ARTICOLO ORIGINALE

Differenze nel decorso clinico intraospedaliero, nella gestione e nella prognosi dello stroke con e senza fibrillazione atriale. Analisi retrospettiva dello studio SETI (Studio Epidemiologico Toscano Ictus)

Differences in in-hospital clinical course, management and outcome between stroke with and without atrial fibrillation. A retrospective analysis from the SETI (Studio Epidemiologico Toscano Ictus) study

P. Biagi[1], S. Bocchini[1], R. Laureano[2], G. Panigada[2], G. Vescovo[3] *

[1] UO Medicina Interna, OO.RR. Valdichiana Montepulciano, USL 7 Siena
[2] UO Medicina Interna, Ospedale di Pescia, USL 3 Pistoia
[3] UO Medicina Interna, Ospedale "San Bortolo", USL 6 Vicenza

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Sommario **Scopo dello studio** Lo Stroke (S) che si presenta in pazienti con Fibrillazione Atriale (FA) differisce da quello che si presenta in soggetti a ritmo sinusale per la gravità dell'insorgenza e per la prognosi, tuttavia altri fattori possono alterare lo scenario clinico. **Materiali e metodi** Abbiamo studiato 738 pazienti (430 femmine e 308 maschi) di età media di 78,7 ± 9,9 anni (femmine 81,0 ± 8,9; maschi 75,2 ± 10,2; $p < 0,001$) ricoverati consecutivamente a causa di S nei reparti di Medicina Interna della Toscana in un periodo di tre mesi (dal 1° marzo al 31 maggio 2003) allo scopo di definire se il decorso clinico e il carico assistenziale degli S con FA fosse differente da quello degli eventi senza FA. Sono stati presi in esame i seguenti punti: dati demografici, condizioni cliniche prima del ricovero, modalità e tempo del ricovero, presentazione clinica, trattamento, complicanze, esito e modalità della dimissione. **Risultati** Gli S con FA sono stati 205 (27,8%). L'età media di questi pazienti era significativamente maggiore. Lo scompenso cardiaco, la cardiopatia ischemica, la cardiomiopatia dilatativa e l'insufficienza renale cronica erano più frequenti in questi soggetti e inoltre avevano una presentazione clinica con un più basso score alla Glasgow Coma Scale (GCS) ($p < 0,01$) all'ingresso. La terapia intraospedaliera evidenziava un più diffuso impiego di antiaggreganti nei soggetti senza FA (97,1% *vs* 63%; $p < 0,001$) e di anticoagulanti orali in quelli con FA (11% *vs* 1,3%; $p < 0,001$). I soggetti con FA avevano più complicazioni, un maggior grado di disabilità alla dimissione e una maggiore mortalità (47 AFS = 23% *vs* 67 NAFS = 12,8%, $p < 0,001$). L'analisi multivariata ha confermato che il peso maggiore ai fini della prognosi nei pazienti con S è definito, oltre che dall'età, dalla presenza o meno della FA, dalla gravità all'ingresso desunta dallo score della GCS e ovviamente dalla durata della degenza. I nostri dati confermano, pertanto, che gli S con FA sono tendenzialmente più gravi di quelli senza FA e tale dicotomia appare già all'insorgenza dell'episodio vascolare.

Summary **Background** Stroke in patients with Atrial Fibrillation (AF) differs from Not Atrial Fibrillation Strokes (NAFS) in severity of onset and outcome but other variables may worsen the clinical scenario. **Materials and methods** We studied 738 patients (430 females and 308 males), with mean age 78.7 ± 9.9 years (female 81.0 ± 8.9; male 75.2 ± 10.2; $p < 0.001$) consecutively admitted for stroke to the Internal Medicine Departments of Tuscany in a three months period (March 1 to May 31, 2003) in or-

* Corrispondenza:
Paolo Biagi, loc. Le Bertille 6, 53045 Montepulciano (SI),
e-mail: chipama@libero.it

der to ascertain if the in-hospital burden of Atrial Fibrillation Strokes (AFS) was different from that of NAFS. Demographic data, clinical conditions before admission, the mode and timing of hospital admission, clinical presentation, treatment, complications, and outcome and the mode of discharge were examined. **Results** AFS were 205 (27.8%) and NAFS 533 (72.2%). Mean age of AFS was significantly higher ($p < 0.001$). Heart failure, ischemic heart disease, dilatative cardiomyopaties and chronic renal insufficiency were more prevalent in the AFS. The clinical presentation with a lower (3-6) Glasgow Coma Scale (GCS) score ($p < 0.01$) prevailed in AFS patients. The in-hospital therapy showed a greater use of antiplatelet agents in the NAFS (97.1% *vs* 63%, $p < 0.001$) and oral anticoagulants in AFS (11% *vs* 1.3%, $p < 0,001$). AFS patients showed much complications, higher degree of disability at discharge and mortality (47 AFS = 23% *vs* 67 NAFS = 12.8%, $p < 0.001$). Multivariate analysis confirms that AFS is more serious than NAFS owing to pathogenetic mechanisms: this results in a higher number of complications, a longer hospitalisation and a worse prognosis in terms of survival and disability. This dycothomy begins early as the symptoms start.

Introduction

Stroke in patients with Atrial Fibrillation (AF) is a peculiar subset among the overall ischemic stroke in terms of pathogenesis and severity of onset and outcome **[1-3]**.

It is not clear if these ischemic events may envisage an in-hospital management different from that of atherothrombotic forms. Possible differences might be the consequence of the arrhythmia itself, representing the cardioembolic genesis of stroke **[4]**, or of other risk factors such as age, comorbidities or the mode of presentation **[5]**.

To see whether the in-hospital course of Atrial Fibrillation Stroke (AFS) was different in comparison to that of Not Atrial Fibrillation Stroke (NAFS), we examined an homogeneous cohort of subjects coming from the same geographical region, with quite similar demographic characteristics, recruited among all the patients consecutively admitted for stroke in the Departments of Internal Medicine in Tuscany in a well defined period of time.

Materials and methods

We analyzed the data of the SETI (*Studio Epidemiologico Toscano Ictus*) study **[6]** relative to all the consecutive patients admitted for stroke in the Internal Medicine Departments of Tuscany in a three months period (March 1-May 31, 2003). Data came from a collecting sheet filled for each patient (discharged or died) and aimed to determine the burden of each single stroke.

The case record form was prepared including the following points: demographic data, clinical situation before admission, mode and the timing (emergency or not) of hospital admission, diagnostic tests performed during the in-hospital staying, pharmacologic treatment, complications, outcome and the mode of discharge.

Data collecting sheet is reported in the Appendix A.

Statistic analysis has been effected applying the Chi^2 test or Fisher test when the number was not enough for Chi^2 test validation. All the results have been expressed in percentages. The results related to continuous variables have been expressed as mean + 1 Standard Deviation (SD). Whereas a normal distribution had been individualized (Kolmogorov-Smirnov test associated to the index of Lilliefors) of the variable in use, the one way ANOVA test has been applied.

Multivariate analysis using some characteristics significantly different as covariate (age, sex, Glasgow Coma Scale, GSC, score, number of copathologies, number of complications and the presence of AF) was performed to identify whether AF was an independent predictor of mortality or residual functional limitation, too.

Statistic analysis has been executed with support software Epi Info 6.0 distributed by the Centers for Disease Control and Prevention (CDC) and with Statistic (data analysis software system), version 6.0 produced by StatSoft Inc. (2001, www.statsoft.com).

The relative burden of each of these variables was defined according to the Wilks' lambda method.

Results

A total of 738 data sheets were analyzed (430 females and 308 males). Mean age was 78.7 ± 9.9 years (female 81.0 ± 8.9 years *vs* male 75.2 ± 10.2, $p < 0.001$).

Patients with AF were 205 (27.8%) and those without AF were 533 (72.2%). The mean age of patients with stroke and AF (AFS) was significantly higher than that of those without AF (NAFS) (77.6 ± 10.1 and 81.8 ± 8.0 years, $p < 0.001$).

The most relevant pre-existing diseases were represented differently in the two groups: heart failure; Coronary Artery Disease (CAD); dilatative cardiomyopaties; chronic renal insufficiency; and heart failure were more prevalent in the AFS.

Hypertension was prevalent in the NAFS group as well as carotid stenosis at echo duplex scan. Uniformly distributed were alcoholic abuse (more than 3 units a week); diabetes; Peripheral Artery Disease (PAD); Chronic Obstructive Pulmonary Disease (COPD); cognitive impairment; and neoplastic diseases **(Tab. 1)**.

The clinical presentation with coma or stupor (36.6% *vs* 24.4%, $p < 0.001$), and a lower (3-6) GCS score (13.6 *vs* 6.7%, $p < 0.01$) **(Tab. 2)** were prevalent in AFS patients.

Table 1 Characteristics and comorbidities of Not Atrial Fibrillation Stroke (NAFS) and Atrial Fibrillation Stroke (AFS) subjects

		Atrial fibrillation (AF, %)			
		Not	Yes	Total	
		533	205	738	
Gender	F	284 (54.2%)	139 (69.2%)	423 (58.3%)	
	M	240 (45.8%)	62 (30.8%)	302 (41.7%)	
Age	Mean age ± 1 SD	77.6 ± 10.1	81.8 ± 8.0	78.8 ± 9.7	p < 0.001
	Comorbidities	NAFS	AFS	Total	p value (OR)
	Alcoholic abuse	5 (0.9%)	1 (0.5%)	6 (0.8%)	NS
	Peripheral artery disease	24 (4.5%)	8 (3.9%)	32 (4.3%)	NS
	Chronic obstructive pulmonary disease	58 (10.9%)	20 (9.8%)	78 (10.6%)	NS
	Dilated cardiomyopathy	13 (2.4%)	16 (7.8%)	29 (3.9%)	< 0.01
	Coronary artery disease	127 (23.8%)	65 (31.7%)	77 (10.4%)	< 0.05
	Cognitive impairment	100 (18.8%)	40 (19.5%)	50 (6.8%)	NS
	Diabetes	119 (22.3%)	43 (21.0%)	54 (7.3%)	NS
	Dislipidemia	90 (16.9%)	31 (15.1%)	121 (16.4%)	NS
	Heart failure	35 (6.6%)	39 (19.0%)	74 (10.0%)	< 0.001
	Hypertension	336 (63.0%)	111 (54.1%)	447 (60.6%)	< 0.05
	Chronic renal insufficiency	18 (3.4%)	21 (10.2%)	39 (5.3%)	< 0.001
	History of cancer (> 6 months before)	26 (4.9%)	15 (7.3%)	41 (5.6%)	NS
	Neoplasia	20 (3.8%)	14 (6.8%)	34 (4.6%)	NS
	Carotid stenosis	43 (8.1%)	8 (3.9%)	51 (6.9%)	< 0.05

SD = Standard deviation; OR = Odds ratio; NS = Not significant.

Table 2 Glasgow Coma Scale (GCS) score distribution of the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Admittance GCS score	NAFS (%)	AFS (%)	p (Chi^2)
3-6	6.75	13.66	0.015
7-11	9.38	15.12	NS
12-14	14.13	13.66	NS
15	73.73	57.58	0.011

NS = Not significant.

Table 3 Percent distribution of type of stroke in the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Type of stroke	AFS (%)	NAFS (%)	
Ischemic*	84.4	70.4	p < 0.001
Hemorragic	5.9	14.6	p < 0.01
Other**	9.7	15.0	NS
Lacunar	9.6	17.9	p < 0.01

* Include lacunar stroke. ** Include subarachnoid hemorrhage and indefinite cases.
NS = Not significant.

The classification of the existing neurological deficit revealed that only the hemiplegia pattern was significantly more represented in the ASF subjects (84 patients [41.0%] *vs* 98 patients [18.4%], p < 0.0001).

The neurological lesions identified by Computed Tomography (CT) scan are shown in **Tab. 3**. The hemorrhagic pattern prevailed in NASF patients (14.6% *vs* 5.9%, p < 0.01) while the ischemic pattern prevailed in AFS patients (84.4% *vs* 70.4%, p < 0.001).

A brain CT scan was performed within 6 hours from the onset of stroke in 51.8% of the cases and in 28.9% of the cases from the 6^{th} to the 24^{th} hour. Only 17% had the CT

scan after 24 hours. The total brain CT performed was 1051 (CT scan/patient ratio = 1.48) and a second CT was done slightly more often in the NAFS patients (1.49 *vs* 1.46 ratio, p = not significant).

The timing of the second CT scan execution was entirely random and scattered.

Only in a very small number of cases (2.3%) the CT scan was not performed: noteworthy, this happened especially in the subjects with AFS (4.5% *vs* 1.5%, $p < 0.05$).

The carotid duplex colour scan was performed in 382 subjects (51%), 41.5% in AFS and 55.7% in NAFS patients ($p < 0.001$); it was done within 6 hours only in a marginal and substantially identical numbers of cases in the two groups.

Major carotid stenoses (> 70%) were detected in none of AFS patients. The right carotid arteries were more frequently involved: 11 *vs* 2 in NAFS, and this was also true for minor stenoses (< 70%): 22 *vs* 12 in NAFS; 9 *vs* 3 in AFS.

The echo-cardiographic examination was performed in 230 (31%) of the patients and more precisely 29.3% in the subjects without AF and 36.1% in the subjects with AF: this difference was not statistically significant. The pattern observed at echoscopy evaluation is reported in **Tab. 4**.

There were more abnormal echo-cardiographic findings in the AFS echoes (68.8% in NAFS and 87.9% in AFS, $p < 0.01$).

We did not find any significant difference among the two groups in terms of in-hospital therapy apart from more antiplatelet agents being used in the NAFS (97.1% *vs* 63%, $p < 0.001$) and more oral anticoagulants in AFS (11% *vs* 1.3%, $p < 0.001$).

Complications worsened the clinical course in 291 (39.4%) cases: this happened more frequently in AFS (99) than in NAFS (191) (48.3% *vs* 35.8%, $p < 0.01$).

AFS had a great number of both overall and single case complications **(Tab. 5)**: above all fever and the complex pneumonia and respiratory failure **(Tab. 6)**. The patients needed the care procedures reported in **Tab. 7**.

The disability at discharge according to the Rankin scale (high score means low autonomy level) between the two groups is reported in **Tab. 8**. Notably, the numbers of deceased patients was higher in AFS group (47 AFS, 23%, *vs* 67 NAFS, 12.8%, $p < 0.001$).

The **Tab. 9** shows the drug prescriptions at discharge: the antiplatelet agents were prescribed in over 81.4% of NAFS patients and in 56.7% of those with AF, oral antico-

Table 4 Percent distribution of the echo-cardiographic patterns in the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Pattern	NAFS (%)	AFS (%)	p value
Atrial or/and ventricular dilatation	6.5	32.8	> 0.001
Parietal hypo-dyskinesia	13.8	15.5	NS
Left ventricular hypertrophy	48.5	39.6	NS
Normal	31.2	12.1	> 001

NS = Not significant.

Table 5 Number of complications and percentage in the Atrial Fibrillation Stroke (AFS) and Not Atrial Fibrillation Stroke (NAFS) patients

N. of complications	AFS	NAFS	p value
0	106 (51.7%)	340 (63.8%)	> 0.01
1	50 (24.4%)	124 (23.6%)	NS
2	26 (12.7%)	50 (10.3%)	NS
3	15 (7.3%)	11 (3.5%)	> 0.01
> 3	8 (3.9%)	8 (2.2%)	NS

NS = Not significant.

Table 6 Six main complications in the Atrial Fibrillation Stroke (AFS) and Not Atrial Fibrillation Stroke (NAFS) patients

Complications	AFS	NAFS	p value
Fever	44 (21.5%)	84 (15.8%)	NS
Mental mess	26 (12.7%)	46 (8.6%)	NS
Need for bladder catheter	28 (9.8%)	38 (7.1%)	NS
Respiratory insufficiency	18 (8.8%)	24 (4.5%)	> 0.05
Pneumonia	13 (6.3%)	18 (3.4%)	NS
Others	13 (6.3%)	18 (3.4%)	NS

NS = Not significant.

Table 7 Distribution of care procedures (with their percentage) in the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Pattern	NAFS	AFS	p value
Early mobilizing	308 (57.8%)	92 (44.9%)	< 0.01
Blood pressure monitoring	186 (34.9%)	74 (36.1%)	NS
Deep vein thrombosis prophylaxis	178 (33.4%)	80 (39.0%)	NS
Crystalloids infusion	175 (32.8%)	84 (41.0%)	< 0.05
Control of dysphagia	189 (35.5%)	92 (44.9%)	< 0.05
Control of hyperthermia	74 (13.9%)	41 (20.0%)	< 0.05
Antibiotics administration	120 (22.5%)	66 (32.2%)	< 0.01
O_2 therapy	128 (24.0%)	72 (35.1%)	< 0.01
Mattress for bedsores	128 (24.0%)	72 (35.1%)	< 0.01
Parenteral feeding	60 (11.3%)	38 (18.5%)	< 0.01
Movements limitations	62 (11.6%)	43 (21.0%)	< 0.01
Urinary catheter	153 (28.7%)	103 (50.2%)	< 0.01

NS = Not significant.

Table 8 Distribution in Rankin scale in all patients and in the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Progressive groups at Rankin scale	All	AFS	NAFS	p value
Rankin 1	129 (24.2%)	24 (17.6%)	105 (26.4%)	0.022
Rankin 2	107 (20.1%)	21 (15.4%)	86 (21.7%)	NS
Rankin 3	101 (18.9%)	22 (16.2%)	79 (19.9%)	NS
Rankin 4	95 (17.8%)	26 (19.1%)	69 (17.4%)	NS
Rankin 5	101 (18.9%)	43 (31.6%)	58 (14.6%)	0.008

NS = Not significant.

Table 9 Differences in drugs prescription at the discharge in the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS])

Drugs	NAFS (%)	AFS (%)	p value
Antiplatelets	81.4	56.7	< 0.001
Anticoagulants	3.0	25.5	< 0.001
Antiplatelets and anticoagulants	84.4	82.2	NS
Anti hypertensive agents	61.6	47.8	< 0.05
Statins	13.8	5.7	NS

NS = Not significant.

agulants were most frequently prescribed in the AFS group (25.5% *vs* 3.0% in NAFS).

To be noted that at admission just 12% of patients with AFS were on oral anticoagulants while at discharge the figure grew up to 25.5%.

The AFS patients in-hospital Length of Stay (LOS) was 2.2 days longer ($p < 0,001$) than that of those without AF ($p = 0.001$) **(Tab. 10)**.

When the number of patients who died in hospital was added to that of those discharged with the highest disability score (Rankin 5), we observed that 54.6% of the AFS patients had a poorer prognosis compared with 31.7% of the NASF patients: this difference was highly significant ($p < 0.001$).

The grouping analysis and the discriminant analysis disclosed age (< 75 years), GCS score (< 6), AF (yes) and LOS (> 14 days) as the most important determinants of a poor prognosis. The relative burden of each of these variables depicted the following order: age, AF, GCS and LOS **(Tab. 11)**. From our data the gender is not an independent variable for a poor prognosis.

Discussion

The SETI survey was carried out in Tuscany, one of the Italian regions with high mean age population **[7]**, and we know that the prevalence of AF arrhythmias and the incidence of ischemic stroke grow in the 8th and 9th decades of life **[8,9]**.

In this study the association between stroke and AF was found in the 28% of the population observed and the high-

Table 10 Distributions of in-hospital length of staying (LOS; days ± 1 SD) between the two groups of patients (Not Atrial Fibrillation Stroke [NAFS] and Atrial Fibrillation Stroke [AFS]) according to gender (females and males)

In-hospital LOS (days ± SD)	NAFS	AFS	All
Females	9.9 ± 8.2	11.5 ± 8.3	10.4 ± 8.3
Males	9.8 ± 8.9	13.1 ± 11.2	10.4 ± 8.0
All	9.8 ± 7.6	12.0 ± 9.3	10.4 ± 8.2

Table 11 Discriminant function analysis summary showing the relative burden of the variables in predicting a worse prognosis of stroke. Age, atrial fibrillation, Glasgow Coma Scale score at the entry and, obviously, length of staying are significantly the most important

	Wilks' lambda**	Partial lambda	F-remove (1.694)	p value
Sex	0.877	0.999	0.516	NS
Age	0.927	0.945	40.699	< 0.001
Co-pathologies	0.877	0.999	0.381	NS
Glasgow Coma Scale	0.882	0.993	5.087	< 0.05
Complications	0.878	0.998	1.348	NS
Atrial fibrillation	0.897	0.976	16.786	< 0.001
Length of staying	0.889	0.985	10.236	< 0.005
CV anamnesis*	0.877	0.999	0.559	NS

* CV anamnesis: any previous cardio-cerebrovascular event.
** Wilks' lambda: 0.87606 approx. F (8.694) = 12.273; Multiple analysis of variance: $p < 0.001$.
NS = Not significant.

er figures were found in women, whose mean age was higher. The frequency is similar to that observed in other epidemiological studies such as the Framingham and Copenhagen studies **[1,10]**, although the observed slightly higher figures may be related to the older age of our population.

The patients presenting with more severe deterioration of conscience, as demonstrated by the GCS, and worse neurological symptoms were those with AF. This reflects a greater degree of overall CNS damage in patients with AF. So our data confirm that clinical conditions of patients presenting with stroke and AF are worse than those of patients without AF **[1]**.

The SETI patients with AF had a greater number of ischemic strokes (84.4%) and a lesser number of lacunar lesions (9.6%) than the NAF patients: it is well known **[11-13]** that the embolus dimension usually produces a complete occlusion of the medium and large size cerebral arteries giving more extensive brain damage and ensuing more serious neurological pictures like partial or total ischemic strokes according to the Oxfordshire Community Stroke Project **[14]**. In the AF stroke group there are 12 patients with cerebral hemorrhage and patients that may not have any sure cardio-embolic stroke despite of the occurrence of AF, however the great majority of strokes in the AF SETI patients may be attributed to a cardio-embolic origin.

In the not AF patients stroke has quite different etiology: hemorrhage; *in situ* thrombosis; embolism from aortic or carotid plaques, etc., but in any case leading to a lesser degree of neurological damage because the size of the arteries involved (very often the penetrating arteries) is much smaller **[15,16]**.

In AF patients there are moreover some other causes that can protract and worsen the cerebral ischemia: one of these factors could be the hemodynamic instability due to the arrhythmia itself **[17,18]**.

As it has been observed in other studies, our NAF patients had a higher incidence of hemorrhagic strokes, probably for cardio-embolism leads to a partial reduction of odds for cerebral hemorrhage in AF patients **[1,16]**.

An interesting observation in the SETI survey is that almost 50% of the patients had a CT scan within 6 hours from the symptoms onset, which is the time window within which a thrombolytic therapy could be still attempted **[19-22]**. This might represent an indirect index of the efficiency of the Internal Medicine structures of Tuscany and suggests that thrombolytic therapy could be in the future used to a larger sample of patients and in a wider setting of that currently applied.

Carotid and vertebral echo-color Doppler has been carried out in nearly 50% of the cases, with greater deal in patients without AF. In these patients the severity of the atherosclerotic lesions was greater both in terms of degree of stenosis and extension of the plaque. Just 12% of the not AF patients had a normal echo-color Doppler. Our survey points out that the echo was performed within 6 hours only in a marginal number of patients (10%): at present there is not routine recommendation for its emergent use in acute stroke **[23-26]**.

Transthoracic echocardiography has been carried out in nearly one third of the patients, with slightly higher figures in those with AF. In two third of the cases echo showed either morphologic or functional abnormalities which were more pronounced in the AF patients (69% *vs* 60%), confirming the data of the literature **[12]**.

There are observations that an impaired myocardial function can worsen the prognosis in patients with stroke and AF **[27,28]**; we have found that nearly all the AF patients with stroke (88%) had abnormal echocardiographic findings so our data from the SETI study suggest that echo should be carried out early after admission and in all the patients with AF. These patients carry a greater risk and a worse prognosis and should be more aggressively treated.

The current technologies allowing a rapid bed side echo execution with high reproducibility and sensitivity can greatly improve its feasibility.

Despite we think that echo execution is a must in patients presenting with stroke and AF, allowing a better prognostication and therapeutical approach, unfortunately it is not very helpful for secondary prevention of stroke, especially as for the indication of anticoagulant or anti platelet treatment is concerned. There is in fact a widespread consensus regarding the use of oral anticoagulants in patients with AF and previous stroke, regardless of any echo information **[29,30]**.

The most frequent and severe complications of AF-ischemic stroke were respiratory insufficiency **[31,32]** and bed sores **[33]**. This can be easily due to the fact that patients with AF have more comorbidities **[34]**.

Rehabilitation should start within 48 hours from symptoms onset according to the most recent guidelines **[35-37]** and what we have observed in our SETI patients with ischemic stroke and AF is that a slight delay occurred.

A more elevated degree of disability as documented by an elevated Rankin score at discharge was also present.

However we are convinced that AF stroke patients have a worse outcome and a greater need of care because of the number of comorbidities, severity of the clinical presentation and age rather than delayed physiotherapy.

Therapy of discharge does not differ between the two groups: anti-platelets drugs have been prescribed nearly to all the patients with no AF. In patients with AF, however, oral anticoagulants have been employed to a lesser degree than it should have done according to the most recent guidelines for the secondary prevention of stroke **[31,37]**.

This is even more important if we take into account that the population is older than that of other studies **[38-40]** and that age by itself is a powerful risk factor for cardioembolic relapse.

Age by itself is not a contraindication for oral anticoagulant provided that we pay attention to careful patients selection and follow up **[41,42]**.

Our data on the percentage of patients treated with warfarin are similar to those of other studies **[43]**. Moreover the number of patients discharged on oral anticoagulants though still not satisfactory is twice as higher than that treated at admittance.

We have to point out that the SETI study is observational and did not envisage any follow-up. For this reason we cannot speculate whether the two groups may have different outcomes after a follow-up period. The disability score at 3 and 6 months could have been a better prognostic index in our patients.

However according to multivariate analysis we may conclude that AF is an independent variable and its relative burden in predicting the stroke prognosis is similar to the age of the patient and heavier than LOS, GCS and sex. So we are convinced that a more severe presentation of the AF stroke may account for any difference in clinical outcome, management and care need during hospitalisation and after discharge: atrial fibrillation, age and comorbidities at admission can be the key factors leading to a dichotomy in clinical course and outcome of stroke.

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Appendix A - Data collecting sheet

Age (years)

Sex

Pre-existing diseases in particular documented history of chronic AF irrespective of the cause desumed by antecedent discharge data sheets or ECG

ECG at entry differentiating AF from not AF

TC or MRI cathegorizing stroke in the following 4 groups
- hemorrhage
- subarachnoid hemorrhage
- ischemia
- other

Timing of the first brain TC scan from clinical presentation
- within 6 hours
- 6 to 24 hours
- over 24 hours
- never done

Clinical severity at entry according to Glasgow Coma Scale (3 to 15 score)

Presence of clinical neurological deficit according to the following definitions
- hemi/monoparesis
- hemiplegia
- aphasia/dysphasia
- disarthria
- dysesthesia
- dysphagia
- ataxia/dizziness/disequilibrium
- amaurosis
- convulsions

Duplex scan carotid type lesions according to the following classes
- intima-media thickness > of 1.2 mm
- stenosis > or < of 70%
- occlusion

Timing of carotid echo-color duplex scan at admission
- within 6 hours
- 6 to 24 hours
- over 24 hours
- never done

Echocardioscopic findings
- normal
- LVH
- parietal hypo-dyskinesia
- ESVD and EDVD widening

In-hospital therapy

Rehabilitation started within 48 hours

Clinical complication

Disability grading at discharge (Rankin scale severity score 1 to 5)

Therapy regimen at discharge

Length of hospital staying in days (LOS)

Outcome

Appendix B - The following Internal Medicine Departments participated in the SETI Study

M. Cipriani (USL 9 Grosseto)

A. Morettini (USL 10 Careggi, Firenze)

A. Tafi (USL 11 Castelfiorentino, FI)

R. Laureano, G. Panigada (USL 3 Pescia, PT)

W. Boddi (USL 7 Poggibonsi, SI)

M. Lomi, D. Degl'Innocenti (USL 4 Prato)

C. Pedace, M. Bernardini, L. Fusconi (USL 8 Arezzo)

A. Cuccuini (USL 8 San Giovanni Valdarno, AR)

D. Vanni, G. Iannelli (USL 8 Arezzo)

C. Passaglia, S. Fascetti (USL 12 Versilia, Lucca)

C. Nozzoli, P. Ricotti (USL 10 Careggi, Firenze)

M. Mazzoli, D. Badii (USL 8 Montevarchi, AR)

A. Lagi, G. Bandinelli (USL 10 Santa Maria Nuova, Firenze)

D. Neri (USL 11 Empoli, FI)

A. Ghetti, G. Landini (USL 10 Santa Maria Annunziata, Firenze)

C. Cappelletti, S. Spolveri (USL 10 San Giovanni di Dio, Firenze)

G. Seghieri, C. Breschi (USL 3 Pistoia)

B. Micheli, M. Giusti (USL 3 Pistoia)

A. Carnicelli, L. Masotti (USL 6 Cecina, LI)

A. Fierro (USL 11 San Miniato, FI)

C. Bartolomei, L. Bocci, M. Barberio (USL 6 Livorno)

R. Capiferri, L. Mangano (USL 5 Volterra, PI)

G. Rinaldi (USL 2 Barga, LU)

G. Berni, Biagini (USL 10 Careggi, Firenze)

P. Biagi, S. Bocchini (USL 7 Montepulciano, SI)

A. Nardini (USL 2 Lucca)

G. Parca, G. Galastri (USL 8 Bibbiena, AR)

L. Cecchi, L. Scarti (Borgo San Lorenzo, FI)

E. Silvestrini, A. Lelli (USL 3 San Marcello Pistoiese, PT)

R. Migliacci, M. Mollaioli (USL 8 Cortona, AR)

U. Giannuzzi, M. Lucarini (USL 8 San Sepolcro, AR)