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# BMJ Open Evaluation of anticoagulation status for atrial fibrillation on early ischaemic stroke outcomes: a registry-based, prospective cohort study of acute stroke care in Surrey, UK

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## ABSTRACT

**Objective** The relationship of anticoagulation therapies with stroke severity and outcomes have been well documented in the literature. However, none of the previous research has reported the relationship of atrial fibrillation (AF)/anticoagulation therapies with urinary tract infection (UTI), pneumonia and length of stay in hyperacute stroke units (HASUs). The present study aimed to evaluate AF and anticoagulation status in relation to early outcomes in 1387 men (median age=75 years, IQR=65–83) and 1371 women (median age=83 years, IQR=74–89) admitted with acute ischaemic stroke to HASUs in Surrey between 2014 and 2016.

**Methods** We conducted this registry-based, prospective cohort study using data from the Sentinel Stroke National Audit Programme. Association between AF anticoagulation status with severe stroke on arrival (National Institutes of Health Stroke Scale score  $\geq 16$ ), prolonged HASU stay (>3 weeks), UTI and pneumonia within 7 days of admission, severe disability on discharge (modified Rankin Scale score=4 and 5) and inpatient mortality was assessed by logistic regression, adjusted for age, sex, hypertension, congestive heart failure, diabetes and previous stroke.

**Results** Compared with patients with stroke who are free from AF, those with AF without anticoagulation had an increased adjusted risk of having more severe stroke: 5.8% versus 14.0%, OR=2.4 (95% CI 1.6 to 3.6,  $P<0.001$ ), prolonged HASU stay: 21.5% versus 32.0%, OR=1.4 (1.0–2.0,  $P=0.027$ ), pneumonia: 8.2% versus 19.1%, OR=2.1 (1.4–2.9,  $P<0.001$ ), more severe disability: 24.2% versus 40.4%, OR=1.6 (1.2–2.1,  $P=0.004$ ) and mortality: 9.3% versus 21.7%, OR=1.9 (1.4–2.8,  $P<0.001$ ), and AF patients with anticoagulation also had greater risk for having UTI: 8.6% versus 12.3%, OR=1.9 (1.2–3.0,  $P=0.004$ ), pneumonia: 8.2% versus 11.5%, OR=1.6 (1.1–2.4,  $P=0.025$ ) and mortality: 9.7% versus 21.7%, OR=1.9 (1.4–2.8,  $P<0.001$ ). The median HASU stay for stroke patients with AF without anticoagulation was 10.6 days (IQR=2.8–26.4) compared with 5.8 days (IQR=2.3–17.5) for those free from AF ( $P<0.001$ ).

**Conclusions** Patients with AF, particularly those without anticoagulation, are at increased risk of severe stroke,

## Strengths and limitations of this study

- The strengths of the present study include its large homogenous cohort of patients derived from one of the largest National Health Service regions in England.
- The analysis was robustly adjusted for age and sex, as well as major chronic conditions known to associate with stroke including hypertension, congestive heart failure, diabetes and previous stroke.
- The data were collected by healthcare providers for the patients using national Sentinel Stroke National Audit Programme protocol.
- Although data are derived only from Surrey, it is likely to be representative of the rest of the UK as stroke prevalence is similar to that of the UK.
- The study did not collect information on types of oral anticoagulants and international normalised ratio. Information on the duration of anticoagulation treatment for individual patients was also not available, but it is likely to be closely related to their age.

associated with prolonged HASU stay and increased risk of early infection, disability and mortality.

## INTRODUCTION

Each year, about 6.7 million people die of stroke worldwide, accounting for 11.9% of all deaths.<sup>1</sup> Stroke results in adverse health consequences including physical disability and cognitive impairment,<sup>2–4</sup> which imposes enormous burdens on patients, their carers as well as social and healthcare systems.<sup>5 6</sup>

Patients with existing comorbidities such as diabetes and cardiovascular diseases including coronary heart disease, poorly controlled hypertension or congestive heart failure



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(CHF) have an increased risk of stroke, but atrial fibrillation (AF) remains the biggest risk factor.<sup>7 8</sup> Although outcomes for stroke patients have improved significantly in the UK since the introduction of organised hyperacute stroke unit (HASU) care provided by multidisciplinary teams,<sup>9 10</sup> the elderly and those who have chronic health conditions continue to have increased risk of mortality and disability, as well as time to recovery requiring longer stay in hospital after a stroke.<sup>11–13</sup> The relationship of anticoagulation therapies with stroke severity and outcomes have been well documented in the literature.<sup>14–16</sup> However, none of the previous research has reported the relationship of AF/anticoagulation therapies with urinary tract infection (UTI), pneumonia and length of stay in HASU.

The present study aimed to evaluate the relationship of patients with AF and their anticoagulation status on the severity of stroke on admission, length of stay in HASU, UTI and pneumonia within the first week in hospital, early disability on discharge and inpatient mortality.

## METHODS

### Study design, patients and setting

We conducted this registry-based, prospective cohort study using data from the Sentinel Stroke National Audit Programme (SSNAP), which is the national register of stroke care in England and Wales. Data were collected prospectively from the time of admission up to 6 months after stroke and validated by stroke teams and entered into the SSNAP database via a secure web interface. These data comprise clinical characteristics and care quality of patients admitted to all acute care hospitals in England and Wales with acute ischaemic stroke or primary intracerebral haemorrhage.<sup>12</sup> We used an anonymised extract of a total of 3309 patients from Surrey, a relatively stable and homogenous population, who were admitted to four HASUs within the county (one of the largest National Health Service (NHS) regions in the England). The hospitals, Ashford and St Peter's (n=1038), Frimley Park (n=1010), Royal Surrey County (n=612) and Epsom (n=649), were surveyed between January 2014 and February 2016. Twenty-two patients were admitted twice, and two patients were admitted three times. For the purpose of analysis, data from the first admission for these 24 patients who were admitted multiple times were used.

SSNAP has approval from the Confidentiality Advisory Group of the Health Research Authority to collect patient data under section 251 of the NHS Act 2006. No additional ethical approval was sought.

### Sociodemographic factors and medical history

Data were collected for sociodemographic factors including age at arrival, sex and ethnicity, as well as medical history including AF, hypertension, CHF, diabetes mellitus, previous stroke and drug history. In addition, details of new-onset AF cases as well as UTI and

pneumonia acquired in hospital within 7 days of admission were documented by the stroke team comprising consultants and stroke nurse specialists, including anticoagulation treatment from the point of admission to discharge.

### Diagnosis of stroke and severity

Stroke was diagnosed based on clinical presentation and brain CT scan as guided by the National Institute for Health and Care Excellence.<sup>17</sup> The severity of stroke symptoms was assessed by the National Institutes of Health for Stroke Scale (NIHSS) with score range from no symptoms to severe stroke symptoms (NIHSS score=0 to 42).

### Disability and mortality

Degree of disability or dependence in daily activities were assessed by a modified Rankin Scale (mRS), ranging from no symptoms to severe symptoms (mRS score=0 to 5) and mortality (mRS score=6).

### Categorisation of variables

Dichotomisation was applied for hypertension, CHF and diabetes according to the presence of history of the condition or not while age was dichotomised at the median value (<79 and ≥79 years). AF and anticoagulation status were categorised into four groups: free from AF, AF with anticoagulation, AF without anticoagulation and AF unsuitable for anticoagulation. Severity of stroke and disability were dichotomised into two groups: no symptoms to moderate symptoms (NIHSS score <16 and mRS score <4) and moderately severe to severe (NIHSS score ≥16 and mRS score=4 and 5). Prolonged stay in HASU was defined as patients who stayed in a HASU >3 weeks (upper fourth quartile of length of stay).

### Statistical analysis

Of the 3309 patients collected in the database, we analysed 2758 (83.3%) patients presented with ischaemic stroke and the remaining 518 (15.7%) patients with haemorrhagic stroke, and 33 (1.0%) patients who were unspecified were excluded. The frequency of patients with AF using anticoagulation before developing an ischaemic stroke was assessed by cross-tabulation and  $\chi^2$  tests. Most variables had no missing data, which were handled in analysis using a 'listwise deletion of missing data' approach.<sup>18</sup> Independent t-tests were performed to compare differences between two groups and analysis of variance (ANOVA) between three or more groups, with post hoc analysis where applicable. Multivariable logistic regression was performed to assess the risk of moderately severe to severe stroke on arrival and disability on discharge, inpatient mortality after stroke and prolonged stay in HASU (dependent variables) from comorbidities including AF, hypertension, CHF, diabetes and previous stroke (independent variables). Two logistic regression models were conducted: the first model was unadjusted, and the second was adjusted for age, sex and comorbidities. Analyses were performed using SPSS V.22.0. The null hypothesis was rejected when  $P < 0.05$ .

**Table 1** Distribution of 2758 patients admitted with acute ischaemic stroke to hospitals in Surrey between January 2014 and February 2016

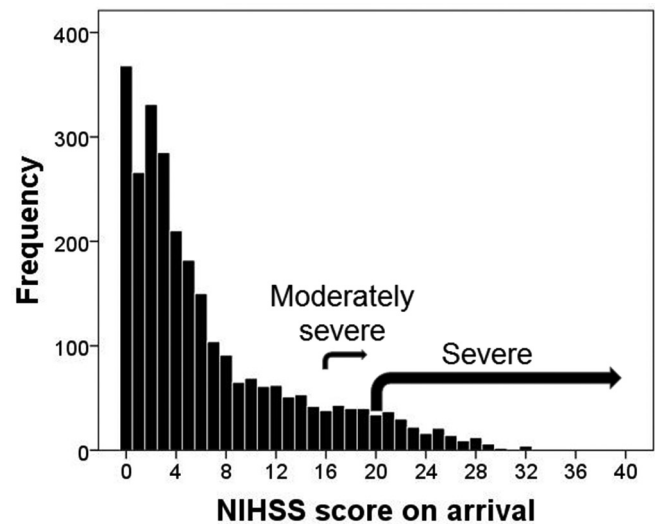
	Median	IQR
Age of men (years)	75.0	65.0–83.0
Age of women (years)	83.0	74.0–89.0
	n	Proportion (%)
Men:women	1387:1371	50.3:49.7
Caucasian: mixed race, black, Asian and other ethnic populations: not stated	2544:180:34	92.2:6.6:1.2
First stroke: recurrent stroke	2123:635	77.0:23.0
AF	564	20.4*
AF with anticoagulation	230	40.8†
AF without anticoagulation	260	46.1†
AF not suitable for anticoagulation	74	13.1†
Hypertension	1446	52.4
CHF	171	6.2
Diabetes	463	16.8
Stroke severity on arrival		
No stroke symptoms (NIHSS score: 0)	368	13.3
Minor stroke (NIHSS score: 1–4)	1092	39.6
Moderate stroke (NIHSS score: 5–15)	930	33.7
Moderate to severe stroke (NIHSS score: 16–20)	195	7.1
Severe stroke (NIHSS score: 21–42)	173	6.3
Modified Rankin Scale (mRS) on discharge		
No symptoms (mRS score: 0)	682	24.7
No significant disability (mRS: 1)	489	17.7
Slight disability (mRS score: 2)	377	13.7
Moderate disability (mRS score: 3)	362	13.1
Moderately severe disability (mRS score: 4)	284	10.3
Severe disability (mRS score: 5)	130	4.7
Dead (mRS score: 6)	333	12.1

\*Proportion relative to the total number of all patients in the present study (n=2758).

†Proportion relative to the number of patients with AF (n=564). AF, atrial fibrillation; CHF, congestive heart failure; mRS, modified Rankin Scale; NIHSS, National Institutes of Health for Stroke Scale.

## RESULTS

Admissions for stroke were almost equally distributed between men (50.3%) and women (49.7%), with the onset of the first stroke 6.5 years (95% CI 5.5 to 7.5,  $P<0.001$ ) earlier in men. **Table 1** shows that there were 77.0% of patients presented with first stroke and 23.0% with recurrent stroke. Most patients were white Caucasians (92.2%) with the remaining 6.6% comprises mixed



**Figure 1** Distribution of patients against severity of stroke on admission based on NIHSS score. NIHSS, National Institutes of Health for Stroke Scale.

race, black, Asian and other ethnic populations and 1.2% not stated. On arrival, 546 (20.4%) patients had a history of AF, in whom 40.8% were treated in the community with an anticoagulant, while 46.1% were untreated, although 13.1% had been considered for anticoagulation and deemed unsuitable by their healthcare providers. Also on arrival, 7.1% of patients had moderate to severe stroke symptoms (NIHSS score=16–20) and 6.3% had severe symptoms (NIHSS=21–42). The remainder had no symptoms (13.3%, NIHSS=0), minor (39.6%, NIHSS=1–4) or moderate (33.7%, NIHSS=5–15) symptoms; a more detailed analysis of NIHSS scores is shown in **figure 1**. On discharge, 10.3% and 4.7% of the original patients, respectively, had moderately severe (mRS score=4) or severe (mRS score=5) symptoms. The rate of inpatient mortality was 12.1% (**table 1**).

Baseline characteristics of patients in different categories of AF and anticoagulation status are shown in **table 2**. The median age of patients without AF were 77 years old, while those with AF were between 83 and 84 years old. Hypertension, CHF and moderate to severe stroke were more commonly observed among patients with AF than those free of AF.

Patients free from AF had significantly less severe stroke on admission as reflected by a lower NIHSS score ( $F=21.8$ ,  $P<0.001$ ) and disability on discharge as indicated by a lower mRS score ( $F=20.9$ ,  $P<0.001$ ) than patients with AF of any anticoagulation status (with anticoagulation, without anticoagulation or unsuitable for anticoagulation in the community) (**figure 2**). ANOVA with post hoc analysis by least significant difference tests showed that NIHSS score on arrival (**figure 2A**) and mRS on discharge (**figure 2B**) were significantly lower ( $P<0.01$ ) for those free from AF compared with any of the other three groups of patients with AF (with anticoagulation, without anticoagulation or unsuitable for anticoagulation). The NIHSS score for those with AF who were treated with anticoagulant was



**Table 2** Baseline characteristics of patients admitted with ischaemic stroke according the AF and anticoagulation status

	Non-AF (n=2194)		AF with anticoagulation (n=230)		AF without anticoagulation (n=260)		AF not suitable for anticoagulation (n=74)	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (years)	77.0	66.0–85.0	83.0	77.0–88.0	84.0	77.0–90.0	84.0	78.8–88.2
	n	%	n	%	n	%	n	%
Men:women	1133:1061	51.6:48.4	111:119	48.3:51.7	106:154	40.8:59.2	37:37	50.0:50.0
Hypertension	1093	49.8	142	61.7	160	61.5	51	68.9
CHF	105	4.8	28	12.2	10	13.5	171	6.2
Diabetes	364	16.6	44	19.1	41	15.8	14	18.9
Moderate to severe stroke on arrival (NIHSS score: $\geq 16$ )	114	5.2	17	7.4	36	13.8	6	8.1

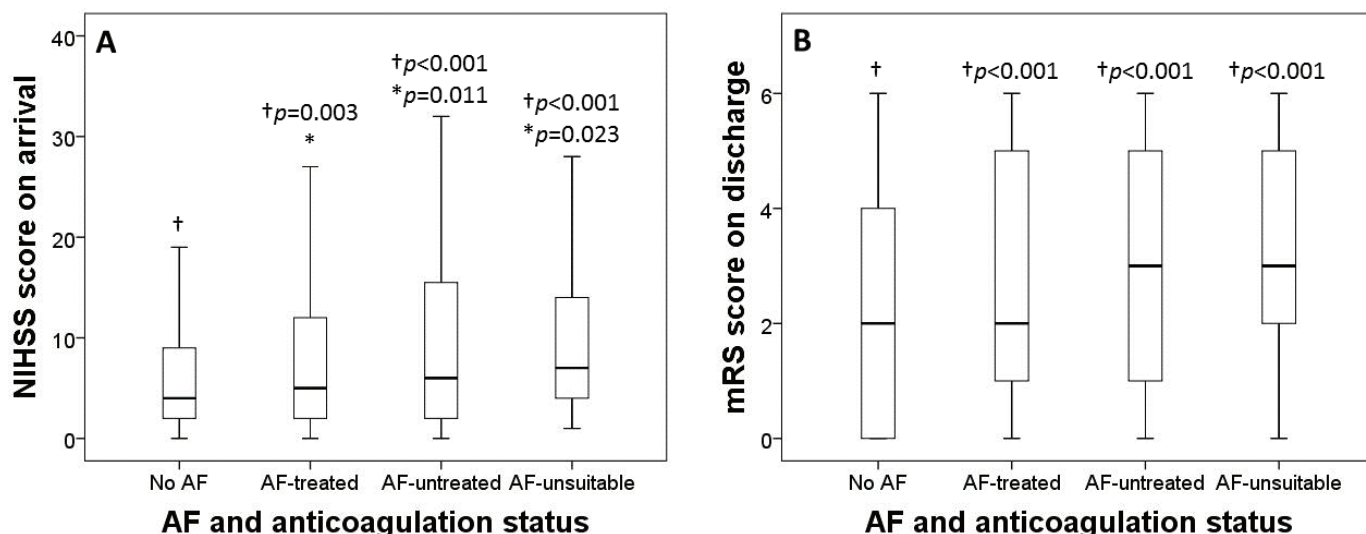
AF, atrial fibrillation; CHF, congestive heart failure; NIHSS, National Institutes of Health for Stroke Scale.

also lower than that of those with AF who were not treated with ( $P=0.011$ ) or considered unsuitable for anticoagulation ( $P=0.023$ ).

**Table 3** shows that compared with patients with stroke who were free of AF, those with AF but not anticoagulated had an increased adjusted risk of having more severe stroke: 5.8% versus 14.0%, OR=2.4 (95% CI 1.6 to 3.6,  $P<0.001$ ), prolonged HASU stay: 21.5% versus 32.0%, OR=1.4 (95% CI 1.0 to 2.0,  $P=0.027$ ), pneumonia: 8.2% versus 19.1%, OR=2.1 (95% CI 1.4 to 2.9,  $P<0.001$ ), more severe disability: 24.2% versus 40.4%, OR=1.6 (95% CI 1.2 to 2.1,  $P=0.004$ ) and mortality: 9.3% versus 21.7%, OR=1.9 (95% CI 1.4 to 2.8,  $P<0.001$ ). Patients with AF with anticoagulation also had greater risk than those free of AF for having UTI: 8.6% versus

12.3%, OR=1.9 (95% CI 1.2 to 3.0,  $P=0.004$ ), pneumonia: 8.2% versus 11.5%, OR=1.6 (95% CI 1.1 to 2.4,  $P=0.025$ ) and mortality: 9.7% versus 21.7%, OR=1.9 (95% CI 1.4 to 2.8,  $P<0.001$ ).

The median length of stay in HASU of 5.8 days (IQR=2.3–17.5 days) for patients with stroke who were free of AF. In comparison, the corresponding values were 10.6 days (IQR=2.8–26.4 days) for patients with stroke with AF without anticoagulant ( $P<0.001$ ) and 9.8 days (IQR=4.0–30.0 days) for stroke patients who were deemed unsuitable for anticoagulation ( $P=0.010$ ), while anticoagulation in patients with AF reduced the median length of stay in HASU to 7.1 days (IQR=3.1–19.3 days), which is not significantly different from patients with stroke who are free of AF ( $P=0.062$ ).



**Figure 2** Box plots showing AF and anticoagulation status in relation to stroke severity on arrival indicated by NIHSS score (A) and severity of disability on discharge indicated by mRS score (B). ANOVA showed significant group differences ( $P<0.001$ ), therefore post hoc least significant difference tests were performed to compare NIHSS score between those †free from AF (no AF) and other three AF groups of different anticoagulation status, and between \*AF with anticoagulation (AF-treated) and AF without anticoagulation (AF-untreated) groups. Box plots represent median and IQR; whiskers represent the 5th and 95th percentiles. AF, atrial fibrillation; ANOVA, analysis of variance; mRS, modified Rankin Scale; NIHSS, National Institutes of Health for Stroke Scale.

**Table 3**  $\chi^2$  test and logistic regression to assess the association of AF and anticoagulation status with moderately severe to severe stroke (NIHSS score  $\geq 16$ ), UTI and pneumonia within 7 days of admission, prolonged stay in HASU, moderately severe to severe disability (mRS score=4 and 5) on discharge and mortality

	$\chi^2$											
	Event rates (%) between study groups					Logistic regression analysis						
	Event rates	%	$\chi^2$	P	Unadjusted	Adjusted for age, sex, comorbidities*	OR	95% CI	P	OR	95% CI	P
<b>Severe stroke on arrival (NIHSS <math>\geq 16</math>)</b>												
Free from AF	114/2194	5.8	30.6	<0.001	1	1	1	–	–	1	–	–
AF with anticoagulation	17/230	8.9			1.46	1.24	0.86 to 2.47	0.164	1.24	0.72 to 2.13	0.440	
AF without anticoagulation	36/260	14.0			2.93	2.42	1.97 to 4.37	<0.001	2.42	1.60 to 3.64	<0.001	
AF not suitable for anticoagulation	6/74	9.4			1.61	1.31	0.68 to 3.79	0.275	1.31	0.55 to 3.14	0.539	
<b>Prolonged stay in HASU (&gt;3 weeks)</b>												
Free from AF	339/1852	21.5	15.0	0.002	1	1	–	–	1	–	–	
AF with anticoagulation	38/169	22.5			1.06	0.87	0.72 to 1.54	0.776	0.87	0.59 to 1.28	0.475	
AF without anticoagulation	64/200	32.0			1.71	1.42	1.25 to 1.35	0.001	1.42	1.03 to 1.97	0.034	
AF not suitable for anticoagulation	18/53	34.0			1.87	1.42	1.05 to 3.34	0.034	1.42	0.79 to 2.58	0.242	
<b>UTI within 7 days of admission</b>												
Free from AF	119/2116	5.6	39.5	<0.001	1	1	–	–	1	–	–	
AF with anticoagulation	27/219	12.3			2.36	1.88	1.52 to 3.68	<0.001	1.88	1.18 to 2.97	0.007	
AF without anticoagulation	28/257	10.9			2.05	1.49	1.33 to 3.17	0.081	1.49	0.95 to 2.33	0.081	
AF not suitable for anticoagulation	14/70	20.0			4.20	2.96	2.27 to 7.75	<0.001	2.96	1.55 to 5.65	0.001	
<b>Pneumonia within 7 days of admission</b>												
Free from AF	173/2116	8.2	59.5	<0.001	1	1	–	–	1	–	–	
AF with anticoagulation	34/219	11.5			2.06	1.60	1.39 to 3.07	<0.001	1.60	1.06 to 2.40	0.025	
AF without anticoagulation	49/257	19.1			2.45	2.05	1.87 to 3.75	<0.001	2.05	1.44 to 2.94	<0.001	
AF not suitable for anticoagulation	19/70	21.7			4.18	3.04	2.42 to 5.25	<0.001	3.04	1.73 to 5.37	<0.001	
<b>Moderately severe to severe disability on discharge (mRS=4 and 5)</b>												
Free from AF	530/2194	24.2	48.7	<0.001	1	1	–	–	1	–	–	
AF with anticoagulation	81/230	35.2			1.71	1.20	1.28 to 2.28	<0.001	1.20	0.90 to 1.66	0.198	
AF without anticoagulation	105/260	40.4			2.13	1.56	1.63 to 2.78	<0.001	1.56	1.18 to 2.06	0.002	
AF not suitable for anticoagulation	31/74	41.9			2.26	1.60	1.41 to 3.63	0.001	1.60	0.97 to 2.62	0.065	
<b>Inpatient mortality</b>												
Free from AF	212/2194	9.7	58.8	<0.001	1	1	–	–	1	–	–	
AF with anticoagulation	50/230	21.7			2.60	1.94	1.84 to 3.66	<0.001	1.94	1.35 to 2.78	<0.001	
AF without anticoagulation	55/260	21.2			2.51	1.86	1.80 to 3.49	<0.001	1.86	1.32 to 2.61	<0.001	
AF not suitable for anticoagulation	16/74	21.6			2.58	1.83	1.46 to 4.57	0.001	1.83	1.01 to 3.30	0.046	

\*Comorbidities: CHF, hypertension, diabetes and previous stroke.

AF, atrial fibrillation; CHF, congestive heart failure; HASU, hyperacute stroke unit; mRS, modified Rankin Scale; NIHSS, National Institutes of Health for Stroke Scale; UTI, urinary tract infection.



Among patients with AF who were not anticoagulated or deemed unsuitable for anticoagulation on admission, 91.8% and 75.0% of these patients, respectively, were treated with an anticoagulant on discharge ( $\chi^2 = 16.2$ ,  $P < 0.001$ ).

## DISCUSSION

We show that compared with patients without a history of AF, those with AF without anticoagulation had a greater risk of severe stroke (NIHSS score  $\geq 16$ ), prolonged stay in HASU ( $>3$  weeks), risk of early pneumonia, more severe disability on discharge (mRS score=4 and 5) and inpatient mortality by 1.4-fold to 2.4-fold. Our study of the association of AF/anticoagulation therapies with pneumonia, UTI and length of stay in HASU is novel. It is notable that patients with AF who were anticoagulated had a reduced risk of severe stroke and length of stay in a HASU to the same level as those who were free from AF. The increased risk of severe stroke on arrival, prolonged stay in HASU, more severe disability on discharge and inpatient mortality in patients with AF without anticoagulation was independent of age, sex, hypertension, CHF, diabetes and previous stroke.

Given the growing ageing population,<sup>19</sup> disability from stroke will continue to impose massive burdens on healthcare systems in the foreseeable future worldwide, including the UK. There is therefore a need for early identification of AF, the biggest treatable risk factor of stroke, through systematic screening of at-risk patients in the community and intensive treatment for those diagnosed with AF.<sup>20</sup> However, there is evidence of undertreatment of AF in the community. In the present study, we observed 46.1% of patients with AF who were not on anticoagulation on admission. This figure is consistent with findings from Bassand *et al*,<sup>21</sup> who observed that 36.9% of AF patients with  $\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$  were not on anticoagulant therapy at inclusion and from Perez *et al*, who found that only 50% of patients with AF who were eligible for anticoagulation were given this treatment.<sup>22</sup> Similarly, Waldo *et al* studied 945 patients and found that of the 86% of patients who were at high risk of stroke, only 55% received warfarin.<sup>23</sup> Data from our study revealed that most patients with AF who were not treated or deemed unsuitable for treatment with an anticoagulant on admission were subsequently treated on discharge. This suggests that the number of patients who are actually contraindicated to anticoagulation is small, with most being simply untreated.

Greater collaboration between primary care and specialist cardiology services is necessary to improve stroke prevention through appropriate treatment of AF. The roles of experts such as cardiologists, neurologists and haematologists are vital in providing specialist advice on anticoagulation therapy for patients who pose as a treatment dilemma for anticoagulation, such as those with a history of bleeding. Other preventable risk factors such as obesity, hypertension, dyslipidaemia and

hyperglycaemia/insulin resistance<sup>20 24 25</sup> should also be managed intensively.

A number of important findings emerge from the present study. All patients with AF, whether treated or untreated with an anticoagulant, have increased risks of early hospital-acquired infections, disability and mortality. This suggests the inherent risk of AF that may be associated with other causes of cardiovascular disease leads to worse outcomes of stroke.<sup>26</sup> In the present study, we observed that there was no greater risk for having more severe stroke or prolonged stay in HASU among stroke patients with AF who were anticoagulated than that of those who were free of AF; this evidence reinforces the value of intensive treatment of AF with anticoagulants.<sup>14</sup>

The strengths of the present study include its large homogenous cohort of patients derived from one of the largest NHS regions in England. The analysis was robustly adjusted for age and sex, as well as major chronic conditions known to associate with stroke including hypertension, CHF, diabetes, previous stroke and in particular stroke subtype. The data were collected by healthcare providers for the patients using national SSNAP protocol. Our study focused on early disability on discharge and inpatient mortality. It would be of interest to assess the impact of AF anticoagulation status on these outcomes in longer term. Although data are derived only from Surrey, it is likely to be representative of the rest of the UK as stroke prevalence is similar to that of the UK.<sup>12</sup> Our study did not collect information on types of oral anticoagulants or INR that could have some bearing on the outcomes. This information is beyond the scope of our study. The length of anticoagulation treatment for individual patients was not available, but it is likely that it is closely related to their age. We chose cut-off point for NIHSS score at 16 based on previous studies showing that a baseline score of  $\geq 16$  (moderately severe to severe stroke) was a strong predictor of mortality or severe disability,<sup>27</sup> while cut-off point for mRS score at 4 indicates that, beyond this point, functional disability begins to worsen due to increasing severity of stroke.<sup>28</sup> 'Prolonged stay' has variably been described.<sup>29</sup> In the present study, we defined prolonged stay for those who stayed in HASU  $>3$  weeks as this point reflects the upper quartile of length of stay in HASU. It should be emphasised that these cut-off points tend to be arbitrary and the higher the level, the more severe is the condition. We have explored various other levels including cut-off points for NIHSS score at 12, mRS score at 3 and length of stay in HASU at 1 week (50th centile), all showing similar patterns of, but weaker, association with AF treatment status.

In conclusion, patients with AF, particularly those without anticoagulation, are at increased risk of severe stroke, associated with prolonged HASU stay and increased risk of early infection, disability and mortality.

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