Atrial fibrillation: Improvement in identification and stroke preventive therapy—Data from the UK Clinical Practice Research Datalink, 2000–2012

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A B S T R A C T

Objective: To investigate recent trends in the diagnosis and treatment of atrial fibrillation.
Results: The incidence of AF in men rose from 1.274 (1.271, 1.276) per 1 000 patient years in 2000 to 1.972 (1.969, 1.975) in 2012. In women, it rose from 1.209 (1.207, 1.211) to 1.609 (1.606, 1.611). 55 647 patients with AF first diagnosed between 2000 and 2012 were included in the study. 54% of men were initiated on anticoagulation therapy in the first year following diagnosis of atrial fibrillation, compared to 45% of women (P < 0.001). This increased from 48% in men and 40% in women in 2000 to 58% in men and 52% in women in 2012.
Conclusions: Identification of atrial fibrillation has improved in recent years, as has treatment for stroke prevention. Although there has historically been a bias towards men in the treatment of stroke prevention in atrial fibrillation, this study shows that the gap has been closing in recent years. Despite this improvement, this study shows that there are still many patients with atrial fibrillation who are not treated optimally to prevent stroke.

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1. Introduction

Atrial fibrillation has been associated with a four to fivefold increase in the risk of stroke, and it has been estimated that 15% of all strokes are caused by atrial fibrillation [1]. The Echocardiographic Heart of England Screening study reported a prevalence of atrial fibrillation of 2%, increasing from 0.2% in people aged 45–54 to 8% in people aged 75 and older [2]. A UK study published in 2002 reported an incidence of AF of 1.7 per 1000 person years in the General Practice Research Database [3] (GPRD) in patients aged 40–89 in 1996.

However there has been evidence to suggest that atrial fibrillation often goes undiagnosed. Fitzmaurice et al. showed that in 50 primary care centres in the UK, diagnosis of atrial fibrillation increased by 60% when screening was introduced compared to routine clinical practice [4].

Anticoagulant and antiplatelet medication are licensed to treat patients with atrial fibrillation to reduce the risk of stroke. In 2006 NICE published guidelines [5] on the treatment of atrial fibrillation, which set out an algorithm for stratifying atrial fibrillation patients by low, moderate and high risk of stroke. The guidelines state that patients at high risk of stroke should be treated with anticoagulation therapy, and those at moderate risk of stroke should be treated with either anticoagulation or antiplatelet therapy.

The BAFTA [6] study published in 2007 showed that treating patients with anticoagulants such as warfarin is highly effective at reducing the risk of stroke in patients with atrial fibrillation, more so than antiplatelet treatment such as aspirin. The European Guidelines published in 2012 state that aspirin should not be considered as an alternative to anticoagulation therapy for stroke prevention in patients with atrial fibrillation [7].

However Gallagher et al. found in 2008 that a high stroke risk was not associated with the initiation of warfarin or aspirin treatment, contrary to current guideline recommendations [8]. Recently Cowan et al. found that between 2009 and 2012 over one third of patients who should have been treated with anticoagulation therapy were not receiving it [9].

Treatment differences between men and women with coronary heart disease have long been the subject of research. Despite the fact that heart disease is the leading cause of death amongst women in the UK [10] there has been evidence historically that women with coronary disease are treated less aggressively than men [11,12], and that there is...
a systematic bias towards men in the secondary prevention of ischemic heart disease [13].

This evidence of treatment differences between men and women extends to patients with diagnosed atrial fibrillation. In 2001 a Canadian study found that anticoagulants were underused in older women with AF relative to older men despite comparable risk profiles [14]. De Wilde et al. reported that in the UK between 1994 and 2003 treatment of atrial fibrillation with oral anticoagulants more than doubled in men (25% to 53%) and rose in women also but to a lesser extent (21% to 40%) [15].

In 2006 atrial fibrillation was added to the Quality Outcomes Framework (QOF) in England, which rewards and incentivises good practice in the way GP surgeries identify and manage patients [16]. In 2008 the GRASP-AF tool was made available nationally [17], an audit tool to help GPs identify suitable patients for anticoagulation treatment, which over 2200 practices are now using [18]. In this study, it was of interest to examine recent trends in atrial fibrillation diagnosis and treatment, to discover whether these initiatives and guidelines have improved clinical practice.

2. Methods

2.1. Data source

The CPRD (previously the GPRD) is a database of longitudinal patient primary care records, containing anonymised data on patient demographics, diagnoses, referrals, prescribing and health outcomes from over 660 GP practices in the UK. At February 2013 when the data for this study were extracted, there were 12.6 million patients of ‘acceptable’ standard in the CPRD. Validation studies have confirmed the high data quality and completeness of clinical records within the CPRD [19–22].

2.2. Population

We included patients in the study if they were registered with a practice at any point between 2000 and 2012 and met the CPRD ‘acceptable’ standard for data quality. Patients had to have been permanently registered with a CPRD practice for at least 12 months prior to their entry to the study, and have at least 12 months of follow-up. This was to ensure that every patient had at least 12 months of medical record prior to diagnosis of atrial fibrillation, and 12 months of follow-up data in which to investigate comorbidities and prescribed therapies.

We identified all patients aged 18 and over who had a first diagnosis of non-valvular atrial fibrillation between 1 January 2000 and 31 December 2011. The Read codes used by GPs to enter atrial fibrillation into a patient record are shown in Appendix A.

2.3. Analysis

Data were extracted using the online version of CPRD, and analysed using SAS® Software version 9.2. Incidence of atrial fibrillation was calculated based on our cohort and the total study population extracted from CPRD. We analysed the trend in incidence between 2000 and 2012 by sex and age.

Baseline characteristics of the cohort were summarised by sex and age group (18–64, 65–74, 75–84, 85+), including co-morbidities at the time of atrial fibrillation diagnosis. Stroke prophylaxis therapies prescribed in the year following diagnosis were summarised (British National Formulary Sections 2.8 [anticoagulants], 2.9 [antiplatelet drugs]). We have assumed that patients were treated with a medication if they received at least two prescriptions for that medication in the year following diagnosis of atrial fibrillation.

Stroke risk was calculated using the algorithm in the NICE guidance [5]. This combines patient age with risk factors including hypertension, diabetes, vascular disease, stroke, TIA, valve disease, heart failure, and impaired left ventricular function.

2.4. Follow-up

Patient data were available from the time of first diagnosis of atrial fibrillation until 31 December 2012 or when the patient transferred out of the practice or died. We examined trends in the proportion of patients treated with anticoagulation and antiplatelet therapy in the year following a diagnosis of atrial fibrillation.

3. Results

3.1. Incidence of atrial fibrillation

Fig. 1 shows how the incidence of diagnosed atrial fibrillation in CPRD has risen over the duration of the study period in both men and women (Cochran–Armitage test for trend: P < 0.0001). This increase is most marked in patients aged over 65, and in the years from 2009 onwards. In men the incidence went from 1.274 (95% confidence interval (1.271, 1.276)) per 1000 patient years in 2000 to 1.972 (1.969, 1.975) in 2012. In women it rose from 1.209 (1.207, 1.211) per 1000 patient years to 1.609 (1.606, 1.611) over the same period.

3.2. Atrial fibrillation cohort

There were 55 847 patients (29 361 men (53%) and 26 486 women) in CPRD who had a first diagnosis of atrial fibrillation between 2000 and 2011 and met our inclusion criteria. The mean age in men was 70.7 (standard deviation 12.0) and 76.3 (10.6) in women.

3.3. Treatment trends—Initiation of treatment in year following diagnosis of atrial fibrillation

54% of men were initiated on anticoagulation therapy in the first year following diagnosis of atrial fibrillation, compared to 45% of women (P < 0.0001). The proportion of patient treated with anticoagulation therapy was highest in patients aged 65–74 (62% in men, 56% in women) and lowest in patients aged 80 and above (34% in men, 27% in women). 49% of men received antiplatelet therapy compared to 53% of women (P < 0.0001).

Fig. 2 shows the trend over time in the proportion of men and women treated with anticoagulant and antiplatelet therapy in the first year following diagnosis of atrial fibrillation. The percentage of patients prescribed neither anticoagulant nor antiplatelet therapy has been decreasing year on year since 2000. The proportion of patients prescribed anticoagulant therapy has increased in both men and women, and the gap between the sexes has decreased year on year, from 48% in men and 40% in women in 2000 to 58% in men and 52% in women in 2012. The proportion of patients prescribed both anticoagulant and antiplatelet therapy in the year following diagnosis has increased, while the
proportion of patients prescribed antiplatelet therapy only rose slightly up until 2009 after which it has been decreasing.

3.4. Treatment by stroke risk

Fig. 3 shows the proportion of patients treated with anticoagulation and antiplatelet therapy in the first year following atrial fibrillation diagnosis, by risk of stroke. This shows that in both men and women the proportion of patients treated with anticoagulation therapy in the first year following atrial fibrillation diagnosis has increased since 2000, and the proportion of patients not treated for stroke prevention has decreased. These increases are more evident in patients regarded as high or moderate risk of stroke using the NICE algorithm [14] than in patients at low risk.

4. Conclusions

4.1. Main results

This study found an increase in the rate of diagnosis of atrial fibrillation since 2000, with a sharper incline starting in 2009. This is in contrast to studies recently published on US patients which showed a constant rate of atrial fibrillation diagnosis from 1993 to 2007 [23], and even a decline in the rate of atrial fibrillation diagnosed at hospital discharge between 2005 and 2009 [24].

It is likely that this difference in trend is caused by an increase in the identification of atrial fibrillation in the UK in recent years. It has been reported that atrial fibrillation is a condition which has frequently been under diagnosed [4]. Recent initiatives in the UK to tackle this include the NICE guidance published in 2006 [5] and the GRASP-AF initiative [18]. Our results suggest that these initiatives may be beginning to produce results.

Studies in the UK have shown under-treatment of patients for stroke prevention in atrial fibrillation [8,9]. The addition of atrial fibrillation to the QoF in 2006 incentivised GPs in England to treat patients with anticoagulation or antiplatelet therapy. This study, which analyses treatment by year over a 12 year period, shows that although there are still patients who should be receiving anticoagulation therapy who are not, the proportion of patients who do receive it has been increasing. The recent change to the QoF measures for atrial fibrillation in 2012 which encourages GPs to treat patients at a high risk of stroke with anticoagulation therapy should address this further [25].

The evidence of an increase in the proportion of patients treated with anticoagulant therapy in patients at high or moderate risk of stroke which is not seen in patients at low risk of stroke suggests that the risk stratification of patients has also been improving. Not only are more patients being treated for stroke prevention, but also these additional patients are the patients who should be receiving it. However there is evidence that the rate of prescribing of antiplatelet therapy has increased over the study period too, and there are also a group of patients who are still not treated for stroke prevention, which suggests that there are still patients who are not being treated optimally.

Despite some suggestion that women with atrial fibrillation are at higher risk of stroke than men [9] NICE concludes that as there is no biological plausibility for a difference in stroke risk between the sexes, female patients should not be considered at greater risk than men [10]. This suggests that for any given set of comorbidities, comediations and stroke risk factors, female patients should have an equal likelihood of being anticoagulated to that of male patients. However, past evidence highlights that this is not the case [17].

Fig. 2. Percentage of patients prescribed stroke prevention therapies in year following atrial fibrillation diagnosis.
The results of this study show a marked improvement in this bias. Between 2000 and 2012 the gender gap in treatment with anticoagulation in patients with atrial fibrillation has been closing, to a point where the difference is minimal.

4.2. Limitations

The CPRD contains prescription data for therapies prescribed in primary care, but it does not include any prescribed in secondary care. Therefore we may fail to identify where patients have been treated if they were prescribed the medication only in secondary care. This issue should be minimal, because even if patients are initiated on stroke prevention treatment in secondary care, the prescription will almost exclusively be continued on this therapy in primary care, so we would identify this.

5. Conclusions

This study shows evidence that identification of atrial fibrillation has increased between 2000 and 2012, probably due to improved awareness of the condition. NICE guidance and the GRASP-AF initiative appear to have had an effect, driving improvements in treating patients for stroke prevention. The gender bias in stroke prevention treatment seen in previous studies, with men being more likely to be treated than women, still exists but the gap has been closing in recent years. The proportion of patients treated with anticoagulation therapy has increased, but there are still patients with atrial fibrillation who are not treated optimally to prevent stroke.

Contributors

AS contributed to the planning and design of the study, performed the data analyses, and helped write the manuscript. MC advised regarding the study design and data analyses, and wrote the manuscript. He is the guarantor for the study.

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Competing interests

Professor Cowie provides consultancy advice to a number of pharmaceutical companies, including Boehringer Ingelheim and Bayer, both of which manufacture oral anticoagulant therapy. He holds no stocks or shares in any such company. Anna Scowcroft is an employee of Boehringer Ingelheim.

Approval

The protocol for the COSMOS study (Comparing the Occurrence of Stroke and anticoagulation treatment between Men and women diagnosed with Atrial Fibrillation) has been approved by the Independent Scientific Advisory Committee (ISAC) at the Medicines and Healthcare products Regulatory Agency (MHRA). (Protocol number 10_187R)
Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijcard.2013.11.086.

References