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## Atrial Fibrillation as a Risk Factor for Deep Venous Thrombosis and Pulmonary Emboli in Stroke Patients

P. Noel, MD; F. Gregoire, MD; A. Capon, MD; and P. Leheret, PhD

**In 539 consecutive stroke patients admitted to a rehabilitation department, we studied the possible role of atrial fibrillation as a risk factor for deep venous thrombosis and pulmonary embolism by analyzing a series of relevant clinical data in patients with and without atrial fibrillation and in patients with and without venous thromboembolic complications. Deep venous thrombosis as well as advanced age and cardiac disease were significantly ( $p < 0.001$ ) more frequent in patients with atrial fibrillation. However, in a model of simultaneous logistic regression carried out on the presence or absence of venous thromboembolic complications, atrial fibrillation was the only significant risk factor. In view of the morbidity and mortality linked to deep venous thrombosis, our findings argue for preventive anticoagulation therapy in stroke patients suffering from atrial fibrillation and merit further study. (*Stroke* 1991;22:760-762)**

The high incidence of deep venous thrombosis and pulmonary embolism in stroke patients is well documented.<sup>1</sup> Among the patients admitted to our rehabilitation unit, we noted the frequent coexistence of deep venous thrombosis or pulmonary embolism and stable atrial fibrillation (AF). The possible role of AF as a risk factor for deep venous thrombosis was questioned. To approach this problem, the distribution of various risk factors for deep venous thrombosis or pulmonary embolism was analyzed first in patients with and without AF and then in patients with and without deep venous thrombosis or pulmonary embolism.

### Subjects and Methods

The data prospectively accumulated from 539 patients consecutively admitted to our rehabilitation department were analyzed. The mean interval from stroke to admission was 16 days, 48% (259) of the patients being admitted before the 15th day. All grades of motor and functional deficits were observed. On admission, 61% (329) of the patients needed maximal help to walk and were confined to a wheelchair or bed, 27% (146) needed passive help to walk, and 12% (64) were able to walk without any help. Only 1.5% (eight) of the patients were treated

with anticoagulants on admission. The following items were taken into account: sex, age, history of heart failure, absence of peripheral arterial pulses in the lower limbs, Quetelet index as an assessment of obesity, cardiomegaly on chest radiography, large size (>50% of hemispheric surface) of the brain lesion on computed tomography, and death.

Deep venous thrombosis was diagnosed on clinical grounds, and the diagnosis was confirmed by phlebography. Pulmonary emboli, when suspected clinically, were confirmed by a perfusion-ventilation isotopic scan. Venous thromboembolic complications between admission and discharge or death were noted. The diagnosis of AF or flutter-fibrillation was made on electrocardiography.

Statistical analysis was achieved by the  $\chi^2$  test, two-sample  $t$  test, and logistic regression.

### Results

The results are summarized in Table 1. When comparing patients with and without AF, deep venous thrombosis was significantly more frequent ( $\chi^2$  test,  $p < 0.001$ ) in the former. Patients with AF were also significantly older than those without and more frequently had a history of heart failure or cardiomegaly. This led us to suspect that AF's effect on the frequency of deep venous thrombosis might be an indirect one, due to the combined presence of older age, congestive heart failure, and cardiomegaly.

A first approach consists of observing that these three risk factors considered in particular do not influence the occurrence of deep venous thrombosis significantly (Table 1). A more accurate method of

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TABLE 1. Comparison of Frequency of Relevant Clinical Data Among 539 Patients Admitted to Rehabilitation Department

Parameter	Atrial fibrillation				Deep venous thrombosis			
	With (n=88)		Without (n=451)		With (n=60)		Without (n=479)	
	No.	%	No.	%	No.	%	No.	%
Sex								
Male	31	35	230	51	24	40	237	49
Female	57	65*	221	49	36	60	242	51
Age (mean±SD) (years)	75±9.1†		68±12.4		71±10.0		69±11	
History of congestive heart failure	36	41†	57	13	11	18	82	17
Peripheral arterial insufficiency	33	38	163	36	17	28	179	37
Quetelet index	24.0±4.3		25.0±4.6		24.9±5.4		24.9±5.1	
Cardiomegaly	67	76†	210	47	37	62	240	50
Large brain lesion	23	26	82	18	15	25	90	19
Death	18	20†	20	4	7	12	31	6
Deep venous thrombosis or pulmonary emboli	20	23†	40	9	...	...	...	...
Atrial fibrillation	...	...	...	...	21	35‡	67	14

n=466 for Quetelet index.

\* $p < 0.01$ , † $p < 0.001$  different from patients without atrial fibrillation by  $\chi^2$  test.

‡ $p < 0.001$  different from patients without deep venous thrombosis by  $\chi^2$  test.

separating the intrinsic effect of AF on deep venous thrombosis consists of using simultaneous logistic regression<sup>2</sup> of the presence versus the absence of deep venous thrombosis or pulmonary embolism as the main criterion, with the additional predictors sex, age, congestive heart failure, peripheral arterial insufficiency, Quetelet index, cardiomegaly, size of the brain lesion, and AF. With this method, the only significant main effect was AF ( $p=0.0049$ , partial correlation coefficient=0.136). No significant interaction of the other factors was found, and the very small values of the other partial correlation coefficients underlined the essential intrinsic effect of AF.

### Discussion

As shown in Table 1, the frequency of thromboembolic events in patients with AF far exceeded that in those without ( $p < 0.001$ ). Patients with AF were significantly older and had higher frequencies of cardiomegaly and history of cardiac failure, both conditions probably being linked. In view of these data, a possible physiopathologic role of a poor hemodynamic situation as the main risk factor for deep venous thrombosis with an indirect effect of AF was considered; this effect was not supported by the statistical analysis. Neither peripheral arterial insufficiency, which may contribute to a poor hemodynamic situation, nor age and a large brain lesion on computed tomography (as an index of functional impairment) showed a significant role in the development of venous thromboembolic complications. Therefore, it seems that AF is an independent risk factor for deep venous thrombosis or pulmonary embolism in stroke patients.

The role of an atrial or platelet humoral factor is hypothesized.<sup>3</sup> However, AF may worsen local venous parameters, which have been implicated in the development of deep venous thrombosis.<sup>1,4</sup> This finding

may have practical implications. The relation between AF and stroke is well known,<sup>5</sup> but there is no consensus for anticoagulation therapy.<sup>6-9</sup> Many stroke patients develop deep venous thrombosis and pulmonary embolism, particularly during the acute stage, but there is also no definite consensus for preventive anticoagulation in hemiplegic patients.<sup>10,11</sup> Mortality in our patients with deep venous thrombosis was twice that in those without (Table 1). Although this difference was not significant, it may be assumed that the thromboembolic disease contributed to the poor prognosis.<sup>1</sup> The greater incidence of deep venous thrombosis and pulmonary embolism in stroke patients with AF or flutter-fibrillation after the acute stage may be an argument favoring preventive anticoagulation therapy and merits further study.

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KEY WORDS • atrial fibrillation • cerebrovascular disorders • thrombosis