

What are the costs of atrial fibrillation?

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The costs of atrial fibrillation (AF) are linked to the general cost of managing AF patients in different health-care systems, as well as the cost of managing AF-related complications (e.g. hospitalizations and long-term complications, such as stroke). In addition, indirect medical costs, such as care for patients who do not recuperate fully from a vascular event, and non-medical costs such as loss of work force add to the costs of AF. All estimations for cost of AF and cost of AF therapy are based on assumptions and markedly influenced by these cost determinants. This urges for extreme caution not to take cost estimates at their absolute values. In fact, even relative comparisons between interventions may have different consequences in terms of direct and indirect costs in different health-care settings. While newer therapeutic options appear to increase the cost of AF management, newer antithrombotic substances and adequate rhythm control therapy also carry the promise of preventing the two major drivers of AF-related cost, hospitalizations and AF-related complications. Formal assessment of the cost of AF requires adjustment to local practice, and more data are clearly needed especially from primary care to better estimate the 'real' cost impact of AF.

Keywords Ablation • Cost • Cost effectiveness • Oral anticoagulation • Stroke

Introduction

The increasing prevalence of atrial fibrillation (AF) is age related, with few (~1%) affected younger than 60 years and a higher prevalence of up to 12% of those aged 75–84 years.¹ Patients with AF commonly have underlying cardiovascular or metabolic disorders, such as heart failure, stroke, valvular disease, hypertension, obstructive sleep apnoea, and diabetes mellitus.^{2–6} Partly related to the increasing mean age of the general population as well as to the improved management and increased survival associated with concomitant diseases such as stroke, heart failure, and myocardial infarction, the prevalence of AF is likely to increase in forthcoming years.^{2–6}

Consequences of atrial fibrillation

Death

Even after adjusting for co-morbid conditions, AF is associated with a two-fold increase in death rates compared to those without the condition.^{7–9} So far, the medical means to prevent AF-related deaths are not sufficiently effective: indeed, no single therapeutic intervention has reduced death rates in AF patients. Even oral anticoagulation, which is highly effective for stroke prevention in AF, only reduces death in a pooled meta analysis,¹⁰ and in the largest published trial (RE-LY), dabigatran reduced cardiovascular

death as a secondary outcome parameter.¹¹ Other therapies, such as dronedarone, reduced a composite endpoint of cardiovascular hospitalizations and death in the ATHENA study, which was largely driven by a significant reduction in hospitalizations, although there was a positive effect on cardiovascular death in a non-hierarchical secondary analysis.¹² Nonetheless, there is a remarkable residual death rate in AF trials (3–4% per year depending on the patient risk profile).

Stroke

Even within large controlled trials, rates of major cardiovascular events remain high. In the general population, approximately every fourth stroke is attributable to AF.^{13–15} Indeed, strokes related to AF are associated with a poorer outcome than those that are not related to AF^{15–18} and stroke patients with AF have higher levels of morbidity and create higher in-patient costs than other non-AF stroke patients.^{18–20} Furthermore, AF-related strokes more often result in permanent disability with severe consequences for patients and their families, and lower rates of patient discharge to their own homes.

Heart failure and acute coronary syndromes

Independently of strokes, AF is commonly associated with heart failure, acute coronary syndromes, and—the most common interruption of normal life in AF patients—with frequent

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Table 1 Direct (medical and non-medical) and indirect costs of atrial fibrillation and of complications

Direct medical costs of AF
Hospitalization (inpatient care)
Electrical cardioversion
AF ablation
Atrioventricular node-ablation including pacemaker therapy
Maze surgery
Other surgery for AF
Hospital-based ambulatory and outpatient care
Visit to a specialist
Electrical cardioversion
Pacemaker interrogation and monitoring
Visit to a general practitioner
AF as secondary diagnosis
Pharmaceuticals
Anticoagulation monitoring
Direct costs of complications (stroke, heart failure, and acute coronary syndromes)
Indirect costs of AF
Production loss
Indirect costs of complications (stroke, heart failure, and acute coronary syndromes)
Production loss

hospitalizations (25% per year in recent controlled trials).^{12,21} In one cohort of almost 1000 patients, the annual medical cost of AF management was high, and that analysis found clear cost increments in patients with persistent or permanent AF compared with paroxysmal AF, as well as in patients with frequent AF recurrences, and the cost increase was largely attributable to hospitalizations.²² Thus, it is not surprising that AF is an increasing public health burden,^{23–26} given the progressive nature of the arrhythmia in almost all patients^{27,28} and the age-dependent increase in AF prevalence (see above).

Medical costs in atrial fibrillation

In addition to the general cost for managing AF patients in different health-care systems,^{29–31} the management of AF-related complications contributes markedly to the medical costs of AF, e.g. through costs for hospitalizations and long-term complications, such as stroke.³² In addition, indirect medical costs, such as care for patients who do not recuperate fully from a vascular event, and non-medical costs such as loss of work force add to the cost of AF (Table 1). All estimations for cost of AF and cost of AF therapy are based on assumptions and markedly influenced by these cost determinants.³³ This urges for extreme caution not to take cost estimates at their absolute values. In fact, even relative comparisons between interventions may have different consequences in terms of direct and indirect costs in different health-care settings (Table 1).

Hospital admissions were reported to cause between 40 and 60% of the direct medical cost in AF patients in different European

countries.^{29,30,33–37} In a medium-sized prospective French survey (671 patients), hospitalizations were more frequent in patients with persistent AF than in those with paroxysmal AF (127 vs. 83, $P < 0.05$).³⁴ The first cost driver was hospitalizations (52%), followed by drugs (23%), consultations (9%), further investigations (8%), loss of work (6%), and paramedical procedures (2%). According to the multivariate analysis, heart failure ($P < 0.04$), coronary artery disease ($P < 0.001$), use of potassium channel blockers ($P < 0.002$), hypertension ($P < 0.002$), and metabolic disease ($P < 0.001$) were significantly associated with higher costs.³⁴ In the EuroHeartSurvey on AF, more than half of the estimated direct medical cost were due to hospitalizations and interventions for AF.^{29,35}

Cost and cost effectiveness of atrial fibrillation management

The main goals with treatment in AF patients are to prevent thromboembolic complications and to alleviate symptoms.³⁸ Treatment of AF thus includes anti-thrombotic therapy, management of concomitant, disease-modifying conditions, and various strategies for symptom relief including rate control, electrical cardioversion, antiarrhythmic drugs for conversion or rhythm control, and left atrial ablation. Consequently, there is increasing attention on the demand of resources for patients with AF and its related diseases. However, there is limited information on cost effectiveness for managing patients with AF in their different clinical settings and on a long-term basis.

Therapy of concomitant conditions

A number of economic analyses have focused on AF-related costs, the majority of which have evaluated the costs of specific interventions or pharmacologic treatments.^{39–41} Treatment of hypertension, a common co-morbid condition in AF patients, has been shown to be cost effective in virtually all patient populations (and circumstances) studied and for a wide variety of drugs, more so with coexisting risk factors.³⁹ In the same study, the cost effectiveness of anticoagulants was favourable for prosthetic valves, although sensitive to imprecision in monitoring, and it was also favourable for mitral stenosis in the presence of AF but not normal sinus rhythm.³⁹

Anticoagulation

In a more recent analysis, anticoagulation is cost effective in patients at high risk of stroke, but not for those with a low risk of stroke.⁴² Furthermore, the additional benefit of newer anticoagulants such as dabigatran may be cost effective according to modelling estimations.⁴³ With the evidence available for stroke risk factors and the various stroke risk stratification models, a review of these models regarding their validity and their performance in representative AF populations would be highly desirable.⁴² The recent guidelines of the European Society of Cardiology have slightly broadened the range of patients in whom oral anticoagulation is recommended, resulting in a recommendation for oral anticoagulation in patients at moderate risk for stroke.³⁸ Although this recommendation is based on a net benefit between bleeding and

ischaemic events in such patients, and supported by the more recent anticoagulation trials in AF patients, formal cost analyses of these recommendations may be of economic interest.

Rate and rhythm control therapy

Cost-effectiveness analyses of 'pure' rate control therapy without a rhythm control comparator are scarce. In combination with antithrombotic therapy, cardioversion followed by the use of amiodarone may be cost effective, at least in patients at moderate or high risk for stroke and according to older analyses.^{40,41} So far, however, most cost analyses suggest that adding rhythm control (albeit using partially ineffective antiarrhythmic drugs and cardioversions) adds cost to the medical management of AF patients rather than avoiding complication-related cost.^{27,44,45} There is a clear need to better delineate which patients may benefit from rhythm control therapy, and when and to what extent such therapy should be pursued.

Limitations of current atrial fibrillation management

The observations discussed so far were made in relatively small patient samples, and extrapolated to the general AF population. Importantly, the majority of patients were enrolled through cardiologists and hospital physicians, while many AF patients are managed in primary care as outpatients,³⁸ with potential implications for the type and quality of management as well as for medical cost. A large recent analysis of health-care provider data, however, confirms that the cost of managing AF-related complications and cost of hospitalizations are the main drivers of direct medical cost in AF patients.⁴⁶ In this survey of over 100 000 patients with AF, major cost drivers were the direct cost of complications (54%) and hospitalization due to AF, including AF as secondary diagnosis (18%), followed by loss of productivity (12%).⁴⁶ Notably, cost of primary care management was not well assessed in this survey, reinforcing the need for data on AF management in primary care. Another indirect confirmation of hospitalizations as a major driver for AF-related medical cost stems from an analysis that demonstrated reduced AF-related cost when management guidelines with a focus on avoiding unnecessary hospitalizations were implemented.⁴⁷

Even though effective treatments are available for the prevention of thromboembolic complications and for rhythm and rate control in AF patients,³⁸ there is not only marked residual stroke and death, but the interventions also have a limited impact on hospitalization rates that may even increase on progression of AF.^{25,48,49} These observations have important implications because estimates of the health-care costs of AF have identified direct costs and hospitalizations as the major cost drivers.^{22,29,30,33–37}

Quo vadis?

In principle, prevention of AF appears an attractive road to preventing the cost of AF-related complications and AF-related hospitalizations. It is conceivable that limiting the duration of

antiarrhythmic drug therapy,^{50–52} the use of newer, potentially safer antiarrhythmic drugs,⁵³ or a wider-spread use of catheter ablation of AF^{54,55} including an earlier rhythm control intervention^{56,57} could help to improve the cost effectiveness of rhythm control therapy in AF patients. This assumption requires formal assessment including a formal demonstration that rhythm control therapy conveys additional benefits for AF patients in addition to improving symptoms.³⁸

Conclusion

The costs of AF are high and are likely to be driven by the consequences of AF-related complications such as strokes, cost of hospitalizations in AF patients, and loss of productivity. While newer therapeutic options appear to increase the cost of AF management, newer antithrombotic substances and adequate rhythm control therapy also carry the promise of preventing the two major drivers of AF-related cost, hospitalizations and AF-related complications. Formal assessment of the cost of AF requires adjustment to local practice, and more data are clearly needed, especially from primary care, to better estimate the 'real' cost impact of AF.

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