



Original article

Sex differences in clinical presentation, severity and outcome of stroke: Results from a hospital-based registry

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ABSTRACT

Background and purpose: Sex related differences in cardiovascular disease and stroke are issues of increasing interest. The aim of this study was to evaluate for sex differences in clinical presentation, severity of stroke and outcome in a population of patients admitted to 4 public and 1 private hospitals in three different regions of Italy.

Methods: All hospital admissions for ischemic and haemorrhagic stroke (ICD-IX code 434 and 431 respectively) between January 1st and December 31st, 2011 at five different hospitals located in three different regions of Italy: Milan (North), Rome and Perugia (Center), and Palermo (South) have been recorded and sex-differences have been evaluated.

Results: A total of 1272 stroke patients were included in the analysis: 1152 ischemic and 120 haemorrhagic strokes, 567 women and 705 men. Compared to men, women were significantly older (mean age 75.2 SD 13.7 vs 71.5 SD 12.5 years, $P < 0.001$) and their stroke severities at onset, measured by NIHSS, were also compared to men (10 SD 8 vs 8 SD 7, $P < 0.001$).

Female sex was associated with a worse functional prognosis measured by *modified Rankin Scale score* ($mRS \geq 3$), as well as in-hospital mortality, without reaching statistical significance.

There were no observed significant differences between sexes regarding the number of patients treated with thrombolytic therapy. Analysis of the distribution of risk factors between sexes showed a prevalence of atrial fibrillation in women (29% vs 21%, $P = 0.003$).

Conclusions: Both stroke severity and functional outcome were worse in women.

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1. Introduction

Stroke in women is a recognized public health issue worldwide because of its influence on post-stroke disability [1]. Since women have longer life expectancies, there is a higher stroke prevalence in women [2,3], and this sex difference in the number of stroke events is expected to increase further over the next few decades [4,5]. Moreover, women have a worse functional outcome after stroke than men

[6,7], and a higher mortality especially in the oldest age groups [8]. In fact, at onset, women tend to be 4 to 5 years older, on average, than men and present more comorbidities [9,10], both these variables affect the severity of stroke at presentation and impact the timelines of acute stroke care.

The aim of this study was to evaluate for sex-differences in clinical presentation, severity of stroke and outcome in patients admitted to five hospitals in three different regions of Italy.

2. Subjects and methods

Consecutive stroke patients admitted to five Italian hospitals, 4 public (Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan; Santa Maria della Misericordia Hospital, Perugia; San Camillo Forlanini Hospital, Rome; and Civico Hospital, Palermo) and 1 private

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(San Raffaele Hospital, Milan) from Northern, Central and Southern Italy, discharged with the codes for ischemic and haemorrhagic stroke according to the International Classification of Diseases (ICD-IX codes 434 and 431 respectively) between January 1st and December 31st 2011, were recorded in the Stroke Units databases.

Each database was analyzed for data on sex differences regarding stroke severity at clinical presentation assessed by *National Institute of Health Stroke Scale (NIHSS)* [11], functional outcome assessed by *modified Rankin Scale score (mRS)* [12] at discharge and in-hospital mortality were recorded.

Each hospital followed Human Research rules and this observational study was approved by the local hospital boards.

All patients were managed in sub-intensive stroke units and standard stroke care guidelines [13,14] were followed.

Patients admitted within 3 h from stroke onset meeting SITS-MOST criteria and according to physicians discretion were treated with thrombolysis [15]. Information concerning inclusion/exclusion criteria for thrombolysis were not collected.

Stroke was classified as large-artery atherosclerotic, cardioembolic, lacunar or cryptogenic according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria [16].

Variables included in study analysis were: (1) baseline demographic characteristics (age and sex); (2) risk factors for stroke (3) clinical stroke severity at admission and at discharge assessed by NIHSS; (4) functional outcome, at discharge and at 3-months follow-up, measured by mRS score; and (5) any difference in thrombolytic treatment and prognosis at the 5 participating hospitals.

Functional outcome was measured according to the mRS: 0, 1, 2 = no- to slight disability; 3, 4, 5 = moderate- to severe disability; 6 = death. For the purpose of this study, clinical outcomes (mortality and disability) were assessed at three months, the functional outcomes were assessed by outpatient visits or by structured telephone interviews using mRS. Time of occurrence and cause of death were also recorded. The causes of death were divided into: neurological (stroke recurrence, status epilepticus, edema or herniation), cardiovascular (myocardial infarction, heart failure, sudden death or other cardiovascular diseases and pulmonary embolus), and other causes (pneumonia, cancer, and other causes).

3. Statistical analysis

Pearson's chi-square or Fisher's Exact Test were used to compare categorized proportions.

A comparison of discrete variables was conducted using a non-parametric test (Mann-Whitney).

Multivariate logistic regression was performed in order to define risk factors for dichotomic outcomes.

Multivariate linear regression was carried out with the aim of evaluating independent variables for NIHSS values at entry. An alpha level of 0.05 was used for each statistical test.

No imputation was done for missing data.

4. Results

Over the 12-month study period, 1272 consecutive patients with acute stroke were included in the databases of the 5 participating hospitals: 567 patients were women (45%) and 705 men (55%); 1152 ischemic (521 women vs 631 men) and 120 haemorrhagic strokes (46 women vs 74 men), not statistically significant differences were observed between sexes.

Women were significantly older than men, (mean age 75.2 SD 13.7 vs 71.5 SD 12.5 years, $P < 0.001$); date of birth was available for all patients except for 1 woman and 2 men. The length of hospital stay was longer for women (11 SD 8 vs 10 SD 8 days, $p = 0.001$), (Table 1).

Table 1

Age, hospital stay and NIHSS at onset and discharge by sex in the whole population.

	Sex	N	Mean	SD	P value
Age	Female	566	75.2	13.7	<0.001
	Male	703	71.5	12.5	
Hospital stay	Female	396	10.8	7.8	0.001
	Male	520	9.5	7.5	
NIHSS at onset	Female	550	9.9	7.8	<0.001
	Male	689	7.9	7.0	
NIHSS at discharge	Female	357	6.7	7.5	0.002
	Male	462	4.9	6.2	

Stroke severity at admission assessed by NIHSS score was significantly worse in women than men (NIHSS 10, SD 8; median 7, interquartile range 13 vs NIHSS 8, SD 7; 5, interquartile range 9, $P < 0.001$). Similarly, women resulted significantly more severely neurologically impaired at discharge than men (NIHSS score 7, SD 8; median 3, interquartile range 10 vs NIHSS 5, SD 6; 2 interquartile range 5 $P = 0.002$), (Table 1) and multivariate linear regression revealed that female sex and age were significantly associated with greater stroke severity at hospital's admission, (Table 3a).

There was no observed significant difference between sexes in terms of receiving thrombolysis treatment even if there was a slight tendency for men to be treated more frequently (10% vs 12%), (Table 2).

The in-hospital mortality was similar for both sexes (women 5% vs male 4%) (Table 2), and the multivariate logistic model suggested that the following were independent predictors of in-hospital death: age, stroke severity at onset, and length of hospital stay (Table 3b).

Regarding functional outcome assessed by mRS score, either at discharge (44% vs 37% $P = 0.030$) or at 90-day follow-up (51% vs 40%, $P = 0.022$), both resulted worse ($mRS \geq 3$) for women compared to men (Table 2); 3-months follow-up data were not available for all patients.

Table 4 lists the distributions of risk factors for both sexes: women were less likely to be smokers and alcohol consumers; whereas, history of hypertension, diabetes and dyslipidemia had similar distributions between the sexes. Obesity [17] was more frequent in women without reaching statistical significance, while atrial fibrillation (AF) was statistically significant in women compared to men (29% vs 21%, $P = 0.003$).

Table 2

Thrombolytic treatment, in-hospital death and functional outcome by sex.

		F	M	Total	P value
Thrombolytic treatment	No	n	369	465	0.392
		%	90.0	88.2	
	Yes	n	41	62	103
		%	10.0	11.8	
Total	n	410	527	937	
	%	100	100	100	
In-hospital death	No	n	425	560	0.499
		%	94.7	95.6	
	Yes	n	24	26	50
		%	5.3	4.4	
Total	n	449	586	1035	
	%	100	100	100	
mRS score at discharge	<=2	n	252	368	0.030
		%	56.1	62.8	
	3+	n	197	218	415
		%	43.9	37.2	
Total	n	449	586	1035	
	%	100	100	100	
3 months-mRS	<=2	n	89	146	0.022
		%	48.9	60.1	
	3+	n	93	97	190
		%	51.1	39.9	
Total	n	182	243	425	
	%	100	100	100	

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