**Mortality after stroke in patients with paroxysmal and chronic atrial fibrillation – The FibStroke Study**

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All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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**Disclosure of conflicts of interest**

Dr Palomäki has given a lecture for Bayer. Dr Mustonen has given lectures for Orion, Boehringer Ingelheim, Bayer, Pfizer, Bristol-Myers Squibb, Sanofi-Aventis and Leo Pharma, and has been a member in the advisory boards for Boehringer Ingelheim, Bayer, Pfizer, Bristol-Myers Squibb and Leo Pharma. Dr Juha Hartikainen has received research grants from the Finnish Foundation for Cardiovascular Research and the European Union Seventh Framework Programme, has given lectures for Cardiome, St Jude Medical and Biotronic, and has been member in the advisory boards for Astra Zeneca, Amgen and Bayer. Dr Kiviniemi has given lectures for Bayer, Boehringer Ingelheim, Medicines Company, Astra Zeneca and St Jude Medical, and received research grants from the Finnish Foundation for Cardiovascular Research and Finnish Cardiac Society. Dr Päivi Hartikainen has received honoraria from Genzyme, Novartis, Biogen Idec, TEVA, and has given lectures for Sanofi-Aventis. Dr Luite has received honoraria from Webster-Biosense, Biotronik, Bayer and St. Jude Medical, and has given lectures for Bristol-Myers Squibb. Dr Airaksinen has received research grants from the Finnish Foundation for Cardiovascular Research, has given lectures for Bayer, Cardiome and Boehringer Ingelheim, and has been a member in the advisory boards for Bayer, Astra Zeneca and Boston Scientific. The other authors report no disclosures.

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**Abbreviations:** AF=atrial fibrillation; $CHA_2DS_2$-VASc = Congestive heart failure, Hypertension, Age ≥ 75 (doubled), Diabetes mellitus, prior Stroke, transient ischemic attack or thromboembolism (doubled), Vascular disease, Age 65 to 74, Sex category (female, unless < 65 years and no other risk factors); $CHADS_2$= Congestive heart failure, Hypertension, Age ≥ 75, Diabetes mellitus, prior Stroke, transient ischemic attack or thromboembolism (doubled); CI=confidence interval; INR=international normalized ratio; IQR=inter-quartile range; TIA=transient ischemic attack

**Abstract**

Background: Recent studies have reported that patients with paroxysmal atrial fibrillation (AF) have lower risk of thromboembolism and better prognosis than patients with chronic AF. We sought to address the differences in ischaemic events in patients with paroxysmal and chronic AF.

Methods: FibStroke study is a cross-sectional observational multicenter registry that included AF patients with an ischaemic stroke, TIA (transient ischaemic attack) or intracranial bleed during 2003-2012 identified from discharge registries of four Finnish hospitals. Altogether 1448 patients with paroxysmal and 1808 patients with chronic atrial fibrillation suffered a total of 707 TIA-episodes and 2549 ischaemic strokes.

Results: Mortality within 30 days after the index event was significantly lower in patients with paroxysmal AF than with chronic AF (7.6% vs 16.9%, $p<0.01$). At the onset of event, 62.8% of the patients with paroxysmal AF were in sinus rhythm, and these patients had better prognosis after the event compared to patients with other rhythm than sinus rhythm (mortality 5.2% vs 15.7%, $p<0.01$). In the propensity score matched analysis mortality after stroke was significantly lower in patients with paroxysmal AF than in patients with chronic AF (11.6% vs 17.8 %, $p<0.01$), while mortality after TIA was also lower, but did not reach statistical significance (0.4% vs 1.7%, $p=0.31$).

Conclusions: Significant proportion of strokes in AF patients occurs in patients with paroxysmal AF, but they have better prognosis than patients with chronic AF. The prognosis is also significantly better in patients, who are in sinus rhythm at the onset of event.

## 1. Introduction

Atrial fibrillation (AF) is the most a common arrhythmia usually progressing from short self-terminating episodes (paroxysmal AF) to more long-lasting episodes requiring termination with cardioversion (persistent AF). As the disease progresses, the ability to maintain sinus rhythm is eventually lost in many of the patients, and AF becomes the prevalent rhythm (chronic AF)[1]. Because of the shifting nature of the AF in a single patient, the prevalence of paroxysmal AF is not totally unambiguous. It has been estimated that of all AF patients about 20% have paroxysmal AF[2,3]. Although the patients with paroxysmal AF are younger and healthier, in previous studies the risk of thromboembolism in paroxysmal AF has been similar to chronic AF[4-6]. However, recent studies have questioned this and demonstrated that patients with paroxysmal AF may have lower risk of thromboembolism as compared to patient with chronic AF [7-10]. The current guidelines suggest similar approach to oral anticoagulation depending on the risk factors for stroke (OAC) regardless of the type of AF[11,12]. Our previous studies suggest that a significant proportion of AF related ischaemic events occur to patients with paroxysmal AF and that these patients are frequently undertreated with OAC [13,14]. In this study we compared the clinical characteristics of thromboembolic events and prognosis in patients with previously diagnosed paroxysmal or chronic AF suffering a stroke or transient ischaemic attack (TIA).

## 2. Methods

### *2.1 Study population*

The FibStroke study (www.ClinicalTrials.gov, identifier NCT02146040) is part of a wider protocol in progress to assess thrombotic and bleeding complications of patients with AF in Finland[15,16].

The FibStroke registry included all consecutive patients with a previously diagnosed AF (paroxysmal, persistent of chronic) who suffered a stroke or intracranial bleed during the study period 2003-2012 [13,14]. Data for the study was collected from two university hospitals and two central hospitals in Finland. The initial screening was conducted by identifying all patients from the hospital discharge records with the following criteria: 1) The patient had been diagnosed with AF or atrial flutter and 2) The patient had been diagnosed with ischaemic stroke, TIA or intracranial bleed between the years 2003-2012 (in one central hospital 2006-2012). A comprehensive list of the ICD 10 codes used for the screening is provided in the Supplementary methods. After the initial screening, each case was individually reviewed from their patient records using a standardized data collection protocol and the diagnosis of AF or atrial flutter and ischaemic stroke, TIA or intracranial bleeding were confirmed case by case. Patient characteristics, risk factors for stroke and bleeding, medication, laboratory results, major operations and bleeding events during the 30 days preceding the stroke, TIA or intracranial bleeding were recorded. Data was collected in a structured electronic case report form.

There were a total 3677 patients with a history of AF and who after the diagnosis of AF developed a total of 3252 ischaemic strokes and 956 TIA episodes. During the study period 433 (11.8%) of the patients suffered more than one event. For this analysis, we chose only the first event for each patient.

The type of AF was chronic in 1808 (49.2 %), paroxysmal or persistent in 1448 (39.4%) and undefined in 349 (11.4 %) of the patients at the time of the first event. For the final analysis we included 3256 patients with a defined type of AF who suffered 707 TIA episodes and 2549 ischaemic strokes.

*2.2 Ethical issues*

The study protocol was approved by the Medical Ethics Committee of the Hospital District of Southwest Finland and the ethics committee of the National Institute for Health and Welfare. Informed consent was not required because of the registry nature of the study. The study conforms to the Declaration of Helsinki.

*2.3 Definitions*

The diagnosis of AF was confirmed by 12-lead electrocardiogram according to the standard criteria. All patients had at least one electrocardiographically confirmed AF episode before the onset of stroke. The nature of the AF (paroxysmal, persistent or chronic) was defined on the basis of the information in the patient records. The diagnoses of stroke and TIA were confirmed from the patient records, as diagnosed by the treating neurologist. Only strokes and TIAs considered as definite by the treating neurologist were included in our study. All patients were imaged by computed tomography or magnetic resonance imaging.

*2.4 Statistical analysis*

Continuous variables were reported as mean ± standard deviation if they were normally distributed, and as median [inter-quartile range (IQR)] if they were skewed unless stated otherwise. Categorical variables were described with absolute and relative (percentage) frequencies. Comparisons between study subgroups were performed with Student's t test or Mann-Whitney test as appropriate for

continuous and Chi-square test or Fisher's exact test as appropriate for categorical variables. A binary stepwise logistic regression analysis (backward Wald) was performed to identify independent predictors of mortality after TIA/stroke. All tests were two-sided and statistical significance was set at 5%. As this observational study does not provide randomization, a propensity score matching method was employed to select two groups of patients with chronic and paroxysmal AF having similar baseline characteristics. The propensity score was estimated using a non-parsimonious logistic regression model with the treatment method as the dependent variable. The following variables have been included as covariates: age; gender; hemoglobin; peripheral vascular disease; hypertension; diabetes; previous myocardial infarction; coronary artery disease; previous stroke or TIA; history of heart failure; estimated glomerular filtration rate < 30 ml/min/1.73m$^2$; treatment with oral anticoagulants; treatment with antiplatelet drugs. Pairs of patients with chronic and paroxysmal AF having the same probability score (nearest neighbour method, caliber = 0.2 * standard deviation of the logit) have been matched. To evaluate the balance between the matched groups, univariate analyses were performed and the analysis of the standardized differences after matching has been performed. A standardized difference less than 0.1 was considered as a negligible difference in the prevalence or mean of covariates between the study groups. Propensity score was used also as covariate in multivariate analysis in order to adjust for baseline differences existing between the study groups. Statistical analysis was performed using IBM SPSS Statistics software version 22.0.

This manuscript was written following STROBE guidelines for the reporting of observational studies[17].

*2.5 Missing data*

For all variables with more than 1.0% missing data, the exact number of patients with missing data is marked in the table. The 66 patients with missing mortality data were omitted from the propensity score analysis.

## 3. Results

### *3.1 Characteristics of the patients*

The characteristics of the study population are depicted in Table 1. Patients with chronic AF were older, had longer duration of AF diagnosis, and had more often diabetes, coronary artery disease and history of heart failure than patients with paroxysmal or persistent AF. As a result, they had more risk factors for AF associated stroke as measured with the $CHA_2DS_2$-VASc and $CHADS_2$ scores (Table 1). The index thromboembolic event was more often TIA in patients with paroxysmal AF as compared to patients with chronic AF (25.6% vs 18.6%, $p<0.01$).

### *3.2 Rhythm at the onset of stroke*

At the time of stroke or TIA, 63% of the patients with paroxysmal or persistent AF were on sinus rhythm (Table 1). The proportion of TIA-episodes was higher in patients who were on sinus rhythm when compared to patients with any other rhythm (28.3% vs 18.8%, $p<0.01$).

### *3.3 Antithrombotic medication*

Patients with paroxysmal AF were significantly less often anticoagulated than patients with chronic AF (32% vs 64%). On the other hand, antiplatelet drugs were more common in patients with paroxysmal AF (48% vs 29%).

### *3.4 Mortality*

After the index event (TIA or stroke) patients with paroxysmal AF had significantly lower 30-day mortality than patients with chronic AF (7.6% vs 16.9%). Mortality in different $CHA_2DS_2$-VASc levels is depicted in Figure 1. Higher $CHA_2DS_2$-VASc score was associated with increased mortality both in patients with chronic AF and in patients with paroxysmal AF. Mortality was lower

both after strokes (10.2% vs 20.3%, p<0.01) and TIA episodes (0.3% vs 2.1%, p=0.02) in patients with paroxysmal AF.

Mortality within 30 days after the index event (TIA or stroke) was significantly lower in patients who were in sinus rhythm at the onset of the event compared to patients who were in any other rhythm (5.2% vs 15.7%, p<0.01). If only strokes were considered, the mortality of patients in sinus rhythm and other rhythm were 10.2% vs 20.3%, p<0.01.

In patients who were in sinus rhythm, the mortality in patients who were using OAC was similar to patients not using OAC (4.9% vs 5.4%, p=0.78). In patients who were not in sinus rhythm, the mortality was higher in patients not using OAC (18.3 % vs. 13.7%, p<0.01).

Independent predictors of mortality within 30 days after the event in the final model were increasing age (per year OR 1.06, 95% CI 1.04–1.07), the use of OAC (OR 0.7, 95% CI 0.6–0.9), chronic AF (OR 2.0, 95% CI 1.5–2.6), history of heart failure (OR 1.8, 95% CI 1.4–2.3), and estimated glomerular filtration rate less than 30 ml/min/1.73 $m^2$ (OR 2.1, 95% CI 1.3-3.3) in a multivariate binary logistic regression analysis initially including age, gender, history of heart failure, hypertension, diabetes, previous stroke or TIA, previous myocardial infarction, the use of OAC, the use of antiplatelet medication, type of AF (chronic or paroxysmal) and eGFR less than 30 ml/min/1.73 m2 as variables.

In patients with paroxysmal AF the independent predictors of mortality within 30 days in the final model after the event were increasing age (per year OR 1.08, 95% CI 1.05–1.1), previous stroke or TIA (OR 1.5, 95% CI 0.95–2.5), history of heart failure (OR 1.98, 95% CI 1.2–3.3), and other than sinus rhythm at the onset of stroke (OR 1.9, 95% CI 1.2–2.9) in a multivariate binary logistic regression analysis initially including age, gender, history of heart failure, hypertension, diabetes, previous stroke or TIA, previous myocardial infarction, the use of OAC, the use of antiplatelet

medication, rhythm at the onset of stroke or TIA (sinus vs any other rhythm) and eGFR less than 30 ml/min/1.73 m2 as variables.

*3.5 Propensity score analysis*

Analysis of the standardized differences showed a significant imbalance in the prevalence and mean of most of the covariates before propensity score matching. Logistic regression (Hosmer-Lemeshow's test: p=0.374) provided a propensity score whose area under the receiver operating characteristics curve was 0.757 (95%CI 0.740-0.774). The 30-day mortality in the overall series was significantly higher in patients with chronic AF when adjusted only for the propensity score (p<0.001, OR 1.84, 95%CI 1.37-2.46) as well as for the propensity score and the time from diagnosis of AF to the neurological event (p<0.001, OR 2.23, 95%CI 1.51-3.30).

Propensity score matching provided 927 pairs of patients with well-balanced prevalence and mean of risk factors between the study groups (Table 2). The time from AF diagnosis, type of heart rhythm at the time of neurological event, severe renal failure and mean HAS-BLED were not balanced between the study groups as indicated by a standardized difference > 0.1. In contrast, the proportion of patients with $CHA_2DS_2$-VASc ≥ 2, $CHADS_2$ ≥ 2 and HAS-BLED ≥ 3 were balanced in the study groups.

The 30-day mortality among propensity score matched pairs was significantly higher in patients with chronic AF as compared with those with paroxysmal AF (14.8% vs. 8.6%, p<0.0001). In this subset of propensity matched pairs, the 30-day mortality among patients with TIA was higher in patients with chronic AF as compared with those with paroxysmal AF (1.7% vs. 0.4%, p=0.317), but the difference did not reach statistical significance. Among patients who suffered stroke, the 30-day mortality was significantly higher in patients with chronic AF (17.8% vs. 11.6%, p<0.0001).

## 4. Discussion

In the present study we showed that about 40 % of strokes and TIA episodes of patients with AF occur to patients with a previously diagnosed paroxysmal AF and they have they have a significantly lower mortality after the event than patients with chronic AF. Moreover, the majority of patients with paroxysmal AF were in sinus rhythm at the time of the event and their mortality was lower than in patients who were in AF at the onset of stroke. Only third of the patients with paroxysmal AF were using anticoagulation at the time of the event. The ischaemic event was more often TIA in patients with paroxysmal AF than during chronic AF.

### *4.1 Paroxysmal and chronic AF*

A significant proportion of strokes in patients with AF occur to patients with a history of paroxysmal AF. In previous studies, the proportion has varied from 31% to 53%[18,19].Whether or not the risk for thromboembolic complications is similar in patients with chronic and paroxysmal AF has been debated for years and the results have been somewhat controversial. Many often cited studies have reported similar risk of thromboembolic complications in paroxysmal and chronic AF [4-6]. However, most recent results from randomized clinical trials have shown significantly lower risk of thromboembolism in patients with paroxysmal AF when compared to chronic AF patients [7-9] and results were similar in a Japanese cohort of AF patients [10].

### *4.2 Rhythm at the onset of stroke*

In our study 63 % of patients with paroxysmal AF were in sinus rhythm at the onset of stroke or TIA. This is in line with a previous smaller study, in which AF was detected in 51.4% of patients with previously diagnosed paroxysmal AF presenting with an acute stroke or TIA[18]. This finding may reflect at least two things: (1) a spontaneous cardioversion has occurred before the onset of the

event predisposing to thromboembolic complication or (2) the patients have been in sinus rhythm and the index event is not embolic in nature but rather atherothrombotic. Since patients with paroxysmal AF had a higher proportion of TIA episodes and better survival after stroke, the latter might be true for some patients, as AF associated strokes have been shown to be more severe and lethal than non-AF related strokes[20,21]. The finding that TIA episodes are more common in patients with paroxysmal AF is also in line with a previous study [18].

*4.3 Antithrombotic medication*

In patients with paroxysmal AF who were in sinus rhythm at the onset of ischaemic event, OAC was not associated with a better outcome during the 30-days follow-up, while in patients who were not in sinus rhythm at the onset of event OAC was associated with a lower mortality. It has been previously shown, that strokes are less severe and mortality is lower in AF patients using OAC at the time of stroke[22,23]. While it seems that not all strokes in patients with paroxysmal AF may not be thromboembolic in nature, they seem to benefit from OAC[4,5].

*4.4 Limitations*

Retrospective design includes some limitations in the accuracy of data collection. However, in our study all patient charts were manually reviewed after the initial screening, and any remaining inaccuracies are compensated by the large number of events in our study. The definition of paroxysmal AF might have been slightly different among different clinicians, but this is unlikely to bring a systematic error, especially since we combined the groups of paroxysmal and persistent AF. While we used propensity score matching and logistic regression to address for confounding factors, there is always the possibility of residual confounding. The strengths of the study include the identification of all consecutive stroke and TIA patients with a diagnosis of AF from reliable hospital discharge records and the thorough individual case by case review of patient records.

## 5. Conclusions

A significant proportion of strokes and TIA episodes in patients with AF occur to patients with a previously diagnosed paroxysmal AF. Patients with paroxysmal AF have better prognosis after the event than patients who have chronic AF. Majority of patients with paroxysmal AF are in sinus rhythm at the onset of the event, and have better prognosis than patients who are not in sinus rhythm.

**References**

[1] Jahangir A, Lee V, Friedman PA*, et al.* Long-term progression and outcomes with aging in patients with lone atrial fibrillation: a 30-year follow-up study. Circulation 2007; 115:3050-3056.

[2] Levy S, Maarek M, Coumel P*, et al.* Characterization of different subsets of atrial fibrillation in general practice in France: the ALFA study. The College of French Cardiologists. Circulation 1999; 99:3028-3035.

[3] Jensen TJ, Haarbo J, Pehrson SM, Thomsen PE. Paroxysmal atrial fibrillation: ectopic atrial activity and prevalence of severely symptomatic patients. Pacing Clin Electrophysiol 2003; 26:1668-1674.

[4] Friberg L, Hammar N, Rosenqvist M. Stroke in paroxysmal atrial fibrillation: report from the Stockholm Cohort of Atrial Fibrillation. Eur Heart J 2010; 31:967-975.

[5] Hohnloser SH, Pajitnev D, Pogue J*, et al.* Incidence of stroke in paroxysmal versus sustained atrial fibrillation in patients taking oral anticoagulation or combined antiplatelet therapy: an ACTIVE W Substudy. J Am Coll Cardiol 2007; 50:2156-2161.

[6] Hart RG, Pearce LA, Rothbart RM, McAnulty JH, Asinger RW, Halperin JL. Stroke with intermittent atrial fibrillation: incidence and predictors during aspirin therapy. Stroke Prevention in Atrial Fibrillation Investigators. J Am Coll Cardiol 2000; 35:183-187.

[7] Al-Khatib SM, Thomas L, Wallentin L*, et al.* Outcomes of apixaban vs. warfarin by type and duration of atrial fibrillation: results from the ARISTOTLE trial. Eur Heart J 2013; 34:2464-2471.

[8] Vanassche T, Lauw MN, Eikelboom JW*, et al.* Risk of ischaemic stroke according to pattern of atrial fibrillation: analysis of 6563 aspirin-treated patients in ACTIVE-A and AVERROES. Eur Heart J 2015; 36:281-7a.

[9] Steinberg BA, Hellkamp AS, Lokhnygina Y*, et al.* Higher risk of death and stroke in patients with persistent vs. paroxysmal atrial fibrillation: results from the ROCKET-AF Trial. Eur Heart J 2015; 36:288-296.

[10] Takabayashi K, Hamatani Y, Yamashita Y*, et al.* Incidence of Stroke or Systemic Embolism in Paroxysmal Versus Sustained Atrial Fibrillation: The Fushimi Atrial Fibrillation Registry. Stroke 2015; 46:3354-3361.

[11] Camm AJ, Lip GY, De Caterina R*, et al.* 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J 2012; 33:2719-2747.

[12] January CT, Wann LS, Alpert JS*, et al.* 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart

Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014; 64:e1-76.

[13] Palomaki A, Mustonen P, Hartikainen JE*, et al.* Underuse of anticoagulation in stroke patients with atrial fibrillation - the FibStroke Study. Eur J Neurol 2015.

[14] Palomaki A, Mustonen P, Hartikainen JE*, et al.* Strokes after cardioversion of atrial fibrillation - The FibStroke study. Int J Cardiol 2015; 203:269-273.

[15] Airaksinen KE, Gronberg T, Nuotio I*, et al.* Thromboembolic complications after cardioversion of acute atrial fibrillation: the FinCV (Finnish CardioVersion) study. J Am Coll Cardiol 2013; 62:1187-1192.

[16] Nuotio I, Hartikainen JE, Gronberg T, Biancari F, Airaksinen KE. Time to cardioversion for acute atrial fibrillation and thromboembolic complications. JAMA 2014; 312:647-649.

[17] von Elm E, Altman DG, Egger M*, et al.* Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ 2007; 335:806-808.

[18] Rizos T, Wagner A, Jenetzky E*, et al.* Paroxysmal atrial fibrillation is more prevalent than persistent atrial fibrillation in acute stroke and transient ischemic attack patients. Cerebrovasc Dis 2011; 32:276-282.

[19] Aronis KN, Thigpen JL, Tripodis Y*, et al.* Paroxysmal atrial fibrillation and the hazards of under-treatment. Int J Cardiol 2015; 202:214-220.

[20] McGrath ER, Kapral MK, Fang J*, et al.* Association of atrial fibrillation with mortality and disability after ischemic stroke. Neurology 2013; 81:825-832.

[21] Wolf PA, Mitchell JB, Baker CS, Kannel WB, D'Agostino RB. Impact of atrial fibrillation on mortality, stroke, and medical costs. Arch Intern Med 1998; 158:229-234.

[22] Hylek EM, Go AS, Chang Y*, et al.* Effect of intensity of oral anticoagulation on stroke severity and mortality in atrial fibrillation. N Engl J Med 2003; 349:1019-1026.

[23] O'Donnell M, Oczkowski W, Fang J*, et al.* Preadmission antithrombotic treatment and stroke severity in patients with atrial fibrillation and acute ischaemic stroke: an observational study. Lancet Neurol 2006; 5:749-754.

## Figure Captions

**Figure 1.** Unadjusted mortality after stroke or TIA in patients with paroxysmal and chronic AF.