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On the outcome in stroke patients one year later: the role of atrial fibrillation

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The post-stroke aftermath of patients suffering from atrial fibrillation (AF) is investigated. A total of 104 consecutive patients (80 with AF and 24 without AF) were referred to a rehabilitation centre and enrolled. They underwent a rehabilitative programme. Disability was assessed by using the Functional Independence Measure (FIM), at the time of admission, discharge and after 1 year. Death was more frequent over the 1-year interval in AF group. Ten patients died (42%), whereas in the non-AF group death occurred in 15 cases (19%). By using chi-square test, the difference was significant ($P < 0.02$). The logistic regression analysis indicated that the unique variable affecting the FIM at follow-up was the FIM at discharge ($P < 0.0001$). AF was not a significant variable in the equation. The result can be attributed to subject attrition in the AF group, as the most severe patients died and survivors could benefit from a better functional status.

Introduction

Atrial fibrillation (AF) is the most frequent dysrhythmia in clinical practice. It is observed in 0.3–0.4% of the adult population and increases significantly with age, reaching values of more than 10% in persons over 75 years of age. The Framingham study (Wolf *et al.*, 1991) and the Cardiovascular Health Study (Furberg *et al.*, 1994) have reported a prevalence of approximately 5% in patients over 65 years of age. Another recent study (Levy *et al.*, 1999) has stated that hypertension is the most frequent associated pathology at presentation of AF (40%), followed by coronaropathy (16%) and myocardial disease (15%). Previous studies, like the Stroke Prevention in AF (SPAF, 1991) had already demonstrated that hypertension and recent heart failure were predictive factors for possible embolism. Moreover, the SPAF and the Copenhagen Atrial Fibrillation Aspirin and Anticoagulation (AFASAK) studies (Petersen *et al.*, 1989) had reported the seriousness of stroke secondary to AF, being fatal and highly invalidating in 63 and 44% of subjects, respectively. Therefore, AF is a well-known independent risk factor for stroke, with a 3–5-fold increased risk (Wolf *et al.*, 1991). Seventy-five per cent of strokes that occur in fibrillating patients are caused by embolism and embolism was already present when AF started, more than 48 h before (Bogousslavsky *et al.*, 1990). Every year 1% of patients with AF experience four or five embolic episodes. The annual frequency of embolism is 12% in patients with recurrent strokes [Ezekowitz *et al.*, 1995; Aronow *et al.*, 1996; EAFT (European Atrial Fibrillation Trial) Study Group, 1996].

Functional condition with AF and stroke is low at the time of admission and discharge from a rehabilitation centre (Jorgensen *et al.*, 1996; Lin *et al.*, 1996; Karatas *et al.*, 2000; Palomeras Soler and Roquer Gonzales, 2000), but the functional gain does not seem to differ compared with stroke patients without AF. It is not clear yet if stroke patients with or without AF present statistically significant differences in functional gain 1 year after discharge.

Therefore, the objective of our study was to verify if stroke patients with and without AF, at the time of admission, discharge and at 1-year follow-up (i) present statistically significant differences in functional gain; (ii) have a different mortality rate; (iii) show an effect of the variables on the final outcome, such as age, sex, diabetes, hypertension, concomitant cardiopathy (hypertensive, coronaric, valvular cardiopathies), cigarette smoking, pulmonary diseases, pharmacological therapy (digital, warfarin, antiplatelets, antidysrhythmics, coronary-vasodilators).

The study was approved by the local Ethical Standards Committee in accordance with the requirements of Good Clinical Practice and with local laws. Informed consent was obtained from the patients or when necessary from their relatives.

Patients and methods

A total of 104 consecutive stroke patients were enrolled and started on a 60-day rehabilitation programme. Eighty patients presented without AF (men/women 39/41) and 24 with AF (men/women 9/15). They were referred to us by general hospitals, none

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from a stroke unit. The mean interval between stroke event and admission to the rehabilitation centre was 18 days. Inclusion criteria were (i) first ever stroke; (ii) interval from stroke no longer than 3 weeks; (iii) compliance to rehabilitation programme. Exclusion criteria were (i) subarachnoid haemorrhage; (ii) neurosurgery of any kind; (iii) severe cases at admission, treatment urgently needed and prognosis guarded. The stroke severity was assessed by means of the Scandinavian Stroke Group (1985). Disability was assessed using the Functional Independence Measure (FIM) (Linacre *et al*., 1994), at the time of admission, discharge, and after 1 year. Comorbidity was assessed by means of the Cumulative Illness Rating Scale (CIRS) (Linn *et al*., 1968). AF was diagnosed at admission on the basis of electrocardiogram and further studies to confirm the presence of chronic AF. One year after discharge, patients and their relatives were contacted in order to fill out the follow-up FIM scale. Patients were treated only with drugs that were strictly necessary.

Statistics were performed by using a logistic regression analysis. Candidate variables were chosen on the basis of bivariate analysis results. Such a method allowed to avoid an adjustment on patients' age and FIM value at entrance. The FIM value at the outcome was the dependent, dichotomic variable (independent patient or not). The cut-off of the minimal independence was set at 90, i.e. score 5 for 18 items. The univariate ANOVA was used to choose the continuous variables, and the Person chi-square was used for the dichotomic variables. Significant continuous variables were age, FIM at admission and FIM at discharge. Significant dichotomic variables were cardiopathies and usage of digital. The comparison of percentage of deaths was performed by the chi-square test. Comparison of age between groups was made by means of *t*-test. Comparison of stroke severity between groups was made by means of Mann–Whitney *U*-test. All statistical tests were developed with 'two tails' and with a significance level of 0.05. Statistical analysis has been performed by using the SPSS Software (1998).

Results

The patients of the AF group were older than the patients of the non-AF group. Indeed, the mean age was 76.0 (SD = 6.64) vs. 70.5 years (SD = 11.0). The difference was significant at the *t*-test ($P < 0.005$). The stroke severity was also higher in this group: Mann–Whitney *U*-test 638, ($P < 0.01$). Median FIM values are indicated in Table 1. AF group values at admission were significantly lower than non-AF group: Mann–Whitney *U*-test 668 ($P = 0.024$). FIM gains at discharge were the same. Other variables were equally distributed between the two groups (Table 2) except for a higher incidence of other cardiopathies in AF group, with a significant difference. Concomitant pharmacological treatments (antihypertensive, digital, anticoagulate, antiplatets, coronary dilators, antidysrhythmics) were also alike.

Death was more frequent over the 1-year interval in the AF group. Ten patients died (42%), whereas in the non-AF group death occurred in 15 cases (19%). By using chi-square test, the difference was significant ($P < 0.02$).

The logistic regression analysis indicated that the unique variable affecting the FIM at follow-up was the FIM at discharge ($P < 0.0001$). The exp *B*-value was 0.91 and the 95% confidence interval was 0.87–0.94. The R was −0.38. The prior bivariate analysis had indicated the following significant candidate variables: age, FIM at admission, FIM at discharge, cardiopathies and usage of digital. Therefore, AF was not a significant variable in the equation.

Discussion

The incidence of AF in our patient population (23%) is similar to that reported in other studies (Sandercock

Table 1 Median FIM values at admission, discharge and follow-up

With AF ($n = 24$)	Without AF ($n = 80$)
30	52
68	83
99.5	104

Table 2 Comparison of demographic and clinical characteristics in patients with and without atrial fibrillation (AF)

	With AF ($n = 24$) (%)	Without AF ($n = 80$) (%)	*P*-value from univariate analysis (chi-square test)
Tobacco Consumption	7 (29.2)	25 (31.2)	0.846
Diabetes	3 (12.5)	14 (17.5)	0.756[a]
Hypertension	14 (58.3)	58 (72.5)	0.187
Other cardiopathies	10 (41.7)	6 (7.5)	0.001[a]
Broncho-pulmonary diseases	4 (16.7)	5 (6.2)	0.206[a]
Concomitant treatments	23 (95.8)	68 (85.0)	0.29

[a]Fisher's exact test.

et al., 1992; Kaarisalo *et al*., 1997). Stroke and also disability were more severe in our patients with AF. Previous finding were therefore confirmed (Jorgensen *et al*., 1996).

Fibrillating stroke patients have a major mortality risk than those without AF, as already reported (Fisher, 1979; Kaarisalo *et al*., 1997), probably for other associated cardiopathy rather than microembolism. The decreased survival observed in patients with AF was present in women and across a wide range of ages (Benjamin *et al*., 1998).

In a review by Roth (1994), it was observed that the presence of cardiac disease, like ischaemic cardiopathy or congestive heart failure, had a negative impact on functional rehabilitation of a stroke patient, also in follow-up. Furthermore, it was suggested by other authors (Keller *et al*., 1982; Britton and Gustafsson, 1985) that a major prevalence of ischaemic cardiopathy and congestive heart failure in patients with AF causes cerebral hypoperfusion and is responsible for ischaemic cerebral lesions. Recently, Sharma *et al*. (2000) found that the pre-existence of associated cardiopathy has a negative influence on stroke mortality, independent of other risk factors. The other clinical variables studied, like cigarette smoking, diabetes, hypertension, bronchopulmonary disease, associated medical treatment did not interfere significantly with functional recovery at discharge and/or at 1-year follow-up. These data confirm the results of a previous study of our group (Giaquinto *et al*., 2001).

The incidence of AF increases in the last decades of life, with a peak of 8.8% in patients between 80 and 89 years old (Tresch and Aronow, 1994; Feinberg *et al*., 1995). Histopathological studies of the heart in the elderly reveal a reduction of muscle mass, increase of elastic fibres, collagen and fat tissue at the interatrial septal level, atrial dilatation and small losses in the conduction fibres (Heger, 1981; Holland and Gravanis, 1989). The incidence of coronaropathy is approximately 30% in patients older than 75 years and increases significantly in the following years (Giaquinto *et al*., 2001).

Neurovegetative changes, histological modifications of the myocardiac tissue in the elderly, hypertension and coronaropathies are all factors facilitating 're-entry mechanisms' that represent the electrophysiological substratum of the AF onset (Rensma *et al*., 1988; Konigs *et al*., 1994). If the role of chronic AF is considered in recent stroke patients, who underwent rehabilitation and subsequently followed at 1 year, it can be observed that many variables are mixed and apparently interfere with functional recovery.

Our statistical analysis revealed that the outcome of stroke patients at 1 year after stroke, as measured by FIM, was solely dependent of the FIM value at discharge. In other words, AF apparently lost importance. In this sense, our data overlap with those presented by Lin *et al*. (1996), but the studies are not similar. Lin *et al*. (1996), performed a study based on a general population sample, and for geographical reasons not every stroke survivor could attend follow-up examination at each set time. Our study was focused on a population admitted to rehabilitation, a field where prognosis is important for both medical and fiscal reasons. Compared with the case selection encountered in hospital-based series, our study is biased by a lesser number of more severe stroke cases, who deceased before admission. By contrast, our data come from a prospective study on patients actively trained for 2 months, whose disability was checked three times during the study by means of the FIM, that provides a better evaluation of dependence compared with Barthel Index which is just a performance scale (Mahoney and Barthel, 1965). All the stroke survivors were checked.

At the best of our knowledge, the present study is the first to provide a follow-up of cases with AF, dismissed from a rehabilitation centre. The offset of AF variable during the follow-up period perhaps is because of subject attrition in the AF population. Indeed, the increased mortality in this group accounts for a selection of less-severe patients, who can benefit from their functional conditions. It has already been postulated that some variables, such as age and other cardiopathies could be associated to a minor ability in participating to an active re-education, more than a direct deleterious effect on the final outcome (Bagg *et al*., 2002).

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