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Pre-stroke disability assessed by modified Rankin Scale is associated with post-stroke adverse outcomes in hospital: a registry-based, prospective cohort study of acute stroke care in Surrey, United Kingdom

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ABSTRACT (245 words)

Objectives: Information concerning pre-stroke disability on stroke outcomes is lacking. We assessed pre-stroke disability in relation to post-stroke outcomes whilst in hospital.

Design: Analysis of prospectively collected data from the Sentinel Stroke National Audit Programme (SSNAP).

Setting: Four major UK hyperacute stroke units (HASUs) between 2014 and 2016.

Participants: 1656 men (mean age ±SD=73.1yrs ±13.2) and 1653 women (79.3yrs ±13.0) admitted with acute stroke.

Main outcome measures: Pre-stroke disability, assessed by modified Rankin Scale (mRS), was tested against post-stroke adverse outcomes, adjusted for age, sex and coexisting morbidities.

Results: Compared with patients with pre-stroke mRS score=0, individuals with pre-stroke mRS scores=4 or 5 had greater adjusted risks of: moderately-severe or severe stroke on arrival (4.4% *vs* 22.1%, OR=4.5, 95%CI=2.9-7.1); urinary tract infection and/or pneumonia within seven days of admission (9.6% *vs* 34.7%, OR=3.4, 95%CI=2.4-5.0); prolonged length-of-stay (LOS) on HASU (20.3% *vs* 34.6%, OR=1.6, 95%CI=1.1-2.5) and mortality (7.2% *vs* 38.1%, OR=5.0, 95%CI=3.5-7.3). Patients with mRS scores=2 or 3 had intermediate risk of adverse outcomes: but for those with mRS score=2 the highest risk of prolonged LOS on HASU (20.3% *vs* 41.8%, OR=2.4, 95%CI=1.8-3.2) and for those with mRS score=3 haemorrhagic stroke (15.5% *vs* 22.5%, OR=1.9, 95%CI=1.4-2.6). Overall, those with a mRS=2 had LOS on HASUs extended by 9.7 days (95%CI=6.8-12.5), mRS=3 by 8.4 days (95%CI=5.2-11.6), and mRS=4 or 5 by 5.2 days (95%CI=1.1-9.3).

Conclusions: Individuals with evidence of pre-stroke disability, assessed by mRS, had significantly increased risk of post-stroke adverse outcomes and prolonged LOS on HASUs.

KEY FINDINGS

- Post-stroke disability, assessed by the modified Rankin Scale (mRS), is commonly used to assess stroke outcomes.
- There is a paucity of information on pre-stroke disability on stroke outcomes.
- More severe pre-stroke disability, assessed by mRS, was related to greater risk of severe stroke at admission, urinary tract infection and pneumonia within seven days of admission, and in-patient mortality by 3.5 to 5-fold, independent of age, sex and co-morbidities.
- Increasing severity of pre-stroke disability also increased the likelihood of prolonged length of stay in hyperacute units, extending by 9.7 days for those with mRS = 2, 8.4 days for those with mRS = 3, and 5.2 days for those with mRS = 4 or 5.

INTRODUCTION

In line with an increasingly ageing population in industrialised nations over the past century [1, 2], the number of adults living with age-related conditions, such as stroke, has risen dramatically [3] which result in long-term poor health and disability [4]. Information on the severity of post-stroke disability allows healthcare teams to arrange appropriate levels of care for patients upon discharge to the community [5], and also provides prognosis on stroke outcomes [6] and recovery [7-10]. The ability to predict post-stroke complications on admission provides important data that can be used to formulate clinical plans for the patient earlier in the care pathway, and allows hospital to strategically organise their day-to-day operational matters with more certainty.

The modified Rankin Scale (mRS) is a widely accepted instrument used to assess disability after stroke as well as endpoints for research trials [11]. There is now increasing interest in the use of pre-stroke disability, assessed by mRS, as a prognostic tool for stroke outcomes [12]. However, there is a paucity of published data on pre-stroke mRS in relation to post-stroke adverse outcomes in hospital. In the present study, we assessed the relationship between pre-stroke disability assessed by mRS and a number of post-stroke outcomes during hospitalisation including: severity of stroke, haemorrhagic stroke, nosocomial infections, length-of-stay in hyperacute stroke units (HASUs) and in-patient mortality.

METHODS

Study design, participants and setting

We performed analysis of prospectively collected data from the national register of stroke care (Sentinel Stroke National Audit Programme (SSNAP)). The data comprise

clinical characteristics and care quality of patients admitted to acute care hospitals in England and Wales [13]. Data from the present study were gathered from the time of admission up to six months after stroke in patients admitted to four major UK hyperacute stroke centres in South East England between January 2014 and February 2016 [14,15].

SSNAP has approval from the Confidentiality Advisory Group of the Health Research Authority to collect patient data under section 251 of the National Health Service Act 2006, so that no additional ethical approval was required [9].

Socio-demographic factors and medical history

Demographic data were collected and documented by stroke consultants and nurse specialists; including age at arrival, gender and coexisting morbidities (atrial fibrillation, hypertension, congestive heart failure, diabetes mellitus and previous stroke) [13-15].

Pre-stroke disability

The degree of pre-stroke disability or dependence with daily activities was assessed by mRS, ranging from no symptoms to severe symptoms: 0 = no symptoms at all, 1 = no significant disability despite symptoms; able to carry out all usual duties and activities, 2 = slight disability; unable to carry out all previous activities, but able to look after their own affairs without assistance; 3 = moderate disability; requiring some help, but able to walk without assistance; 4 = moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance; 5 = severe disability; bedridden, incontinent and requiring constant nursing care and attention [16].

Stroke diagnosis and severity

Stroke was diagnosed based on clinical presentation and brain imaging [14,15]. The severity of stroke symptoms at arrival was assessed by the National Institutes of Health for Stroke Scale (NIHSS) with a score range from no symptoms to severe stroke symptoms (NIHSS score=0 to 42).

In-patient infections, length of stay and mortality

Details of new cases of urinary tract infection (UTI) and pneumonia acquired in hospital within seven days of admission, length of stay on HASUs and in-patient mortality were documented.

Categorisation of variables

Dichotomisation was applied for atrial fibrillation, congestive heart failure, hypertension and diabetes, type of stroke, and in-patient infections and mortality according to the presence or absence of history of the condition. Prolonged length of stay (LOS) on HASUs was defined as those who stayed longer than three weeks (4^{th} quartile) [14,15]. Pre-stroke mRS was categorised into five groups: group 1, mRS score = 0; group 2, mRS score = 1; group 3, mRS score = 2; group 4, mRS = 3; and group 5, mRS score = 4 or 5 (these last two mRS categories were grouped together due to small numbers). Moderately-severe to severe stroke on arrival was defined as an NIHSS score ≥16.

Statistical analysis

Multivariable logistic regression analysis was carried out to estimate the risk of severe stroke at admission, haemorrhagic stroke, in-patient mortality, urinary and pneumonia infections within seven days of admission and LOS on HASUs (dependent variables) from pre-stroke disability using patients with mRS score = 0 as the reference group (independent variable). The results are presented as two models: model 1, unadjusted; model 2, adjusted for age, sex and co-morbidities (atrial fibrillation, hypertension, congestive heart failure, diabetes and previous stroke). Results are expressed as odds ratios (OR) and 95% confidence intervals (CI). Analyses were performed using SPSS V.23.0 (SPSS Inc, Chicago, Illinois, USA). The null hypothesis was rejected when p <0.05.

RESULTS

A total of 3309 patients were admitted with an acute stroke, 1656 men (mean age ±SD = 73.1 yr ±13.2) and 1653 women (79.3 yr ±13.0). From these 2758 (83.3%) patients presented with ischaemic stroke; of the remainder 518 (15.7%) patients had a haemorrhagic stroke and 33 (1.0%) were unspecified. The mean LOS on HASU was 16.1 days (±21.2). There were 480 (14.5%) patients who died during admission. The prevalence of co-existing morbidities including atrial fibrillation and congestive heart failure and previous stroke (except a smaller proportion in the mRS = 5 group) rose progressively with increasing severity of pre-stroke mRS scores: there was no such relationship for diabetes or hypertension. The proportions of individuals with adverse post-stroke outcomes also increased progressively with increasing severity of pre-stroke disability: these included moderately-severe to severe stroke (NIHSS score ≥16) on admission, UTI and pneumonia within seven days of admission and mortality.

However, the rates of prolonged LOS on HASU were greatest in those with mRS scores between 2 and 4 (**Table 1**).

There were significant increases in LOS on HASUs for patients with higher pre-stroke mRS scores (p<0.001) **(Figure 1**). ANOVA showed that compared with patients with a pre-stroke mRS score = 0 (reference group), LOS on HASUs was longer for those with a pre-stroke mRS score = 1 by 2.6 days (95% CI: 0.3-4.9 days, p = 0.027), pre-stroke mRS score = 2 by 9.7 days (95% CI: 6.8-12.5 days, p <0.001), pre-stroke mRS score = 3 by 8.4 days (95% CI: 5.2-11.6 days, p <0.001), and pre-stroke mRS score = 4 and 5 by 5.2 days (95% CI: 1.1-9.3 days, p = 0.013).

Logistic regression showed progressive increase in the risk of having adverse outcomes with increasing pre-stroke mRS (**Table 2**). Compared with patients with mRS scores = 0 (reference group), individuals with mRS scores = 4 and 5 had greater adjusted risks of: moderately-severe or severe stroke on arrival (4.4% *vs* 22.1%, OR = 4.5, 95%CI = 2.9-7.1); UTI (4.6% *vs* 23.2%, OR = 4.2, 95%CI = 2.7-6.5), pneumonia within seven days of admission (6.7% *vs* 26.7%, OR = 3.7, 95%CI = 2.5-5.8), UTI and/or pneumonia within seven days of admission (9.6% *vs* 34.7%, OR = 3.4, 95%CI = 2.4-5.0); prolonged LOS on HASUs (20.3% *vs* 34.6%, OR = 1.6 (1.1-2. 5) and mortality (7.2% *vs* 38.1%, OR = 5.0, 95%CI = 3.5-7.3). Patients in with mRS scores of between 2 and 3 had intermediate risk of severe stroke at admission, nosocomial infections and mortality. However, for those with mRS score = 2 there was the highest risk of prolonged LOS on HASU (20.3% *vs* 41.8%, OR = 2.4, 95% CI=1.8-3.2) and for those with mRS score =3 the greatest risk of haemorrhagic stroke (15.5% *vs* 22.5%, OR = 1.9, 95%CI = 1.4-2.6).

DISCUSSION

The majority of studies concerned with the management of stroke patients focus on post-stroke disabilities, assessed by mRS. By contrast, there are few data on the use of a pre-stroke mRS score as a prognostic indicator of stroke outcomes. For individuals with moderately-severe to severe pre-stroke disabilities (mRS score = 4 or 5) there was a 3- to 4-fold increase in the risk for having severe stroke itself, nosocomial infections, in-patient mortality and a 2-fold increase for prolonged stay on HASU; all these outcomes were independent of age, sex and a range of major co-existing morbidities.

We found the severity of pre-stroke disability related continuously with some post-stroke outcomes including: the severity of stroke at admission; nosocomial infections; and in-patient mortality. However, the risk of prolonged LOS in HASU and haemorrhagic stroke was highest among those with intermediate pre-stroke mRS scores (2 or 3). It is possible that the higher in-patient mortality of those patients with greater severe pre-stroke disability (mRS score 4 or 5) may contribute to the shorter LOS among these patients and that those with haemorrhagic stroke are at greater risk of death.

Although effort was made to adjust for major co-existing morbidities in our analysis, the risk of pre-stroke mRS with post-stroke adverse outcomes suggests that patients with pre-existing disabilities are more likely to be more frail and susceptible to common infections with diminished ability to recover from an illness [19,20], leading to increased risk of prolonged LOS on HASUs and mortality. Our observations are

consistent with a previous study on the associations between pre-stroke mRS scores and adverse outcomes [12].

Acute stroke usually evolves into a chronic condition. The majority of individuals with a stroke require after-care including rehabilitation and frequent hospital admissions or clinic visits, as well as more different medications [17,18]. Disability [21], frailty [22], impaired quality of life [23] and cognitive impairment [4], that arising from stroke, impose enormous personal costs and burdens on healthcare systems [24]. Given the increasing life expectancy of the population in the UK and other industrialised nations [1, 2], more people are living with stroke than ever. This means the adverse health outcomes from stroke will continue to increase these personal and healthcare costs. Therefore it is necessary to recognise earlier those patients with pre-stroke disability, indicated by high mRS scores, to reduce the risk of adverse complications from stroke, including nosocomial infections, as well as increased in-patient LOS and mortality.

Strengths and limitations

The strengths of the present study lie in its large cohort of patients derived from one of the largest NHS regions in the UK and who have similar characteristics to the rest of the UK [18, 19, 22]. The data were collected in accordance with the national SSNAP protocol and analysis took a range of confounding factors known to associate with stroke outcomes into account. We chose a cut-off point for NIHSS scores of ≥16 (moderately-severe to severe stroke) based on previous studies that demonstrated a strong prediction of mortality or severe disability [25], while cut-off intervals for mRS score at 0-1, 2-3, and 4-5 indicated worsening functional disability due to increasing severity of stroke [26]. “Prolonged stay” tends to vary between studies which

generates a problem that the longer is this time, the greater is the severity of conditions that cause a prolonged stay. In this study, we specifically defined it as for patients who stayed on HASUs for more than three weeks, which represents the upper quartile of LOS on HASUs.

In conclusion, individuals with increasing pre-stroke disability, assessed by mRS, were at higher risk of post-stroke adverse outcomes, independent of age, sex and coexisting morbidities.

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LEGENDS

Figure 1. Plot showing mean LOS on HASUs in relation to different level of pre-stroke disability assessed by mRS scores. *Significances from pre-stroke mRS score = 0 (reference group).

Table 1. Proportions of patients (1288 men and 1255 women) admitted with first stroke with co-existing morbidities and adverse outcomes.

	mRS = 0 (*n* = 2003)	mRS = 1 (*n* = 476)	mRS = 2 (*n* = 340)	mRS = 3 (*n* = 309)	mRS = 4 (*n* = 143)	mRS = 5 (*n*=38)	Group differences	
Co-existing morbidities	%	%		%		%	χ^2	*p*
Atrial fibrillation	15.6	24.2	25.6	30.1	36.4	18.4	79.5	<0.001
Congestive heart failure	3.6	8.6	9.1	9.4	11.9	10.5	49.6	<0.001
Hypertension	50.4	60.3	53.2	53.1	51.0	39.5	18.0	0.003
Diabetes mellitus	15.0	19.1	14.4	17.2	21.0	21.1	9.3	0.099
Previous stroke	16.4	30.7	31.8	36.6	39.9	34.2	136.6	<0.001
Post-stroke adverse outcomes								
Haemorrhagic stroke	15.0	13.7	17.9	22.5	13.5	19.4	14,7	0.012
NIHSS ≥16 on arrival	4.4	6.5	7.6	13.6	22.4	21.1	107.3	<0.001
UTI within 7 days of admission	4.6	6.5	9.2	17.7	24.5	18.4	131.2	<0.001
Pneumonia within 7 days of admission	6.7	10.7	13.5	29.7	25.4	31.6	186.2	<0.001
UTI and/or pneumonia within 7 days of admission	9.6	13.0	19.3	36.7	34.1	36.8	213.8	<0.001
Prolonged LOS on HASUs	20.3	26.9	41.8	38.4	37.2	23.8	80.8	<0.001
Mortality	7.2	14.1	25.1	36.3	37.1	42.1	320.6	<0.001

Table 2. Logistic regression to assess the risk of post-stroke adverse outcomes in older patients with acute stroke. Reference group: mRS = 0 (*n* = 2012).

	mRS = 1 (*n* = 476)			**mRS = 2 (*n* = 340)**			**mRS = 3 (*n* = 309)**			**mRS = 4 and 5 (*n* = 181)**		
Unadjusted	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Intracranial haemorrhagic stroke	0.90	0.68-1.20	0.482	1.23	0.91-1.68	0.176	1.64	1.22-2.20	0.001	0.97	0.63-1.50	0.906
NIHSS ≥16 on arrival	1.52	0.99-2.31	0.053	1.80	1.15-2.84	0.011	3.42	2.32-5.05	<0.001	6.17	4.09-9.31	<0.001
UTI within 7 days of admission	1.43	0.94-2.18	0.098	2.08	1.35-3.21	0.001	4.41	3.96-6.35	<0.001	6.20	4.12-9.33	<0.001
Pneumonia within 7days of admission	1.65	1.17-2.34	0.004	2.16	1.50-3.12	<0.001	5.85	4.31-7.94	<0.001	5.05	3.46-7.38	<0.001
UTI and/or pneumonia within 7days of admission	1.41	1.04-1.93	0.029	2.26	1.65-3.09	<0.001	5.46	4.13-7.22	<0.001	5.00	3.54-7.06	<0.001
Prolonged LOS on HASUs	1.44	1.11-1.85	0.005	2.82	2.12-3.75	<0.001	2.50	1.83-3.43	<0.001	2.08	1.38-3.16	0.001
Mortality	2.12	1.56-2.88	<0.001	4.31	3.20-5.80	<0.001	7.34	5.52-9.74	<0.001	7.98	5.66-11.24	<0.001
Adjusted												
Intracranial haemorrhagic stroke	0.98	0.73-1.32	0.910	1.37	1.00-1.88	0.051	1.89	1.38-2.59	<0.001	1.15	0.73-1.82	0.534
NIHSS ≥16 on arrival	1.29	0.84-1.99	0.246	1.45	0.91-2.32	0.122	2.56	1.68-3.89	<0.001	4.53	2.90-7.07	<0.001
UTI within 7 days of admission	1.13	0.73-1.76	0.580	1.58	1.01-2.48	0.045	3.08	2.07-4.57	<0.001	4.16	2.66-6.51	<0.001
Pneumonia within 7days of admission	1.33	0.93-1.90	0.120	1.70	1.16-2.48	0.006	4.34	3.11-6.06	<0.001	3.72	2.47-5.81	<0.001
UTI and/or pneumonia within 7days of admission	1.10	0.80-1.52	0.557	1.71	1.23-2.38	0.001	3.86	2.85-5.23	<0.001	3.44	2.37-5.00	<0.001
Prolonged LOS on HASUs	1.25	0.96-1.63	0.093	2.38	1.77-3.20	<0.001	1.92	1.38-2.68	<0.001	1.63	1.06-2.51	0.027
Mortality	1.66	1.20-2.28	0.002	3.21	2.35-4.37	<0.001	4.92	3.61-6.69	<0.001	5.03	3.48-7.28	<0.001

[†]Adjusted for age, sex and co-existing morbidities (AF, CHF, HT, diabetes and previous stroke).

Figure 1. Plot showing mean LOS on HASUs in relation to different level of pre-stroke disability assessed by mRS scores. *Significances from pre-stroke mRS score = 0 (reference group).