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EDITORIAL

Incidence and outcome of atrial fibrillation: diversity throughout Europe

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This editorial refers to 'Paradoxical impact of socioeconomic factors on outcome of atrial fibrillation in Europe: trends in incidence and mortality from atrial fibrillation'†, by B.M. Al-Khayatt *et al.*, on page 847.

The incidence and prevalence of atrial fibrillation (AF) have been increasing over time and are expected to rise further due to extended life expectancy, accumulation of lifestyle-related risk factors such as obesity and diabetes mellitus, and a better survival after myocardial infarction and heart failure (HF). In addition, a better awareness of AF and improved and intensified technology for undiagnosed AF contribute to an increase in AF burden.[1–3] In addition to the incidence and prevalence of AF, the AF-associated mortality rate is increasing.[1,3] Mortality is the highest early after diagnosis of AF, being 5–6% in the first year after the initial presentation due to as yet undiagnosed underlying cardiovascular diseases and therefore far less well treated AF.[4,5] Many associated conditions contribute to incident AF as well as to AF-related mortality including increasing age, hypertension, diabetes mellitus, HF, coronary artery disease, obesity, and chronic kidney disease.[4] The incidence of AF is higher in men than in women.[3] The moment of onset of AF as well as the associated comorbidities differ between men and women. Women are older, have a higher prevalence of hypertension, valvular heart disease, and HF with a preserved ejection fraction (HFpEF), and less often have coronary artery disease.[6,7] Most data on the incidence of AF and AF-related mortality come from higher income Western countries. Recent data, however, show that there exists a large global variation in age of onset, risk factors, and concomitant diseases associated with AF and treatment of AF among different regions.[8] This may all contribute to European regional differences in incidence of AF and AF-associated mortality.

In this issue of the *European Heart Journal*, Al-Khayatt *et al.* provide us with timely information about the incidence of AF and AF-associated mortality during the last 28 years in men and women from 20 countries in Europe. Data on trends in incidence and mortality, and the incidence and mortality in 2017, are presented.[9] A comparison is made between Western and Eastern European countries, higher vs. lower gross domestic product (GDP) countries, and men vs. women. Incidence and AF-associated mortality were determined from the Global Burden of Disease (GBD) Study database, a comprehensive global programme that assesses mortality and morbidity from major diseases. These were subsequently collated by the Institute of Health Metrics and Evaluation. The countries were chosen to provide a representative sample across Europe, but only if they had a population >4 million and met the data reliability criteria. Trends were analysed using Joinpoint regression analysis; missing data were imputed using the last observation carried forward method.

Key findings include, first, that the rates of change of AF incidence are heterogeneous throughout Europe, with some nations with substantially lower rates than others. Some Western European countries experienced peaks in incidence in the middle of the study period. In contrast, most lower GDP countries showed a gradual decline in AF incidence over the years. AF incidence was consistently higher in the Western European countries as compared with Eastern European countries, and in men as compared with women. Interestingly, incidence rates were not increasing as much as might have been expected.[10]

Second, AF-related mortality is increasing more rapidly than AF incidence, especially in the higher GDP countries. As a result, AF-related mortality is significantly greater in higher GDP countries. Remarkably, mortality was not different between men and women, in

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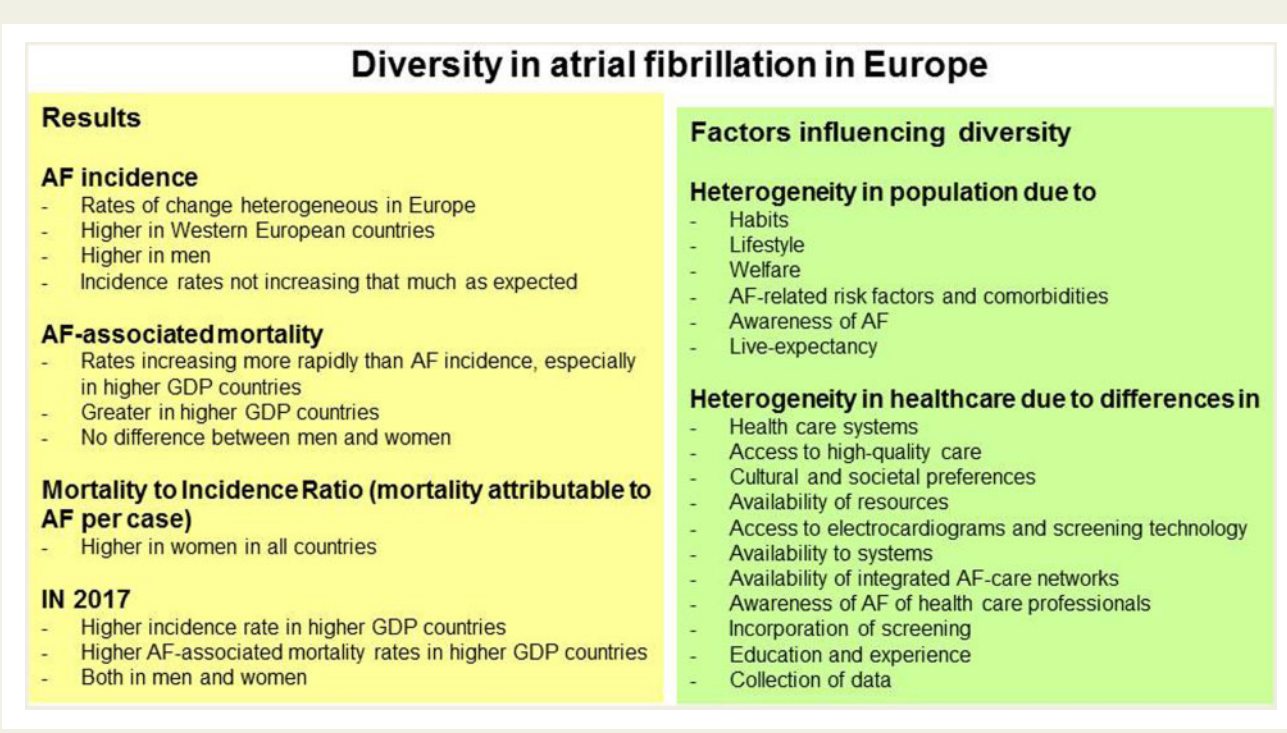

Figure 1 Diversity in atrial fibrillation in Europe.

contrast to the observed difference in AF incidence. Mortality to incidence ratios (MIRs), an approximation of mortality attributable to AF per case, however, were higher in women in all countries, with the disparity increasing the most over time in Germany. Finally, the authors show that in 2017 the countries above the mean GDP had higher incidence and mortality rates, in both men and women. The highest incidence rates were seen in Sweden for men (80.04 per 100 000) and Austria for women (52.36 per 100 000). The highest mortality rates for men and women were seen in Sweden (8.83 and 8.88 per 100 000, respectively).

The authors should be congratulated for their excellent contribution to our knowledge on the diversity of incidence of AF and AF-related mortality in Europe. The main conclusion is not unexpected, but it is interesting that both incidence and mortality are heterogeneous throughout Europe. This diversity may be explained by the fact that Europe is a non-homogeneous region. Although not many data are available, there are apparent differences between European countries with regard to habits and lifestyle, welfare, AF-related risk factors, and comorbidities. In addition, large variation exists between European countries with regard to access to high-quality care. This is a result of different healthcare systems, but also due to differences in cultural and societal preferences and availability of resources. As a result, populations in low GDP countries will have less widespread access to electrocardiograms (ECGs) and screening technology.[11] In addition to the observed differences between high and low GDP countries, heterogeneities are also observed between Western European countries and between Eastern European countries, suggesting multifactorial reasons for the observed differences (*Figure 1*). In addition to population- and healthcare-driven differences between countries, collection of patient data in the GBD database may also have contributed to the observed variations. The higher incidence in Western European countries may also have been caused by more integrated AF care networks, with increased awareness of AF both by healthcare professionals and by individuals at risk. Opportunistic and systematic screening may nowadays have been better incorporated in higher GDP countries, in this way contributing to the higher incidence rates in those countries, e.g. in Sweden.[12] Interestingly, incidence rates were not rising as much as might have been expected.[10]

A second important observation is that AF-related mortality is increasing more rapidly than AF incidence, especially in the higher GDP countries. How can that be explained? On one hand, this may be due to, as the authors suggest, a survivor effect, i.e. in higher GDP countries individuals live long enough to be diagnosed with and die due to AF. On the other hand, improved awareness and detection of AF may have contributed to higher mortality associated with AF, especially in the higher GDP countries. In a recent worldwide registry in 47 countries, of those patients who were admitted to the emergency room because of AF, 11% died within 1 year.[4] AF is a difficult to treat disease as it is not only the ECG but in particular the risk factors and comorbidities that necessitate treatment. Identification and treatment of these risk factors and comorbidities warrants a holistic, inclusive, and personalized treatment strategy. Recently, exploratory analyses suggested that in experienced centres, an integrated nurse-led care approach could reduce the risk of cardiovascular death or hospital admission compared with usual care.[13] The latter observation suggests that experience and education may improve outcome

in AF patients. This is currently under investigation in the Stroke prevention and rhythm control Treatment: Evaluation of an Educational programme of the European Society of Cardiology in AF (STEEER-AF) trial.[14] The primary objective is to determine whether a comprehensive educational programme for healthcare professionals who treat AF patients, compared with no added education, will improve guideline-adherent treatment. In addition to education, implementation of a patient-centred systematic healthcare pathway throughout Europe may contribute to improved outcome of AF in Europe. This will be studied in the EHRA-PATHS trial which aims to improve clinical practice in AF to holistic, inclusive personalized treatment strategies throughout Europe. Needless to say, access to education may vary among countries and warrants attention.

Finally, although the incidence of AF was lower in women, MIRs, an approximation of mortality attributable to AF per case, were higher in women in all countries. This obviously needs further research. So far research on sex differences in AF has been limited.[7] Risk factors and comorbidities are different; AF starts at an older age in women, but adverse events associated with therapies may also differ. The RAte Controle versus Electrical cardioversion showed that a rhythm control strategy was associated with more cardiovascular morbidity and mortality in women as compared with men. Morbidity included especially HF, thrombo-embolic complications, and serious adverse effects of antiarrhythmic drugs, the latter being predominantly sick sinus syndrome and pacemaker implantation.[6] In this respect, it is interesting to consider bradyarrhythmias more often contributing to morbidity and mortality in AF patients. Recently, the Ventricular tachyarrhythmia detection by Implantable loop recording in Patients with HFpEF (VIP-HF) with and without AF study emphasized that clinically relevant bradyarrhythmias were observed more often than expected.[15]

The present study has limitations, as also acknowledged by the authors. In particular, the process of collecting data for the database may have influenced the observed heterogeneity among countries, e.g. access to such information may be limited in lower GDP countries. Also, the Joinpoint regression analysis has some limitations. Imputing missing data using the last observation carried forward method may be likely to underestimate the true incidence and mortality rates; also missing data may not have occurred randomly, but may be more of a problem in some countries than in others.

In conclusion, this study emphasizes the diversity of incidence of AF and AF-related mortality throughout Europe. It underlines the differences in integrated AF care and access to it, and the clinical profile of AF patients in Europe. In addition, sex differences are emphasized. It is a call for more research in individual European countries and more multinational studies including Western and Eastern European countries, as is currently being done in the STEEER-AF and EHRA-PATHS trials.

Conflict of interest: none declared.

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