 two described a study protocol,146,147 two focused only on children,148,149 and 23 were either editorials or clinical/economic reviews.150-172 None of these were included in this analysis.

Of the 21 papers remaining, only three studies were considered for the primary analysis of cost-effectiveness studies of RFA (Table 11).173-175 A total of 12 studies considered only costs (Table 12).176-187 Six studies considered QOL and cost or QOL only (Table 13).55,56,188-191 The following discussion is focussed on the analysis of cost-effectiveness studies, and then provides some general discussion about the costing and QOL studies.

4.2.1 Cost-effectiveness studies
None of the cost-effectiveness studies considered the identical interventions and patient populations. All of these studies173-175 were Markov decision analysis models based on resource use data and practice patterns in the United States.

- Cheng et al. (2000)173 used a state-transition Markov model to compare RFA versus medical management for adult patients with SVT. Medical management included either long-term antiarrhythmic drug therapy (LTDT) or treatment of acute episodes with antiarrhythmic drugs (EDT). The study population primarily consisted of unselected patients with severely symptomatic SVT due to AVNRT referred for RFA at the Kaiser Permanente Medical Care Program in Northern California. Patients with WPW syndrome were excluded.
Effects were estimated by synthesizing published efficacy data and expert opinion from the Cardiac Arrhythmia Patient Outcome Research Team Project when necessary. Direct medical care cost data were collected from a cohort sample of patients (n=60) seen at a major academic hospital. Complications of the intervention were incorporated into the model, including hospitalization, adverse clinical events and mortality. Direct medical care costs related to SVT were considered over patients’ lifetime. All costs and effects were discounted at three per cent and reported in 1999 US dollars. Assumptions were stated and justified.

Morbidity was incorporated into the model by using preferences that were elicited from patients by using results from a published study that used the time trade-off (TTO) technique. Although extensive one-way, multiway, and best-case vs. worst-case sensitivity analyses were performed, there was no estimate of the confidence interval for effects and costs.

In patients with severely symptomatic SVT, RFA was associated with increased quality-adjusted life-years (QALYs) and decreased costs, and dominated 1 both LTDT and EDT treatment options. LTDT was associated with increased QALYs and decreased costs compared to EDT.

- Calkins et al. (2000) 174 used a state-transition Markov model to compare RFA versus drug therapy with amiodarone for adult patients with an ICD with sustained VT. Incremental effects were estimated by collecting cost and effect data as a sub-study of an RCT. The trial evaluated use of a single type of catheter (Chilli Cooled Ablation System) to treat patients with VT due to ischemic heart disease or cardiomyopathy. Complications of the intervention were incorporated into the model, including hospitalization, adverse clinical events and mortality. Direct medical care costs were calculated based on medical resource utilization estimated by a panel of three clinical experts. The analytic time horizon for this study was five years. All costs and effects were discounted at three per cent per annum and reported in 1998 US dollars. Assumptions were stated and justified.

Morbidity was incorporated into the model by eliciting SF-36 scores from patients enrolled in the randomised trial then applying a previously published statistical algorithm (Shumeli equations 192) to convert these scores into utilities. These estimates were supplemented with data obtained from an expert panel. Extensive sensitivity analyses were performed but there was no estimate of the confidence interval for effects and costs.

In patients with VT, RFA was associated with an incremental cost of US$ 20,923 per QALY over a five-year period.

- Hogenhuis et al. (1993) 175 was the only cost-effectiveness study to specifically evaluate RFA in adults with WPW syndrome. Four other alternative treatment approaches were considered: 1) observation alone, 2) observation until cardiac arrest and then initiate therapy, 3) non-invasively guided drug therapy, and 4) surgical ablation. The analysis was stratified based on patient cardiac history and age. Effects were estimated from the published literature and supplemented by clinical input from an expert panel when data were not available. Costs were estimated from a small convenience sample of patients by using a hospital cost-

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1 One strategy is said to dominate another if it is both more effective and less costly than its comparator.
accounting system. Costs and health effects were discounted at 5% per annum and appear to be reported in 1992 US dollars. Opinions from the authors were used to assign utility scores to each relevant health state without deriving values using a validated instrument.

This model showed that RFA was generally favoured as a treatment approach, but varies with clinical category and age. RFA dominated both drug therapy and surgical ablation for survivors of cardiac arrest. For asymptomatic patients, the model supported observation as a first line approach.

4.2.2 Costing studies

Twelve costing studies were identified. These are summarised in a standard format in Table 12. One of the costing studies described patients with AF; one was for patients with atrial flutter, and the rest described patients with PSVT. Of the twelve studies, three were Australian, six were American, two were British, and one was Japanese. Most of these studies used a retrospective design. Two studies compared in-patient care; one had no comparison group.\(^{177,184}\)

In general, these studies suggested that RFA has lower costs than alternative treatments over the long-term. However, the overall quality of these studies is poor because they tended to be small (n<40) retrospective studies with no comparison group and used charge data rather than costs.

4.2.3 QOL studies

Six studies of the QOL of patients who had RFA were identified (Table 13). All surveyed adult patients. Of these, one used the SF-36 to assess QOL;\(^{56}\) one used a linear rating scale and time-tradeoff technique;\(^{55}\) one used a validated and modified version of the SF-36;\(^{191}\) one used both the cardiac specific Karolinska Questionnaire and the Nottingham Health Profile;\(^{190}\) and two used novel questionnaires to assess QOL without any apparent validation.\(^{188,189}\)

All of these studies suggested that RFA was associated with an improvement in QOL, however, not all the studies had a comparison group. The studies by Bathina et al.,\(^{56}\) Gerstenfeld et al.,\(^{191}\) and Levy et al.,\(^{190}\) included a comparison group.

Bathina et al. (1998) compared RFA (n=39) and drug therapy (n=40) using the SF-36 and found an improvement in SF-36 scores for patients with SVT in both the RFA and drug therapy group.\(^{56}\) However, as stated in the review of clinical studies on AVNRT, ablation patients had significantly better bodily pain, general health vitality and emotional-role subscales than the drug treated group at the end of the follow-up period.\(^{56}\) Gerstenfeld et al. (2001) found that AF patients who underwent electrophysiological mapping without ablation reported no significant improvement in any QOL score, compared to patients who had long-term successful ablation who had significant improvements in all QOL measures with six months of follow-up.\(^{191}\) However, patients who developed AF recurrence after ablation still reported significant improvements in four of six QOL measures.\(^{191}\)

The study by Levy et al. (2001), which was the only randomised QOL study, reported less optimistic findings regarding ablation in patients with permanent AF.\(^{190}\) QOL improved significantly in both treatment arms (pacemaker plus ablation vs. pacemaker plus drug therapy),
but there were no significant differences in baseline results or between the groups at follow-up for either of the two study QOL instruments. In fact, there was a tendency for greater improvement in the drug therapy group for individual subgroup symptoms on the Nottingham Health Profile. The authors concluded that neither technique showed any significant advantage over the other, but recommended drug therapy first to avoid an initial irreversible ablation procedure.\textsuperscript{190}

### 4.3 Discussion

Only three cost-effectiveness analyses (CEAs) were identified and they focused on different and specific patient groups with selected target disorders. Based on these CEAs, RFA appears to be economically attractive compared to drug therapy in adult patients with frequently symptomatic PSVT or in VT patients with an ICD.\textsuperscript{173,174} In these patients, RFA dominates drug therapy options with a cost-effectiveness ratio within US $21,000 (C $33,000) per QALY. Specifically, in adult patients with WPW syndrome, the range of cost-effectiveness for RFA varies depending on baseline risk, but seems to either dominate other options of drug therapy, surgical therapy or observation, or lie within the above cost-effectiveness ratio. This is particularly true with younger age groups. RFA would not be considered cost-effective in the treatment of asymptomatic WPW syndrome adult patients at any age.\textsuperscript{175}

There are major limitations of the CEAs considered in this review. First, evidence of the cost-effectiveness of RFA is limited due to the paucity of rigorous analyses available. The three eligible analyses considered only selected target disorders. It is unclear whether such data are generalizable to other patient populations. The underlying effectiveness data in these analyses were derived from a single RCT or from small studies performed in high-volume centres. Only two studies use a lifetime perspective.\textsuperscript{173,175} All focused on direct medical costs, without consideration of indirect costs to patients or caregivers. Utility estimates were methodologically strong in one study only.\textsuperscript{173}

Second, the modelling efforts are all based on data from the United States for practice patterns and costs. There are no Canadian cost-effectiveness studies on cardiac ablation. It is unclear whether such data is generalizable to the Canadian context, but Canadian practice patterns and unit costs are likely to be different from the U.S.

Although several studies have evaluated the costs and QOL associated with ablation techniques independently, there are insufficient data to determine whether such interventions are cost-effective relative to other interventions.
5 HEALTH SERVICES IMPACT

There exist no Canadian guidelines for catheter ablation but current Canadian practices do not appear to vary markedly from guidelines or recommendations by international specialty societies.\textsuperscript{10,195-195} Currently in Canada, individuals with drug refractory tachycardias are offered catheter ablation. It is also common practice to offer the procedure electively to individuals as an alternative to lifelong drug therapy. Catheter ablation is also considered a reasonable treatment choice for life-threatening WPW syndrome.

Catheter ablation is performed on both an in-patient and out-patient basis. In the absence of Canada-wide estimates, based on data provided by the Canadian Institute for Health Information for the fiscal year 1998/99, over 1,000 ablation procedures are performed on an annual basis in Ontario.\textsuperscript{196,197} In the absence of direct data and given the geographical disparities in the accessibility of catheter ablation across provinces, it is difficult to extrapolate this figure to all of Canada. The average cost of an ablation procedure is estimated at C $1,700.\textsuperscript{2} This cost estimate includes in-patient charges, building and plant indirect costs, staff costs in the EP laboratory, and material & supplies. It is important to note that this estimate excludes physician fees and is based upon re-use of catheters in the RFA procedure.

\textsuperscript{2} This estimate is derived from the procedure costs at the London Health Sciences Centre, Ontario.
6 CONCLUSIONS

Catheter ablation for most cardiac arrhythmias is associated with good procedural success rates but there remains insufficient evidence to draw specific conclusions about its long-term clinical efficacy and cost-effectiveness. RFA is considered primarily as an adjunct procedure to pacemaker implantation for AF, and to antiarrhythmic drugs and ICD therapy for VT.

For all the different types of ablation procedures, there is a paucity of high quality outcome studies comparing ablation with alternative therapies. There exist no Canadian guidelines for catheter ablation but current practices do not appear to vary markedly from the guidelines or recommendations made by international specialty societies. If future evidence from controlled trials, especially in patients with AF and atrial flutter, demonstrates more conclusive benefits of ablation as technique and experience advance, utilization could climb significantly.
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### Appendix 1: Literature Search Strategies

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<td>SEARCH TERMS</td>
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| EMBASE* (File 73) | 41. (Set 2 OR Set 3 OR Set 4 OR Set 17) AND economic aspect!  
42. (Set 2 OR Set 3 OR Set 4 OR Set 17) AND Set 30  
43. Set 41 OR Set 42 | |
| BIOSIS Previews* (File 5) | 44. (Set 2 OR Set 3 OR Set 4 OR Set 21 OR Set 22) AND (Set 5 OR Set 6) AND [(economics/mc) OR (economic factors OR economic impact OR economic value OR cost OR cost analysis OR cost effectiveness OR cost savings OR cost-benefit analysis OR costs)/de]  
45. (Set 2 OR Set 3 OR Set 4 OR Set 21 OR Set 22) AND (Set 5 OR Set 6) AND Set 30  
46. Set 44 OR Set 45 | |
| PASCAL (File 144) SciSearch® (Files 34, 434) | 47. arrhythmia? OR Set 2 OR Set 3 OR Set 4 OR Set 21 OR Set 22  
48. Set 47 AND Set 6 AND Set 30 | Reduce Duplicates: Set 40 OR Set 43 OR Set 46 OR Set 48 = 192 refs. |

**The Cochrane Collaboration and Update Software**  
Cochrane Library 1985-2000  
2000 Issue I  
1. arrhythmia[MeSH] OR arrhythmia* OR (atrial and fibrillation) OR (ventricular and tachycardia*) OR (fasicular and tachycardia*) OR (ventricular and ectopic and tachycardia*) OR (atrial and tachycardia*) OR (cardiac and arrhythmia*) OR (cardiac and arrhythmia*) OR (supraventricular and tachycardia*) OR (atrioventricular and tachycardia*) OR (accessory and atrioventricular and pathway*) OR (accessory and pathway*) OR (ectopic and atrial and tachycardia*) OR (bypass and tract and tachycardia*) OR (multifocal and atrial and tachycardia*) OR (atrioventricular and junction*) OR (junctional and tachycardia*) OR (sinus and tachycardia*) OR (reentrant and tachycardia*) OR (reciprocating and tachycardia*) OR (WPW and syndrome*) OR (bundle and branch and reentry) OR (catecholamine and sensitive and tachycardia*) OR (microand reentrant and tachycardia*)  
2. catheter ablation[MeSH] OR fulguration OR electrofulguration OR cryoablation OR (catheter and ablation) OR (radiofrequency and ablation) OR (atrial and flutter and ablation) OR (ablation and catheter) OR (transcatheter ablation*) OR (ablative and cure*) OR (arrhythmia and ablation*) OR (high and frequency and catheter and ablation) OR (transcoronary and ablation*) OR (His and bundle and ablation*) OR (radiofrequency and linear and ablation*)  
3. electrocoagulation [MESH] OR electrocoagulation  
4. Set 1 AND (Set 2 OR Set 3)  
5. Set 4 and 1985:2000 = 88 hits  
I. Cochrane Database of Systematic Reviews = 2 Protocols  
II. Database of Reviews of Effectiveness. Abstracts of Quality Assessed Systematic Reviews = 1  
III. Cochrane Reviews/Protocols Listed by Collaborative Review Group = 1  
IV. Cochrane Trials Register. References = 77  
V. Health Technology Assessment Database. Abstracts from NAHTA and other healthcare agencies = 2  
VI. NHS Economic Evaluation Database. Abstracts of Economic Evaluation of Health Care Technologies = 6 |

**GUIDELINES SEARCH**  
MEDLINE® (File 154) 1995-2001 Human 1. arrhythmia!  
2. catheter ablation/de  
3. (fulguration OR electrofulguration OR ablation?)/ti,ab  
4. Set 1 AND (Set 2 OR Set 3)  
5. guidelines!
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<td>8. Set 5 OR Set 6 OR Set 7</td>
<td>8. Set 5 OR Set 6 OR Set 7</td>
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<td>9. Set 4 AND Set 8</td>
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<td></td>
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<td>18. Set 17/human from 72</td>
</tr>
<tr>
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<td>19. cardiac arrhythmia/de OR atrial arrhythmia/de OR arrhythmia?/ti,ab</td>
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<td>21. practice guidelines/de OR guidelines/de OR guideline?/ti,ab</td>
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<tr>
<td></td>
<td>22. Set 20 AND Set 21</td>
<td>22. Set 20 AND Set 21</td>
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<tr>
<td>PASCAL</td>
<td>25 arrhythmia?/ti,ab AND Set 3 AND guideline?/ti,ab</td>
<td>25 arrhythmia?/ti,ab AND Set 3 AND guideline?/ti,ab</td>
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<tr>
<td>(File 144)</td>
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<td>26. Set 25/human from 144</td>
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<td><strong>Reduce Duplicates: Set 11 OR Set 12 OR Set 18 OR Set 24 OR Set 26=42 refs.</strong></td>
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<td>“CCOHTA HTA Check list of websites”</td>
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<td>HTA Agencies (such as ANAES), near HTA agencies, and specialized databases (such as NHS CRD), for relevant literature and guidelines</td>
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Appendix 2: Summary Tables - Clinical and Economic Review

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Table 1: Accessory pathway (AP) ablation

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
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<tbody>
<tr>
<td>Scheinman, 1994</td>
<td>2,527</td>
<td>--</td>
<td>87</td>
<td>24</td>
<td>--</td>
<td>2</td>
</tr>
<tr>
<td>Jackman, 1991</td>
<td>166</td>
<td>32 ± 16</td>
<td>99</td>
<td>8</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Calkins, 1991</td>
<td>40</td>
<td>43 ± 18</td>
<td>93</td>
<td>6</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Lesch, 1992</td>
<td>100</td>
<td>31 ± 2</td>
<td>89</td>
<td>10</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Kuck, 1991</td>
<td>105</td>
<td>40</td>
<td>89</td>
<td>7.5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Thakur, 1994</td>
<td>200</td>
<td>34 ± 18</td>
<td>96</td>
<td>6</td>
<td>-</td>
<td>3.5</td>
</tr>
<tr>
<td>Timmermans, 1994</td>
<td>163</td>
<td>36 ± 14</td>
<td>92</td>
<td>14</td>
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</tr>
<tr>
<td>Schlüter, 1997</td>
<td>1,280</td>
<td>34 ± 18</td>
<td>96</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Chen, 1992</td>
<td>62</td>
<td>47 ± 6</td>
<td>96</td>
<td>10</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Chen, 1994</td>
<td>45</td>
<td>69 ± 3</td>
<td>95</td>
<td>18</td>
<td>--</td>
<td>9</td>
</tr>
<tr>
<td>Calkins, 1999</td>
<td>500</td>
<td>27 ± 17</td>
<td>95</td>
<td>24</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Chen, 1993</td>
<td>145</td>
<td>45 ± 16</td>
<td>95</td>
<td>12</td>
<td>11</td>
<td>0-3</td>
</tr>
<tr>
<td>Kay, 1993</td>
<td>363</td>
<td>35 ± 16</td>
<td>95</td>
<td>9</td>
<td>5.5</td>
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</table>

Table 2: AV node pathway ablation

<table>
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<tr>
<th>Author, Year (ref. #)</th>
<th># Patients [Slow/Fast Pathway]</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
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<tbody>
<tr>
<td>Langberg, 1993 RCT</td>
<td>28/22</td>
<td>47 ± 19</td>
<td>68/55</td>
<td>3</td>
<td>29/41</td>
<td>4/5</td>
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<tr>
<td>Jazayeri, 1993</td>
<td>104/16</td>
<td>--</td>
<td>94/81</td>
<td>--</td>
<td>6/19</td>
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<tr>
<td>Mitranı, 1993</td>
<td>29/13</td>
<td>48</td>
<td>90/46</td>
<td>12</td>
<td>0/64</td>
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</tr>
<tr>
<td>Chen, 1993</td>
<td>68/32</td>
<td>45 ± 10</td>
<td>100/94</td>
<td>12</td>
<td>2/3</td>
<td>0/6</td>
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</table>
### Table 3: Atrial flutter isthmus (AFI) ablation for lone atrial flutter

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natale, 2000 RCT⁶⁶</td>
<td>31/30</td>
<td>67 ± 18/66 ± 11</td>
<td>100-RFA</td>
<td>21</td>
<td>6/93</td>
<td>22% rehospitalized &amp; 29% AF vs. 63% rehospitalized &amp; 53% AF</td>
</tr>
<tr>
<td>Fischer, 1995⁶⁶⁶</td>
<td>110</td>
<td>59 ± 12</td>
<td>93</td>
<td>28</td>
<td>16</td>
<td>0</td>
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<tr>
<td>Ward, 1995⁶⁶⁶</td>
<td>15</td>
<td>50</td>
<td>33</td>
<td>19</td>
<td>67</td>
<td>0</td>
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<tr>
<td>Fischer, 1996⁶⁶⁶</td>
<td>200</td>
<td>60 ± 12</td>
<td>95</td>
<td>24</td>
<td>15.5</td>
<td>0</td>
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<tr>
<td>Poty, 1996⁶⁶⁶</td>
<td>44</td>
<td>57 ± 12</td>
<td>98</td>
<td>12</td>
<td>9</td>
<td>0</td>
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<tr>
<td>Welch, 1999⁶⁶⁶</td>
<td>14</td>
<td>69 ± 8</td>
<td>93</td>
<td>1.5</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Jais, 1998⁶⁶⁶</td>
<td>13</td>
<td>56 ± 10</td>
<td>92</td>
<td>5</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Tai, 1997⁶⁶⁶</td>
<td>30</td>
<td>57 ± 18</td>
<td>100</td>
<td>17</td>
<td>10</td>
<td>--</td>
</tr>
<tr>
<td>Tai, 1998⁶⁶⁶</td>
<td>144</td>
<td>56 ± 18</td>
<td>100</td>
<td>17</td>
<td>10</td>
<td>--</td>
</tr>
<tr>
<td>Lee, 1999⁶⁶⁶</td>
<td>100</td>
<td>56</td>
<td>97</td>
<td>6</td>
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<td>(12-56% AF)</td>
</tr>
<tr>
<td>Anselme, 1999⁶⁶⁶</td>
<td>100</td>
<td>60 ± 11</td>
<td>83</td>
<td>15</td>
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<td>(36% AF)</td>
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### Table 4: Atrial tachycardias and sinus tachycardias

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients [SANRT]</th>
<th>Success Rate (%) [SANRT]</th>
<th># Patients [FAT]</th>
<th>Success Rate (%) [FAT]</th>
<th># Patients [IART]</th>
<th>Success Rate (%) [IART]</th>
<th>Recurrence (%)</th>
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<tr>
<td>Kalman, 1996⁷⁴</td>
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<tr>
<td>Triedman, 1997⁷⁵</td>
<td>--</td>
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<td>--</td>
<td>45</td>
<td>73</td>
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<tr>
<td>Baker, 1996⁷⁶</td>
<td>--</td>
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<td>--</td>
<td>--</td>
<td>--</td>
<td>14</td>
<td>93</td>
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<tr>
<td>Sanders, 1994⁷⁷</td>
<td>10</td>
<td>100</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>Lee, 1995⁷⁷</td>
<td>16</td>
<td>100</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>12.5</td>
</tr>
<tr>
<td>Kay, 1993⁷⁹</td>
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<td>11</td>
<td>91</td>
<td>--</td>
<td>--</td>
<td>18</td>
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<tr>
<td>Goldberger, 2001⁷⁶</td>
<td>--</td>
<td>--</td>
<td>11</td>
<td>80</td>
<td>--</td>
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<td>18</td>
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<tr>
<td>Lesh, 1994⁷⁷</td>
<td>3</td>
<td>100</td>
<td>12</td>
<td>92</td>
<td>8</td>
<td>87</td>
<td>--</td>
</tr>
<tr>
<td>Chen, 1994⁷⁷</td>
<td>41</td>
<td>98</td>
<td>16</td>
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<td>20</td>
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SANRT- Sinoatrial node re-entrant tachycardia; FAT- Focal atrial tachycardia; IART- Intra-atrial re-entrant tachycardia
### Table 5: AV node ablation for chronic AF

<table>
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<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brignole, 1994 RCT&lt;sup&gt;23&lt;/sup&gt; RFA+PM vs. PM</td>
<td>12/11</td>
<td>64±10/70±6</td>
<td>54-92/17-40 (improved symptoms)</td>
<td>(3 weeks)</td>
<td>0/0</td>
<td>0</td>
</tr>
<tr>
<td>Brignole, 1998 RCT&lt;sup&gt;25&lt;/sup&gt; RFA+PM vs. Drug therapy</td>
<td>32/34</td>
<td>72±9/72±9</td>
<td>17-78 (improved symptoms compared to drug therapy)</td>
<td>12</td>
<td>--</td>
<td>6/29</td>
</tr>
<tr>
<td>Curtis, 2000&lt;sup&gt;26&lt;/sup&gt;</td>
<td>156</td>
<td>66±11</td>
<td>99</td>
<td>3</td>
<td>4</td>
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</tr>
<tr>
<td>Twidale, 1998&lt;sup&gt;27&lt;/sup&gt;</td>
<td>44</td>
<td>71±10</td>
<td>100</td>
<td>17</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Yamane, 1997&lt;sup&gt;28&lt;/sup&gt;</td>
<td>41</td>
<td>--</td>
<td>100</td>
<td>3</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>Natale, 1996&lt;sup&gt;29&lt;/sup&gt;</td>
<td>14</td>
<td>69±9</td>
<td>100</td>
<td>16</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>Kay, 1988&lt;sup&gt;30&lt;/sup&gt;</td>
<td>12</td>
<td>67</td>
<td>100</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Natale, 1999&lt;sup&gt;31&lt;/sup&gt;</td>
<td>75</td>
<td>69±9</td>
<td>100</td>
<td>6</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>Buys, 1997&lt;sup&gt;32&lt;/sup&gt;</td>
<td>25</td>
<td>58±11</td>
<td>100</td>
<td>7</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Edner, 1995&lt;sup&gt;33&lt;/sup&gt;</td>
<td>29</td>
<td>65±7</td>
<td>100</td>
<td>7</td>
<td>0</td>
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</tr>
</tbody>
</table>

RFA= radiofrequency catheter ablation; PM= pacemaker

### Table 6: AV node modification

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stabile, 1998&lt;sup&gt;34&lt;/sup&gt; RCT- Anterior vs. Posterior approach</td>
<td>17/16</td>
<td>67±7</td>
<td>82/25</td>
<td>16</td>
<td>4</td>
<td>6/0</td>
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<tr>
<td>Lee, 1998&lt;sup&gt;35&lt;/sup&gt; RCT-Complete AV junction ablation vs. AV modification</td>
<td>30/30</td>
<td>69±9/66±10</td>
<td>100/93</td>
<td>6</td>
<td>3/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Menozzi, 1994&lt;sup&gt;36&lt;/sup&gt;</td>
<td>78</td>
<td>69±10</td>
<td>99</td>
<td>3</td>
<td>6</td>
<td>6</td>
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<tr>
<td>Tebbenjohanns, 1995&lt;sup&gt;37&lt;/sup&gt;</td>
<td>34</td>
<td>46±13</td>
<td>100</td>
<td>12</td>
<td>3</td>
<td>0</td>
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<tr>
<td>Della, 1995&lt;sup&gt;38&lt;/sup&gt;</td>
<td>14</td>
<td>55±11</td>
<td>100</td>
<td>6</td>
<td>79</td>
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</table>

### Table 7: Linear AF ablation

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haïssaguerre, 1996&lt;sup&gt;39&lt;/sup&gt;</td>
<td>45</td>
<td>51±12</td>
<td>53</td>
<td>11</td>
<td>--</td>
<td>4</td>
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<tr>
<td>Jais, 1999&lt;sup&gt;40&lt;/sup&gt;</td>
<td>54</td>
<td>54±7</td>
<td>57</td>
<td>19</td>
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<td>15</td>
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<tr>
<td>Natale, 2000&lt;sup&gt;41&lt;/sup&gt;</td>
<td>18</td>
<td>61±7</td>
<td>28</td>
<td>22</td>
<td>39</td>
<td>50</td>
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</table>
### Table 8: Focal and pulmonary vein ablation for AF

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haïssaguerre, 1998</td>
<td>45</td>
<td>54±11</td>
<td>62</td>
<td>8</td>
<td>38</td>
<td>--</td>
</tr>
<tr>
<td>Shah, 2000</td>
<td>225</td>
<td>55</td>
<td>70</td>
<td>--</td>
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<td>4</td>
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<tr>
<td>Haïssaguerre, 2000</td>
<td>90</td>
<td>51±12</td>
<td>71</td>
<td>8</td>
<td>10</td>
<td>4</td>
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<tr>
<td>Haïssaguerre, 2000</td>
<td>70</td>
<td>53±13</td>
<td>73</td>
<td>4</td>
<td>44</td>
<td>0</td>
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<tr>
<td>Hsieh, 1999</td>
<td>42</td>
<td>65±14</td>
<td>88</td>
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<td>2</td>
</tr>
<tr>
<td>Chen, 1999</td>
<td>79</td>
<td>64</td>
<td>86</td>
<td>6</td>
<td>--</td>
<td>3</td>
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</tbody>
</table>

### Table 9: Ventricular tachycardia with structural heart disease

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rothman, 1997</td>
<td>35</td>
<td>62±13</td>
<td>86</td>
<td>3</td>
<td>54</td>
<td>--</td>
</tr>
<tr>
<td>Callans, 1998</td>
<td>66</td>
<td>67±8</td>
<td>71</td>
<td>--</td>
<td>--</td>
<td>9</td>
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<tr>
<td>Stevenson, 1998</td>
<td>52</td>
<td>65±10</td>
<td>40</td>
<td>18</td>
<td>33</td>
<td>10</td>
</tr>
<tr>
<td>Stevenson, 1993</td>
<td>15</td>
<td>66±7</td>
<td>80</td>
<td>10</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Gonska, 1994</td>
<td>136</td>
<td>56</td>
<td>75</td>
<td>24</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Kim, 1994</td>
<td>21</td>
<td>--</td>
<td>81</td>
<td>--</td>
<td>--</td>
<td>1</td>
</tr>
<tr>
<td>Jadonath, 1994</td>
<td>10</td>
<td>58±19</td>
<td>80</td>
<td>12</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Fontaine, 1994</td>
<td>89</td>
<td>32</td>
<td>80</td>
<td>52</td>
<td>--</td>
<td>16</td>
</tr>
<tr>
<td>Fontaine, 1996</td>
<td>58</td>
<td>55</td>
<td>76</td>
<td>17</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Calkins, 2000</td>
<td>146</td>
<td>65±13</td>
<td>75</td>
<td>8</td>
<td>46</td>
<td>8</td>
</tr>
<tr>
<td>Sosa, 2000</td>
<td>14</td>
<td>54±14</td>
<td>37</td>
<td>14</td>
<td>0</td>
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</table>

**Bundle Branch/Fascicular VT**

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mehdird, 1995</td>
<td>16</td>
<td>60±9</td>
<td>100</td>
<td>22</td>
<td>--</td>
<td>6</td>
</tr>
<tr>
<td>Blanck, 1993</td>
<td>28</td>
<td>62</td>
<td>100</td>
<td>16</td>
<td>--</td>
<td>14</td>
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</tbody>
</table>

### Table 10: Primary ventricular tachycardia

<table>
<thead>
<tr>
<th>Author, Year (ref. #)</th>
<th># Patients</th>
<th>Mean Age ± SD (yrs)</th>
<th>Success Rate (%)</th>
<th>Follow-up (months)</th>
<th>Recurrence (%)</th>
<th>Complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calkins, 1993</td>
<td>18</td>
<td>41±13</td>
<td>78</td>
<td>8</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>Lauribe, 1999</td>
<td>12</td>
<td>43±16</td>
<td>92</td>
<td>25</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Coggins, 1994</td>
<td>28</td>
<td>46±12</td>
<td>86</td>
<td>10</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Lin, 1996</td>
<td>18</td>
<td>29±11</td>
<td>100</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Thakur, 1996</td>
<td>15</td>
<td>31±12</td>
<td>93</td>
<td>24</td>
<td>13</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 11: Cost-effectiveness studies of catheter ablation

<table>
<thead>
<tr>
<th>Authors, Year (ref. #)</th>
<th>Ablation Technique and Energy Form</th>
<th>Indication</th>
<th>Comparators</th>
<th>Study Population and Size</th>
<th>Study Design</th>
<th>Analytic Horizon</th>
<th>Perspective</th>
<th>Data Sources for Effects</th>
<th>Data Sources for Costs</th>
<th>Discounting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheng, 2000173</td>
<td>RFA</td>
<td>Severely symptomatic SVT due to AVNRT (65%) or concealed bypass tract</td>
<td>1. long-term antiarrhythmic drug therapy (LTDT), 2. treatment of acute episodes of arrhythmia with antiarrhythmic drugs (EDT)</td>
<td>Model estimates were based on an unselected patient population referred for RFA at the Kaiser Permanente Medical Care Program of Northern California which cares for 2.9 million subscribers. Patients experienced an average of 4.6 unscheduled visits per year, had been symptomatic for a median of 3 years, were 70% women, physically active, with a mean age of 40 years. Patients with WPW syndrome were excluded.</td>
<td>Markov model using Decision Maker with cycle length of 1 month</td>
<td>Lifetime</td>
<td>Stated as societal, however, the analysis only included direct costs of care related to SVT, and lifetime medical expenditures unrelated to arrhythmia therapy.</td>
<td>Literature, efficacy from RCT’s and effectiveness from experienced centres; when literature was conflicting or inadequate, experts from the Cardiac Arrhythmia Patient Outcome Research Team Project and experts in electrophysiologic testing and RFA were consulted.</td>
<td>Direct costs of care related to SVT and lifetime medical expenditures unrelated to arrhythmia therapy based on a cohort of 60 patients seen at a major academic hospital between 1997 and 1998, as well as published data on costs. Professional fees were estimated using the 1998 National Physician Fee Schedule Relative Value File. Wholesale drug costs were estimated by using the Red Book, assuming that patients would be prescribed metoprolol. Lost time not accounted for explicitly.</td>
<td>Costs and health effects both discounted at 3%.</td>
</tr>
<tr>
<td>Calkins, 2000174</td>
<td>RFA with the Chilli Cooled Ablation System</td>
<td>Sustained VT in patients with an implantable cardioverter-defibrillator (ICD).</td>
<td>Medical therapy with amiodarone (400 mg daily) (MT).</td>
<td>Patients with sustained monomorphic VT with 2 or more episodes during 2 months prior to enrollment were included in the Chilli randomized trial (n=107). Patients had ICD and were candidates for RFA and amiodarone. Mean left ventricular ejection fraction was 31%, with ischemic heart disease in 82%. Simulated results treat severe patients with good ejection fraction who suffer their first VT episode assuming increased success rates, increased survival rates, decreased ablation complication rates, and increased utilities.</td>
<td>Markov model using DATA with 24 health states and cycle length of 1 month.</td>
<td>5 years</td>
<td>Societal, however, the analysis included only direct medical costs, and assumed indirect costs and intangible costs were implicitly incorporated in the utility values.</td>
<td>Effect (efficacy) data for model based on premarket approval RCT data for Chilli Cooled Ablation System. 5 year follow up data on amiodarone treatment from the literature, but follow up data on RFA was limited to 3 years.</td>
<td>Panel of 3 cardiac electrophysiologists enumerated medical resource utilization associated with treatments and their sequelae. A physician experienced in medical reimbursement assigned procedure and diagnosis codes to hospitalizations, physician office visits, laboratory tests and professional services. Cost estimates were from 1998 national Medicare reimbursement schedule, 1998 Clinical Laboratory Information Act Fee Schedule, and drug costs from the 1998 Drug Topics Red Book (less 20% of the average wholesale price).</td>
<td>Costs and health effects both discounted at 3%.</td>
</tr>
<tr>
<td>Hogenhuis, 1993175</td>
<td>RFA (if fails after two attempts, then may follow with observation, drug therapy, surgery)</td>
<td>WPW syndrome</td>
<td>1. observation alone, 2. observation until cardiac arrest and then initiate therapy, 3. noninvasively guided drug therapy (DT), 4. surgical ablation (ST)</td>
<td>Adults with WPW syndrome. Subgroup analysis for: 1. cardiac arrest survivors, 2. history of PSVT/AF associated with hemodynamic compromise, 3. history of PSVT/AF without hemodynamic compromise, 4. asymptomatic patients with delta wave on ECG. Each subgroup was analysed for three age groups (20, 40 and 60 years).</td>
<td>Markov model using Decision Maker with cycle length of 1 year.</td>
<td>Lifetime</td>
<td>--</td>
<td>Literature for data on natural history of WPW syndrome and incidence of symptomatic events. Where data were not available, a modified nominal group process with a panel of four electrophysiologists was used to reach a consensus estimate.</td>
<td>Variable costs were from the Clinical Cost Manager cost-accounting system (Transition Systems Inc.) for 13 consecutive patients who underwent RFA between 1991 and 1992 at New England Medical Center. Cost of physician services were estimated by multiplying physician charges by the mean reimbursement to charge ratio for the cardiology practice (0.7). For drug therapy, annual average costs included cost of prescriptions, physicians visits, and routine laboratory studies.</td>
<td>Costs and health effects both discounted at 5%.</td>
</tr>
</tbody>
</table>
Table 11: cont’d

| HRQL | Patient based TTO utilities before and after RFA from Larson et al. (55) based on 161 patients receiving drug therapy before ablation (median utility = 0.833) and after ablation (median utility = 0.983). For episodic drug therapy, utility was decreased by 0.25 quality adjusted life days for each event in excess of those experienced by patients receiving long-term drug therapy. | SF-36 quality of life scores from patients at 6 months after therapy in the Chilli trial for catheter ablation success and drug therapy success. SF-36 scores were transformed to utilities based on equations from Shmueli (192). Estimates for all other health states were from the clinical panel of experts using trial data as the reference point. Assumed indirect costs of lost productivity and intangible costs of pain and suffering related to VT morbidity were implicitly incorporated in the utility values. | Quality of life utilities were assigned by the authors for each health state in the model. |
| Base Case ICER Results | RFA vs. EDT = -$81,640, -8.8 days, 3.75 QALY; LTDT vs. EDT = -$53,700, 0 days, 0.38 QALY; RFA vs. LTDT = -$27,900, -8.8 days, 3.10 QALY. LTDT more effective and lower costs than EDT. RFA dominated both drug therapy options. | RFA vs. MT = $2,720, 0.13 QALY = $20,923 per QALY. For survivors of cardiac arrest, RFA dominates both DT and ST for all age groups. For patients with history of PSVT and hemodynamic complications, surgical ablation after RFA failure ranges from $770 (20 years) to $2800 (40 years) per QALY, and drug therapy after RFA failure ranges from $60,000 (20 years) to $8,400 (60 years). For patients with history of PSVT and no hemodynamic complications, RFA ranges from $6,600 (20 years) to $19,000 (60 years) per QALY, and drug therapy after RFA failure ranges from $55,000 (20 years) to $74,000 (60 years) per QALY. For asymptomatic patients, RFA ranges from $33,000 (20 years) to $52,000 per QALY, and for drug therapy after RFA failure from $174,000 (20 years) to $540,000 (60 years) per QALY. CUA of RFA generally very favourable, but varies with clinical category and age. Does not support RFA in asymptomatic patients (not cost-effective). |
| Sensitivity Analyses | One way for frequency of unscheduled visits, cost of drug therapy, change in utilities, rate of post-procedure atioventricular node block, RFA complications, RFA death, arrhythmia recurrence, efficacy of drug therapy. Selected two- and three-way sensitivity analyses, five-way sensitivity analyses and n-way (Monte Carlo) probabilistic sensitivity analysis for all variables. This showed that RFA dominated LTDT in 93.7% of simulations, and more effective yet more costly in an additional 2.2% of simulations. LTDT was dominant compared to EDT in 99.8% of simulations. | One way and multi way sensitivity analysis on assumptions about the initial success, 5-year treatment success, cost of both therapies, risk and timing of adverse events, survival rates, daily dose of amiodarone, utilities for health states, crossover to ablation on amiodarone failure or severe adverse event, population disease severity, discount rate, and analytic time horizon. Results were most sensitive to assumptions about the cost of RFA, survival rate of catheter ablation patients, and time horizon. Sensitivity analysis of the cost-effectiveness in a population with less severe disease estimated $6,028 per QALY. | One way sensitivity analyses indicated that the model was sensitive to two parameters: the cost of RFA and 2) the overall annual incidence of PSVT/AF in asymptomatic patients. |
| Conclusions | RFA improves QOL and reduces costs in treating highly symptomatic patients. | RFA of VT is a cost-effective alternative to amiodarone patients with frequent VT episodes. | The model supports initial RFA in patients with WPW syndrome who survive a cardiac arrest or experience hemodynamic compromise during an episode of PSVT/AF. RFA is comparable in cost-effectiveness to many commonly used therapies for patients with PSVT/AF who have not yet experienced hemodynamic compromise. RFA is expensive in asymptomatic patients and the model supports observing these patients. |

GCA = general CA, CA = catheter ablation, APA = accessory pathway ablation; SAVNPA = slow AV node pathway ablation, AVNA = AV node ablation, PVA = pulmonary vein ablation, HISCA = HIS-bundle CA, AVNM = AV node modification; RFA = Radiofrequency catheter ablation, SVT = supraventricular tachycardia, PSVT = paroxysmal SVT, VT = ventricular tachycardia, AF = atrial fibrillation, AVNRT = AV node re-entrant tachycardia, AT = atrial tachycardia and flutter, PS = pre-excitation syndromes, Wolf-Parkinson-White (WPW) syndrome; RCT = randomized controlled trial.
Table 12: Cost studies of catheter ablation

<table>
<thead>
<tr>
<th>Ablation Technique and Energy Form</th>
<th>Mitchell, 2001&lt;sup&gt;186&lt;/sup&gt;</th>
<th>Fragakis, 2001&lt;sup&gt;187&lt;/sup&gt;</th>
<th>Knight, 1997&lt;sup&gt;176&lt;/sup&gt;</th>
<th>Weerasooriya, 1996&lt;sup&gt;177&lt;/sup&gt;</th>
<th>Ikeda, 1994&lt;sup&gt;182&lt;/sup&gt;</th>
<th>Weerasooriya, 1994&lt;sup&gt;183&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modification of AV node (AVNM) vs. ablation of AV node (AVNA) and pacemaker implant</td>
<td>RFA APA</td>
<td>RFA</td>
<td>Transcatheter RFA of accessory pathway (APA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug-refractory patients with chronic AF and an uncontrolled ventricular rate</td>
<td>SVT related to an accessory AV pathway or dual AV nodal pathways.</td>
<td>PSVT (WPW syndrome and AVNRT)</td>
<td>Symptomatic SVT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSVT (WPW syndrome and AVNRT)</td>
<td>Symptomatic SVT</td>
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<td></td>
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<tr>
<td>Symptomatic SVT</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Indication</td>
<td>Various cardiac arrhythmias</td>
<td>Clinically documented classical anti-clockwise or clockwise rotation atrial flutter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study Population and Size</td>
<td>Consecutive patients referred for RFA of atrial flutter over a period of 16 months. 24 were studied using a decapolar electrode (12 men, mean age 50 years). 12 had a Halo catheter (7 men, mean age 40 years). One patient in the Halo group did not proceed.</td>
<td>Adults, 60 men (mean age 58.4) and 80 women (mean age 58.6) undergoing diagnostic and therapeutic electrophysiology at Eastbourne District General hospital from Jan 1, 1997 to July 1, 2000. 34 procedures were APA, 42 AVNM, 70 total AV node ablation, 3 flutter ablation, 5 atrial tachycardia, 1 VT.</td>
<td>Adults (mean age 66 years) with successful modification of AV node (n=10), or successful ablation of AV node (n=14) selected from a pool of patients who underwent modification (n=82) and ablation (n=109) between March 1993 and June 1996 at the University of Michigan. Inclusion criteria: chronic AF, a successful long-term outcome, and availability of complete billing records. Exclude previous permanent pacemaker, hospitalization immediately before or after for reason other than procedure, prosthetic heart valve requiring hospitalization.</td>
<td>Consecutive adult patients (mean age 44 years) with PSVT refractory to antiarrhythmic drug therapy (WPW syndrome n=15 and AVNRT n=5) having successful RFA between July and December 1992 at Ohashi Hospital of Toho University in Japan.</td>
<td>Adults (all &gt; 20 years) at Royal Perth Hospital, Australia. For RF APA, consecutive patients between May 19 and Oct 19, 1992 (n=20, mean age 34 years). For surgical division, most recent patients between Aug 10, 1986 and Mar 27, 1991 (n=20, mean age 37 years). For long term antiarrhythmic medication, all patients between Jan 1, 1985 and Jul 1, 1992 (n=12, mean age 47 years).</td>
<td></td>
</tr>
<tr>
<td>Comparators</td>
<td>None</td>
<td>Decapolar electrode in infero-lateral wall of right atrium vs 'Halo' catheter.</td>
<td>Compare modification of AV node (AVNM) vs. ablation of AV node (AVNA) and pacemaker implant</td>
<td>Compare costs for day stay vs. inpatient ablation therapy</td>
<td>Compare RFA vs. continuing pharmacologic treatment</td>
<td>Compare RFA vs. surgical division vs. long term antiarrhythmic medication.</td>
</tr>
<tr>
<td>Study Design</td>
<td>Prospective data collection in computer database</td>
<td>Retrospective review of billing records combined with modelling to estimate charges during follow-up on AV modification (n=62) over 30 months for long term estimates of additional procedures, and on AV ablation repeats over 3 months (n=109), assuming a standardised follow-up schedule</td>
<td>Retrospective review of charts for inpatient.</td>
<td>Retrospective review of medical charges from hospital bills (less health insurance payments) compared with outpatient charges for the year before ablation (historical controls)</td>
<td>Retrospective review of medical records, theatre and catheter lab records</td>
<td>Retrospective review of medical charges from hospital bills (less health insurance payments) compared with outpatient charges for the year before ablation (historical controls).</td>
</tr>
<tr>
<td><strong>Analytic Horizon</strong></td>
<td>Mitchell, 2001(^{186})</td>
<td>Fragakis, 2001(^{187})</td>
<td>Knight, 1997(^{176})</td>
<td>Weerasooriya, 1996(^{177})</td>
<td>Ikeda, 1994(^{182})</td>
<td>Weerasooriya, 1994(^{183})</td>
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<td>Date of preadmission visit to date of discharge.</td>
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<td><strong>Perspective</strong></td>
<td>Hospital care provider</td>
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<td>Health care provider</td>
<td>Health care provider (government)</td>
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<td><strong>Data Sources for Effects</strong></td>
<td>Hospital database for procedure indication, arrhythmia type, findings, duration, success rate and complications.</td>
<td>Based on follow up data over 30 months (n=62) for AV modification, it was assumed that 31% of patients would undergo pacemaker implantation within 3 months of the procedure. Based on the results of ablation of AV node in 109 consecutive patients, it was assumed that the initial success rate was 100% and 2% of patients would require a second ablation procedure.</td>
<td>Success rates based on ECG next day or immediately afterwards.</td>
<td>Source is not clear.</td>
<td>Review of medical records for success of procedure determined at follow-up at least two months post ablation or surgery. Questionnaires were administered to medically treated patients to determine tachycardia incidence, re-hospitalisations, dosage of medication and frequency of physician visits.</td>
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<tr>
<td><strong>Data Sources for Costs</strong></td>
<td>Hospital database for procedure costs, equipment used, fluoroscopy items, and personnel involved. Capital investment for equipment, additional cardiac technician time, and management system service costs.</td>
<td>Price of equipment and expected costs in an electrophysiology centre.</td>
<td>Initial charges were determined for each patient by review of the computerised billing system of the Patient Accounts Department and included professional fees, laboratory fees, and hospital fees. Follow up charges assumed a standardised follow-up schedule for both groups of patients.</td>
<td>Major resources were identified and counted by direct observation (preadmission costs, procedural costs, ward costs, investigation costs). The total cost was derived by multiplying the cost of each item by the number of items used. A mixture of costs and charges were used - public hospital fees for preadmission clinic cost, clinical costing estimates, procedural and ward costs, and Medicare charges for investigations. Only direct medical costs were included - overhead costs (depreciation, catheter lab cleaning, waste disposal, sterilisation).</td>
<td>Direct medical charges for ablation from the bills less health insurance payments sent to patients by the hospital. Charges for ablation included radical cure (electrophysiologic study, ablation), examination (ECG, ECC, chest x-ray, blood tests) and hospital charges (room, board, nursing and drugs). No professional fees were charged. Charges for drug therapy were based on the charges as outpatients during the year before ablation, and estimated for the patient's lifetime.</td>
<td>Medical records for duration of hospitalisation(s), laboratory investigations, number of procedures, and complications. Theatre and catheter lab records for procedure durations. Where follow-up and treatment of complication were required, costs were included in the overall patient cost. Direct medical costs were estimated according to actual resources utilised (multiplied by unit costs from fees, costs, and Medicare fees) and did not include overhead costs (depreciation, catheter lab cleaning, waste disposal, sterilisation). Cost for surgical and medical treatment were also estimated using a DRG based costing model.</td>
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<td><strong>Discounting</strong></td>
<td>No</td>
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<td>5%</td>
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Success rates in RF APA were 90%, surgical 100%, and medical 83% (measured as symptom free). Total costs for RF APA = AUS $2,746 +/- 800, surgery $12,141 +/- 4465, and medical $1,713 +/- 748. Projected costs for 20 years (discounted) for RF APA $2,911, surgery $17,467, and medical $4,959.

All patients had a successful outcome and none required additional antiarrhythmic therapy.

Day stay and inpatient RFA successful in 96% and 84% respectively. 96% asymptomatic during 6 months follow up for day stay, and 84% asymptomatic during 17 months follow up for inpatient. Mean cost per patient $1,876 +/- $595 AUS$ and $2,354 +/- $642 respectively (p<0.01).

Total nominal charges (per patient) for first year $14,369 +/- 2002 for modification vs. $28,935 +/- 2023 for ablation. Adjusted (for additional procedures) charges in first years were $20,453 +/- 2002 vs. $29,118 +/- 2023 respectively. Cumulative adjusted charges over 10 years follow up were $27,331 +/- 2002 and $47,347 +/- 2023 respectively.

Success rates in the group with decapolar electrode was 22/24 (92%) compared to 9/11 (82%) in the Halo catheter group. Current price for decapolar catheter is Pounds 358 (US$572) and Pounds 1,507 (US$2,411) for a Halo catheter. Assuming that 30% of the cases are atrial flutter, the cost saving for the decapolar catheter over the Halo catheter was about US$ 25,000 per year for a low-volume centre, US$110,000 per year for a medium volume centre, and US$ 160,000 for a high volume centre.

Conclusions

RFA can be performed safely, effectively and cheaply in a district general hospital setting with a satisfactory success rate and a low complication rate. The present study suggests that use of a single decapolar catheter electrode for atrial flutter can have a significant impact on the cost of the procedure. These data indicate a substantial cost saving by using a decapolar catheter, depending on the volume of flutter ablation procedures performed in a centre.

Initial charges for AVNM are significantly lower than for AVNA in patients with chronic atrial fibrillation. Even when adjusted for higher failure and recurrence rates, the modification procedure retains a major cost advantage over ablation during long-term follow-up.

RFA of PSVT is of clinical benefit and dramatically reduces the medical costs of definitive therapy. RFA would appear to be more economical than pharmacologic treatment.

RFA of slow AV nodal pathway.

RFA of accessory AV connections on an outpatient basis or limited overnight hospital stay in low risk patients.

Comparators

RFA of accessory AV connections on an outpatient basis or limited overnight hospital stay in low risk patients.

Study Population and Size

Adults (n=95) (mean age 36 years) with 100 outpatient procedures between Sept 1, 1991 and April 20, 1992 at University of Michigan, USA. The costing study.

Adults (n=139) (mean age 45 years) between Aug 20, 1991 and Dec 2, 1992 at University of Michigan, USA. The costing study.

Adults (n=30) (age 16-68 years) who had RFA between Jan and Sept 1992 at Austin Hospital, Melbourne, Australia. 26

Adults (n=15) (mean age 50 years) with successful CA between Jan and July 1990 at University of Michigan Medical Centre, USA.

Adults (n=50) (mean age 40 years and for surgery 30 years) as consecutive patients for RF APA (n=25) in 1990 and

Adults (n=22) (RF APA mean age 34 years and for surgery 31 years) as consecutive patients with WPWS for RF APA (n=11)
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<td>USA. Patients excluded if already inpatients, &lt; 13 or &gt; 70 years old, morbidly obese, anterosetal accessory AV connection, had complications, required transseptal approach, or required observation or treatment for other medical conditions. The costing study included a subset of 30 consecutive patients who underwent RFA between Jan 1, 1992 and March 1, 1992.</td>
<td>Included 40 consecutive patients selected from the study sample.</td>
<td>patients responded to the questionnaire, for whom results are reported.</td>
<td>Patients were selected if they had successful outcome of ablation after unsuccessful pharmacologic therapy and were available for questioning by phone.</td>
<td>consecutive patients for surgical ablation (n=25) in 1989 at the University of Michigan Medical Centre, USA, and surgical ablation (n=11) between 1984 and 1988 at the University of Michigan Medical Centre, USA.</td>
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<td>Study Design</td>
<td>Prospective study and follow up with retrospective review of patients' billing records for costing.</td>
<td>Prospective study and follow up with retrospective review of patients' billing records for costing.</td>
<td>Retrospective review of hospital billing records to determine hospital and physician charges related to ablation. Patients were contacted by phone to determine symptoms, medications, presence of structural heart disease, use of health care prior to ablation, and number of days missed from work.</td>
<td>Retrospective review of patient clinical record to determine number, duration and dates of hospital admissions, and the number and dates of office visits related directly to ablation procedure.</td>
<td>Retrospective review of patient records to extract age, sex, location of accessory pathway, duration of hospital admission after ablation, and associated complications. Review of hospital billing records for charges and independent physician associate groups for physician fees.</td>
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<tr>
<td>Analytic Horizon</td>
<td>Immediate postprocedure recovery, short term follow up mean of 17 +/- 7 days after RFA procedure. Charges for costing included physicians' fees and hospital charges.</td>
<td>Immediate postprocedure recovery, short term follow up 2-4 weeks after RFA procedure. Charges for costing included physicians' fees and hospital charges.</td>
<td>Short term hospital costs for procedure related costs, and projection for 20 years for continued medical therapy costs.</td>
<td>Short term for CA hospital stay and procedures; long term projections for medical from phone interview and surgical from literature</td>
<td>Short term for procedure, including 1 month follow-up (office visit and EPS for ablation and chest x-ray at office visit for surgery).</td>
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<td>Perspective</td>
<td>Health care provider</td>
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<td>Data Sources for Effects</td>
<td>Prospective case series follow up study.</td>
<td>Prospective case series follow up study.</td>
<td>Hospital records and replies to a questionnaire.</td>
<td>Hospital records and responses to telephone interview.</td>
<td>Patient case records for success, hospitalization, and complications.</td>
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<tr>
<td>Data Sources for Costs</td>
<td>Review of patients' billing records for physicians' fees and hospital charges.</td>
<td>Review of patients' billing records for physicians' fees and hospital charges. Hospital charges included room and board, EPS lab, recovery room and lab tests. Professional charges included physician fees for RFA and patient care.</td>
<td>Direct medical charges for hospital costs and Schedule of Medical Benefits for physician fees. Professional fees incurred by all patients were averaged to yield a mean per patient value.</td>
<td>For ablation, hospital billing records were reviewed to determine hospital and professional charges during hospital admission in which the EPS was performed. All charges related to management of patient's AVNRT were included (all ECG studies, blood tests, chest x-ray, echocardiograms, medications, and EPS studies). For prior medical</td>
<td>Direct medical costs were estimated from billed charges, including hospital and physician charges. Hospital costs included charges for room and board, operating room or EPS lab charges, and charges for nursing and ancillary care, drugs, blood tests, x-rays, electrocardiograms and echocardiograms. Physician charges for hospital</td>
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<tr>
<td>Data Sources for Costs</td>
<td>Direct medical charges were estimated from billed charges for ablation and hospitalization. Hospital bill included charges for room and board, use of operation room and EPS lab, x-rays and blood tests. Physician fees were provided by the independent physician associate groups. The cost estimate for RF APA was adjusted for unsuccessful RFA that required additional surgery.</td>
<td>Direct medical charges were estimated from billed charges for ablation and hospitalization. Hospital bill included charges for room and board, use of operation room and EPS lab, x-rays and blood tests. Physician fees were provided by the independent physician associate groups. The cost estimate for RF APA was adjusted for unsuccessful RFA that required additional surgery.</td>
<td>Direct medical costs were estimated from billed charges, including hospital and physician charges. Hospital costs included charges for room and board, operating room or EPS lab charges, and charges for nursing and ancillary care, drugs, blood tests, x-rays, electrocardiograms and echocardiograms. Physician charges for hospital</td>
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Table 12: cont’d

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<td>expenses, direct medical charges for office visits, emergency room, and hospital admissions were based on billing fees. Medication charges were determined from the outpatient pharmacy based on a 1-month refill schedule. admissions and office visits were obtained from physician-associates groups. Charges were converted to costs using cost to charge ratio for RF APA of 0.56 and surgery of 0.81.</td>
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<td>Discounting</td>
<td>No.</td>
<td>No.</td>
<td>Projection over 20 years assumed an annual inflation factor of 5%.</td>
<td>No.</td>
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<td>Results</td>
<td>Accessory pathway conduction was no longer present by the end of the ablation procedure in 97 of 100 cases. At follow up (mean 17 days after procedure), 9 patients had recurrence of accessory pathway conduction or symptoms or PSVT. Mean total charges (n=30) were US$10,183 +/- 1,082. Outpatients only (n=22) had total charges of $9,873 +/- 932, and those with an overnight stay (n=8) had total charges of $11,034 +/- 1,056.</td>
<td>Of 139 patient who underwent RFA of slow AV nodal pathway, 120 qualified for early discharge with successful ablation in 119. 119 patients had no recurrence of symptomatic tachycardia during 7 +/- 3 months of follow-up. Mean total charges (n=40) were US$10,547 +/- 1,082. Outpatient only (n=27) had total charges of $10,192 +/- 846 and those with overnight stay (n=13) had total charges of $11,240 +/- 763.</td>
<td>RFA was successful in 89% of patients with recurrence of tachycardia in 1 patient. Permanent cure (at 9 months follow-up) was achieved in 85% of patients. Mean total charges per patient for RFA were AUS $4,067. For continued medical therapy, charges were $700/ year. When projected for 20 years, then medical is 4-5x cost of RFA.</td>
<td>Mean total charges for cure of AVNRT with ablation were US$15,893 +/- $3,338. At a mean of 15 months after ablation, no patient had a recurrence of symptomatic tachycardia or required antiarrhythmic drug therapy, office visits, emergency room visits, or hospital admission for PSVT. Prior to the ablation procedure a mean of 13 +/- 26 days of work were missed. After ablation, 0 days of work were missed. Total costs of medical before ablation were $7,651 +/- $9,496. If only one emergency visit was required per year, then medical costs were $1,501. In patients who respond well to pharmacologic therapy, charges would exceed charges for ablation after approximately 15-60 years, depending on the type of medication used. In patients who do not respond well to pharmacologic therapy and assume only 1 emergency visit/year is required, then medical charges exceed ablation charges after 10 years.</td>
<td>RF APA successful in 88% during single hospital admission and 8% during 2 hospital admissions. Surgery successful in 96% and 84% had a single hospital admission. The mean time lost from work for RF APA was 11 +/- 19 days and for surgery 55 +/- 26 days (p&lt;.0001). The mean total cost of definitive therapy with RF APA was US$14,919 +/- $6,740 compared to $53,265 +/- 12,755 for surgery (p&lt;.0001). Based on a subset of uncomplicated patients (n=10 in each group) the total cost for RF APA was $11,012 +/- $2,886 compared with $47,726 +/- $3,817 for surgery (p&lt;.0001).</td>
<td>RF APA success rate was 73%. Mean time lost from work was based on average annual per capita income in US of $15,495. The time lost for RF APA was 10 +/- 5 days and for surgery 60 +/- 16 days. The estimated cost of lost time from work for RF APA was $424 and for surgery was $2,547. The direct cost of RF APA was US$14,116 +/- 4,493 and surgery $34,175 +/- 5,434 (p&lt;.0001). The adjusted cost (for unsuccessful RF APA) was $24,382 +/- 4,741.</td>
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<tr>
<td><strong>Conclusions</strong></td>
<td>In properly selected patients, outpatient management for RFA of accessory AV connections, is both safe and feasible and results in significant cost savings.</td>
<td>Substantial cost savings can be achieved when RFA of slow pathway is performed on an outpatient basis and safety is not compromise when early discharge is limited to patients who are appropriate candidates for outpatient therapy.</td>
<td>In the long term, RFA is more cost effective than continued medical therapy in patients with SVT.</td>
<td>RF AVN is not only of clinical benefit, but also results in a dramatic long-term reduction in medical expenses.</td>
<td>RF APA results in dramatic reduction in cost of definitive therapy compared to surgical ablation in patients with SVT (WPWS).</td>
<td>For patients with posteroseptal accessory pathway who require definitive therapy, it is cost effective to offer RF APA as the initial therapy of choice.</td>
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GCA=General CA, CA=Catheter ablation, APA=Accessory pathway ablation, SAVNPA=Slow AV node pathway ablation, AVNA=AV node ablation, PVA=Pulmonary vein ablation, HISCA=HIS-bundle CA, AVNM=AV node modification, AVJRT=atrioventricular junctional re-entry tachycardia, RFA=radiofrequency catheter ablation, SVT=supraventricular tachycardia, PSVT=paroxysmal SVT, VT=ventricular tachycardia, AF=Atrial fibrillation, AVNRT=AV node re-entrant tachycardia, ATR= atrial tachycardia and flutter, PS=pre-excitation syndromes, Wolff-Parkinson-White (WPW) syndrome; RCT=randomized controlled trial, EPS=electrophysiologic studies
<table>
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<th>Table 13: QOL studies of catheter ablation</th>
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<tr>
<td><strong>Author, Year (ref. #)</strong></td>
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<tr>
<td>Levy, 2001**</td>
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<td>Gerstenfeld, 2001**</td>
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<td>Fitzpatrick, 1996**</td>
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<td>Sareewiwatthana, 1999**</td>
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<td>Bathina, 1998**</td>
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<td>Larson, 1999**</td>
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*Note: RCT = Randomized Controlled Trial*
Table 13: cont’d

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HRQOL Instrument

**Modified Karolinska Questionnaire (KQ)** that is cardiac specific and validated for pacemaker patients. Nottingham Health Profile (NHP) for general quality of life validated for cardiac patients. Both questionnaires were administered at baseline, 1, 3, 6 and 12 months post ablation.

A validated quality of life questionnaire (based on the Medical Outcomes Study SF-36 and developed specifically for patients with supraventricular arrhythmias). Questions were combined to form six QOL measures (current health, physical function, energy, health distress, mental health, disease impact), four symptom scores and the number of work days missed due to AF. The questionnaire was distributed to all patients 1 month before and 3 to 6 months after the procedure.

A customised questionnaire using Zhao conceptual framework and SF-36 that had 45 items with 4 dimensions 1) life satisfaction, 2) self concept and psychosocial well being, 3) health and function and physical well being, 4) socio-economic and social well being.

**Medical Outcomes Study Short Form Health Survey (SF-36)** was used to measure quality of life. This validated instrument includes 6 concepts: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health.

Two rating systems were used. A linear rating scale from 0 (worst health) to 100 (excellent health) was used to assess current health and pre-RFA health. The time-tradeoff method was used to assess the amount of a projected 30-year life expectancy that patients would be willing to give up to achieve excellent health.

Results

Significant improvement in total KA for both Med group and HBA group, with a mean reduction in scores of about 50%. No significant difference in baseline or follow up results between Med and HBA groups.

Significant improvement in total NHP (Part 1) score at all follow ups, with a mean reduction of 40% for Med and 20% for HBA. No significant differences in baseline or follow up results between Med and HBA.

No significant change from baseline for NHP (Part 2) in either group at any time or any differences between groups.

The initial QOL questionnaire was completed by 55 (77%) of 71 patients and the follow-up questionnaire by 41 (75%) of 55 patients. Of the 41 patients who completed both initial and follow up questionnaire by 41 (27%) of 41 did not undergo an attempt at ablation, 18 (44%) of 41 underwent RFA with AF recurrence after ablation, and 12 (29%) of 41 underwent ablation and were in persistent sinus rhythm without antiarrhythmic drugs at the time of last follow up.

Comparing the differences between preablation and postablation scores among the three groups, patients with successful maintenance of sinus rhythm at follow-up reported significantly greater improvement in QOL score before treatment increased from 1.9 +/- 1.2 to 3.6 +/- 1.1 (p<.001) (3=good). Patients also reported an improvement in quality of life as 3.5 +/- 0.9 (unchanged), 1.5 (p<.001). Patients' activities of daily living became easier with pooled score rising from 2 +/- 0.4 to 2.4 +/- 0.3 (p<.01). Hospital admissions decreased (2.8 +/- 6.8 to 0.17 +/- 0.54, p<.03), emergency room visits decreased (3.1 +/- 8 to 0.2 +/- 0.62), physician visits decreased (10 +/- 13 to 5.08 +/- 7 visits per year, p<.03) and antiarrhythmic drug trials decreased (6.2 +/- 4 to 0.46 +/- 1.5, p<.001).

HRQOL scored increased after RFA. Overall QOL score improved from 132 to 180 (p<.000), life satisfaction increased from 29.0 to 44.6 (p<.000), self-concept and psychological well being increased from 27.1 to 40.5, health functioning increased from 41.7 to 56.1, and socio-economic and social well being increased from 33.7 to 37.9 (p<.000). Origin of clinical arrhythmias had impact on QOL.

RFA primary success rate was 100%. Both medical therapy and ablation were associated with improvements in SF-36 scores. Ablation therapy resulted in significant improvements in all QOL categories. A statistically significant difference in QOL favours ablation was found for bodily pain, general health, vitality, and role emotional categories; no QOL categories favoured medical therapy. Average cumulative cost for procedures, hospital, complications, and 1 follow up visit was $7722 +/- 1019 for ablation. The yearly cost for medical therapy was $3422 (atenolol) and $548 (verapamil). During the follow-up period, the cost of emergency room visits for medical therapy.
Table 13: cont’d

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<td>improvement than patients with recurrences after ablation for 2 of 6 QOL measures (current health, p&lt;0.05, and health distress, p&lt;0.01), as well as an incremental improvement in the number of days activities cut down (p&lt;0.05). There were trends toward additional improvement for all other QOL measures in patients with successful maintenance of sinus rhythm at long-term follow-up.</td>
<td>p&lt;.0001. Significant events were documented in 19 patients before treatment and in 8 afterwards.</td>
<td>group was $1,039 +/- 680 per visit, so that cost of medical therapy would exceed RFA in 9-12 years.</td>
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Conclusions

In patients with permanent AF with mixed ventricular response rate, quality of life improved significantly with either MED or HBA treatment. However, there was a tendency for greater improvement in the medical group for individual subgroup symptoms. Neither technique shows any significant advantage over the other, with equal improvement in rate control. However, we would recommend medical treatment first with a VVIR pacemaker as it avoids initial irreversible ablation.

Patients undergoing successful ablation with persistence of sinus rhythm at last follow-up reported a dramatic improvement in QOL and reduction in all symptoms associated with AF. The patient who underwent ablation but had recurrent AF at the time of follow-up also reported significant (but smaller) improvements in symptoms and QOL after ablation. Patients who underwent the same extensive mapping but in whom no ablation was performed had no significant improvement in QOL or symptoms.

There are statistically significant positive outcomes in terms of improved QOL symptoms, performance of daily activities, and consumption of health care resources for RF catheter AVJ ablation and permanent pacing for established or paroxysmal AF.

Patients with arrhythmias perceived negative impact of their condition on the quality of their lives. 80% of patients with SVT reported improvements in HRQOL after RFA.

Although both medical therapy and RFA were associated with improved QOL, the benefits of medical therapy were limited to improvements in physical functioning, social functioning, and mental health. RFA resulted in higher QOL in all health concepts. In patients with symptoms that can be controlled with medications, the initial large cost of ablation therapy is equalled by the cumulative cost of medical therapy after about 9-12 years. The cost data in this study would suggest that ablation therapy may be most appropriate in young patients who would be subject to life-long medical therapy.

RFA for patients with highly symptomatic AVNRT leads to a substantial improvement in QOL, utility, and health care resource utilisation.

AVJ = Atrioventricular junction, Wolff-Parkinson-White (WPS) syndrome, AVRT=atrioventricular reentrant tachycardia, AVNRT=atrioventricular nodal reentrant tachycardia concealed bypass tract, AF=atrial fibrillation, AT=atrial tachycardia, SAVNPA=slow AV node ablation, RCT=Randomized controlled trial, AF=atrial fibrillation, VT=ventricular tachycardia