Adherence to Oral Anticoagulation in Secondary Stroke Prevention—The First Year of Direct Oral Anticoagulants

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Background: Patients with ischemic stroke caused by atrial fibrillation (AF) have a high risk of recurrence without adequate secondary prevention with oral anticoagulation (OAC). We investigated adherence to OAC in the first year after introduction of direct oral anticoagulants. *Methods:* In 284 appropriate patients, the rate of anticoagulation (AC) at discharge, adherence at 90 days and 1 year, changes between substances, and predictors for adherence to AC were analyzed. Functional outcome was assessed using the modified Rankin Scale score. *Results:* AC was initiated in 70.3% of survivors before discharge. In these patients, only 8.6% and 9.9% discontinued AC after 90 days and 1 year, respectively. In 22.1%, AC was recommended but not started before discharge. Only 53.2% of them received AC at 90 days, increasing to 67.5% at 1 year. A total of 7.6% of patients were deemed unsuitable for AC, none of them subsequently received AC. Overall, 85.4% of patients suitable for AC were treated at 1-year follow-up. No independent predictors for withholding AC were identified. Switching of medication occurred in only a minority of patients within the first year. *Conclusions:* AC is feasible in more than 90% patients with acute ischemic stroke and AF. When initiated during the acute hospital stay, AC is discontinued in only a minority of patients. However, if AC is recommended but not started during initial hospitalization the rate of AC treatment at 90 days and 1 year is much lower. Therefore, AC should be initiated within the acute hospital stay whenever possible. **Key Words:** Atrial fibrillation—ischemic stroke—oral anticoagulation—adherence.
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Introduction

Patients with acute ischemic stroke and underlying atrial fibrillation (AF) have a high risk of recurrent embolic events without adequate secondary prevention. Timely initiation of oral anticoagulation (OAC) is highly effective and reduces the risk for recurrence dramatically.[1] Nevertheless, previous studies have shown that because of the difficult handling of vitamin K antagonists and the fear for complications, OAC is often avoided and particularly prone to be discontinued by patients or treating physicians, even in the high-risk situation after previous embolic stroke.[1-3] We investigated whether the introduction of fixed dose direct oral anticoagulants (DOACs) with an improved safety profile has influenced initiation and adherence to OAC in secondary prevention after stroke.

Materials and Methods

Study Population

Data of all consecutive stroke patients treated on our stroke or neurointensive care unit (University Hospital,

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Erlangen, Germany) are entered into a prospective observational database, which was approved by the institutional ethics committee. Patient characteristics, stroke specific information, medication, and outcome data are recorded. For the present analysis, data of all patients between September 2011 and September 2012 with cerebral ischemia (stroke or transient ischemic attack) and underlying AF were extracted. The study period was chosen to cover the first year after approval of the first DOAC (dabigatran) in Germany. Mortality rate, functional outcome, and adherence to OAC after 90 days and 1 year were assessed in a standardized telephone interview with patients or their legal representatives as part of the general database.

Statistical Analysis

Data were tested for normality using the Kolmogorov–Smirnov test and presented as mean (standard deviation) or median (interquartile range) as appropriate. In non-normally distributed data nonparametric statistical tests (Mann–Whitney *U* test) were used. To identify predictors associated with anticoagulation (AC) at 1-year follow-up, binary logistic regression was performed. Potential factors investigated in previous studies were tested: age, age greater than 80 years,[4] Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism ($CHADS_2$) score[5] at discharge, and functional outcome.[6] Statistical significance was set at *P* less than .05. Data were analyzed using the SSPS 20.0 for Windows software (SPSS Inc, Chicago, IL).

Results

Overall, 284 patients with cerebral ischemia and underlying AF were included into the analysis. Baseline data are given in Table 1. In 210 patients, AF was known before the present stroke and antithrombotic premedication is

Table 1. *Baseline characteristics*

Parameter	N = 284
Age, mean ± SD, y	78.1 ± 9.5
Women	144 (50.7)
NIHSS score on admission, median (IQR)	5 (2-13)
Ischemia, n (%)	233 (82.0)
TIA, n (%)	51 (18.0)
Intravenous thrombolysis with rtPA, n (%)	69 (24.3)
Acute coronary syndrome, n (%)	6 (2.1)
Prior myocardial infarction, n (%)	31 (10.9)
Pre-existing coronary heart disease, n (%)	151 (53.2)
Prior ischemic stroke or TIA, n (%)	113 (39.8)
Prior hemorrhagic stroke, n (%)	3 (1.1)
Diabetes mellitus, n (%)	98 (34.5)
Arterial hypertension, n (%)	271 (95.4)
Hyperlipidemia, n (%)	145 (51.1)
Current smoking, n (%)	19 (6.7)
Previously known atrial fibrillation, n (%)	210 (73.9)
Anticoagulation on admission	98 (98/210 = 46.7%)
INR 2-3, n (%)	26 (26.5)
INR <2, n (%)	61 (62.2)
INR >3, n (%)	11 (11.2)
Platelet inhibition on admission	68 (68/210 = 32.4%)
ASA 100 mg/d, n (%)	60 (88.2)
Clopidogrel 75 mg/d, n (%)	5 (7.4)
ASA + ER-dipyridamole, n (%)	3 (4.4)
No antithrombotic treatment	44 (44/210 = 21.0%)
Newly detected atrial fibrillation, n (%)	74 (26.1)
$CHADS_2$ score on admission (index ischemia/TIA not counted), median (IQR)	3 (2-4)
$CHADS_2$ score at discharge in survivors (actual ischemia/TIA is counted), median (IQR)	4 (4-5)
Renal impairment on admission (estimated glomerular filtration rate eGFR <60 mL/min/1.73 m^2), n (%)	114 (40.1)
eGFR <30 mL/min/1.73 m^2, n (%)	18 (6.3)

Abbreviations: ASA, acetylsalicylic acid; $CHADS_2$, Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus, Prior Stroke or TIA or Thromboembolism; eGFR, estimated glomerular filtration rate; ER-dipyridamole, extended-release dipyridamole; INR, international normalized ratio; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; rtPA, recombinant tissue plasminogen activator; SD, standard deviation; TIA, transient ischemic attack.

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