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ORIGINAL RESEARCH

Atrial fibrillation in patients with ischemic stroke: A population-based study

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Background: Atrial fibrillation is a major risk factor for ischemic stroke. However, the prognostic impact of atrial fibrillation among patients with stroke is not fully clarified. We compared patient characteristics, including severity of stroke and comorbidity, quality of in-hospital care and outcomes in a cohort of first-time ischemic stroke patients with and without atrial fibrillation.

Methods: Based on linkage of public medical databases, we did a population-based follow-up study among 3,849 stroke patients from the County of Aarhus, Denmark admitted in the period of 2003–2007 and prospectively registered in the Danish National Indicator Project.

Results: Atrial fibrillation was associated with an adverse prognostic profile but not with an overall poorer quality of in-hospital care. Patients with atrial fibrillation had a longer total length of stay (median: 15 vs 9 days), and were at increased risk of in-hospital medical complications (adjusted relative risk = 1.48, 95% CI: 1.23–1.79) and recurrent stroke (adjusted hazard ratio = 1.30, 95% CI: 0.93–1.82) when compared with patients without atrial fibrillation. The adjusted hazard ratios for 30 days and one year mortality were 1.55 (95% CI: 1.20–2.01) and 1.55 (95% CI: 1.30–1.85), respectively. Patients not eligible to oral anticoagulant treatment had an increased risk of recurrent stroke (adjusted hazard ratio = 1.92, 95% CI: 1.19–3.11).

Conclusion: Atrial fibrillation is associated with a poor outcome among patients with ischemic stroke particularly among patients, who are not eligible to oral anticoagulant treatment.

Keywords: atrial fibrillation, stroke, quality of care, prognosis, mortality, epidemiology

Introduction

Atrial fibrillation is the most common cardiac arrhythmia and a major risk factor for ischemic stroke,[1] in particular among elderly patients.[2] Atrial fibrillation is present in approximately 1% of the general population, but is mainly found among elderly where the prevalence is substantially higher (eg, approximately 9% of people older than 80 years).[3]

Stroke is one of the most feared complications in patients with atrial fibrillation, in particular since atrial fibrillation has been reported to be associated with a higher short- and long-term case fatality following stroke.[4–12]

A number of mechanisms have been suggested to explain this increased mortality among stroke patients with atrial fibrillation, including a higher stroke severity,[4,7,13–15] higher age,[16] more comorbidity[17,18] and poorer quality of care.[6] However, the impact of these individual factors remains to be clarified. Furthermore, more information is needed on the prognosis of atrial fibrillation patients, who are not eligible to oral anticoagulant therapy.

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We therefore examined the prognosis among patients with ischemic stroke in a population-based cohort to clarify whether atrial fibrillation is an independent prognostic factor among patients with ischemic stroke.

Methods

The Danish National Indicator Project

The Danish National Health Service provides tax-supported health care to the country's 5.4 million residents, all of whom have free access to hospital care. The Danish National Indicator Project is a nationwide initiative to monitor and improve the quality of care for specific diseases, including stroke.[19] The project focuses on the development and implementation of evidence-based indicators of quality of care related to the structure, process and outcome of health care. Participation in the project is mandatory for all hospital departments treating patients with stroke.

The study was approved by The Danish National Indicator Project and the Danish Data Protection Agency (record number: 2007-41-0012).

Study population

We conducted this cohort study using population-based medical databases covering the population of the former County of Aarhus (approximately 650,000 people or 12% of the entire Danish population).

Our study population (n = 3,849) included patients ≥18 years old admitted between Jan 13, 2003–Dec 31, 2007. We included patients diagnosed with an acute first-time ischemic or unspecific stroke event according to the World Health Organization (WHO) criteria (ie, rapidly developing clinical symptoms and signs of focal or global loss of cerebral function lasting more than 24 hours or until death, with no apparent cause other than vascular origin).[20]

We excluded patients with intracranial hemorrhage, subdural hematoma, epidural hemorrhage, retinal infarct, and infarct caused by trauma, infection, or an intracranial malignant process.

Our study population included 741 patients with atrial fibrillation (19%) and 3,108 patients without atrial fibrillation (81%). Atrial fibrillation was defined as a history of atrial fibrillation and/or atrial fibrillation diagnosed during the index admission with stroke. No distinction was made between chronic and paroxystic atrial fibrillation.[21]

Prognostic factors

The following prognostic factors were registered in the Danish National Indicator Project: gender, age, civil status (alone or living with someone), housing situation (own home, nursing home or other institution), pre-admission Rankin Scale score, Scandinavian Stroke Scale score, Barthel Index score, hypertension, hypercholesterolemia (total cholesterol >5 mmol/L and/or low-density lipoprotein [LDL] >3 mmol/L), smoking habits (current (≥1 cigarette/day), former smoker (≥6 months), sometimes (<1 cigarette/day) and never), alcohol intake (≤14/21 or >14/21 units/week for women and men, respectively) and hospital department. Further, we computed the Charlson Index of Comorbidity for each patient based on data from the National Registry of Patients which contains data on all discharges from all nonpsychiatric hospitals in Denmark since 1977. The files include information on the civil registry number; date of admission and discharge; and up to 20 discharges diagnoses and procedures coded according to the International Classification of Diseases, 8th revision until the end of 1993 and 10th revision thereafter. The Charlson Index of Comorbidity covers 19 conditions, including chronic obstructive pulmonary disease, diabetes mellitus, intermittent claudication, acute myocardial infarction, congestive heart failure, carotid stenosis, and cancer, each weighted according to its impact on survival.[22,23] We defined three levels of comorbidity for each patient, based on their complete hospital discharge history, as follows: 0 comorbidities ("low"), 1–2 comorbidities ("moderate") and ≥3 comorbidities ("high").

Stroke severity was assessed by the Scandinavian Stroke Scale score <24 hours of admission (very severe (≤14), severe (15–29), moderate (30–44), and mild (≥45 pts)). The scale is a validated and widely used neurological stroke scale in Scandinavia that evaluates level of consciousness; eye movement; power in the arm, hand, and leg; orientation; aphasia; facial paresis; and gait on a total score that ranges from 0 to 58.[24,25]

The patients' pre-stroke functional ability was assessed with the modified Rankin score which scales the patients from 0 (no symptoms) to 5 (bedridden, incontinent and requiring constant nursing care and attention).

During hospitalization the patients' functional status was measured with Barthel Index score on day 7 ± two days (low (<60) to high (≥60)). Barthel Index is commonly used to score a patient's self-care performance and consists of 10 different rated items including bladder and bowel control, bathing, and feeding. The score ranges from 0 (inability to perform) to 100 (complete independence).[26]

Quality of care criteria

Quality of in-hospital care was defined as fulfillment of a set of quality of care criteria. An expert panel including

physicians, nurses, physiotherapists, and occupational therapists defined 14 quality of care criteria covering the acute phase of stroke based on a systematic search of the scientific literature:[19] admission to a specialized stroke unit, antiplatelet therapy initiated among patients with ischemic stroke without atrial fibrillation, oral anticoagulant therapy initiated among patients with ischemic stroke and atrial fibrillation, examination with computed tomography (CT) or magnetic resonance imaging (MRI) scan, assessment by a physiotherapist, assessment by an occupational therapist, assessment of nutritional risk, mobilization, screening for dysphagia with water swallow test, individual nutritional therapy initiated among patients with a nutritional risk score >3, use of sterile intermittent catheterization among patients with urinary retention, assessment by a logopedic, a neuropsychologist and a social worker.

A time frame was defined for each criterion to capture the timeliness of the interventions. The time frame was the first day of hospitalization for examination with CT/MRI scan, mobilization and screening for dysphagia. The time frame was second day of hospitalization for admission to a specialized stroke unit, antiplatelet therapy, assessment by a physiotherapist, assessment by an occupational therapist, and assessment of nutritional risk, whereas time frame for anticoagulant therapy was the 14th day of hospitalization for initiation of oral anticoagulant therapy and before discharge for individual nutritional therapy, sterile intermittent catheterization and assessment by a logopedic, a neuropsychologist and a social worker.

A specialized stroke unit was defined as a hospital department/unit that exclusively or primarily is dedicated to patients with stroke and which is characterized by multidisciplinary teams, a staff with a specific interest in stroke, involvement of relatives and continuous education of the staff. Initiation of antiplatelet (acetylsalicylsyre, dipyridamol, and clopidogrel) and oral anticoagulant (warfarin and phenprocoumon) therapy was defined as continuous use of the drugs and not merely a single dose. Assessment by a physiotherapist, occupational therapist, logopedic, neuropsychologist and social worker was defined as a formal in-person assessment of the patient's needs, whereas assessment of nutritional risk was defined as an assessment following the recommendations of the European Society for Parenteral and Enteral Nutrition, ie, calculation of a score which both accounts for the nutritional status and for the stress induced by the stroke.[27]

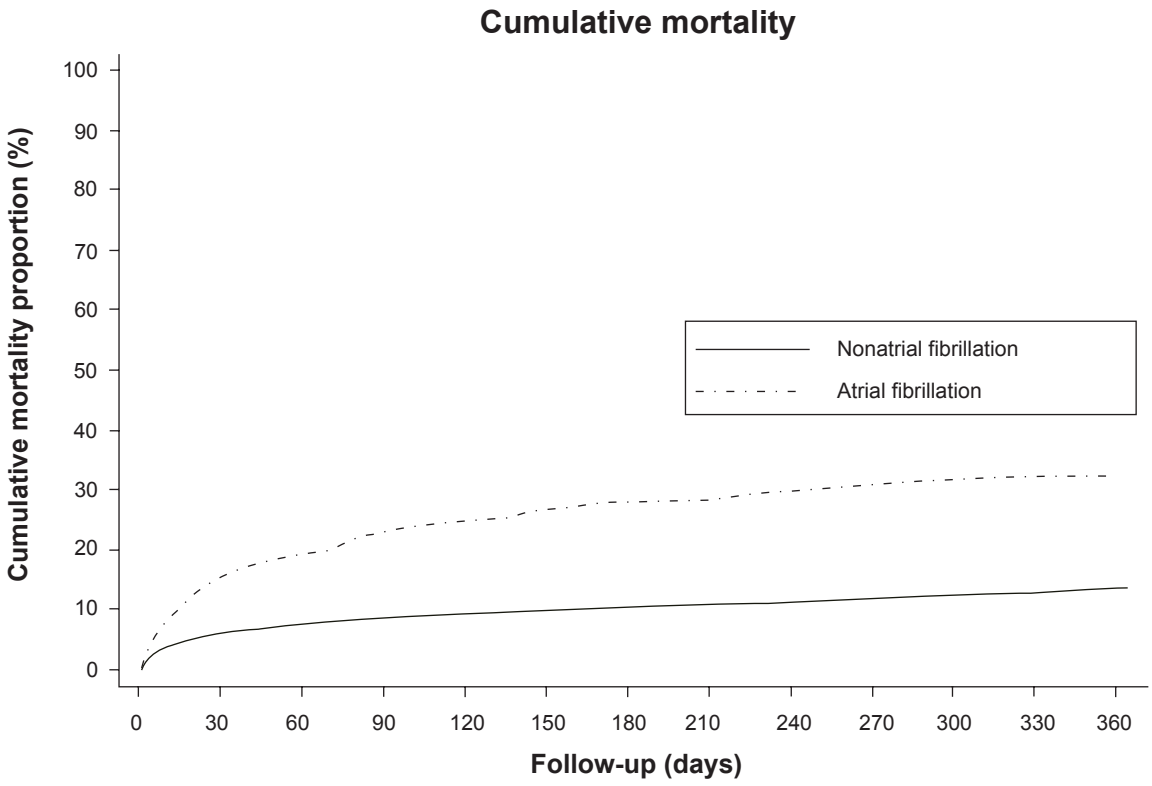

Figure 1 The cumulative mortality in stroke patients with and without atrial fibrillation.

Upon hospital admission, data on care, and patient characteristics were prospectively collected for each patient using a standardized form. After hospital discharge the data were entered into a central database. Patients were classified as eligible or noneligible for the specific processes of care depending on whether the stroke team or physician treating the patient identified any contraindications. The specific contraindications for the individual patient were not registered; however, decisions on eligibility or noneligibility for treatment made by the staff followed national guidelines for stroke treatment as described in the national Danish guidelines for treatment of patients with stroke which is comparable to international guidelines for stroke treatment.[28] Thus, with these national guidelines in mind, it was ultimately left to the staff to decide whether or not contraindications to the specific criteria were present. Guidelines from the Danish Society of Cardiology on oral anticoagulant treatment were followed, eg, severe dementia, recent major surgery, antiplatelet therapy, uncontrolled hypertension, alcoholism, pregnancy (first trimester) and lack of acceptance from the patient were contraindications in a patient with ischemic stroke and atrial fibrillation.

Clinical outcomes

We assessed the following clinical outcomes:

Medical complications

Included in-hospital urinary retention, pneumonia, urinary tract infection, obstipation and other complications (including pressure ulcers, trauma from falling, deep venous thrombosis, and lung embolism).

Length of hospital stay

Length of stay was defined from the day of admission to a hospital department to the day of discharge to either own residence, care home or other type of institution. Length of stay included both the acute inpatient hospital stay and the inpatient rehabilitation stay. Restricting the analyses to the acute inpatient hospital stay yielded similar results and thus, we present the results only for the total length of stay.

Recurrent stroke

Included both ischemic and hemorrhagic strokes. To be considered a recurrent stroke, the patients needed to be discharged for at least one day before readmission to the hospital.

Mortality

Short- (30 days) and long-term (one year) mortality. Data on vital status were obtained from the Civil Registration System which is a unique personal identification number issued to all Danish citizens that allows unambiguous linkage between various public registries and contains complete electronic follow-up data on civil registry number, name, gender, date and place of birth, citizenship, vital status, address and emigration for the entire Danish population since 1968. A minimum of one month of follow-up was available on all patients included in the study.

Statistical analyses

We first computed the relative risk (RR) for patients with atrial fibrillation meeting the quality of care criteria compared with patients without atrial fibrillation. Only the crude RRs were computed since the care processes had been considered relevant by the staff treating the patients included in these analyses.

We then used logistic regression analysis to compute odds ratios as an estimate of the RRs of in-hospital medical complications, including both specific complications and any type of complication. Decubitus, falls, deep venous thrombosis and pulmonary embolism were combined into one category ("Other") as there were few events.

Linear regression was used to compare length of stay. A natural log (ln) transformation was used to correct for the right skewness of length of stay. When reporting the findings of the analyses, we transformed the regression estimates back into the original units by exponentiating the estimates and thereby obtained the ratios of the geometric means of length of stay. The analyses were done both with and without inclusion of the patients who died in hospital.

We used the life table technique to compute the absolute risk of recurrent stroke, 30 day- and one year mortality and Cox's proportional regression analysis to compute crude and adjusted hazard ratios as an estimate of the incidence rate ratios of recurrent stroke and mortality. Follow-up started on the day of admission to any hospital department/ward and ended on the day of readmission with stroke, death, emigration or end of the study period, respectively, whichever came first. In the analyses on mortality follow-up ended on the day of death, emigration or after 30 days and one year respectively.

We adjusted for fulfillment of the quality-of-care criteria and the prognostic factors in all regression analyses using a two-step approach, where we first adjusted for the proportion of fulfilled quality of care criteria and all prognostic factors except Scandinavian Stroke Scale score and Barthel Index score followed by adjustment for all factors including Scandinavian Stroke Scale score and Barthel Index score.

This approach was used in order to explore to which extent the prognostic impact of atrial fibrillation is mediated through stroke severity and consequently impaired functional level. In cases of missing data on the covariates, a separate category for missing data was added to the specific covariate. We computed 95% confidence intervals (CI) for all estimates. Finally, we stratified all analyses according to the patients' eligibility to oral anticoagulant treatment.

All analyses were performed using STATA (version 9.2; StataCorp, College Station, TX, USA).

Results

Table 1 displays the descriptive characteristics of the study population. Patients with atrial fibrillation were characterized by a higher proportion of women, higher age, increased stroke severity, lower functional level and more co-morbidities compared to patients without atrial fibrillation. Among the patients with atrial fibrillation, a total of 136 patients (18.4%) had previously been admitted to the hospital with atrial fibrillation.

Quality of care

Table 2 presents the fulfillment of quality of care criteria among patients with and without atrial fibrillation. The differences in quality of care were in general minor. However, patients with atrial fibrillation were less likely to be mobilized (RR = 0.90, 95% CI: 0.86–0.94), treated in a stroke unit (RR = 0.93, 95% CI: 0.88–0.98), have an assessment by a physiotherapist (RR = 0.91, 95% CI: 0.84–0.99), a occupational therapist (RR = 0.92, 95% CI: 0.84–0.99), an early assessment of nutritional risk (RR = 0.89, 95% CI: 0.82–0.97) and evaluation by a neuropsychologist (RR = 0.61, 95% CI: 0.38–0.98) when compared to patients without atrial fibrillation. In contrast, patients with atrial fibrillation were more likely to receive individual nutritional therapy (RR = 1.07, 95% CI: 1.03–1.11).

A sub-analysis of quality of care stratified according to eligibility to oral anticoagulant treatment among the patients with atrial fibrillation showed no substantial differences (data not shown).

Medical complications

The absolute risk of any in-hospital medical complication was 43.3% for those with atrial fibrillation and 24.4% for patients without atrial fibrillation (adjusted RR = 1.48, 95% CI: 1.23–1.79) (Table 3). The adjusted RR estimates for the individual medical complications ranged from 1.02 (95% CI: 0.76–1.36) to 1.66 (95% CI: 1.29–2.13) when comparing patients with atrial fibrillation to those without. This pattern was independent of eligibility to oral anticoagulant treatment.

Length of hospital stay

Patients with atrial fibrillation had a median length of stay of 15 days (interquartile range: 6–31) whereas patients without atrial fibrillation had a median length of stay of 9 days (interquartile range: 4–24). The adjusted relative length of stay was 1.32 (95% CI: 1.18–1.46). The results remained virtually unchanged when restricting the analyses to include only the acute phase defined as the length of stay until the date of transfer to a rehabilitation facility which applied for 16% of our study population (n = 620). Atrial fibrillation patient had a median length of acute stay of 11 days (interquartile range: 5–22) and patients with no atrial fibrillation of 8 days (interquartile range: 3–16). There was no difference when restricting the analyses only to patients discharged alive whether or not the sub acute rehabilitation phase was included (data not shown).

The increased length of stay was both found among atrial fibrillation patients eligible to oral anticoagulant treatment (adjusted relative length of stay = 1.49, 95% CI: 1.30–1.70) and among patients with contraindications against oral anticoagulant treatment (adjusted relative length of stay = 1.31, 95% CI: 1.13–1.52).

Recurrent stroke

The median follow-up time for all patients was 1.8 years (interquartile range: 0.6–3.2 years). The cumulative risk of recurrent stroke during follow-up was 6.6% and 5.8% among patients with and without atrial fibrillation, respectively, corresponding to an adjusted hazard ratio of 1.30 (95% CI: 0.93–1.82) (Table 4). Further adjustment for Scandinavian Stroke Scale and Barthel Index had virtually no effect on the hazard ratio. The increased risk of recurrent stroke was restricted to atrial fibrillation patients with contraindications against oral anticoagulant treatment (adjusted hazard ratio 1.92, 95% CI: 1.19–3.11).

Short and long term mortality

The absolute 30-day mortality risk for patients with atrial fibrillation was 14.7% compared with 5.8% for patients without atrial fibrillation. Adjusting for differences in quality of care and patient characteristics resulted in a 30-day hazard ratio of 1.55 (95% CI: 1.20–2.01). Further adjustment for stroke severity and Barthel Index resulted in an adjusted 30-day hazard ratio of 1.24 (95% CI: 0.95–1.61) (Table 4).

Table 1 Characteristics of 3,849 patients with ischemic stroke from the County of Aarhus registered in the Danish National Indicator Project, 2003–2007

	Atrial fibrillation (n = 741)	No atrial fibrillation (n = 3,108)
Sex		
Female	411 (55.5%)	1,390 (44.7 %)
Male	330 (44.5%)	1,718 (55.3 %)
Age		
≤65	89 (12.0%)	1,142 (36.7 %)
>65–80	287 (38.7%)	1,288 (41.4 %)
>80	365 (49.3%)	678 (21.8 %)
Civil status		
Co-habiting	299 (40.4%)	1,764 (56.8 %)
Alone	398 (53.7%)	1,244 (40.0 %)
Other	24 (3.2%)	71 (2.3 %)
Missing	20 (2.7%)	31 (1.0 %)
Type of residence		
Own residence	628 (84.8%)	2,847 (91.6%)
Care home	81 (10.9%)	164 (5.3%)
Other	14 (1.9%)	54 (1.7%)
Missing	18 (2.4%)	43 (1.4%)
Modified Rankin scale (pre-admission)		
No/Minor symptoms	427 (57.6%)	2,132 (68.6%)
Modest/Moderate symptoms	153 (20.6%)	471 (15.2%)
Much/Constant help needed	53 (7.2%)	119 (3.8%)
Missing	108 (14.6%)	386 (12.4%)
Scandinavian Stroke Scale		
Very severe (0–14 pt)	107 (14.4%)	182 (5.9%)
Severe (15–29)	103 (13.9%)	222 (7.1%)
Moderate (30–44)	149 (20.1%)	522 (16.8%)
Mild (46–60)	245 (33.1%)	1,689 (54.3%)
Missing	137 (18.5%)	493 (15.9%)
Bartel Index		
Low (<60)	296 (39.9%)	700 (22.5%)
High (≥60)	238 (32.1%)	1,315 (42.3%)
Missing	207 (27.9%)	1,093 (35.2%)
Charlson Comorbidity Index		
No comorbidity	251 (33.9%)	1.466 (47.2%)
Moderate comorbidity	323 (43.6%)	1.193 (38.4%)
Severe comorbidity	167 (22.5%)	449 (14.4%)
Missing	0 (0%)	0 (0%)
Diabetes mellitus		
Yes	108 (14.6%)	413 (13.3%)
No	601 (81.1%)	2,662 (85.7%)
Missing	32 (4.3%)	33 (1.1%)

(*Continued*)

Table 1 (*Continued*)

	Atrial fibrillation (n = 741)	No atrial fibrillation (n = 3,108)
Hypertension		
Yes	401 (54.1%)	1,593 (51.3%)
No	303 (40.9%)	1,431 (46.0%)
Missing	37 (5.0%)	84 (2.7%)
Hypercholesterolemia		
Yes	241 (32.5%)	1,489 (47.9%)
No	364 (49.1%)	1,314 (42.3%)
Missing	136 (18.4%)	305 (9.8%)
Smoking status		
Smoker	152 (20.5%)	1,287 (41.4%)
Occasional	16 (2.2%)	61 (2.0%)
Former (> 6 months)	182 (24.6%)	648 (20.8%)
Never	248 (33.5%)	837 (26.9%)
Missing	143 (19.3%)	275 (8.9%)
Alcohol status		
≤14/21 drinks/week	549 (74.1%)	2,479 (79.8%)
>14/21 drinks/week	39 (5.3%)	258 (8.3%)
Missing	153 (20.7%)	371 (11.9%)

The absolute one-year mortality risk was 31.7% among patients with atrial fibrillation and 13.7% for patients without atrial fibrillation and the corresponding adjusted hazard ratio was 1.55 (95% CI: 1.30–1.85). The adjusted hazard ratio dropped to 1.33 (95% CI: 1.12–1.59) after further adjustment for stroke severity and Barthel Index.

Major differences in risk of death were found when stratifying the analyses according to patients' eligibility to oral anticoagulant treatment. Thus, patients with atrial fibrillation eligible for oral anticoagulant treatment had a tendency towards a lower adjusted hazard ratio of 30-day (0.91, 95% CI: 0.60–1.40) and one-year mortality (0.74, 95% CI: 0.48–1.15) compared with patients without atrial fibrillation. In contrast, patients with atrial fibrillation not eligible for oral anticoagulant treatment had an adjusted hazard ratio of 30-day and one-year mortality of 2.24 (95% CI: 1.59–3.13) and 1.68 (95% CI: 1.20–2.36), respectively, compared to patients without atrial fibrillation.

Discussion

In this population-based cohort study we found atrial fibrillation to be associated with an overall poorer outcome following ischemic stroke, including increased in-hospital medical complications, length of stay, mortality and possibly also an increased risk of recurrent stroke. The risk of recurrent stroke and mortality differed substantially among atrial fibrillation patients according to eligibility for oral anticoagulant treatment. The poor prognosis appeared only partly to be explained by a more adverse prognostic patient profile, including a higher stroke severity, and not by a poorer quality of acute hospital care.

Methodological considerations

The main strengths of our study are its large size, the uniformly organized health care system facilitating a prospective population-based design, with complete long-term follow-up and use of data collected independently of the study objectives. Further, our analyses were based on detailed clinical data and included information on a wide range of prognostic factors.

Our study was based on data collected during routine clinical work, which may potentially have affected the data accuracy. Still, participation in the Danish National Indicator Project is mandatory for all departments treating patients with stroke in Denmark, and extensive efforts are made to ensure the validity of the Danish National Indicator Project, including regular structured audit and validation of the completeness of patient registration against county hospital discharge registries. Furthermore, any misclassification of data in the Danish National Indicator Project is unlikely to depend on atrial fibrillation and would therefore most likely result in conservative risk estimates. Although we adjusted for quality of care and a wide range of prognostic factors, we cannot entirely exclude the possibility that our results may still be influenced by residual confounding due to the use of crude categories (eg, diabetes mellitus and hypertension) or

Table 2 Fulfilment of quality of care criteria among ischemic stroke patients with and without atrial fibrillation

Quality of care criterion	Atrial fibrillation (%) (n = 741)	No atrial fibrillation (%) (n = 3,108)	RR (95%CI)
Treatment/rehabilitation in stroke unit (days after admission)	509/719 (70.8%)	2,246/2,955 (76.0%)	0.93 (0.88–0.98)
Antiplatelet therapy (<2 days after admission)	448/641 (69.9%)	2,176/2,858 (76.1%)	0.93 (0.88–0.98)
Oral anticoagulant therapy (<14 days after admission)	266/383 (69.5%)	130/365 (35.6%)	1.82 (1.57–2.12)
CT/MRI scan (≤1 days after admission)	409/723 (56.6%)	1,672/3,063 (54.6%)	1.04 (0.96–1.11)
Assessment by a physiotherapist (<2 days after admission)	336/625 (53.8%)	1,492/2,537 (58.8%)	0.91 (0.84–0.99)
Assessment by an occupational therapy assessment (<2 days after admission)	325/630 (51.6 %)	1,458/2,587 (56.4%)	0.92 (0.84–0.99)
Nutritional risk evaluation (<2 days after admission)	314/592 (53.0%)	1,466/2,463 (59.5%)	0.89 (0.82–0.97)
Dysphagia screening (<24 hours)	386/509 (75.8%)	1,650/2,053 (80.4%)	0.94 (0.89–1.00)
Individual nutritional therapy when nutritional score > 3	247/258 (95.7%)	621/694 (89.5%)	1.07 (1.03–1.11)
Mobilized (<24 hours)	472/617 (76.5%)	2,232/2,616 (85.3%)	0.90 (0.86–0.94)
Urinary retention treated with sterile intermittent catheterization	89/92 (96.7%)	174/182 (95.6%)	1.01 (0.96–1.06)
Evaluated by a logopedic	263/297 (88.6%)	886/1,033 (85.8%)	1.03 (0.98–1.08)
Evaluated by a neuropsychologist	16/89 (18.0%)	107/364 (29.4%)	0.61 (0.38–0.98)
Evaluated by a social worker	44/90 (48.9%)	244/441 (55.3%)	0.88 (0.70–1.11)

Notes: *Patients with no atrial fibrillation are the reference group; †Because the proportion of patients eligible for the specific care interventions differs, the total amount of patients included differed between each criterion.

unaccounted confounding from factors not included in the analyses (eg, mental function).

Scandinavian Stroke Scale and Barthel Index are measures which reflect stroke severity and they may as such be considered intermediate steps in the association between atrial fibrillation and patient outcome. Adjusting for stroke severity and Barthel Index are therefore questionable when examining the prognostic role of atrial fibrillation although it has been done in a number of studies.[4,6,7,14,17,29,30] Thus, if stroke severity and Barthel Index are adjusted for, the association between atrial fibrillation and adverse outcomes is likely to be underestimated as demonstrated in our analyses. Finally, it should be noticed that some of the studied outcomes (eg, medical complications) were quite common. As a consequence the rare disease assumption was not fulfilled in all analyses and the computed odds ratios to some extent overestimated the true RR.

Comparisons with existing studies

The higher stroke severity found in our study confirms findings from other studies[4,6,7,13,14] and most likely reflects that ischemic stroke in patients with atrial fibrillation is mainly caused by cardiogenic embolisms.[31] Ischemic stroke of cardioembolic origin is in general associated with a higher mortality and a worse functional outcome than other subtypes of stroke probably due to the underlying pathophysiology (ie, sudden occlusion, often of a relatively large vessel).[4,7,13,32,33]

Previous studies have indicated that inequalities may exist in the quality of care offered to patients with stroke, in particular elderly and female patients have been reported to be less likely to receive adequate treatment and care.[34,35] Differences in quality of care are important to identify as they may contribute to potentially avoidable adverse outcomes for selected patient groups. Thus, in a previous study we have found a strong association between meeting the quality of care criteria in the Danish National Indicator Project and short-term mortality.[36] However, to our knowledge only one study has previously compared the quality of care of patients with atrial fibrillation versus patients without atrial fibrillation. In a multinational European multicenter study of 4462 stroke patients including 803 with atrial fibrillation, Lamassa and colleagues have found brain imaging and other diagnostic procedures to be used less frequently among patients with atrial fibrillation. Moreover, patients with atrial fibrillation received a lower number of physiotherapy and occupational therapy sessions.[6] However, the study had some methodological shortcomings as it was based on patients from selected, specialized centers, had incomplete follow-up and lacked detailed data on diagnosis and care, including timing of the diagnostic procedures and other interventions. We only

Table 3 Risk of medical complications among ischemic stroke patients with atrial fibrillation compared to patients without atrial fibrillation

Medical complications	Atrial fibrillation Absolute risk* (%)	No atrial fibrillation Absolute risk* (%)	Crude odds ratio (95% CI)	Adjusted odds ratio† (95% CI)	Adjusted odds ratio† incl. stroke severity and Barthel Index (95% CI)
Urinary retention	109/741 (14.7%)	216/3,108 (6.9%)	1.04 (1.01–1.08)	1.47 (1.17–1.83)	1.25 (0.99–1.58)
Pneumonia	124/741 (16.7%)	212/3,108 (6.8%)	1.11 (1.05–1.17)	1.66 (1.29–2.13)	1.29 (0.99–1.69)
Urinary tract infection	187/741 (25.2%)	444/3,108 (14.3%)	1.12 (1.06–1.18)	1.29 (1.04–1.59)	1.05 (0.84–1.32)
Obstipation	61/741 (8.2%)	172/3,108 (5.5%)	1.06 (1.00–1.11)	1.02 (0.76–1.36)	0.82 (0.60–1.12)
Other‡	40/731 (5.5%)	87/3,086 (2.8%)	2.00 (1.36–2.93)	1.57 (1.03–2.39)	1.38 (0.88–2.15)
Any§	319/736 (43.3%)	757/3,098 (24.4%)	2.37 (2.00–2.80)	1.48 (1.23–1.79)	1.19 (0.96–1.48)

Notes: *Includes only patients with nonmissing values; †Adjusted for prognostic factors (gender, age, civil status, type of residence, pre-admission Rankin scale, Charlson Comorbidity Index, hypertension, hypercholesterolemia, smoking, alcohol, hospital department, and proportion of fulfilled quality of care criteria). ‡'Other' includes decubitus, trauma from falling, venous thromboembolism. Patients are only included once, even though they may have suffered more than one of the four mentioned complications. §'Any' includes one or more of the categories above.

found modest differences in quality of in-hospital care in our study and adjusting for these differences had virtually no impact on patient outcomes. This finding strongly indicates that inadequate treatment and care in general is not a major contributor to the higher mortality among stroke patients with atrial fibrillation.

There are few published data on in-hospital medical complications among stroke patients with atrial fibrillation. However, our finding of an increased risk of in-hospital complications is supported by findings from the Austrian Stroke Registry,[30] where atrial fibrillation was associated with an increased risk of pneumonia and urinary tract infection.

The increased length of stay in our study for patients with atrial fibrillation is in accordance with some[4,5] but not all existing studies.[6,37] An increased length of stay among patients with atrial fibrillation may be due to the higher risk of in-hospital medical complications, which will require further treatment and care before the patient can be discharged. It was remarkable that the length of stay was longest among the atrial fibrillation patients, who were eligible to anticoagulant treatment. This could possibly reflect a longer and more intense rehabilitation period in these patients compared with atrial fibrillation patients who were not eligible to anticoagulant treatment; however we did not have data to clarify this hypothesis.

We did not find atrial fibrillation in general to be a strong independent predictor for recurrent stroke. This finding is consistent with some other studies[10,38–41] but not all.[42,43] The inconsistencies may at least partly be explained by differences in adjustment for other prognostic factors and in particular differences related to the effective use of oral anticoagulant treatment. Thus, in our study, patients that were ineligible to oral anticoagulant treatment had a higher stroke recurrence rate.

The overall increased short- and long-term mortality among patients with atrial fibrillation in our study is consistent with a number of other studies.[4–11,44] Different mechanisms have been suggested to underlie the increased mortality, yet no definitive answer has emerged. The higher frequency of in-hospital medical complications and the higher risk of recurrent stroke among patients not eligible to oral anticoagulant treatment found in our study are, however, likely to be important contributors.

Conclusion

Atrial fibrillation is associated with a poorer outcome following ischemic stroke, including increased in-hospital medical complications, length of stay, mortality and possibly

Table 4 Risk of recurrent stroke and mortality among ischemic stroke patients with atrial fibrillation compared to patients without atrial fibrillation

	Atrial fibrillation Absolute risk* (%)	No atrial fibrillation Absolute risk* (%)	Crude hazard ratio (95% CI)	Adjusted hazard rate† (95% CI)	Adjusted hazard ratio† incl. stroke severity and Barthel Index (95% CI)
Recurrent stroke	49/741 (6.6%)	181/3,106 (5.8%)	1.44 (1.05–1.98)	1.30 (0.93–1.82)	1.31 (0.93–1.84)
Short-term mortality (30 days)	109/741 (14.7%)	181/3,106 (5.8%)	2.67 (2.12–3.38)	1.55 (1.20–2.01)	1.24 (0.95–1.61)
Long-term mortality (1 year)	235/741 (31.7%)	409/3,106 (13.2%)	2.70 (2.30–3.17)	1.55 (1.30–1.85)	1.33 (1.12–1.59)

Notes: *Includes only patients with non-missing values; †Adjusted for prognostic factors (gender, age, civil status, type of residence, pre-admission Rankin scale, Charlson Comorbidity Index, hypertension, hypercholesterolemia, smoking, alcohol, hospital department, and proportion of fulfilled quality of care criteria).

also an increased risk of recurrent stroke. The prognosis is particularly poor among patients where oral anticoagulant treatment is contraindicated. This is only partly explained by a more adverse prognostic patient profile, including a higher stroke severity, and not by a poorer quality of acute hospital care. Continued efforts are warranted in order to improve the prognosis of stroke patients with atrial fibrillation, in particular patients who are not eligible to oral anticoagulant treatment.

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