

# Atrial fibrillation – European and Swiss perspectives

Reflections on epidemiology, costs and treatment options: an article from the series  
“Atrial fibrillation – update 2014”

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## Summary

Atrial fibrillation is the most common arrhythmia in the general population and its prevalence is increasing as the population becomes older. It is related to an increase in the incidence of stroke, but also to an overall increased morbidity and mortality. Huge efforts are made by the medical community to try and reduce the burden of atrial fibrillation in the general population and to reduce the negative impact on morbidity and mortality. While some of these goals have been achieved with the use of drugs, namely anticoagulants, there is a plethora of unmet needs in patients with atrial fibrillation. Pulmonary vein isolation has emerged as a treatment option for selected patients with atrial fibrillation with a high aim of curing the arrhythmia. The treatment has been shown to reduce symptoms and improve quality of life in patients with atrial fibrillation but whether it impacts survival remains to be shown. The increase in atrial fibrillation prevalence as well as novel drugs and therapies increase the treatment costs of patients with atrial fibrillation. Increased treatment costs are reflected in higher healthcare expenditures in all European countries which are becoming a significant financial burden for health care systems. The economic burden of atrial fibrillation influences the availability of treatment options in some European countries.

*Key words: atrial fibrillation; epidemiology; anticoagulation; pulmonary vein isolation; healthcare costs*

## Epidemiology

Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general population [1] with a marked increase in incidence with age [2]. It is estimated that AF occurs in 1–2% of the general population [1, 3]. It has been strongly associated with increased age, hypertension, ischemic heart disease and heart failure [4]. The prevalence of AF is predicted to increase significantly in the years to come [5, 6] and could even double in the next 50 years [1]. There are,

among others, two important reasons for this increase. First, the population in developed countries is aging with more people at risk for AF and second, treatments of confounding factors for AF are leading to increased survival (hypertension, heart failure, valvular heart disease). Assuming that the prevalence of AF is 1% in the general population, it affects more than 5 000 000 people in the European Union and more than 80 000 people in Switzerland. These numbers are calculated conservatively for the general population, not taking into account differences in age distribution between countries and with the lowest described prevalence of 1%. However, although these numbers are high, they are lower than prevalence of other “modern epidemics” such as hypertension or diabetes. On the other hand, true prevalence of AF could be even higher since AF can be asymptomatic and hence undiagnosed in up to one third of patients [1]. How these numbers impact both patients and physicians, and national healthcare systems will be further discussed in this review.

## Impact on morbidity and mortality

AF is associated with a decrease in functional status, quality of life and an increase in heart failure, stroke and mortality [7, 8]. AF has been shown to be an independent predictor of mortality with a 1.5- to 2.5-fold increase and these results are consistent in different trials [1, 9]. However, the increase in mortality is independent of commonly measured confounders such as hypertension, diabetes, obstructive sleep apnea and obesity. Since the mortality risk can only partially be explained by AF itself (tachycardia, irregular heart rhythm, loss of atrial systole, thromboembolism), other potential confounding factors likely co-exist (myocardial fibrosis, systemic inflammation, endothelial dys-

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function) which are not routinely measured. AF should be recognised as a predictor of mortality and management should be driven towards treatment of predisposing factors of AF. However, further research is needed to gain a better understanding of the mechanisms causing the increase in mortality in AF patients.

### Costs of atrial fibrillation

The socio-economic burden of AF is considerable [10]. In several reports, AF was associated with average healthcare costs from 971 euros per patient per year (Poland) up to 3027 euros per patient per year (France, Italy) [11]. Total costs for treating AF were 655 million euros in the UK in year 2000 [10] and 690 million euros in Germany in 2006. The Euro Heart Survey which included 5333 patients in 35 countries identified hospitalisations and interventional procedures in patients with AF as main determinants of costs accounting for >70% of total costs [11]. Except from direct healthcare costs, indirect costs also rise as a consequence of early retirement or sick leaves and are assumed to be from 39 euros average per patient per year (Poland) to more than 3000 euros average per patient per year in Italy or Germany [11] adding an additional 20% to the total costs of treatment [11, 12]. In Switzerland, the DRG-derived reimbursement (DRG = diagnosis-related group) for a patient undergoing pulmonary vein isolation (PVI) is approximately 25 000 CHF and with >1500 PVIs performed in Switzerland in 2012 this results in costs of approximately 40 million CHF per year. This number only includes costs of PVI which is only performed in a small portion of selected patients, whereas real costs include medication, hospitalisations, treatment of complications, disability and sick leave. Since the number of patients with AF is rising and new, more expensive pharmacologic and non-pharmacologic therapies are constantly being developed, we can assume that these costs will further increase and represent a significant burden for countries and their healthcare systems. In the UK, direct costs of AF treatment were 0.6–1.2% of total healthcare expenditure in 1995 and almost doubled by 2000 (0.9–2.4%). From both a European and Swiss perspective, it can be assumed that AF-associated costs will further increase, but differences between countries are quite significant.

### Treatment options

The most important goals of AF treatment are stroke reduction, mortality reduction and symptom improvement. Anticoagulation therapy, first with vitamin K antagonists and today with novel anticoagulants, has been shown to reduce the risk of stroke and it is still the only treatment that has been shown to have an impact on mortality so far [13, 14]. Pharmacological and non-pharmacologic treatments reduce AF burden and

improve symptoms with different success rates, but these treatment modalities have so far not shown an impact on mortality.

As the impact of rhythm control on mortality raises many questions and is still debatable, it is discussed in more detail in the following paragraph.

The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study compared two treatment modalities in patients with AF [15]. Patients were randomised to a rhythm control strategy (maintenance of sinus rhythm with cardioversion and anti-arrhythmic drugs) or rate control strategy (persistence of AF with control of ventricular rate). The study showed no reduction in mortality with rhythm control strategies with a higher incidence of adverse drug effects. However, post hoc analysis of the trial showed that sinus rhythm was a marker of improved survival with 47% lower risk of death. On the other hand, the use of anti-arrhythmic drugs was associated with a 49% increase in mortality [14]. The interpretation of the data was that, although maintenance of sinus rhythm (SR) improves survival, the use of AADs for this purpose nullifies that benefit. It is important to note that the AFFIRM study compared a rhythm control to a rate control strategy, not sinus rhythm to atrial fibrillation and a significant proportion of patients in the rhythm control strategy group were actually in AF because of unsuccessful treatment with anti-arrhythmic drugs.

After the advent of pulmonary vein isolation it became a widely used non-pharmacologic method for the treatment of AF and maintenance of sinus rhythm (SR) [16]. Pulmonary vein isolation has been compared to anti-arrhythmic drugs in several trials and has been shown to be a safe and effective method for AF treatment in selected patients, namely those with paroxysmal AF and absence of structural heart disease [17–19]. Besides radiofrequency point-by-point ablation, novel technologies with the aim of single shot PVI have been developed in order to simplify the procedure and potentially increase success rates [20–22]. Available data show that most of these methods perform comparably to standard RF point-by-point ablation and add to the broad spectrum of treatment modalities used for AF treatment.

Two important questions regarding PVI remain. First, whether PVI has a similar benefit in maintaining sinus rhythm in a broader patient population (heart failure, post cardiac surgery, chronic AF, valvular heart disease) and second, whether maintenance of sinus rhythm after PVI has a significant impact on survival. These questions are currently addressed in several ongoing trials. Two major trials are the Catheter Ablation versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (CABANA, NCT00911508) and Catheter Ablation Versus Standard Conventional Treatment in Patients With Left Ventricular Dysfunction and Atrial Fibrillation (CASTLEAF, NCT00643188)

trials. The CABANA trial includes both patients with paroxysmal and non-paroxysmal AF and those with additional comorbidities and is the first trial powered with the possibility of showing differences in mortality. The CASTLE AF trial is designed to evaluate the impact of catheter ablation of AF on morbidity and mortality of patients with heart failure.

### Use of pulmonary vein isolation in Switzerland and other European countries

PVI has become the cornerstone of interventional treatment of AF. In Western European countries, the number of PVI procedures is constantly increasing. According to the EHRA White book 2012, the five countries with the most PVIs per million inhabitants are Norway, Switzerland, Denmark, Germany and Belgium with more than 180 PVIs per million [20]. Among EU countries, the five countries with the lowest number of procedures per million were Bulgaria, Romania, Croatia, Slovakia and Lithuania with less than 20 PVIs per million [23]. The total number of PVIs was 44 185 in all reporting countries. Of these, 1525 were performed in Switzerland. A large gap is seen between EU's 27 countries and the total of 54 countries included in the White book, with the exceptions of Switzerland and Norway which are in the top five countries with most PVIs performed but are not EU members. There are several reasons for this difference among European countries. According to available data, countries with a low PVI rate per million lack infrastructure (ablation centres), have a low capacity of existing centres and have a low referral rate for PVI. Also, among the 54 included countries, there are big differences between healthcare systems, gross domestic product per capita and healthcare expenditure (both in absolute number in USD and as a percentage of GDP). For comparison, the country with the lowest healthcare expenditure among countries included in the White book was Armenia (143 USD per capita) whereas Switzerland had the highest with 9603 USD per capita. Countries with most ablations per million inhabitants also had the highest healthcare expenditures and all had health care expenditure of more than 10% of GDP [23]. While low PVI numbers in some countries can be explained with both lower GDP and healthcare expenditure, the question is whether the numbers in countries with a high number of PVIs are justified by the need and whether they should increase further to meet the needs of patients with AF or whether there is "overtreatment".

It is the strong opinion of the authors that PVI is all about patient selection. As discussed before, patients who benefit the most and where the data are strong are those with paroxysmal AF and absence of structural heart disease. However, in Switzerland and other Western European countries, many PVIs are performed based on referral and in patients with non-par-

oxysmal AF and/or structural heart disease. Especially in countries with high GDP and a high number of PVIs, referral patterns, insurance coverage and good reimbursement as well as the availability of centres performing PVI and the presence of competitors may lead to heterogeneous patient selection with the result that "not always the best candidates are ablated". This pattern is hardly going to change since the AF Guidelines are expanding the indications [1, 24] and more data on PVI success rates in different population groups are becoming available [25]. However, even if PVI were to be curative and equally successful in all patients with AF, without any new cases of incident AF, it would take us more than 60 years to perform PVIs in all 80 000 to 100 000 patients with AF in Switzerland based on the current prevalence and PVI rate. With the same assumptions, it would take us more than 100 years to treat all AF patients in Europe with the current ablation rates.

### Conclusion

Atrial fibrillation is the most common arrhythmia in the general population and its prevalence is increasing. While our knowledge and understanding on pathophysiology, complications and treatment of AF is constantly but slowly expanding it seems that we are still far away from reaching the goal of curing AF. With the development of pulmonary vein isolation for AF treatment, we have successfully achieved a reduction of AF burden in a significant proportion of selected patients. Whether this can apply to a broader spectrum of patient groups and whether it has an impact on mortality still remains to be shown. The number of PVIs differs significantly between European countries, and is mostly influenced by GDP, healthcare expenditures and infrastructure. Therefore, whereas AF prevalence is probably similar between European countries, available treatment differs substantially. Efforts should be made to improve the availability of different treatment modalities across all European countries.

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