



Prognosis in atrial fibrillation

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This editorial refers to 'Incidence and mortality risk of congestive heart failure in atrial fibrillation patients: a community-based study over two decades' by Y. Miyasaka *et al.*, doi:10.1093/eurheartj/ehi694

The public health importance of a disease is related to the number of people affected and to the mortality and morbidity that it causes. This metric underscores the clinical importance of atrial fibrillation (AF). AF is the most common of the supraventricular arrhythmias. Recent data suggest that there are 2.3 million individuals with AF in the USA alone.¹ Also, there is a strong association of AF with advancing age. About 1% of individuals between 60 and 69 years of age have AF but this rises to 5% for individuals older than 69 years and to 9% for individuals in their ninth decade.^{2,3} With the known, dramatic aging of the population, the number will climb to more than five million by mid-century.¹ Aging of the population alone would increase AF prevalence. There is also a suggestion that the age-adjusted prevalence of AF is also increasing,² although the underlying mechanisms have not been defined.

The clinical sequelae of AF are several, for some of which there is a clear mechanistic connection between AF and events. Stroke is likely related to stasis of blood in the non-contracting atria and occurs annually in 4.5% of un-anticoagulated patients.³ Significant progress has been made in the treatment of stroke. A series of major trials has demonstrated that anticoagulation with warfarin reduces the stroke rate by almost 70%.⁴⁻⁶ Aspirin also reduces the risk of stroke in these patients but is less effective than warfarin.⁷ Patients with rapid ventricular response to their AF may experience dyspnoea with exertion because of non-physiologic reduction in filling time. While not as ominous as stroke, the impact on exercise tolerance does have a significant effect on quality-of-life and much of the day-to-day treatment of AF revolves around optimizing rate control or maintaining sinus rhythm to minimize exertional dyspnoea and/or palpitations. In patients with other haemodynamic compromise, new onset of AF or inadequate ventricular rate control can result in heart failure.

A number of studies have found an association between AF and reduced survival. For instance, in a multivariable

analysis of data on more than 5000 Framingham patients,⁸ AF was a risk factor for reduced survival independent of stroke or transient ischaemic attack, myocardial infarction, hypertension, age, smoking, ECG diagnosed left ventricular hypertrophy, heart failure, or valvular heart disease. Interestingly, the mode of death was similar to control patients. This multivariable analysis cannot take into account the time course and severity of the various variables and did not account all of the risk factors now known to be important (such as renal function). Other studies have not found an independent association of AF and survival. Further, the prognosis of younger (less than 60 years old) AF patients without cardiovascular disease appears similar to that of the general population, suggesting that it may be the underlying disease or non-cardiac causes, rather than AF, *per se*, driving prognosis.⁹ Attempts to maintain sinus rhythm in the AFFIRM trial¹⁰ were associated with a trend towards increased mortality, rather than a reduction, but this may have been medication-related. Finally, in general, the risk factors for AF are also risk factors for major adverse cardiovascular events and distinguishing an independent effect of AF from the effect of these risk factors is difficult.

It is into this context that the study of Miyasaka *et al.*,¹¹ enters. These authors report a study of AF using data collected between January 1, 1980 and December 31, 2000 in patients residing in Olmsted County, Minnesota.¹ The specific purpose of the study was to investigate the development of heart failure in patients with diagnosed AF and determine whether there has been any change over time in the incidence of first diagnosis of heart failure in these individuals. Of the 4618 patients in that cohort identified as having a first episode of AF in the timeframe of the study, 1330 were eliminated because of heart failure diagnosed before the AF diagnosis. The 3288 subjects of the study, then, were individuals with AF but without prior heart failure. Their mean age was 71 ± 15 years and 53% were men. The mean follow-up was 6.1 years. Most of the patients (76%) presented with paroxysmal AF and 17% of these progressed to chronic AF.

Among these patients, 24% developed a first episode of heart failure and an additional 60% died during follow-up. Age was strongly associated with the development of heart failure, as was presentation with LVEF <0.50, compared with those presenting with LVEF >0.50. There was also an early clustering of first heart failure events after the diagnosis of AF. The rate of heart failure development was greater for patients presenting with chronic, rather than

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paroxysmal, AF. After adjustment for age and sex, there was no influence of calendar year of AF diagnosis on new heart failure diagnosis. Heart failure, as would be expected, was a strong predictor of mortality and, despite reductions in overall heart failure mortality resulting from drug treatment (ACE-inhibitors, β -blockers, aldosterone antagonists) demonstrated in randomized trials, there was no improvement over time in the prognosis of heart failure patients in this cohort.

What new understandings do we derive from this study? Certainly, the prognosis of these patients is poor and new onset heart failure is frequent. There appears no marked change over the years in either new heart failure onset or in survival of AF patients. A number of methodological issues are present that bears on how the results of this study might be used. The influence of medications used to treat these patients was not accessible but might have influenced the outcomes. It is, after all, treatment with ACE-inhibitors, β -blockers, and aldosterone antagonists that has been shown to improve longevity in heart failure patients. The large number of patients for whom echocardiographic examination was unavailable could introduce an important bias, depending on why the echocardiogram was unavailable. Further, cause-specific mortality is not provided. Hence, we cannot determine whether there was any change over the years in cardiovascular death that was simply insufficient to make a significant change in overall mortality. The design of this study is such that the data do not speak directly to the important question of whether AF is an independent predictor of adverse events or simply a marker of underlying severe disease. Finally, the population of Olmstead County, Minnesota, is homogeneous with respect to race and region. Nonetheless, this concern affects more the precise quantification of risk rather than the conclusions.

Central among the residual questions, is whether curing AF will reduce the risk of heart failure or cardiovascular death. More epidemiologic study would no doubt improve our understanding but the study design that would likely be the most useful in informing practice would be a randomized trial comparing curative catheter ablation to standard therapy. The timing of such a study is critically dependent on waiting long enough so that the technical aspects of the study are unlikely to dramatically change over the

course of the study. In addition, the authors identify a number of independent risk factors for the development of heart failure in the AF patients. At least some of these, such as obesity, could be studied as potential therapeutic targets of attempts to prevent the development of heart failure in the setting of AF.

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