



**Title: Outpatient Pulmonary Vein Ablation for Atrial Fibrillation: Clinical and Cost-Effectiveness Review**

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**Context and policy issues:**

A type of supraventricular arrhythmia in the upper chambers of the heart, known as atrial fibrillation (AF), affects approximately 200,000 to 250,000 Canadians.<sup>1</sup> Accounting for 15% of all strokes, AF is commonly associated with aging, thromboembolism, hypertension, heart failure, and valve disease.<sup>1</sup> The clinical impact of AF is underestimated as it is often asymptomatic until a stroke or heart failure occurs.

Management of AF involves medication, brief electrical shock or cardioversion, and surgical or catheter-based therapies.<sup>1,2</sup> When antiarrhythmic drugs are ineffective and normal rhythm can not be restored by cardioversion, pulmonary vein ablation (PVA), also known as atrial fibrillation ablation or pulmonary vein isolation, may be used to destroy cells near the pulmonary veins where AF originates.<sup>3</sup> Most AF ablations consist of isolating abnormal electrical pathways from the pulmonary veins and destroying them using radiofrequency energy.<sup>3</sup>

Since its introduction in 1990, catheter ablation has almost replaced surgical intervention with the numbers of procedures increasing from 500 in 1991 to greater than 15,000 in 1993.<sup>4</sup> Over the last seven years, PVA has evolved and the patient population has expanded.<sup>5</sup> Patients undergoing PVA in 2005 were older, with larger atrial size, more persistent or permanent AF, and had taken fewer antiarrhythmics than those who underwent the procedure in 1999.<sup>5</sup> In 2001, the Ontario Consensus Panel on Arrhythmia Management concluded that radiofrequency ablation is likely to be an economically attractive intervention when performed in high-volume centres with low complication rates.<sup>6</sup> However, at that time, the panel concluded there was insufficient Canadian data on which to base health policy and there were inherent limitations in existing non-Canadian data.<sup>6</sup>

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Outpatient cardiac catheterizations and diagnostic procedures have been shown to be safe and cost effective compared to inpatient procedures.<sup>7</sup> Similarly, while PVA is effective and improves quality of life when performed during surgery, evidence is sought to support the use of PVA in the outpatient setting.

## Research questions:

1. What is the clinical effectiveness of outpatient PVA for adults with AF?
2. What impact does outpatient PVA have on quality of life (QoL) for adults with AF?
3. What complications are associated with outpatient PVA for adults with AF?
4. What is the cost-effectiveness of outpatient PVA for adults with AF?
5. What are the guidelines for outpatient PVA for adults with AF?

## Methods:

A limited literature search was conducted on key health technology assessment resources, including PubMed, the Cochrane Library (Issue 4, 2007), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 1993 and the present, and are limited to English language publications. No filters were applied to limit the retrieval by study type.

## Summary of findings:

The literature search yielded two observational studies on clinical effectiveness,<sup>8,9</sup> three observational studies on cost-effectiveness,<sup>10-12</sup> and one observational study on adverse events.<sup>13</sup> Studies were prospective or retrospective in design, conducted between 1991 and 2007, with follow-up ranging from six to 22 months. Outcomes include successful ablation, same day discharge and costs. Study details are provided in appendix A.

## Health technology assessments, systematic reviews, meta-analyses, guidelines

No health technology assessment reports, systematic reviews, meta-analyses, or guidelines were identified that specifically addressed outpatient PVA.

## Randomized controlled trials

No randomized controlled trials involving outpatient PVA were identified.

## Observational studies

### *Clinical effectiveness*

A prospective study of the first 50 patients admitted to the Royal Perth Hospital in Australia reported the safety and efficacy of day stay transcatheter radiofrequency ablation in patients treated for supraventricular tachyarrhythmias.<sup>8</sup> Nineteen males and 31 females, with a mean age of 42±14 years, underwent outpatient transcatheter radiofrequency ablation for supraventricular tachyarrhythmias due to aberrant atrioventricular pathways. The number of patients with atrial fibrillation was not specified, nor was the recruitment period. Patients were followed-up for a mean of 6.2±3.1 months. Accessory pathways were successfully ablated in

30 of 32 patients; dual atrioventricular nodal pathways were successfully ablated in 18, and slow pathways were successfully ablated in 17. Of the 38 patients discharged on the same day, 24 were treated for accessory pathways and 14 were treated for dual atrioventricular nodal pathways. Eight patients were admitted overnight because of a long and difficult procedure (four), need for intravenous anticoagulation (one), and complications detected during the procedure (cardiac perforation during mapping in one patient, and retrograde dissection of the femoral artery in another). No readmissions or complications were observed in patients discharged on the same day. The authors concluded that day stay transcatheter ablation for supraventricular tachyarrhythmia can be planned without prior diagnosis of physiological cause.<sup>8</sup> Day stay catheter ablation affords the use of day ward beds that can be reliably booked in advance, avoiding the need for coronary care unit beds typically allocated to life-threatening cardiac conditions.<sup>8</sup>

The safety and efficacy of outpatient radiofrequency ablation was evaluated in a retrospective analysis of 60 consecutive patients admitted to the New York Medical Center between 1994 and 1997.<sup>9</sup> Forty-three males and 17 females, with a mean age of  $38 \pm 15$  years, underwent outpatient transseptal radiofrequency ablation of left sided accessory pathways with a mean follow-up of 22 months. Fifty patients (83%) had supraventricular tachycardia, 7 (11%) had AF, and 3 (6%) had complex tachycardia. Following diazepam sedation, a mean of 3.5 radiofrequency applications were given per case and procedure time ranged from 1.25 to 3.5 hours. Post-procedure subcutaneous heparin precluded the need for overnight intravenous anticoagulation to prevent thromboembolic events. All patients had successful ablation of the accessory pathway without complication. One patient with left anterolateral concealed pathway experienced a recurrence of symptoms three months after the procedure. Authors concluded that this study suggests transseptal radiofrequency ablation of the left sided accessory pathways is a safe and effective procedure when performed in an outpatient setting. Patients could be safely discharged four hours following the procedure, barring complications. These results were obtained at a high volume centre, experienced in using the transseptal technique.<sup>9</sup>

### *Cost-effectiveness*

A prospective study of 95 patients admitted to the University of Michigan Medical Centre between 1991 and 1992 reported the safety and cost of outpatient radiofrequency catheter ablation of accessory atrioventricular connections.<sup>10</sup> Sixty three men and 32 women, with a mean age of  $36 \pm 13$  years, underwent ablation; five of whom underwent two ablation procedures. The pathway was left-sided in 67 cases and right-sided or posteroseptal in 33 cases. Ablation was successful in 97 of 100 cases, with a mean procedure duration of  $99 \pm 42$  minutes. The patient was discharged on the same day in 70 cases and the day following the procedure in 30 cases. Complications were observed in two patients with femoral artery pseudoaneurysm requiring surgical repair.<sup>10</sup> Of the 30 consecutive patients chosen for the cost analysis, 22 were outpatients and eight were hospitalized overnight. The mean cost of the procedure was US\$  $10,183 \pm 1,082$ .<sup>10</sup> The authors concluded that most patients undergoing catheter ablation for an accessory atrioventricular connection can be treated as safely as outpatients.<sup>10</sup>

The safety and cost of outpatient radiofrequency ablation was evaluated in an observational study of 139 consecutive patients who underwent ablation of the slow pathway to treat atrioventricular nodal reentrant tachycardia at the University of Michigan from 1991 to 1992.<sup>11</sup> The patient population comprised of 38 men and 101 women with a mean age of  $45 \pm 16$  years. Ablation was successful in 119 of 120 patients, that qualified for early discharge, up to  $7 \pm 3$

years following the procedure. One patient underwent repeat slow pathway ablation for tachycardia recurrence three weeks after their first procedure. Ninety patients were discharged on the same day, 30 were discharged the next day, and 19 were hospitalized due to complications (2 cases), ablation of the fast atrioventricular pathway (6 cases), clinical indication for hospitalization unrelated to tachycardia (4 cases), and inpatient status at the time of ablation (7 cases). The two complications consisted of complete atrioventricular block that resolved in one patient and persisted in another, resulting in pacemaker implantation.<sup>11</sup>

Of the 40 consecutive patients selected for the cost analysis, 27 were outpatients and 13 were admitted for an overnight hospital stay.<sup>11</sup> The mean total charge for 40 patients was US\$ 10,547 ± 1,062, of which US\$ 6,267 ± 481 was due to professional fees and US\$ 4,327 ± 867 was due to in-hospital charges. The mean total charge for outpatients was US\$ 10,192 ± 846, of which US\$ 6,407 ± 463 was due to professional fees and US\$ 4,028 ± 710 was due to in-hospital charges. The mean total charge for patients who were admitted overnight was US\$ 11,240 ± 763, of which US\$ 6,407 ± 485 was due to professional fees and US\$ 4,833 ± 946 was due to in hospital charges.<sup>11</sup> Authors concluded that outpatient ablation of the slow pathway is safe and cost-effective in low-risk patients. The mean total charges were reduced to US\$ 10,191 ± 846 for patients undergoing slow pathway ablation on an outpatient basis, representing a savings of 36% compared to overnight stay.<sup>11</sup>

The cost-effectiveness of outpatient versus inpatient radiofrequency ablation for the treatment of supraventricular arrhythmias was reported in a retrospective analysis conducted at the Royal Perth Hospital in Australia from 1992 to 1993.<sup>12</sup> Twenty-five consecutive patients underwent day stay (outpatient) ablation and 25 underwent inpatient ablation for the treatment of supraventricular tachycardia due to accessory atrioventricular or dual nodal pathways. Patients in the inpatient group were historical controls who underwent ablation before outpatient PVA was introduced. These patients may have been eligible for same day discharge based on current criteria. The outpatient population was comprised of ten males and 15 females with a mean age of 40 years. The inpatient population was comprised of 11 males and 14 females with a mean age of 41 years. Day stay ablation was successful in 24 (96%) patients for a follow-up of 6 ± 3 months without complication. Twenty-two patients had one procedure and three underwent two procedures. The mean estimated cost per patient for day stay ablation was AUS\$ 1,876 ± 595.<sup>12</sup> Inpatient ablation was successful in 24 (96%) of patients with a follow-up of 17 ± 1 month without complication. Twenty-three patients had one procedure and two patients underwent two procedures. The mean estimated cost per patient of inpatient ablation was AUS\$ 2,354 ± 642.<sup>12</sup> Authors concluded that while outpatient ablation is a less costly and equally effective alternative to inpatient ablation, not all patients are suitable candidates for outpatient ablation. There are limitations to the cost-effectiveness studies as it is difficult to determine how many patients had atrial fibrillation and what costs were considered in the cost analysis.

#### *Adverse events*

Propofol is frequently used to maintain the deep sedation necessary to immobilize patients during catheter-based ablation. The incidence of propofol infusion syndrome during noninvasive PVA was evaluated in a retrospective chart review where blood gasses were used to study metabolic acidosis.<sup>13</sup> Thirteen of 55 (24%) AF patients had unexplained metabolic acidosis following propofol compared to 22 of 267 (8.2%) carotid endarterectomy patients who did not receive propofol ( $p < 0.1$ ).<sup>13</sup> While this study suggests prolonged high-dose propofol infusion is

associated with metabolic acidosis, it is limited by its retrospective design, small sample size, and lack of baseline arterial blood gas data.<sup>13</sup>

### **Conclusions and implications for decision or policy making:**

One small observational study suggests that day stay transcatheter ablation is effective in treating supraventricular tachyarrhythmia.<sup>8</sup> A small retrospective observational study suggests that transseptal radiofrequency ablation of the left-sided accessory pathway is effective in the outpatient setting; however, only seven of 50 patients had atrial fibrillation.<sup>9</sup> Two prospective studies conducted between 1991 and 1992 suggest outpatient radiofrequency ablation is cost-effective.<sup>10,11</sup> However, it is unclear as to what costs were considered in one study.<sup>10</sup> In addition, a retrospective study comparing outpatient radiofrequency ablation to inpatient ablation suggests day stay is less costly and equally effective.<sup>12</sup> All studies reviewed were conducted in the United States or Australia. All studies are dated, limited in size, study design and relevance to the current Canadian context.

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Appendices: Appendix A: Clinical and Cost-Effectiveness of Outpatient PVA for AF

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
<b>Clinical Effectiveness</b>						
Weerasooriya et al., 1995 Australia <sup>8</sup>	Prospective Observational  Intention to treat and discharge same day  Study period: not given  Mean follow-up: 6.2 ±3.1 months	n=50 patients with supraventricular tachyarrhythmias due to aberrant atrioventricular pathways selected consecutively  Males: 19 Females: 31  Mean age: 42 ±14 years	Day stay transcatheter radiofrequency ablation	Successful ablation  Same day discharge	30 of 32 patients were successfully ablated (18 dual atrioventricular nodal pathways; 17 slow pathways)  38 patients discharged on same day (24 accessory pathways; 14 dual atrioventricular nodal pathways)  8 patients were admitted overnight (4 for lengthy procedure; 1 intravenous anticoagulation; 1 patient preference; 2 complications)	Day stay transcatheter ablation for supraventricular tachyarrhythmia can be planned without prior diagnosis of cause.  Small sample size  Entry and exit dates for study are not provided  Published in 1995, procedures conducted in 2007 may differ
Sorbera et al. 1999 USA <sup>9</sup>	Retrospective Observational  Study period: 1994 to 1997  Mean follow-up: 22 months	n=60 patients selected consecutively  Males: 43 Females: 17  Mean age: 38±15 years  50 patients had supraventricular	Outpatient transeptal radiofrequency ablation of the left accessory pathways  Mean procedure duration: 2.5 hours	Successful ablation  Same day discharge  Complications	All cases were successfully ablated  One patient with left anterolateral concealed pathway had a recurrence three months post-procedure  No complications were observed	Authors conclude transeptal radiofrequency ablation of the left sided accessory pathway is a safe, effective procedure in the outpatient setting of an experienced high-volume centre.

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
		tachycardia; 7 had atrial fibrillation; 3 complex tachycardia				Small sample size and 7 of 50 patients had atrial fibrillation (indication of interest)  Published in 1999, procedures conducted in 2007 may differ
<b>Cost-Effectiveness</b>						
Kalbfleisch et al. 1993 USA <sup>10</sup>	Prospective  Observational  Study period: 1991 to 1992	n=95 undergoing 100 separate procedures n=90 single ablation n=5 two ablation procedures  Males: 63 Females: 32  Mean age: 36 ±13 years  Accessory pathway Right-sided: 33 Left-sided: 67 Overt: 70 Concealed: 30  30 consecutive patients were chosen for cost analysis (22 outpatients; 8	Radiofrequency catheter ablation of an accessory atrioventricular connection  Mean procedure duration: 99±42 minutes	Successful ablation  Same day discharge  Cost	97 of 100 cases were successfully ablated  70 of 95 patients were treated as outpatients  30 patients were admitted for overnight stay 2 complications (femoral artery pseudoaneurysm requiring surgical repair)  Mean cost: US\$ 10,183±1,082 outpatient procedure	Authors conclude patients undergoing radiofrequency catheter ablation of an accessory atrioventricular connection are safely treated as outpatients. Small sample size for cost analysis  Selection unclear  Costs considered unclear  Published in 1993, procedures and associated costs in 2007 may differ

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
		overnight)				
Man et al. 1993 USA <sup>11</sup>	Prospective Observational  Study period: 1991 to 1992  Mean follow-up: 7±3 months	n=139 consecutive patients  Males: 38 Females: 101  Mean age: 45 ±16 years  40 consecutive patients were selected for cost analysis (27 outpatients; 13 overnight)	Outpatient radiofrequency ablation of the slow pathway for treatment of atrioventricular nodal reentrant tachycardia	Successful ablation  Same day discharge  Cost-professional fees and hospital charges	119 patients had no recurrence during 7±3 months follow-up  1 patient had a recurrence of tachycardia 3 weeks post-procedure  90 patients were discharged same day  30 patients were discharged the day following the procedure  19 hospitalized (2 complications, 6 ablation of fast atrioventricular node, 4 unrelated indication, 7 inpatients)  2 complications: complete atrioventricular block  Mean cost: US\$ 10,1927±846 outpatients	Authors conclude a substantial cost savings is achieved when radiofrequency ablation of the slow pathway is performed on an outpatient basis.  Small sample size for cost analysis  Published in 1993, procedures and costs in 2007 may differ

Author, Year, Country	Study Design	Participants	Intervention versus Comparator	Outcomes	Results	Conclusions and Limitations
					Mean cost: US\$ 11,2407±763 overnight	
Weerasooriya et al. 1996 Australia <sup>12</sup>	Retrospective Observational  Study period: 1992-1993  Mean follow-up: 6±3 months	n=25 consecutive patients for day stay Males: 10 Females: 15 Mean age: 40 years  n= 25 consecutive inpatient historic controls Males: 11 Females: 14 Mean age: 41 years	Day stay radiofrequency ablation for supraventricular tachycardia versus inpatient radiofrequency ablation (historic controls)	Successful ablation  Same day discharge  Cost	24 of 25 outpatients were successfully ablated without complication  Overall cost per inpatient in 1994 Australian dollars: AUS\$ 2,354±642  Overall cost per outpatient in 1994 Australian dollars: AUS\$ 1,876±595	Authors conclude that while day stay ablation is less costly and equally effective, not all patients are suitable candidates for same day discharge.  Small sample size  Unclear how patients were matches
<b>Adverse Events</b>						
Cravens et al. 2007 USA <sup>13</sup>	Retrospective chart review  Observational  Study period: 1999 to 2001	n=301 radiofrequency ablation outpatients: only 55 blood gases taken  n=293 carotid endarterectomy patients: 267 had blood gases taken	Outpatient radiofrequency ablation for atrial flutter or atrial fibrillation receiving propofol as sedative versus carotid endarterectomy patients who did not receive propofol	Metabolic acidosis based on blood gases	13 of 55 outpatient radiofrequency ablation patients had metabolic acidosis  22 of 267 carotid endarterectomy patients had metabolic acidosis	Authors conclude prolonged, high-dose propofol may experience metabolic acidosis.  Retrospective  Baseline blood gases are missing  Small sample size