

Oral anticoagulation in hospitalised patients with newly diagnosed AF: a story of too little, too late

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Current guidelines make no recommendations regarding the strategy for initiation of oral anticoagulant (OAC) therapy in patients who are hospitalised with newly diagnosed atrial fibrillation (AF). This was a single-centre, retrospective, observational study that included patients admitted in 2013 with newly diagnosed AF (ICD-10 I48). There were 234 patients hospitalised with newly documented AF. The mean CHA₂DS₂-VASC score was 3.8: 201 (86%) patients had a CHA₂DS₂-VASC score ≥ 2 . Out of the 179 patients considered for anticoagulation, only 115 patients were intended to receive OAC therapy: 56 (49%) as an inpatient and 59 (51%) as an outpatient, either by anticoagulation clinic or primary care. In the outpatient group, only 41 patients (69%) were actually initiated on OAC, with a mean time delay of 10 and 93 days in anticoagulation clinic and primary care group, respectively. During mean follow-up of 194 days, there were two strokes in the outpatient group in patients intended to start anticoagulation but did not (2/59), while no episodes occurred in the inpatient group.

In summary, only 82% of patients with newly diagnosed AF and CHA₂DS₂-VASC score ≥ 2 were referred for initiation of OAC, and still fewer actually received such therapy. Outpatient anticoagulation is associated with poor uptake and significant delays.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a reported worldwide prevalence of 0.6% in men and 0.4% in women.¹ AF is independently associated with a five-fold increased

rate of stroke, which is comparable with the risk seen in patients with three or more other stroke risk factors.^{2,3} Furthermore, strokes related to AF are associated with higher rates of disability and mortality than other strokes.^{4–6} The cost of AF-related strokes in the UK is estimated to be around £750 million per year.⁷

AF-related stroke is thought to be secondary to thromboembolism from the left atrium to the cerebral circulation. Oral anticoagulation (OAC) with warfarin and novel oral anticoagulants (NOACs) reduces the risk of AF-related stroke by about two-thirds.^{8,9} Clinical guidelines recommend that patients with AF should undergo formal risk stratification for stroke and those without contraindications should be treated with OAC.¹⁰

AF is commonly first diagnosed in hospitalised patients. In this patient group, OAC can be initiated either during the inpatient stay or following hospital discharge. There are no published data comparing these two strategies in relation to time to initiation of OAC, length of hospital stay, patient outcomes, or cost. Nor do current clinical guidelines specify the preferred strategy for initiation of OAC in hospitalised patients with newly diagnosed AF.

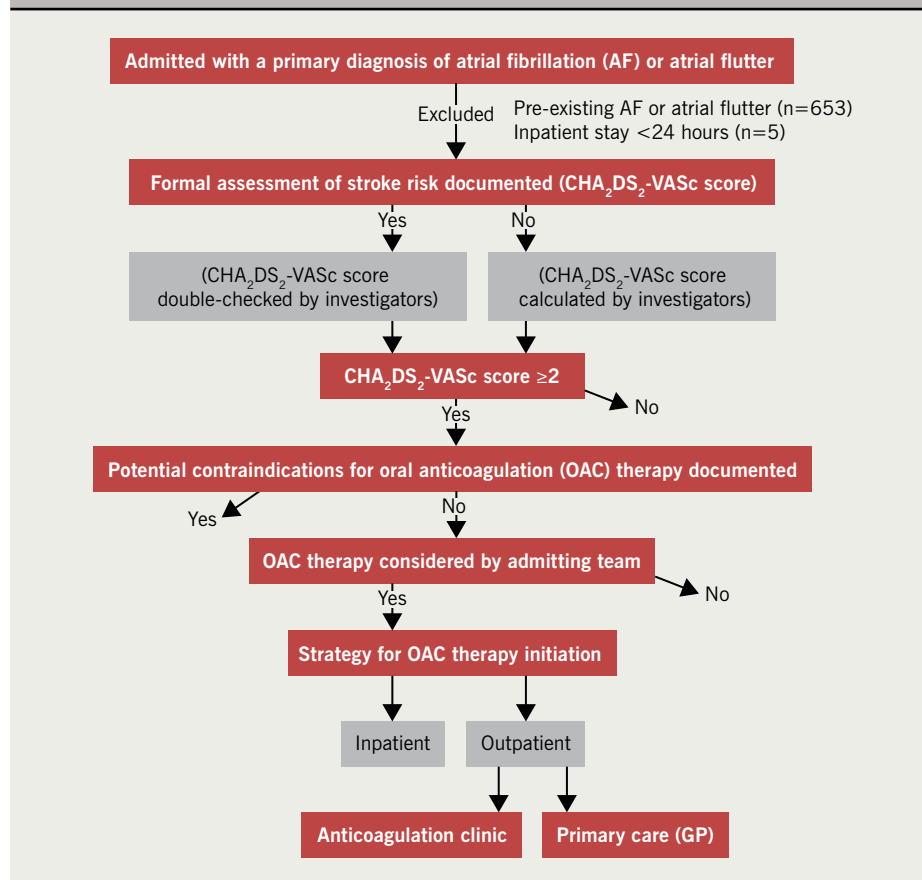
This study described the strategies used to initiate OAC in hospitalised patients with newly diagnosed AF, and the rate of uptake and time delay in initiating OAC in this group of patients. In addition, we aimed to determine whether there were factors that influenced the strategy used.

Method

This was a single-centre, observational, cohort study based in a district general hospital in London. The study cohort comprised all patients admitted between 1 January to 31 December 2013 for more than 24 hours, with one of the primary diagnoses being newly documented AF or atrial flutter. Patients were identified retrospectively using

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Figure 1. The data collection process



t-test, and the Mann Whitney U-test was used to compare non-normal data. Categorical variables were compared using the Z-test. Odds ratios and relative risks were also calculated. All analyses were conducted using SPSS statistical software. A *p* value <0.05 was considered to be significant. This study was approved as an audit/quality improvement project.

Results

In the one-year study period, 234 patients were newly diagnosed with AF or atrial flutter during a hospital admission >24 hours. Their baseline characteristics are shown in **table 1**. Two hundred and one (86%) patients had a CHA₂DS₂-VASc score ≥2, eight patients had a CHA₂DS₂-VASc score of 1 and 25 patients had a CHA₂DS₂-VASc score of 0.

Formal assessment of stroke risk

CHA₂DS₂-VASc scores were documented in the medical records of 202 (86%) of 234 patients. Among the 201 patients in whom we determined that OAC was clearly indicated, CHA₂DS₂-VASc scores were documented in 179. In the remaining 22 patients, there was no documentation to suggest that stroke risk had been assessed or that OAC therapy had been considered. Our retrospective assessment of stroke risk showed that these patients had a mean CHA₂DS₂-VASc score of 3.8. None of these patients were commenced on OAC therapy. Neither were any of the 33 patients with a CHA₂DS₂-VASc score ≤1.

Initiation of oral anticoagulation

Among the 179 patients who were considered for OAC therapy, 61 had documented contraindications or declined therapy (**table 2**). Three further patients were not anticoagulated (inappropriately) because of the paroxysmal nature of their AF. The remaining 115 patients were intended to receive OAC: 56 were initiated as an inpatient (49%) and 59 (51%) were referred for outpatient initiation (**table 1**).

Those with CHA₂DS₂-VASc scores above the mean (≥4) were not more likely to have inpatient OAC compared with those below the mean (odds ratio [OR] 0.72; 95% confidence interval [CI] 0.39–1.34; *p*=0.31). Cardiologist compared with non-cardiologist was not more likely to use inpatient initiation (OR 1.08;

discharge diagnosis coding data I48 (AF or atrial flutter) according to the World Health Organization's International Classification of Diseases 10th revision (ICD-10) coding system. We did not differentiate between AF and atrial flutter because the indications for OAC are the same for both arrhythmias. **Figure 1** demonstrates the data collection process. Pre-existing AF was identified from previous discharge diagnosis coding data, paper health records, or from electrocardiogram (ECG) or Holter-monitor reports. In line with current clinical guidelines, we considered that there was a clear indication for OAC in patients whose CHA₂DS₂-VASc score was ≥2. In the outpatient group, we identified the rate of uptake, time delay and reason(s) for lack of initiation of therapy through directly contacting GPs and anticoagulation clinics. Duration of hospital stay and the specialty team in charge of the patient's care were recorded. The occurrence of cerebrovascular and major bleeding events during a mean follow-up of around six months after hospital discharge

were recorded in all patients. Major bleeding events were defined as bleeding that required invasive intervention such as endoscopic or surgical procedures and/or treatment with blood products.

Clinical information was obtained from paper and electronic health records. The following baseline clinical characteristics were recorded: age, sex, hypertension, diabetes mellitus, congestive heart failure (CHF), ischaemic heart disease (IHD), peripheral vascular disease (PVD), and previous stroke. CHF was defined by prior history or imaging evidence of a left ventricular ejection fraction <40%. IHD was defined by a history of angina, myocardial infarction, myocardial revascularisation, or by use of anti-anginals. PVD was defined by self-reported lower limb claudication or a history of lower limb arterial angioplasty or bypass surgery.

Statistical analysis

Continuous variables with a normal distribution were compared using the student

Table 1. Baseline patient cohort characteristics

	Total (n=234)	Inpatient (n=56)	Outpatient (n=59)	p value
Mean age, years (range)	75 (22–99)	72.8 (45–97)	77.1 (32–94)	0.07
Females	125 (53.4%)	32 (57.1%)	34 (57.6%)	0.11
Diabetes mellitus	57 (24%)	13 (23%)	22 (37%)	0.10
Hypertension	169 (72%)	46 (82%)	51 (86%)	0.86
Ischaemic heart disease	47 (20%)	11 (20%)	19 (32%)	0.13
Congestive heart failure	90 (39%)	26 (46%)	24 (41%)	0.54
Peripheral vascular disease	9 (4%)	1 (2%)	2 (3%)	0.59
Stroke	37 (16%)	11 (20%)	13 (22%)	0.75
Mean CHA ₂ DS ₂ -VASc score	3.8 (95% CI 2.7–5.0; SD 1.4)	3.7 (95% CI 3.3–4.1; SD 1.2)	4.0 (95% CI 3.6–4.4; SD 1.6)	0.23
Median hospital stay (days)	6 (range 1–75; SD 11.6)	7 (range 1–75; SD 12.8)	6 (range 1–63 days; SD 9.9)	0.42

Key: CI = confidence interval; SD = standard deviation

Table 3. The number of patients that were initiated on oral anticoagulant (OAC) therapy as an outpatient, the time taken, the reason(s) for lack of initiation and the number of cerebrovascular events during follow-up

	Outpatient (n=59)	Anticoagulation clinic (n=32)	Primary care (n=27)
Initiated OAC therapy	41 (69%)	29 (91%)	12 (44%)
Reason(s) for lack of initiation of OAC therapy	–	Administrative error (n=3)	Failure to attend appointment (n=4) Not referred for initiation (n=4) GP not aware of the need for OAC (not receiving or lack of information on discharge summary; n=7)
Mean time taken for initiation of OAC therapy (range)	33 days (2–207)	10 days (2–48)	93 days (16–207)
Cerebrovascular events	2 (3.4%)	0	2 (7.4%)

95% CI 0.58–2.00; $p=0.81$), however, they were more likely to utilise anticoagulation clinics rather than GPs for outpatient OAC (OR 13.67; 95% CI 6.14–30.38; $p<0.0001$).

Initiation of OAC as an outpatient was associated with poor uptake, with 18 patients failing to commence on therapy, and mean delays of 33 days as a whole, and 93 days in the primary care arm (table 3). Those that failed to be initiated on OAC had a mean and maximum CHA₂DS₂-VASc score of 4.6 (range 2–6; standard deviation [SD] 1.4) and 6, respectively. Those patients with a scheduled (n=25) versus non-scheduled

(n=4) anticoagulant clinic appointment were commenced on OAC within a mean of six and 37 days, respectively.

Clinical events during mean follow-up of 194 days (range 76–365, table 3)

In the two patients (CHA₂DS₂-VASc score of 4) that suffered a stroke, OAC therapy was planned but was not started due to, either the GP not receiving the discharge summary, or failing to refer the patient for initiation of OAC therapy. There were no reported episodes of major bleeding among the patients who were commenced on OAC.

Table 2. Contraindications to oral anticoagulation

Contraindication	Number of patients (%)
Intracranial bleeds	4 (6.6%)
Gastrointestinal bleeds	13 (21.3%)
Unexplained microcytic anaemia	4 (6.6%)
Recurrent falls	18 (29.5%)
Poor medication compliance	2 (3.3%)
Receiving end-of-life care	6 (9.8%)
Active chemotherapy	1 (1.6%)
Patient declined therapy	13 (21.3%)
Total	61 (30.3%)

Discussion

Stroke is a potentially devastating condition, which is associated with rates of death and major disability of 7–10%¹¹ and 10–12%¹² respectively. The efficacy of OAC in preventing AF-related strokes is well established. Despite this, only 82% of these patients in our cohort with CHA₂DS₂-VASc score ≥ 2 , and no contraindications, were referred for OAC, and still fewer (69% of those in whom OAC was indicated) were initiated on such therapy.

These data add to the considerable weight of evidence, which shows that OAC is underused in patients with AF,¹¹ irrespective of the way in which they present. Patients are only likely to receive OAC if their increased risk for stroke is recognised. In this study, 32 (14%) of 234 patients did not have a CHA₂DS₂-VASc score documented in their medical records. Among the 201 patients in whom OAC was clearly indicated, 22 (12%) patients did not undergo formal risk stratification for stroke. This emphasises the importance of education.

Among the patients who were considered for OAC, more than one-third were felt to have contraindications to therapy, with recurrent falls or gastrointestinal bleeding being most common, or the patient declined therapy. Many of the contraindications were relative ones, which do not preclude OAC if the stroke risk is high.^{13–15} A study has demonstrated that the calculated risk of subdural haematoma from falling was such that a patient with a

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5% annual stroke risk for AF would need to fall 295 times in a year for the fall risk to outweigh the stroke reduction benefit of OAC.¹⁶ Among patients who are at increased risk of bleeding, clinicians appear more ready to prescribe aspirin than OAC therapy despite its limited efficacy for stroke prevention and a similar rate of major bleeding compared with OAC.^{8,17,18}

Outpatient OAC therapy was associated with a high failure rate, and the main explanation for this, in more than 56% of cases, was poor discharge communication from secondary to primary care and administrative errors. Outpatient initiation of OAC therapy was also associated with considerable delays to initiation of treatment (mean 33 days). Patients who were dependent upon their GP to organise initiation of OAC therapy waited an average of three months before they were initiated on OAC therapy. By contrast, those who left hospital with a scheduled anticoagulation clinic appointment waited a significantly shorter time to start therapy (six days). It is difficult to see the rationale for introducing an additional step in the clinical pathway by asking the GP to organise OAC therapy. It is, thereby, the discharging team's responsibility to organise outpatient anticoagulation. Interestingly, patients who had a CHA₂DS₂-VASC score above the mean were no more likely to be initiated on OAC as an inpatient than other patients (OR 0.72; 95% 0.39–1.34; *p*=0.31).

In our cohort, two patients that were intended to initiate OAC therapy but did not, suffered an ischaemic stroke. Inpatient OAC therapy initiation negates the possibility that it will

not be started later, but there is a fear that the time to achieve therapeutic international normalised ratios (INRs) will prolong hospital stay. However, we have demonstrated that this approach does not cause longer hospital stays compared with outpatient initiation (median 6 vs. 7 days; *p*=0.42) and it has been reported that therapeutic INRs can be achieved within this timeline.^{19,20}

Three NOACs are approved by the National Institute for Health and Care Excellence (NICE) for the prevention of non-valvular AF-related strokes.²¹ Despite faster onset of action compared with warfarin, in our centre, their use is restricted to those either allergic to warfarin or who have erratic INRs, and they are not widely prescribed. Indeed, in our cohort, only three patients were commenced on a NOAC. Their wider use might reduce the length of stay through obviating the need to achieve therapeutic INRs. A third approach, which was not used in this study, is to use a low molecular weight heparin in discharged patients until a therapeutic INR is achieved.

Limitations

The retrospective design of this study makes it more prone to bias than prospective studies. The composition of the study population, for example, was dependent upon the accuracy of hospital discharge coding data. Its accuracy for the positively identified cases was validated by a review of the medical records of a random subgroup of 80 patients among whom the discharge code I48 was correct in 79 (99%) cases. However, it is not known how many hospitalised patients with AF were not given the correct discharge code and were, consequently, not included in the study population.

Key messages

- Formal risk stratification for stroke is still not performed in all patients with atrial fibrillation (AF)
- A large group of patients with AF where oral anticoagulation (OAC) is indicated still fail to receive such therapy
- Inpatient OAC does not result in longer hospital stays
- Outpatient OAC is associated with poor uptake and significant delays

In this study, we described physician-reported contraindications to OAC but we did not record whether bleeding risk was formally assessed using a tool such as the HAS-BLED score.

Conclusion

In this single-centre study of hospitalised patients with newly diagnosed AF, only 82% of patients with a CHA₂DS₂-VASC score ≥ 2 were referred for initiation of OAC, and still fewer actually received treatment. Outpatient referral for OAC therapy was associated with poor uptake and significant delays. Patient pathways that maximise treatment uptake and minimise delays are required ●

Conflict of interest

None declared.

Editors' note

See also the editorial on page 87 of this issue.

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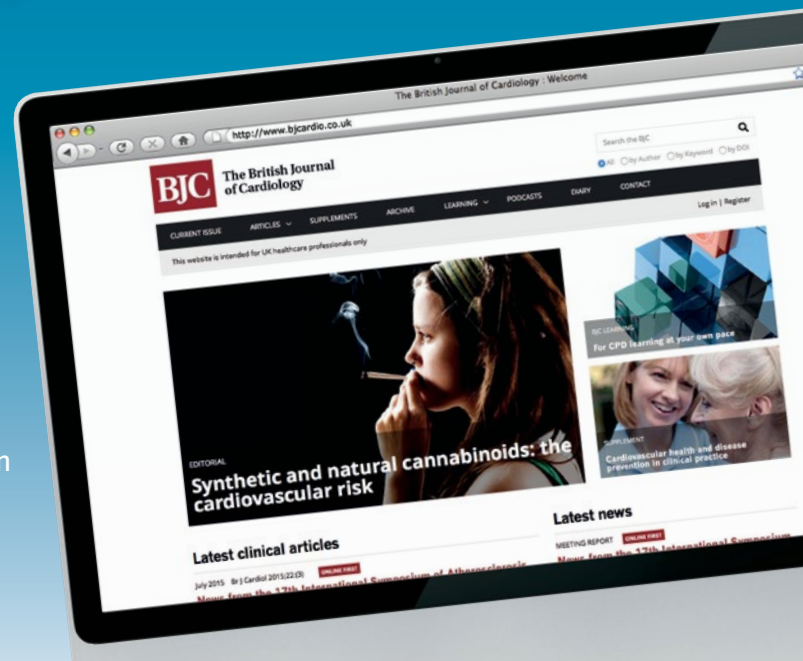
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