Incidence of Stroke and CHADS2 Score in Patients with Paroxysmal, Persistent or Permanent Atrial Fibrillation: Prognosis at 1 Year of Follow-Up

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Objectives: our main endpoints were to determine the incidence of fatal or nonfatal stroke either ischemic or hemorrhagic or transient ischaemic attack, associated with paroxysmal versus persistent and permanent atrial fibrillation (AF), in patients receiving oral anticoagulation therapy (OAC) compared to antiplatelet group, and to test the accuracy of CHADS2 score for the prediction of tromboembolic and hemorrhagic complications, at one year follow up. Secondary endpoints were the hospitalization rate, case fatality at one year and rate of progression of paroxysmal to persistent/permanent AF.

Material and methods: we performed a retrospective (2007–2008) observational study on 468 patients admitted to our department with paroxysmal, persistent and permanent nonvalvular AF, on oral anticoagulation or antiplatelet therapy. We compared the incidence of thromboembolic and hemorrhagic events in patients with paroxysmal AF, persistent and permanent AF, and in patients undergoing anticoagulation versus antiplatelet therapy.

Results: we found a statistically difference between the group of patients treated with OAC and the one treated with antiplatelet therapy in favor for the OAC group of AF in what concerns one year rate of stroke. We also found a statistical difference between the CHADS2 score values and the rate of stroke after during one year.

Conclusions: permanent form of atrial fibrillation carries a higher risk of tromboembolic events than persistent and paroxysmal AF. OAC therapy is superior to platelet therapy in all forms of cardiac arrhythmia in preventing the tromboembolic events. CHADS2 score is a good predictor for stroke.

Keywords: atrial fibrillation, stroke, CHADS2 score

Introduction

Atrial fibrillation is the most common sustained cardiac arrhytmia encountered in clinical practice and is associated with an increased mortality and morbidity, mainly as a result of tromboembolic complications and of heart failure [1]. Several risk stratification models of different complexity have been introduced to identify AF patients who benefit from oral anticoagulation but in none of these models the type of AF, paroxystical versus permanent has emerged as an independent predictor of thromboembolic events. Accordingly, a contemporary study is needed to confirm the stroke risk of patients with paroxysmal as compared with sustained AF [2,4].

Definitions

Ischaemic stroke – Focal neurological deficit of sudden onset as diagnosed by a neurologist, lasting >24 h, and caused by ischaemia [2].

Transient ischaemic attack – Focal neurological deficit of sudden onset as diagnosed by a neurologist, lasting <24 h [2].

Hemorrhagic stroke – Focal neurological deficit of sudden onset as diagnosed by a neurologist, lasting >24 h, and caused by a bleeding [2].

CHADS2 score is a clinical prediction rule for estimating the risk of stroke in patients with non-rheumatic atrial fibrillation (AF), a common and serious heart arrhythmia associated with thromboembolic stroke [3].

Atrial fibrillation progression – First detected becoming paroxysmal, persistent or permanent AF, paroxysmal becoming persistent or permanent AF, persistent becoming permanent AF [2].

	Condition points	
C	Congestive heart failure	1
H	Hypertension (history): blood pressure consistently above 140/90 mmHg (or treated hypertension on medication)	1
A	Age ≥75 years	1
D	Diabetes Mellitus	1
S2	Prior Stroke or TIA	2

Materials and methods

We performed a retrospective observational-analytic study with a duration of 1 year, between January 1, 2007 and January 1, 2008, in the Internal Medicine Department of the 4th Medical Clinic and the Neurology Clinic from Tîrgu Mureș. Data was collected through medical records, medical information systems or entered by the attending physician and was introduced in a software for statistical analysis. A consentment has been obtained for accessing the database.

We classified AF in three categories: paroxysmal AF, (episodes of recurrent arrhythmia that terminates spontaneously in seven days), persistent AF (episodes that are sustained longer than 7 days, or last for less than seven days but necessitate electrical or pharmacological cardioversion) and permanent AF (patients to which cardioversion was not attempted) [3].

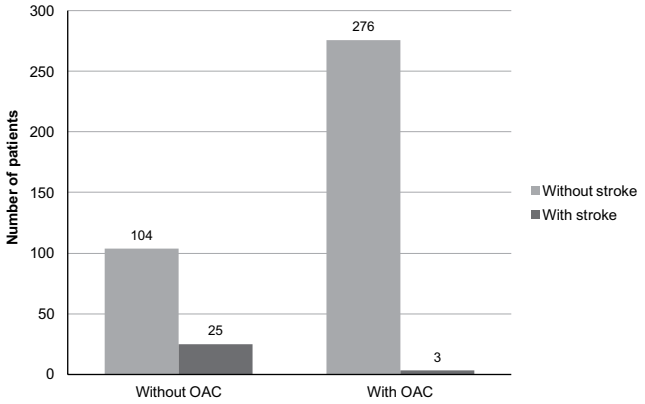

Fig. 1. Stroke rate in the oral anticoagulated group (OAC) compared to the non-anticoagulated group

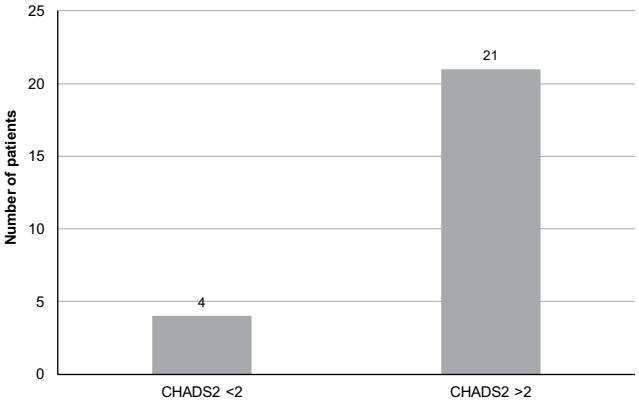

Fig. 2. CHADS2 score in non-anticoagulated group

Patients with permanent AF had a documented ECG at the time of the enrollement that showed AF, and no evidence of sinus rhythm in the year before randomization. Patients with paroxysmal or persistent AF had an ECG documented AF on two separate occasions, at least 2 weeks apart in the 6 months before randomization.

The mean age of the study population was 68.53 years, irresepective of sex and ethnic or demographic origin. We excluded patients with a history of heart valve problem and/or valve replacement.

Statistical analysis

We performed the analysis with the Epi Info software, Chi square, 1 tailed p and Fisher exact tests, with a confidence limit of 95%. A p value of <0.05 was considered statistically significant.

Results

We enrolled 468 cases of atrial fibrillation in January 2007 and we followed them for a period of 1 year. We separated the patients into two groups, one of 279 patients treated with oral anticoagulation therapy (OAC) with Acenocumarol with a INR in therapeutical range (2–3) and the other of 189 patients on antiplatelet therapy. We divided them in three groups depending on the type of AF: paroxysmal, persistent and permanent.

Table I. Correlation between the incidence of stroke in the anticoagulated group versus platelet treated group

Fisher's exact test			
P value	P<0.0001		
P value summary	***		
One- or two-sided	Two-sided		
Statistically significant? (alpha <0.05)	Yes		
Strength of association			
Odds ratio	0.07130		
95% confidence interval	0.02119 to 0.2399		
Data analyzed	Without AVC	With AVC	Total
Without anticoagulant	164	25	189
With anticoagulant	276	3	279
Total	440	28	468

At one year of follow-up we found a statistical difference concerning the stroke rate between the group of patients treated with OAC and those treated with antiplatelet therapy (p <0.0001, OR = 0.07130). A percentage of 5.98% patients developed tromboembolic complications, 3 ischaemic strokes in the anticoagulated group (0.72%) and 25 (4 transient ischaemic attacks and 21 ischaemic strokes) in the non-anticoagulated group.

A CHADS score ≥2 was found in 21 patients (11.11%) from the non-anticoagulated group, and 4 (2.12%) had a CHADS score <2. The CHADS2 score strongly associates with the stroke rate, which suggests a good accuracy of this score and further investigation is needed to decide the superiority of CHADS2 VASC score.

In patients with a CHADS2 score ≥2, chronic therapy with OAC is recommended in a dose-adjusted approach to achieve an international normalized ratio (INR) target of 2–3, unless contraindicated [4].

We found a higher risk of developing tromboembolic events in favor of permanent atrial fibrillation (75%) compared with two other types: paroxysmal (25%), and persistent (0%), in the non-anticoagulated group (p = 0.0056465).

59.62 % of all patients received OAC and 40.38% were assigned to antiplatelet therapy, the criteria of anticoagulation being established on the basis of CHADS2 score, with a therapeutic range of INR 2–3. In function of patient compliance to INR surveillance, all patients with a CHADS2 score ≥2 were assigned to OAC therapy. The patient's lack of compliance was considered a reason in favor of antiplatelet therapy. During one year of follow up 26 cases were electrically converted to sinus rhythm (5.6%),

Table II. Correlation between stroke rate and permanent AF in the non-anticoagulated group

STATISTICAL TESTS	Chi-square	1-tailed p	2-tailed p
Chi-square – uncorrected	25,0000		<0.01
Chi-square – Mantel-Haenszel	24,0000		<0.01
Chi-square – corrected (Yates)	19,8181		<0.01
Mid-p exact		<0.01	
Fisher exact		<0.01	

25 were farmacologically converted (5.34%), while 13 cases presented a spontaneous conversion (2.78%) and they continued anticoagulation.There was a progression of atrial fibrillation in 2.56% of cases (2 cases from paroxysmal to persistent AF, 10 from persistent into permanent). There was a case fatality of 0.64 % (3 cases), 1 of non-cardiovascular cause and 2 of cardiovascular death (0.43%). 64.5% of all patients had a single hospitalization during the follow-up, 4.27 % had at least three hospitalizations in our clinic and 3 patients were hospitalized in the Neurology Clinic.

Discussions

The rate of ischaemic stroke was higher in the antiplatelet group compared to OAC group ($p < 0.0001$). One year mortality was not high, but it is possible to have underestimated it, due to patient transfer at a nursing home [8]. This is in concordance with the prior studies.

Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study showed that OAC (target INR 2–3) was superior to aspirin 75 mg daily in reducing the primary endpoint of fatal or disabling stroke (ischaemic or haemorrhagic), intracranial haemorrhage, or clinically significant arterial embolism by 52%, with no difference in the risk of major haemorrhage between warfarin and aspirin [4].

In the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events–Warfarin arm (ACTIVE W) trial, anticoagulation therapy was superior to the combination of clopidogrel plus aspirin (RR reduction 40%; 95% CI 18–56), with no difference in bleeding events between treatment arms [4].

An important finding in this study is that permanent AF carries a higher risk of tromboembolic events than persistent and paroxysmal AF ($p = 0.0056465$) in non-anticoagulated patients.

In our study the rate of stroke and transient ischaemic attack was lower compared to ACTIWE W study, probably due to absence of death from hemorrhagic stroke due to single antiplatelet therapy and not combined [5,7].

While OAC is an effective therapy for the prevention of stroke in atrial fibrillation, the need for frequent monitoring of the INR, frequent medication adjustments, food and drug interactions, risk of bleeding, and patient/physician resistance has generally led to an under-utilization of OAC in patients who might benefit from this therapy [3].

Alternative agents to OAC have recently been studied. The ACTIVE A trial showed that in patients unable or unwilling to take warfarin, the combination of aspirin plus clopidogrel compared with aspirin alone reduced the risk for stroke by 28%, although it also increased the risk for major bleeding events. There was a net benefit in favor of dual antiplatelet therapy, because in general bleeding events are easier to treat than a massive ischemic stroke, which is a frequent scenario in strokes caused by atrial fibrillation [3,5].

The studies with anticoagulation not requiring constant INR monitoring are very promising and could make treatement more stable, but for the moment their clinical daily use is cost-limited [6,11,12].

Conclusions

1. The rate of ischemic strokes was higher in the antiplatelet group compared to OAC group.
2. Permanent AF carries a higher risk of tromboembolic events than persistent and paroxysmal AF in non anticoagulated patients.
3. A CHADS2 score equal or superior to 2 necessitates chronic OAC, irrespective of the category of AF, unless contraindicated.
4. The progression of AF to more severe forms during one year of follow up was superior in persistent form of AF.

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