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Atrial fibrillation ablation: a cost or an investment?

Josef Kautzner[1]*, Veronika Bulkova[1], Gerhard Hindricks[2], Nikos Maniadakis[3], Paolo Della Bella[4], Pierre Jaïs[5], and Karl-Heinz Kuck[6]

[1]Department of Cardiology, Institute for Clinical and Experimental Medicine, Vídeňská 1958/9, 140 21 Prague 4, Czech Republic; [2]University of Leipzig-Heart Center, Leipzig, Germany; [3]Department of Health Services Management, National School of Public Health, Athens, Greece; [4]Arrhythmology Unit, San Raffaele Hospital, Milan, Italy; [5]Hôpital Cardologique du Haut-Lévêque, Université Bordeaux II, Bordeaux, France; and [6]Hanseatisches Herzzentrum, Asklepios Klinik St Georg, Hamburg, Germany

In the last decade, catheter ablation (CA) became a viable therapeutic approach for symptomatic patients with atrial fibrillation (AF) non-responsive to antiarrhythmic drugs (AAD). The economic analysis of CA is complex due to the presence of several confounding factors, such as the pattern of AF (paroxysmal AF, persistent or long-term persistent AF), the patient population (age, presence/absence of underlying structural heart disease, comorbidities, etc.), the different techniques for ablation (with impact on complexity and cost of the procedure, as well as on efficacy and safety), and the learning curve and experience of an individual centre (with impact on efficacy and cost effectiveness). At present, CA appears to be cost effective mainly in patients with paroxysmal AF who are refractory to AADs, especially if the success of the procedure and, thus, the benefit in quality of life remains >5 years, with a low complication rate. More data are needed on cost effectiveness of CA of persistent and long-term persistent AF or of AF associated with heart failure. Atrial fibrillation ablation is unlikely to be cost effective for patients who have preserved quality of life despite their AF or for patients whose quality of life is not expected to improve substantially despite elimination of AF (e.g. patients with poor quality of life mainly due to other health problems). These observations may help in the selection of candidates for AF ablation.

Keywords Ablation • Atrial fibrillation • Cost • Cost effectiveness • Quality of life

In the last decade, catheter ablation (CA) became a viable therapeutic approach for symptomatic patients with atrial fibrillation (AF) non-responsive to antiarrhythmic drugs (AAD). It has evolved from early attempts to ablate triggering ectopic foci within pulmonary veins to strategies targeting entire regions critical for initiation and maintenance of AF.[1–4] Currently, isolation of pulmonary veins is considered a key step of the procedure, often supplemented in patients with persistent or long-term persistent AF by linear lesions and/or ablation of fractionated potentials.[5] Several small randomized studies performed in populations of patients with predominant paroxysmal AF who failed to respond to previous AAD treatment have established that CA reduces AF recurrence more effectively than AADs.[6–10] In this context, CA proved to be superior in alleviation of symptoms and improvement of quality of life. However, there is incomplete data on the long-term efficacy of this intervention[11,12] and even less is known on potentially positive impact of CA on morbidity and mortality.[13] Similarly, evidence on the efficacy of CA in patients with long-term persistent AF[14,15] and in those with heart failure is also sparse.[16,17] Since the population of patients with AF is large and growing,[18] management decisions about AF are likely to have important implications for future health-care spending. To date, information regarding the cost effectiveness [i.e. the estimation of the difference in relative cost and efficacy (or effectiveness) of two compared therapeutic interventions] of CA for AF relative to medical therapy is limited. This review aims at analysing current literature on this subject.

Costs of medical therapy

Atrial fibrillation is a progressive disease that requires long-term management and follow-ups.[19] One reason is a variable risk of thromboembolic complications that can be minimized by using anticoagulation therapy with the need for close monitoring. The other reason reflects general management strategy: rhythm or rate control. Whichever strategy is selected, it again requires long-term monitoring of efficacy and safety. Last but not least, patients with bradycardia–tachycardia syndrome usually have a cardiac pacemaker implanted to prevent symptomatic bradycardia episodes and enable administration of AADs to suppress runs of tachyarrhythmia. Although many subjects are followed in an outpatient setting, numerous patients present at emergency departments for acute onset of AF, initiation of AAD therapy or cardioversion, and for management of AF-related complications.

The cost of conventional management of AF is significant. It has been calculated that the total cost burden of AF may be as much as

* Corresponding author. Tel: +420 261 365 009; fax: +420 261 362 985, Email: josef.kautzner@medicon.cz

1% of the total health-care system expenditures in the United Kingdom.[20] A study from France included direct medical costs, pharmacological expenditures, and costs of thromboembolic and other complications.[21] Costs per year per patient were calculated at 3308 € and the main drivers identified were the cost of hospitalization (1296 €) and expenses on heart failure therapy (998 €). Expenditures on treatment of stroke reached 334 € per patient. Other European studies showed that the average yearly cost of conventional therapy varied ∼1010–3225€/year.[22,23] These findings correspond to similar data obtained in the Czech Republic where the mean individual expenditures on conventional AF therapy reached 1462 €/year.[24]

Importantly, according to the results of the Fractal Registry,[25] costs of conventional AF management vary considerably according to the individual patient and arrhythmia characteristics. Although the annual costs related to permanent AF were calculated to be US$3.222, the costs calculated for paroxysmal AF were significantly dependent on the number of (symptomatic) arrhythmia recurrences and mainly driven by hospital costs. With no documented AF recurrence, annual costs equalled US$3.385, whereas 1–2 recurrences increased costs to US$6.331. However, three or more recurrences further increased costs to US$10.312.

Although the average therapeutic costs may differ according to individual national economics and the level of health-care funding, costs of conventional treatment of AF represent a considerable burden for every European economy.

Costs of catheter ablation

There have been a great variety of techniques for CA of AF.[5,26] Although some of them are relatively simple, the majority of them utilize several catheters and/or electroanatomical mapping. Other may include novel ablation or imaging tools such as balloon catheters and/or intracardiac echocardiography. On one hand, the use of advanced mapping and imaging technologies seems to increase the efficacy and safety of the procedure. On the other hand, this is reflected by an increased cost of the procedure that is generally 2–3 times more than for CA of other arrhythmias. The costs of CA are influenced by many other factors such as the length of the follow-up and by the variable use of additional tests such as CT angiography of pulmonary veins. Perioperative complications are also generally higher than in conventional ablations for supraventricular tachycardias and contribute to the price tag for the ablation procedure. All these factors, together with the selected efficacy measure (e.g. quality of life vs. mortality), influence cost-effectiveness measures such as the incremental cost-effectiveness ratio (ICER). This is defined as the ratio of the estimated difference in cost to the difference in efficacy measure and considered a reliable index of cost effectiveness.[27] Another frequently used approach in cost-effectiveness analysis is to calculate the incremental cost per quality-adjusted life year (QALY) associated with a new therapeutic intervention (e.g. ablation) in relation to an existing reference treatment (e.g. drug therapy). The critical issue in such analysis is the threshold used as a measure to define whether a new technology is deemed good value for money (i.e. cost-effective) or not, relative to an existing one. Although the level of this threshold is often debated, there is prevailing agreement that technologies with an incremental cost per QALY up to €20 000 are considered very good value for money, while ∼€ 40–60 000 represents the borderline, and >€ 60 000 is deemed expensive. Regarding the cost effectiveness of CA for AF, several studies of variable complexity of analysis have been published on this topic.

One of the first studies from Bordeaux calculated costs of CA in 118 patients with paroxysmal, drug-refractory AF who underwent one to four procedures to cure arrhythmia.[28] During a follow-up period of 32 ± 15 weeks, 72% were free of AF. The costs of CA were expressed in 2001 Euros and compared with retrospectively analysed costs of medical therapy in 20 consecutive patients. No mapping system was used and no complications were observed and calculated. All future costs were discounted by 5% per year. The projected annual costs of medical therapy were estimated at €1590 and the up-front cost of CA at €4715. Given the assumption that ablation was not successful in 28% of patients, the ongoing care in ablated patients was valued at €445 per year. The costs of both treatment strategies reached equilibrium between 4 and 5 years. This could be the most optimistic figure as others showed less freedom from AF after CA and substantial utilization of AADs and resources (cardioversions) in 67 patients over the first year after the procedure with a steep decline during the second year (*Figure* 1) (Della Bella, P, unpublished data). Indeed, Khaykin *et al.*[29] presented a cost comparison of CA for AF and AAD therapy based on health-care utilization patterns from Canada and France. Using Canadian price weights, these authors concluded that costs would equalize over 3–8 years of follow-up (4.5–11 years with 3% discounting applied) due to higher long-term costs of AAD treatment. More recently, the same group used an economic model of a randomized pilot study of AF ablation as first-line therapy for paroxysmal AF, again using Canadian price weights.[30] In this study, costs were nearly equal after 2 years, in large part because of a 49% rate of crossover to CA in patients initially assigned to drug therapy. Thus, this model may exaggerate the cost effectiveness of CA. A more realistic figure seems to be in the range of 5–8 years.

However, some studies show even less favourable data on cost effectiveness of CA. Chan *et al.*,[31] using a disease simulation Markov model, projected the potential cost effectiveness of CA for AF, compared with amiodarone or rate control in a population of patients with moderate-to-low risk of stroke. The analysis was based on hypothetical reductions in the risk of stroke following CA. Costs from a health service perspective and outcomes were measured as QALYs. They concluded that with expected 80% efficacy rate for sinus rhythm restoration, the relative reduction in stroke risk would need to be 42 and 11% to yield ICERs US $50 000 and US $100 000 per QALY, respectively. In other words, in patients at a low stroke risk CA is unlikely to be cost effective. However, this study did not consider potential improvements in quality-adjusted life expectancy due to maintenance of sinus rhythm alone.

Reynolds *et al.*[32] used a similar Markov model for a hypothetical cohort of patients with paroxysmal AF who had failed to respond to previous treatment with one or more AADs. They attempted to estimate costs, quality-adjusted life expectancy, and cost effectiveness of CA with or without AAD relative to continued drug

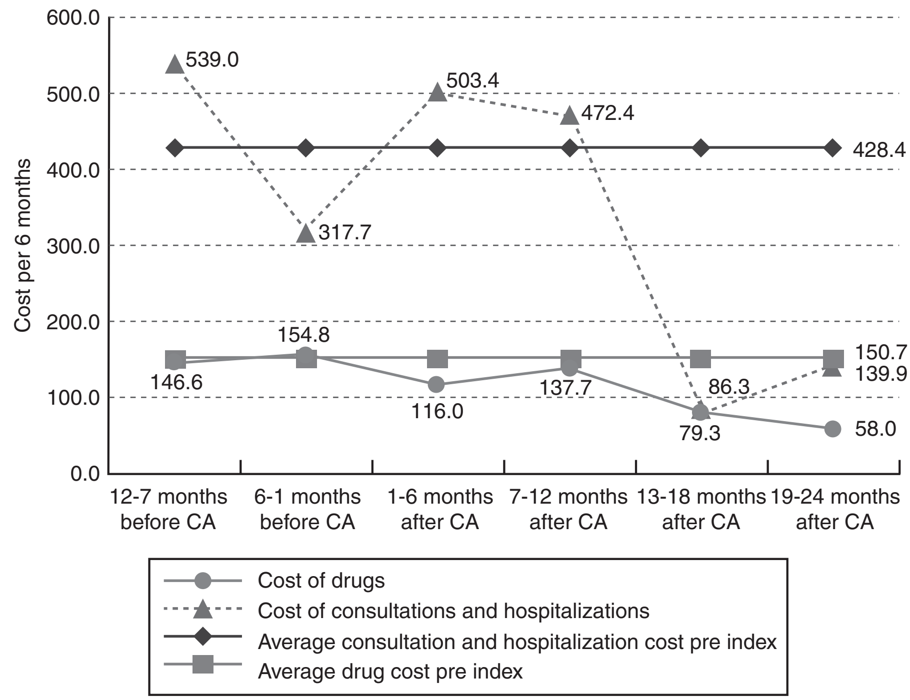

Figure 1 Comparison of costs of drugs, consultations, and hospitalizations before and after index catheter ablation of atrial fibrillation. Note the substantial drop in utilization of resources over time compared with preablation average costs. Average costs are estimated based on the average of observations during the two 6-month periods before index procedure.

therapy alone over a 5-year follow-up. Cumulative costs with CA and AAD strategies were US $26 584 and US $19 898, respectively. Over 5 years, quality-adjusted life expectancy was 3.51 QALYs for ablation vs. 3.38 for the AAD group. Therefore, the ICER for both strategies reached US $51 431/QALY. Longer-term extrapolations of this model indicate cost neutrality after about 10 years. The longer time for equalization of costs in the US model may be due both to the higher up-front cost of CA in the USA, and to the fact that this model incorporates a switch towards less expensive rate controlling drugs over time.

The most robust analysis of the cost effectiveness of radiofrequency CA for AF in comparison with AAD therapy was performed by a group of experts working for NICE in the United Kingdom.[33] They used a systematic review of the literature and meta-analysis, and applied Bayesian statistical methods to synthesize the effectiveness evidence from randomized controlled trials. A decision analytical model was developed to assess the costs and consequences associated with the primary outcome of the trials over a lifetime time horizon. Costs were again measured as QALYs. This study found that the ICER of CA varied between £7763 and £7910 for each additional QALY according to baseline risk of stroke, and with a probability of being cost effective from 0.98 to 0.99 (using a cost-effectiveness threshold of £20 000). The results were again sensitive to the duration of quality-of-life benefits from CA. This group concluded that CA is a potentially cost-effective strategy for paroxysmal AF in patients predominantly refractory to AAD therapy, provided the quality-of-life benefits are maintained for $>$5 years.

Summary of cost-effectiveness analyses

The above analyses seem to indicate that, until and unless morbidity and mortality benefits are proven, the cost effectiveness of AF ablation relative to AADs principally reflects long-term maintenance of quality of life after CA. This holds true at least over a short- to medium-term time period. Obviously, if such benefits are maintained over the remaining lifespan of the patient, the cost effectiveness would be very attractive. However, the results of a 5-year analysis of the outcome of CA suggest that cost effectiveness may not be so favourable. Any shorter benefit in quality of life leads to an increase in the ICER above an acceptable level. Therefore, the short-term cost benefit of CA for AF could be mainly improved by documentation of additional benefit beyond improvement in quality of life such as stroke reduction and by a cheaper initial procedure with less complications and/or reduction of a need for repeated procedures after the first CA.

In reality, the economic analysis of CA is even more complex due to the presence of several confounding factors. One of them is the technique of ablation that may differ significantly, the degree of complexity and cost as well as efficacy and safety. The other factors include the learning curve and variable experience of an individual centre that influence efficacy and cost effectiveness. It is well known that an increased volume of cases is associated with a lower complication rate and higher success rate. Thus, in experienced and high-volume centres, the cost effectiveness of AF ablation is likely to be more favourable.

Since the majority of clinical studies dealt with paroxysmal AF, more data are needed before extending the results of studies on cost effectiveness to a population of patients with persistent or long-term persistent AF. So far, clinical evidence suggests that these patients have a higher probability of repeated procedure as compared with paroxysmal form. This implies significantly poorer cost effectiveness of CA in this form of disease. Similarly, the efficacy of CA for AF is likely to be worse in patients with concomitant structural heart disease or in older patients. Results of prospective trials are awaited to demonstrate the efficacy of CA in preventing recurrences of persistent AF or in patients with risk factors for thromboembolism. One of them is the CA for the Cure of AF 2 study[34] and the other the CABANA trial.[35]

Conclusions

To answer the question as to whether CA for AF is a cost or an investment, we may conclude that at present CA is cost effective mainly in patients with paroxysmal AF who are refractory to AADs. This holds true especially if the success of the procedure and, thus, the benefit in quality of life remain >5 years and complication rate is low. More data are needed on the cost effectiveness of CA of persistent and long-term persistent AF or AF associated with heart failure. In these situations, CA has to be compared with strategies such as AV nodal ablation and cardiac resynchronization therapy or single-chamber pacemaker. However, AF ablation is unlikely to be cost effective for patients who have preserved quality of life despite their AF or for patients whose quality of life is not expected to improve substantially despite elimination of AF (e.g. patients with poor quality of life mainly due to other health problems). These observations may help in patient selection for AF ablation.

Conflict of interest: J.K. is a member of an Advisory Board for Biosense-Webster and St Jude Medical and have received honoraria for lectures from Biotronik, Biosense-Webster, Hansen Medical, and St Jude Medical. G.H. received research support from St Jude Medical, Biotronik, and Medtronic. He is a consultant for St Jude Medical, Biotronik, and Biosense Webster and a member or promotional speakers' Bureau for St Jude Medical, Biotronik, and Medtronic. He also has received modest lecture honoraria from St Jude Medical, Biotronik, Medtronic, and Biosense and is a member of the St Jude Medical and Biosense advisory board. N.M. is received research grants and honoraria from the pharmaceutical companies Sanofi-Aventis, Roche, Astra-Zeneca, Pfizer, Merck-Serono, Amgen, Genesis, Alexion, Boehringer-Ingelheim, Servier, Janssen-Cilag, and Novartis. P.D.B. is a consultant for St Jude Medical and obtained research grants from Biosense Webster, Biotronik, Medtronic, and St Jude Medical and received lecture honoraria from Biosense Webster and St Jude Medical. P.J. obtained research grant from Philips and received lecture honoraria from Biosense Webster and St Jude Medical. K.H.K. is a consultant for Biotronik, Endosense, and Stereotaxis, obtained research grant from St Jude Medical and received lecture honoraria from Biosense Webster and St Jude Medical.

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