Received: 15 January 2021 | Accepted: 4 February 2021

DOI: 10.1111/ene.14769

european journal of neurology
the official journal of the european academy of neurology

ORIGINAL ARTICLE

Gender differences in post-stroke functional outcome at discharge from an intensive rehabilitation hospital

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Funding information
The study was supported by Fondazione Don Carlo Gnocchi (Ricerca Corrente 2020) and Fondazione Cassa di Risparmio di Firenze (Bando Ricerca Scientifica e Tecnologica 2020).

Abstract

Background: Gender differences in stroke functional recovery after rehabilitation are poorly investigated. Our aim was to compare functional outcomes at discharge from an intensive rehabilitation hospital after stroke in men and women, and to analyze their prognostic factors.

Methods: Retrospective observational study of consecutive stroke patients discharged from an intensive neurological rehabilitation hospital, from January 2018 to June 2019. Modified Rankin Scale (mRS) at discharge was the main outcome measure.

Results: Among the 208 included patients (mean age 73.4 ± 13.6 years), 105 (50.5%) were women. Women were significantly older (75.3 ± 13.8 vs. 71.4 ± 13.2 years, respectively, $p = 0.041$), and less often had a history of smoking habit (27% vs. 50%, $p < 0.001$). No gender differences emerged for vascular risk factors and comorbidities, pre-stroke functional status, length of hospital stay, stroke type, and number of clinical deficits. At admission to the rehabilitation hospital, mRS score distributions were not different ($p = 0.795$). At discharge, mRS score distributions and destinations did not differ between men and women ($p = 0.391$, $p = 0.785$, respectively). A significant interaction between gender and the change in mRS score from admission to discharge was found ($F = 6.6$, $p = 0.011$) taking into account age, stroke type, and number of initial clinical deficits. Dividing the cohort according to age, elderly women showed a better functional recovery compared to men.

Conclusions: At admission to an intensive rehabilitation hospital, men and women presented a similar functional and clinical status and a substantial overlap of functional recovery after stroke. At higher ages, the potential for recovery appeared better in women compared to men.

KEYWORDS
function recovery, gender, outcome, rehabilitation, stroke

INTRODUCTION

Stroke is one of the leading causes of death and the main cause of long-term disability in Western society.[1] Differences between women and men in relation to stroke are increasingly being recognized. Age-specific incidence rates are substantially lower in women than men in younger and middle-age groups, but these differences narrow so that in the oldest age groups, incidence rates in women are approximately equal to or even higher than in men.[1] Each year, ≈55,000 more women than men have a stroke with a

higher lifetime risk, attributed to women's higher life expectancy. Vascular risk factors act differently in men and women, symptoms at onset are more often non-specific in women, and the time interval between symptoms onset and both the presentation to hospital and the beginning of treatment is longer in women than in men.[2–4] Overall women have worse outcomes after stroke.[3,4] Women have an increased thromboembolic risk, mainly cardioembolic strokes due to atrial fibrillation, while men have more atherothrombotic strokes.[5]

Despite the growing body of knowledge in many stroke fields, the existing literature on the role of gender in functional recovery after stroke rehabilitation is limited and still controversial. Some reports have shown no differences in functional outcome between men and women,[6,7] some have reported better functional outcome in men,[8] while others point to better recovery in women.[9,10]

The present study is based on a retrospective revision of clinical records of consecutive stroke patients, ischemic stroke, and intracerebral haemorrhage, discharged from an intensive neurological rehabilitation hospital, and was aimed at: (1) evaluating and comparing functional outcomes of men and women at discharge and (2) evaluating the predictive value of baseline characteristics, and of their possible interaction, on functional outcomes.

METHODS

The present study was a single-center, retrospective observational study based on data collected from the revision of clinical records of consecutive patients discharged from an intensive rehabilitation hospital after stroke. All adult (age >18 years) patients discharged from the Intensive Rehabilitation Hospital IRCCS Fondazione Don Carlo Gnocchi in Florence, Italy, with a diagnosis of stroke (ischemic or hemorrhagic) from 1 January 2018 to 30 June 2019 were included in the study.

In the Tuscany region, the rehabilitation pathway for stroke patients is as follows: (1) patients are admitted to an acute hospital (of the four acute hospitals in Florence, one is a university hospital and a stroke center) where they may receive acute treatments and, if needed, rehabilitation and (2) patients presenting with complex modifiable disability are transferred to one of the three intensive rehabilitation hospitals. Each rehabilitation hospital may receive patients from any of the acute hospitals.

IRCCS Fondazione Don Carlo Gnocchi is one of the three rehabilitation hospitals in Florence. It has one high-specialty neurological intensive rehabilitation ward, that is, severe acquired brain injury, mainly dedicated to patients with disorders of consciousness, and one intensive neurological rehabilitation ward. According to national requirements, the interdisciplinary rehabilitation assessment and process of care provide at least 3 hours per day of specific rehabilitation including physiotherapy, with or without neuropsychological, speech, swallowing and/or occupational therapies, according to baseline screening or to emerging needs. Assessment and training in the use of aids are also provided, if needed. When deemed appropriate, psychological support to patients and/or families is also provided. The individual rehabilitation project is developed and carried out according to patient-centered objectives by an interdisciplinary team of health professionals.

The study was conducted in accordance with the Helsinki Declaration, and was approved by the local ethics committee. The following data, when available, were collected from clinical records: (1) sociodemographic characteristics (age, sex), vascular risk factors, and history of previous stroke; (2) referral hospital, length of stay (LOS) in the acute care hospital and in the rehabilitation hospital; (3) classification of stroke type: non-traumatic intracerebral hemorrhage and ischemic strokes, categorized according to TOAST classification; (4) types and overall burden of clinical deficits (motor deficits, aphasia, neglect, and dysphagia); (5) types of rehabilitation (physiotherapy, speech and swallowing therapy, neuropsychological stimulation/rehabilitation); (6) discharge destinations (home, other hospital, death); and (7) modified Rankin Scale (mRS) scores referred to premorbid status (pre-stroke), and at admission and discharge from the rehabilitation hospital.

Study outcome

The primary outcome was the degree of dependence in daily activities as measured by means of the mRS. The mRS is a broadly used disability scale ranging from 0 (no symptoms) to 6 (death), and the most widely used outcome measure in stroke clinical trials.[11,12] As primary outcomes, in the present study the mRS was used either as distribution of mRS categories at different time points (i.e., on admission and discharge) or as change in mRS scores during the stay in the rehabilitation hospital.

Statistical analyses

Descriptive analyses (means and standard deviations or frequencies and percentages) were used to illustrate the total sample characteristics. Independent sample*t* tests, Mann–Whitney U tests and chi-squared tests were used to compare men and women for demographics, vascular risk factors, referral hospital, LOS in the acute and rehabilitation hospitals, types of rehabilitation, and clinical characteristics. Clinical deficits were defined as the presence of: motor deficit (absent = 0, paresis = 1, plegia = 2), aphasia (absent = 0, present = 1), dysphagia (absent = 0, present = 1), and neglect (absent = 0, present = 1). These scores were summed into a variable representing the total burden of clinical deficits (range 0–5). The presence of the above-mentioned neurological symptoms was based on the need of rehabilitation for the specific deficit.

For statistical analysis purposes, the mRS was analyzed according to different approaches. For the analyses of mRS categories at different time points, non-parametric methods (independent samples Mann–Whitney U and Jonckheere–Terpstra tests) were used

for the comparisons between men and women. In order to adjust for confounders, as a sensitivity analysis, multivariate ordinal regression models (complementary log-log function) were used taking into account the effect of age, total number of clinical deficits, and stroke type. For the analyses of change in mRS scores during the stay in the rehabilitation setting, delta scores (mRS Δs) were calculated using the following formula: admission mRS−discharge mRS (positive score=improvement); and then dichotomized as 'not-improved' (mRS Δs ≤ 0) versus 'improved' (mRS Δs ≥ 1). The dichotomized functional outcome was then used to compare the rates of men and women with an improvement stratified according to mRS at admission (Mantel–Haenszel test). Δs mRS were used to calculate efficiency and effectiveness scores according to the approach described by Paolucci et al.[8] Efficiency score was computed using the formula: mRS Δs/rehabilitation LOS, representing the average increase per day, and effectiveness score was computed with the formula: (mRS Δs/admission mRS)*100, representing the proportion of improvement achieved during rehabilitation. Mann–Whitney U test was used to compare efficiency and effectiveness scores between men and women.

Multivariate logistic regression models on the association between baseline characteristics (demographics, vascular risk factors, and clinical deficits) used as potential predictors, and the improvement in functional status (mRS Δs ≥ 1) used as the dependent variable, were carried out separately for men and women. Regression analyses were conducted in two steps: (1) models including each potential predictor independently (Models 1) and (2) models including all predictors that gave statistically significant results in Models 1 (Models 2). All regression Models 1 and 2 were adjusted for LOS in acute and rehabilitation hospitals and for premorbid mRS score.

Finally, repeated measures multivariate ANOVA models were used to study the trajectory of mRS variations from admission to discharge in men and women (gender*time) taking into account the effect of age, total number of clinical deficits, and stroke type.

RESULTS

From 1 January 2018 to 30 June 2019, 229 patients were consecutively discharged from the Intensive Rehabilitation Hospital IRCCS Fondazione Don Carlo Gnocchi with a diagnosis of stroke. Of these, 17 were excluded because their stroke was due to subarachnoid hemorrhage, and four patients were further excluded because data on the primary outcome (mRS) were not available. Demographics and clinical characteristics of the 208 patients included in the final study cohort, as well as comparisons between men and women, are shown in Table 1. Mean age was 73.4 ± 13.6 years, 103 (49.5%) were men and 105 (50.5%) were women. Women were significantly older (75.3 ± 13.8 vs. 71.4 ± 13.2 years, $p = 0.041$). Women less often had a history of (current or past) smoking habit (27% vs. 50%, $p < 0.001$).

Almost half of the study cohort came from the university hospital ($n = 91$, 44%), half came from one of the other three hospitals

TABLE 1 Age, vascular risk factors, pre-stroke functional status, and hospitalization stay of the study cohort, and comparisons between men and women

Parameter	Total cohort (*n* = 208)	Women (*n* = 105)	Men (*n* = 103)	*p*
Age (years)	73.4 ± 13.6	**75.3 ± 13.8**	**71.4 ± 13.2**	**0.041**[*]
Hypertension	170 (82%)	84 (80%)	86 (83%)	0.514[**]
Diabetes	51 (24%)	23 (22%)	28 (27%)	0.376[**]
Dyslipidemia	45 (22%)	23 (22%)	22 (21%)	0.924[**]
Atrial fibrillation	62 (30%)	35 (33%)	27 (26%)	0.262[**]
Smoking habits	80 (38%)	**28 (27%)**	**52 (50%)**	**0.001**[**]
History of previous stroke	21 (10%)	10 (9.5%)	11 (11%)	0.782[**]
Pre-stroke mRS[a] (score)	0.7 ± 1.1	0.7 ± 1.1	0.6 ± 1.1	0.444[***]
Pre-stroke mRS[a]				
0	128 (67%)	62 (64%)	66 (71%)	0.653[**]
1	25 (13%)	16 (17%)	9 (10%)	
2	16 (8.5%)	9 (9%)	7 (7%)	
3	16 (8.5%)	8 (8%)	8 (9%)	
4	5 (3%)	2 (2%)	3 (3%)	
LOS in acute hospital (days)	25.7 ± 32.7	23.9 ± 27	27.5 ± 37.7	0.430[*]

Note: Bold values denote statistical significance at the $p < 0.05$ level.

Abbreviations: mRS, modified Rankin Scale; LOS, length of stay.

[a]Available for 190 patients.

*Independent samples *t* tests.

**Chi-squared tests.

***Independent samples Mann–Whitney U test.

(*n* = 106, 51%), and the rest were mainly patients that had a stroke away from home and accessed the rehabilitation hospital from another city hospital (*n* = 11, 5%). Patients coming from the university hospital, compared to those from other hospitals, did not differ in terms of mRS on admission (median, interquartile range [IQR]: 4, 4–5, vs. 5, 4–5, $p = 0.469$), age (71.3 ± 14.3 vs. 74.9 ± 12.9 years, $p = 0.056$), stroke type (ischemic stroke 74% vs. 66%, $p = 0.226$) or gender (women 54% vs. 49%, $p = 0.392$).

Of the 208 included patients, 144 (69%) had ischemic stroke (72 men, 72 women). According to the TOAST classification, 24 patients (17%) had a stroke related to large-artery atherosclerosis, 53 (37%) to cardioembolism, 16 (11%) to small-vessel occlusion, 16 (11%) to other determined etiology, and 35 (24%) to undetermined etiology. No significant difference between men and women emerged concerning ischemic stroke subtypes, although women more often had cardioembolic strokes (44% vs. 29%, $p = 0.062$). Acute stroke treatments, intravenous thrombolysis and/or mechanical thrombectomy, were performed in 29 patients (20%). More women received acute stroke treatments compared to men (28% vs. 12%, $p = 0.022$). Fourteen women and five men received intravenous thrombolysis (19% vs. 7%, $p = 0.027$), and nine women and four men received mechanical thrombectomy (12% vs. 6%, $p = 0.146$).

Sixty-four patients (31%) had hemorrhagic stroke, of whom 18 (28%) underwent hematoma evacuation, without any gender difference (Table 2).

Considering the clinical status at admission, the overall mean number of clinical deficits was not significantly different between the two groups. While plegia was equally distributed in men and women, the absence of motor deficit was more common in men (Table 2). No differences emerged in terms of mRS scores either pre-stroke (Table 1) or at admission to the rehabilitation hospital (Figure 1a). Pre-stroke mRS scores were not available

TABLE 2 Rehabilitation stay and clinical characteristics of the study cohort and comparison between men and women

Parameter	Total cohort (*n* = 208)	Women (*n* = 105)	Men (*n* = 103)	*p*
Rehabilitation ward				
Severe acquired brain injury	49 (24%)	24 (23%)	25 (24%)	0.810**
Standard neurological unit	159 (76%)	81 (77%)	78 (76%)	
LOS in rehabilitation hospital (days)	51.8 ± 41	51.9 ± 40.9	51.7 ± 41.3	0.971*
Hemorrhagic stroke	64 (31%)	33 (31%)	31 (30%)	0.835**
Surgical hematoma evacuation	18 (28%)	9 (27%)	9 (29%)	0.876**
Ischemic stroke	144 (69%)	72 (69%)	72 (70%)	0.835**
Acute ischemic stroke treatments[a]	29 (20%)	**20 (28%)**	**9 (12%)**	**0.022***
Total number of clinical deficits (range 0–5)	2.3 ± 1.3	2.4 ± 1.2	2.1 ± 1.3	0.218*
Motor deficit				
Absent	18 (9%)	**3 (3%)**	**15 (15%)**	**0.011****
Paresis	111 (53%)	**60 (57%)**	**51 (49%)**	
Plegia	79 (38%)	**42 (40%)**	**37 (36%)**	
Aphasia	72 (35%)	38 (36%)	34 (33%)	0.630**
Neglect	49 (24%)	25 (24%)	24 (23%)	0.931**
Dysphagia	81 (39%)	42 (40%)	39 (38%)	0.752**
Nutrition[b]				
Oral	133 (65%)	70 (67%)	63 (62%)	0.339**
Nasogastric tube	31 (15%)	17 (16.5%)	14 (14%)	
Percutaneous endoscopic gastrostomy	42 (20%)	17 (16.5%)	25 (24%)	

Note: Bold values denote statistical significance at the $p < 0.05$ level.

Abbreviation: LOS, length of stay.

[a]Acute ischemic stroke treatments: intravenous thrombolysis and/or mechanical thrombectomy.

[b]Available for 206 patients.

*Independent samples *t* tests.

**Chi-squared tests.

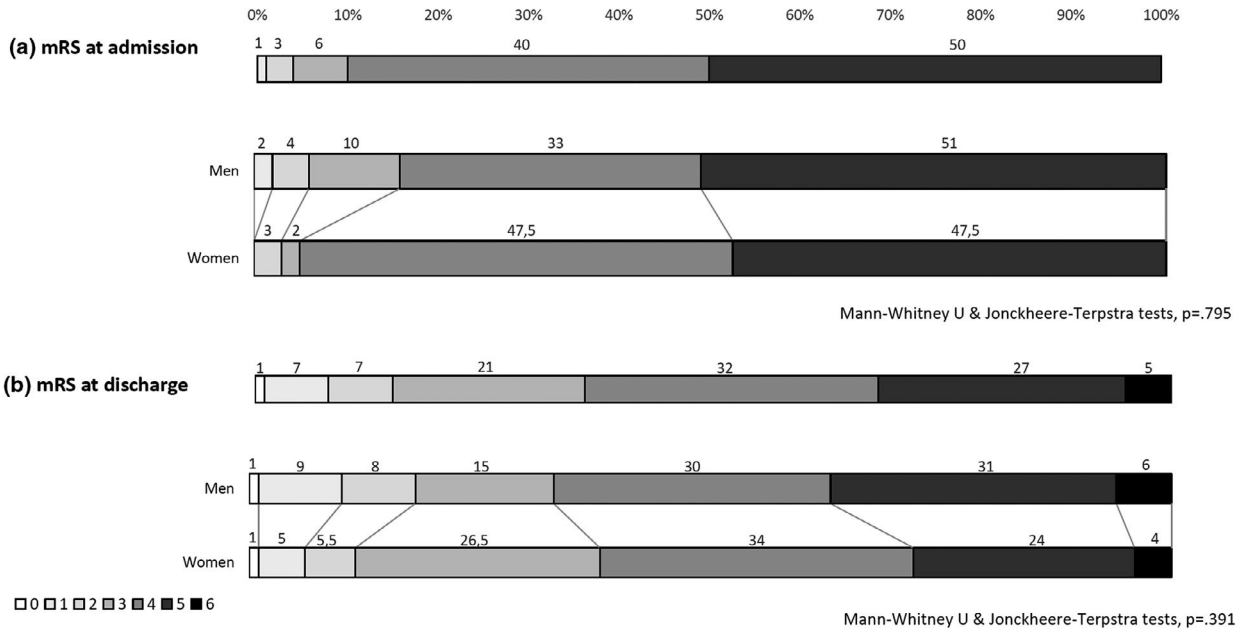

FIGURE 1 Modified Rankin Scale (mRS) score distributions at admission (a) and discharge (b) from the rehabilitation hospital: overall sample and comparisons between men and women.

for 18 (9%) patients (10 men, 8 women). In the ordinal regression model, the association between mRS at admission and gender was confirmed as non-significant (odds ratio [OR] = 0.814, 95% CI 0.541–1.226, p = 0.325) adjusting for age (OR = 1.008, 95% CI 0.993–1.023, p = 0.321), total number of clinical deficits (OR = 2.201, 95% CI 1.767–2.741, p < 0.001), and stroke type (OR = 1.017, 95% CI 0.633–1.634, p = 0.943). All patients received physiotherapy: 204 (98%) speech and swallowing therapy and 39 (19%) neuropsychological stimulation/rehabilitation. No differences between women and men emerged concerning rehabilitation types (speech and swallowing therapy: 67% vs. 69%, p = 0.727; neuropsychological stimulation/rehabilitation: 17% vs. 20%, p = 0.549).

At discharge, mRS score distributions were not significantly different between men and women (Figure 1b). After accounting for the effects of age (OR = 1.020, 95% CI 1.008–1.031, p = 0.001), total number of clinical deficits (OR=1.429, 95% CI 1.250–1.635, p < .001), and stroke type (OR = 0.889, 95% CI 0.632–1.252, p = .501), the ordinal regression model showed a possible significant association between mRS at discharge and gender (OR=0.678, 95% CI 0.499–0.922, p = 0.013), pointing towards a better functional outcome in women compared to men.

One hundred and five (50.5%) patients improved their mRS score after rehabilitation (mRS Δs ≥ 1).

The stratification of improved patient according to mRS at admission did not show any significant difference, although women had a trend toward a better functional outcome than men (Figure 2). In the multivariate logistic regression models, conducted separately in men and women, the only variable that was associated with functional improvement (mRS Δs ≥ 1) in both groups was the total number of clinical deficits, independently of LOS in acute and rehabilitation hospitals and premorbid mRS. Age was associated with functional outcome only in men (Table 3).

No differences between men and women emerged concerning the final discharge destination (i.e., back home: 56% vs. 58%; other hospital: 38% vs. 38%; death 6% vs. 4%, respectively; p = 0.785; data available for 205 patients).

No significant differences between men and women were found in effectiveness (12.5 ± 25.4 vs. 16.5 ± 20.8, p = 0.192) and efficiency (0.011 ± 0.04 vs. 0.014 ± 0.1, p = 0.110) scores.

Looking at the variation of mRS scores from admission to discharge in men and women with repeated measures multivariate ANOVA, taking into account the significant effects of age (F = 17.8, p < 0.001) and total clinical deficits (F = 15.9, p < 0.001), the interaction between gender and time was significant (F = 6.6, p = 0.011) (Figure 3a). Women showed a better functional recovery compared to men. These results did not change even when controlling for stroke type (data not shown).

To further explore the effect of age, the sample was divided into three numerically homogeneous groups according to percentiles distribution: (1) age ≤71 years, n = 72 (34.5%), of whom 29 were women; (2) age 72–80 years, n = 66 (32%), of whom 32 were women; and (3) age ≥81 years , n = 70 (33.5%), of whom 44 were women. Multivariate ANOVA models were repeated separately in each age group.

As shown in Figure 3b, up to the age of 80 years, no significant interactions were found between gender and time, while total clinical deficits remained significantly associated with mRS score variation over time. Above the age of 81 years, the interaction between mRS change and the total clinical deficits was no more significant, while gender was associated with mRS score variation, confirming a better functional recovery of women compared to men.

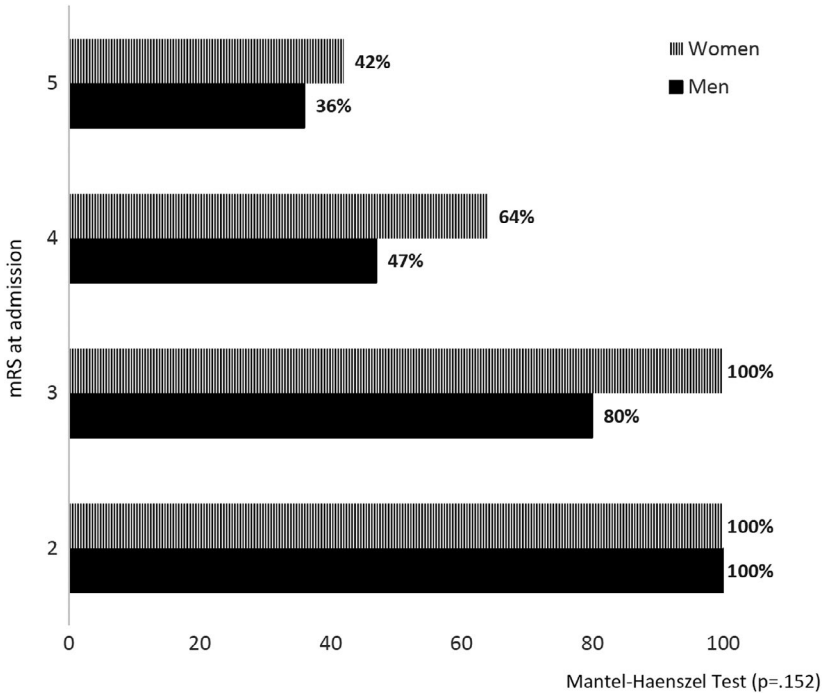

FIGURE 2 Rates of patients with an improved functional status (modified Rankin Scale [mRS] Δs ≥ 1) at discharge from the rehabilitation hospital stratified according to the mRS score distribution at admission: comparisons between men and women.

TABLE 3 Association between age, vascular risk factors, and clinical deficits and the improvement in functional status (mRS Δs ≥ 1) at discharge

	Women				Men			
	Model 1		Model 2		Model 1		Model 2	
Parameter	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Age (years)	0.96 (0.92–1.00)	0.056	0.96 (0.92–1.00)	0.050	**0.95 (0.91-.99)**	**0.013**	**0.95 (0.91-0.99)**	**0.015**
Hypertension	0.56 (0.16–1.95)	0.359			1.29 (0.38–4.32)	0.682		
Diabetes	2.09 (0.65–6.71)	0.212			1.24 (0.44–3.54)	0.683		
Dyslipidemia	0.90 (0.31–2.57)	0.845			1.60 (0.52–4.95)	0.411		
Atrial fibrillation	0.67 (0.26–1.75)	0.415			0.45 (0.16–1.23)	0.120		
Smoking habits	0.85 (0.31–2.34)	0.749			0.94 (0.38–2.29)	0.885		
Type of stroke	0.97 (0.32–2.98)	0.963			0.95 (0.36–2.47)	0.911		
History of previous stroke	0.84 (0.17–4.20)	0.829			1.68 (0.38–7.36)	0.491		
Total number of clinical deficits (range 0–5)	**0.66 (0.44-.99)**	**0.048**	**0.65 (0.43–0.98)**	**0.042**	**0.56 (0.37-0.83)**	**0.004**	**0.55 (0.36-0.84)**	**0.006**

Notes: Model 1: multivariate logistic regression models including each potential predictor independently. Model 2: multivariate logistic regression model including all predictors that resulted in statistical significance in Model 1. All Models 1 and 2 were adjusted for length of stay in acute and rehabilitation hospitals and for the premorbid mRS. Bold values denote statistical significance at the $p < 0.05$ level.

Abbreviations: mRS, modified Rankin Scale; OR, odds ratio; CI, confidence interval.

DISCUSSION

Our study on stroke patients showed that on admission to a rehabilitation hospital, men and women presented similar functional and clinical status and that functional recovery achieved after in-hospital rehabilitation substantially overlapped in the two groups. Age appeared to influence the association between gender and functional outcomes in stroke patients in different ways, as women were older than men, and the trajectory of mRS change over time was influenced by age. Trajectories of functional recovery in men and women changed according to age: older women continued to improve, regardless of the severity of the initial deficit, while recovery in men appeared to decrease with increasing age. Surprisingly, despite their average older age compared to men, women seemed to continue to benefit from rehabilitation also in the oldest groups.

Among the demographics, vascular risk factors and clinical characteristics are taken into consideration as possible predictors of improvement in functional status at discharge, and initial stroke

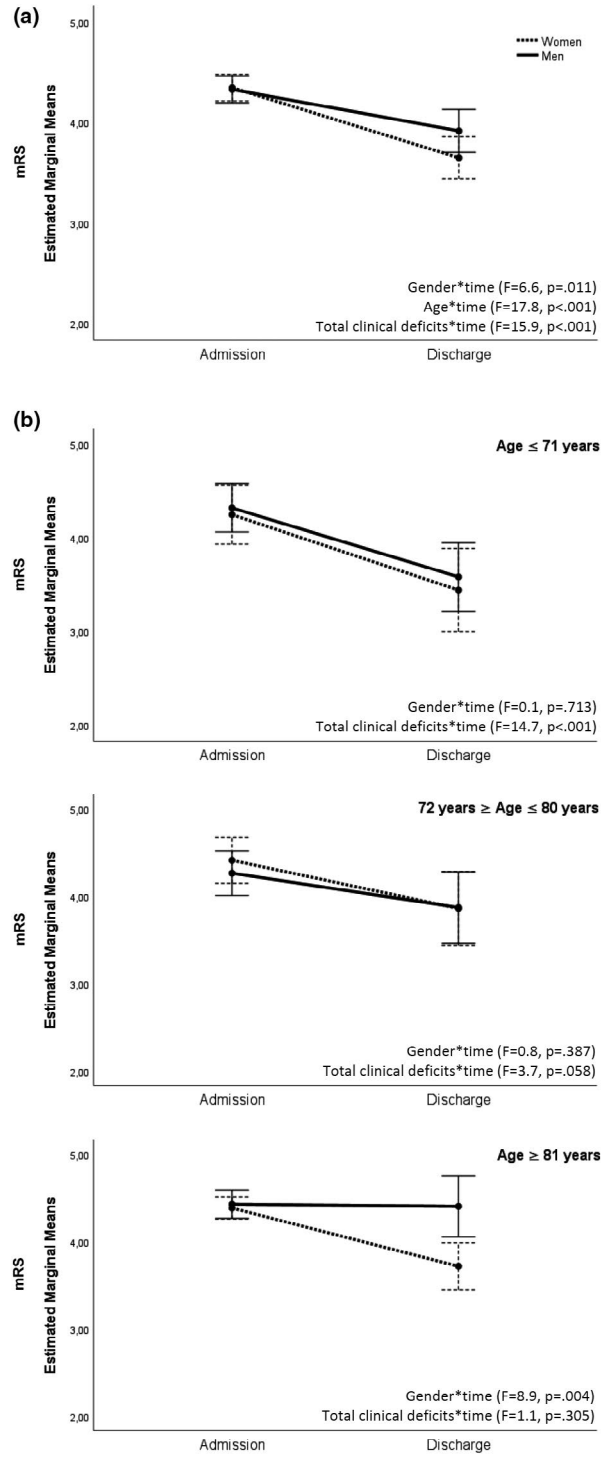

FIGURE 3 Variation in modified Rankin Scale (mRS) scores from admission to discharge from the rehabilitation hospital: comparisons between men and women in the total sample (a) and divided according to age categories (b).

severity was confirmed as the main prognostic factor both in men and women.

Stroke types were equally distributed among men and women. Looking at acute ischemic stroke treatments, interestingly more than twice as many women than men received intravenous thrombolysis or mechanical thrombectomy. Although these are very small numbers, this result is not in line with the evidence that women generally receive less treatment compared to men.[3]

In the context of stroke and gender medicine, our results confirm the need for a better comprehension of the possible underlying mechanisms subsiding the overall worst prognosis in women after stroke. Despite older age, women seem to recover as much as men, or even more after rehabilitation. Thus, the question remains as to why women have a worse long-term prognosis.[13,14] Many hypotheses have been explored, none of which seems to be sufficient in itself.[4,15] Gender difference regarding access to rehabilitation services after stroke are lacking, and a huge variability in access is observed across different countries and healthcare systems.[4] Although our data do not allow the evaluation of differences in access to care in men and women, in our cohort of consecutive stroke patients men and women are equally represented. Our findings may not be generalized to all patients with stroke, but are representative of moderate-to-severe stroke patients who undergo intensive neurological rehabilitation.

Several limitations need to be acknowledged. First, the retrospective study design did not allow the collection of many important clinical determinants of functional outcome. Demographics, such as education, living conditions (alone or with others), and marital status, could not be collected from the available clinical records. We were also not able to consider important clinical outcomes such as quality of life and depression. These factors are known to influence the worse prognosis in women that is often reported in the available literature.[3] Stroke severity and clinical deficits were based on clinical judgment and not defined by means of any standardized instrument, such as the National Institutes of Health Stroke Scale, because of lack of availability of this information in the clinical records. Each clinical deficit (i.e., motor impairment, aphasia, neglect, and dysphagia) was defined as present if a rehabilitation program was assigned to the patients for the specific deficit. Despite this important limitation, clinical severity considered in this study reflected the burden of cumulative deficit after stroke with a known impact on functional outcome.[16] The choice of mRS as the main functional outcome was driven by the availability of this score for all patients at admittance and at discharge. Despite the fact that the mRS is recognized as a valid instrument for clinical trials in acute stroke, its reliability and sensitivity to change in a rehabilitation setting may be limited by the use of large categories, whose scoring is based on the overall impression of function, and by the clinical significance of any change between the categories.[12] From a methodological point of view, the use of mRS according to the conventional categories may further decrease statistical power in the limited sample size of our study cohort. We decided to analyze mRS as a score, and thus to control for the effect of possible confounders, but we are aware that this use of mRS is unconventional and potentially prone to introducing a statistical shortcoming.

In conclusion, our data confirm that functional recovery after stroke rehabilitation is present in both men and women, and that women, despite being older, benefit from rehabilitation also at

advanced age. These findings support the importance of offering adequate rehabilitation services after stroke even to the oldest patients. Future studies are needed to assess the responsiveness of women and men to physical, cognitive, and social interventions during the post-stroke period, taking into account subjective (i.e., quality of life) and objective (i.e., cognitive functioning, depression, disability) outcome measures in stroke survivors, as well as all potentially relevant pre-existing conditions. Further research is needed to establish why outcomes are worse in women than in men, and to identify effective interventions to reduce the unequal burden of stroke in women.

ACKNOWLEDGMENTS

The authors would like to thank Prof. Maria Chiara Carrozza and Prof. Sandro Sorbi for their kind support, and Ing. Federica Vannetti for assiting with administrative issues.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTION

Anna Poggesi: Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Supervision (equal); Writing-original draft (equal). **Greta Insalata:** Investigation (equal); Writing-review & editing (equal). **Giele Papi:** Investigation (equal); Writing-review & editing (equal). **Valentina Rinnoci:** Investigation (equal); Writing-review & editing (equal). **Ida Donnini:** Investigation (equal); Writing-review & editing (equal). **Monica Martini:** Writing-review & editing (equal). **Catuscia Falsini:** Writing-review & editing (equal). **Bahia Hakiki:** Validation (equal); Writing-review & editing (equal). **Annamaria Romoli:** Writing-review & editing (equal). **Carmen Barbato:** Writing-review & editing (equal). **Paola Polcaro:** Writing-review & editing (equal). **Francesca Casamorata:** Writing-review & editing (equal). **Claudio Macchi:** Validation (equal); Writing-review & editing (equal). **Francesca Cecchi:** Validation (equal); Writing-review & editing (equal). **Emilia Salvadori:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Validation (equal); Writing-original draft (equal).

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

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How to cite this article: Poggesi A, Insalata G, Papi G, et al. Gender differences in post-stroke functional outcome at discharge from an intensive rehabilitation hospital. *Eur J Neurol*. 2021;00:1–8. https://doi.org/10.1111/ene.14769