Are there differences in long-term functioning and recovery between hemorrhagic and ischemic stroke patients receiving rehabilitation?

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Are There Differences in Long-Term Functioning and Recovery Between Hemorrhagic and Ischemic Stroke Patients Receiving Rehabilitation?

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Objective: Previous research suggested better recovery in functioning of patients with hemorrhagic as compared to ischemic stroke. Now that more effective acute treatment for ischemic stroke, i.e. thrombolysis and thrombectomy, has become available, this observational cohort study aimed to examine if current rehabilitation outcomes differ between patients with hemorrhagic and ischemic stroke. *Materials and Methods:* The Barthel Index, 4 domains of the Stroke Impact Scale (SIS) and the EuroQol 5Dimensions were completed in all consecutive patients who received stroke rehabilitation at start of rehabilitation and during follow-up (for Barthel Index at discharge, SIS and EuroQol 5D after three and six months). Outcomes and recovery (i.e. change of scores between baseline and last follow-up) were compared between patients with hemorrhagic stroke and ischemic stroke (total and categorized by initial hospital treatment) using the Kruskall Wallis test. In addition, recovery was compared between ischemic and hemorrhagic stroke in multiple regression analyses with bootstrapping. *Results:* Baseline functioning did not differ between 117 patients with a hemorrhagic stroke, 118 ischemic stroke patient treated with reperfusion therapy, and 125 ischemic stroke patients without reperfusion therapy. There were no differences in functioning at follow-up nor in recovery concerning the Barthel Index, SIS domains 'mobility', 'communication', 'memory and thinking' and 'mood and emotions', and EuroQoL 5D between the three categories. *Conclusions:* In a rehabilitation population the recovery and functioning at three or six months did not differ between ischemic stroke patients and hemorrhagic stroke patients, regardless of the hospital treatment they had received.

Key Words: Stroke—Stroke type—Rehabilitation—Outcome—Recovery of function—Intracerebral hemorrhage—Infarction

Introduction

Stroke is one of the leading causes of disability.[1] Strokes are broadly classified as hemorrhagic or ischemic. Hemorrhagic stroke accounts for approximately 10−15% of all strokes and often has a different etiology than ischemic stroke.[2] While a hemorrhagic stroke occurs from rupture of cerebral vessels, ischemic stroke is the result of a thrombus or embolus blocking a cerebral vessel. Treatment of ischemic stroke has improved over the last two decades by resolving this cerebral vessel blockage using intravenous thrombolysis and/or endovascular thrombectomy. These reperfusion treatments salvage the prenumbra aera leading to improved outcomes for ischemic stroke patients.[3,4] Unfortunately, treatment possibilities for hemorrhagic stroke have globally remained the same, including mainly blood-pressure lowering, reversal of anticoagulation medicine, and neurosurgery.

Before these reperfusion treatments for ischemic stroke were available, differences in rehabilitation outcomes

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were found between stroke types.[5–7] Although patients with hemorrhagic stroke started rehabilitation with more impairments, they showed greater recovery (i.e. change of scores) during inpatient rehabilitation.[5,6] Another study did not find differences at admission in a rehabilitation center, but did report better functioning at discharge in patients with hemorrhagic stroke compared to those with ischemic stroke.[7] Similarly, patients with a hemorrhagic stroke showed greater recovery during inpatient rehabilitation than those with an ischemic stroke with similar impairments at baseline.[7] However, a more recent article did not show any differences in functioning at discharge nor in recovery in patients receiving outpatient rehabilitation.[8] This observation might indicate that long-term functioning and recovery have become more comparable for patients with hemorrhagic and ischemic stroke now that more effective acute treatments are available. Unfortunately, no data on hospital treatment were mentioned.

Given the scarcity of recent data from the rehabilitation population, we aimed to investigate differences in functioning between patients with hemorrhagic and ischemic stroke receiving stroke rehabilitation now treatment options for ischemic stroke have improved. We hypothesized that patients with ischemic stroke who received reperfusion therapy function at least equally, three and six months after start of rehabilitation compared to patients with hemorrhagic stroke with a similar magnitude of recovery. In addition, we hypothesized that ischemic stroke patient without reperfusion therapy will do worse on these endpoints because of less brain tissue recovery.

Methods

Design and setting

The Stroke Cohort Outcomes of REhabilitation (SCORE) study is an ongoing observational, prospective cohort study, which started March 10, 2014 (Netherlands Trial registry no.4292).[9] This study collects data from stroke patients who receive inpatient and/or outpatient multidisciplinary rehabilitation in two locations of one Dutch rehabilitation center, located about 20 kms apart from each other. The study was approved by the Medical Ethics Committee of the Leiden University Medical Center (P13.249). The study was conducted in compliance with the Declaration of Helsinki[10] and reported in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines.[11] All patients signed informed consent before participation in the study.

Patients

All consecutive stroke patients were included in the SCORE study when they were diagnosed with a first or recurrent stroke no more than six months before and aged ≥18 years. Patients with dementia or a psychiatric disorder and patients that were unable to complete questionnaires in Dutch were excluded from the study. For this research question we additionally excluded patients of whom the type of stroke was not known, who did not reach the six months follow-up yet (i.e. six months after start of rehabilitation) or were lost to follow-up at 6 months.

Sociodemographic and clinical characteristics

Sex, age, stroke type and treatment in the referring hospital were extracted from the medical files of the rehabilitation centers. Ethnicity, education level, living situation and employment were collected through a standardized questionnaire at start of the rehabilitation (baseline). Comorbidities were determined at baseline by the Dutch Life Situation Cohort Questionnaire, comprising 16 chronic diseases, including diabetes, hypertension and heart disease.[12]

Measurements of functioning and recovery

Functional dependence was measured with the Barthel Index (BI), a score ranging from 0 (e.g. totally dependent) to 20 (e.g. totally independent).[13] The Barthel index was completed by a nurse at admission and at discharge only in patients who received inpatient rehabilitation.

All other measurements of functioning were completed at baseline (i.e. start of rehabilitation) and during follow-up three and six months after baseline. Recovery was defined as change of score between baseline and follow-up at six months.

The Stroke Impact Scale (SIS) version 3.0 is a stroke-specific, self-report, health status measure, that assesses several domains.[14] The domains ‘communication’ and ‘memory and thinking’ were administered in all patients. In April 2015, SIS domains ‘mobility’ and ‘mood and emotions’ were added. Scores for each SIS domain range from 0 to 100, with higher scores indicating better functioning on that specific domain.

Health-related quality of life was measured with the EuroQol 5 dimensions (EQ5D), version EQ-5D 3 levels. The EQ5D is a standardized instrument in which patients rate their health on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension has three levels of severity. The total score ranges from −0.33 (serious problems on all 5 dimensions) to 1 (healthy). In addition, the EuroQol comprises a vertical visual analogue scale, ranging from 0 to 100, that is used as a quantitative measure of overall health status.[15]

Statistical analyses

All data were anonymized when entered in a database and were analyzed with IBM SPSS 24.0 for Windows. A

two-sided p-value of 0.05 was considered statistically significant.

Ischemic stroke patients were categorized in patients with ischemic stroke with reperfusion therapy (i.e. patients who received intravenous thrombolysis, endovascular thrombectomy or both), and patients with ischemic stroke without reperfusion therapy. Recovery for the Barthel Index was calculated by subtracting baseline score from score at discharge. Recovery for the SIS domains and EQ5D was calculated by subtracting baseline scores from follow-up scores six months after baseline.

Descriptive statistics were used to describe the baseline characteristics using numbers (N) with percentages (%), medians with interquartile range (IQR) or means with standard deviation (SD), depending on the nature of the variables and their distribution. The Kolmogorov-Smirnov test was performed to assess whether or not continuous variables were normally distributed.

The Fisher's exact test, Mann Whitney U test (hemorrhagic stroke versus total group of ischemic stroke) and the Kruskall Wallis test (hemorrhagic stroke and the two categories of ischemic stroke) were used to compare baseline characteristics, follow-up and recovery scores. In addition, recovery scores were analyzed with multiple regression analyses with bootstrapping (dependent: recovery score; independent: type of stroke (hemorrhagic or ischemic) adjusted for age and sex.

Post hoc testing with Bonferroni correction were performed when significant differences were found in baseline characteristics or outcome measurements between the three categories (hemorrhagic stroke and the two categories of ischemic stroke).

Results

Between March 2014 and February 2020 839 stroke patients were included in the SCORE study. Of those, 14 patients were excluded because type of stroke was unknown, 129 because they did not reach the six months follow-up and 127 (27 with hemorrhagic stroke of which 1 (3.7%) died and 100 with ischemic stroke of which 3 (3.0%) died) because they were lost to follow-up at 6 months.

Of the remaining 569 patients, 117 (20.6%) patients had a hemorrhagic stroke and 452 (79.4%) patients had an ischemic stroke. Of 243 ischemic stroke patients treatment in the referring hospital was known: 94 (38.7%) patients received intravenous thrombolysis, 8 (3.3%) received thrombectomy and 16 (6.6%) received both thrombolysis and thrombectomy; the remaining received only pharmacological treatment.

Characteristics of patients with hemorrhagic and ischemic stroke

Baseline characteristics of patients with hemorrhagic stroke and with ischemic stroke are shown in Table 1. Comparison of patients with hemorrhagic stroke with all ischemic stroke patients demonstrated that patients with hemorrhagic stroke were on average younger than ischemic stroke patients (61 years versus 63 years, p 0.03), had less often diabetes mellitus (9.9% versus 18.5%, p 0.03) and started more often with inpatient rehabilitation (88.0% versus 76.3%, $p < 0.01$).

Regarding the comparison among the three categories (patients with hemorrhagic stroke, patients with ischemic stroke with reperfusion therapy, and patients with ischemic stroke without reperfusion therapy), there were significant differences in age, diabetes mellitus and living status (Table 1). Post hoc testing demonstrated that patients with hemorrhagic stroke were younger than both patients with ischemic stroke with and without reperfusion therapy (p 0.02 and $p < 0.01$, respectively). In addition, patients with ischemic stroke without reperfusion therapy more often lived alone compared to those with hemorrhagic stroke (p 0.02) and those with ischemic stroke with reperfusion therapy ($p < 0.01$). Patients with ischemic stroke without reperfusion therapy also had more frequent diabetes mellitus than patients with hemorrhagic stroke ($p < 0.01$).

Functioning at baseline and follow-up, and recovery

Between patients with hemorrhagic stroke and all patients with ischemic stroke there were no statistically significant differences in the Barthel Index, SIS domains 'mobility', 'memory and thinking' and 'mood and emotions', and EQ5D at all time points (Table 2). Patients with a hemorrhagic stroke scored significantly higher on the SIS domain 'communication' than patients with ischemic stroke (93 versus 89, p 0.04) at six months follow-up.

Comparing the three categories there were no statistically significant differences in the Barthel Index, all SIS domains and the EQ5D at baseline nor at three or six months follow-up.

When looking at recovery, there were no differences in recovery between patients with hemorrhagic stroke and ischemic stroke nor between the three categories, looking at the measured Barthel Index, SIS domains and EQ5D (Table 2).

In line with these results, no differences in recovery were found between patients with hemorrhagic stroke and ischemic stroke, even when corrected for age and sex (Table 2).

Discussion

We found no significant differences in functioning at six months nor recovery between patients hemorrhagic stroke and patients with ischemic stroke. In line with this, there were no differences found between patients with hemorrhagic stroke and categories of ischemic stroke based on the hospital treatment. These results are in line

Table 1. . *Baseline characteristics of patients with hemorrhagic stroke and ischemic stroke (total and subdivided by therapy).*

	N	Hemorrhagic stroke	N	Ischemic stroke total	*p*-value #	N	Ischemic stroke with reperfusion therapy	N	Ischemic stroke without reperfusion therapy	*p*-value ##
Male sex	117	67 (57.3)	452	283 (62.6)	0.29	118	82 (69.5)	125	82 (65.6)	0.14
Age (years)	117	61 (17)[a,b]	452	63 (14)	**0.03**	118	63 (15)[b]	125	66 (14)[a]	**0.01**
Dutch ethnicity	113	98 (86.7)	434	387 (91.5)	0.15	114	106 (93.0)	120	114 (95.0)	0.07
Low education level	112	45 (40.2)	436	157 (36.0)	0.44	113	43 (38.1)	122	41 (33.6)	0.57
Alcohol use >2 a day	111	10 (9.0)	432	42 (9.7)	1.00	111	8 (7.2)	121	16 (13.2)	0.34
Smoking	112	25 (22.3)	433	130 (30.0)	0.13	111	31 (27.9)	122	38 (31.1)	0.30
Hypertension	111	60 (54.1)	429	208 (48.5)	0.34	112	48 (42.9)	118	65 (55.1)	0.13
Diabetes Mellitus	111	11 (9.9)[a]	432	80 (18.5)	**0.03**	110	17 (15.5)	121	29 (24.0)[a]	**0.02**
Previous heart disease	110	18 (16.4)	416	71 (17.1)	1.00	109	21 (19.3)	116	15 (12.9)	0.43
Paid work*	71	54 (76.1)	246	177 (72.0)	0.55	62	45 (72.6)	59	46 (78.0)	0.76
Living alone	113	24 (21.2)[b]	437	121 (27.7)	0.19	113	21 (18.6)[a]	122	45 (36.9)[a b]	<**0.01**
Start with inpatient rehabilitation	117	103 (88.0)	452	345 (76.3)	<**0.01**	209	100 (84.7)	125	109 (87.2)	0.79
Discharge destination	101		373		0.65	106		113		0.61
Home		100 (99.0)		362 (97.1)			104 (98.1)		108 (95.6)	
Nursing home		1 (1.0)		5 (1.3)			1 (0.9)		3 (2.7)	
Hospital		0 (0.0)		6 (1.6)			1 (0.9)		2 (1.8)	
Duration admission (days)	37	44 (29)	125	42 (44)	0.98	36	41 (62)	23	42 (38)	0.86

Continuous variables are described as median (interquartile range) and dichotomous variables as N (%). Abbreviations: n Number of patients.

*Paid work is only asked in patients who were 65 years or younger; #*p*-value of Fisher's Exact or Mann Whitney U test comparing patients with hemorrhagic stroke with those with ischemic stroke; ## p-value of Fisher's Exact or Kruskall Wallis test comparing the three patient categories (hemorrhagic stroke, ischemic stroke with reperfusion therapy and ischemic stroke without reperfusion therapy)

[a]Post-hoc testing $p < 0.01$.

[b]Post-hoc testing $p < 0.05$.

Table 2. . *Baseline functioning, functioning at 3 and 6 months and recovery of patients with hemorrhagic stroke and ischemic stroke (total and categorized by therapy).*

	N	Hemorrhagic stroke	N	Ischemic stroke total	*p*-value*	*p*-value**	N	Ischemic stroke with reperfusion therapy	N	Ischemic stroke without reperfusion therapy	*p*-value#
Barthel Index											
Baseline	70	15 (9)	273	17 (7)	0.15		81	17 (9)	88	17 (6)	0.17
At discharge	54	20 (0)	218	20 (0)	0.31		76	20 (0)	82	20 (0)	0.70
Recovery	48	4 (9)	203	3 (6)	0.40	0.30	71	3 (9)	79	3 (5)	0.34
SIS mobility											
Baseline	63	81 (39)	251	84 (37)	0.58		82	85 (42)	95	81 (38)	0.65
3-months follow-up	53	92 (15)	247	92 (25)	0.53		76	92 (14)	97	92 (14)	0.44
6-months follow-up	62	94 (22)	264	92 (19)	0.68		84	92 (19)	103	92 (19)	0.86
Recovery	59	6 (26)	245	3 (22)	0.82	0.97	79	6 (26)	94	7 (23)	0.71
SIS communication											
Baseline	105	93 (23)	416	93 (25)	0.64		108	93 (25)	115	89 (25)	0.92
3-months follow-up	100	93 (14)	412	93 (21)	0.24		107	93 (21)	116	93 (18)	0.67
6-months follow-up	114	93 (14)	445	89 (21)	**0.04**		115	89 (18)	124	93 (18)	0.13
Recovery	103	0 (11)	411	0 (13)	0.13	0.10	105	0 (14)	115	0 (12)	0.38
SIS memory and thinking											
Baseline	109	86 (25)	418	86 (25)	0.15		107	86 (25)	116	86 (27)	0.27
3-months follow-up	101	89 (20)	412	86 (21)	0.67		107	89 (25)	116	89 (18)	0.82
6-months follow-up	116	89 (21)	446	86 (21)	0.81		115	86 (21)	124	89 (18)	0.23
Recovery	108	0 (17)	414	0 (14)	0.31	0.07	104	0 (17)	116	0 (11)	0.68
SIS mood and emotions											
Baseline	63	81 (22)	253	78 (22)	0.36		83	81 (22)	96	76 (19)	0.52
3-months follow-up	54	78 (20	249	81 (19)	0.97		77	81 (17)	98	78 (22)	0.55
6-months follow-up	64	78 (29)	265	78 (25)	0.92		84	81 (28)	103	78 (17)	0.96
Recovery	61	−3 (19)	248	1 (18)	0.16	0.16	80	0 (19)	95	3 (19)	0.21
EQ5D											
Baseline	99	0.77 (0.37)	400	0.77 (0.26)	0.44		104	0.79 (0.26)	112	0.78 (0.33)	0.50
3-months follow-up	100	0.81 (0.29)	401	0.81 (0.20)	0.73		103	0.81 (0.20)	112	0.81 (0.20)	1.00
6-months follow-up	115	0.81 (0.31)	443	0.81 (0.20)	0.79		114	0.81 (0.16)	124	0.81 (0.24)	0.76
Recovery	97	0.04 (0.25)	393	0.03 (0.19)	0.27	0.26	101	0.00 (0.25)	111	0.04 (0.21)	0.63
EQ5D VAS											
Baseline	101	65 (30)	414	68 (29)	0.47		107	69 (27)	114	65 (30)	0.71
3-months follow-up	100	70 (20)	405	70 (20)	0.89		105	70 (20)	113	70 (25)	0.30
6-months follow-up	115	70 (23)	441	70 (24)	0.74		116	71 (26)	122	74 (26)	0.35
Recovery	99	4 (22)	405	5 (25)	0.62	0.52	105	10 (25)	112	5 (29)	0.33

All variables are described in median (interquartile range). Abbreviations: EQ5D EuroQoL 5 dimensions; n number of patients; SIS Stroke Impact Scale; VAS visual analogue scale.

*p-value of Mann Whitney U test comparing patients with hemorrhagic stroke with those with ischemic stroke;.

**p-value of multiple regression analyses with bootstrap correcting for age and sex; #p-value of Kruskall Wallis test comparing the three patient categories (hemorrhagic stroke, ischemic stroke with reperfusion therapy and ischemic stroke without reperfusion therapy).

with more recent studies which did not find differences in functioning at discharge of rehabilitation.[8,16]

The results are only partially in line with our hypothesis, in which we expected that no differences in functioning at three and six months and recovery between patients with ischemic strokge treated with reperfusion therapy and patients with hemorrhagic stroke. However, surprisingly, functioning or recovery was also not worse in the group ischemic stroke patients who had not received reperfusion therapy. A possible explanation is that there is a favorable shift in discharge destination due to reperfusion therapy and that a group of patients with reperfusion therapy now receives inpatient rehabilitation that previously would not have received this as reported by Tate et al.[17] They found that ischemic stroke patients treated with thrombectomy were discharged more often to home and less often to institutionalized care than patients treated with medication only (27% versus 10%, 21% versus 33%, respectively), but that similar a proportion of patients went to a rehabilitation facility (42% versus 38%). Another possible explanation is that there was some selection bias in the categorial analyses, because there was a group of whom hospital treatment was not known. Baseline characteristics of this group were comparable with the other categories with exception that these patients less often started with inpatient rehabilitation (data not shown). Therefore influence on recovery in the categorial analyses cannot be excluded.

Interesting additional finding of our study is that ischemic stroke patients who did not receive reperfusion therapy more often lived alone than those who did receive reperfusion therapy, and there is a trend towards more cardiovascular risk factors. This is in line with previous literature describing that patients who live alone are less likely to arrive within 4.5 h in the hospital, to receive thrombolysis and to be discharged home.[18] In addition, more health-compromising behaviors and higher mortality after stroke in persons living alone is found previously.[19]

Strengths and study limitations

The strength of our study was the availability of hospital treatment data in a large number of ischemic stroke patients. In previous research studying rehabilitation populations hospital treatment was not known and therefore the influence of this treatment on their results could not be investigated. Another strength is that we used functioning six months after start of the rehabilitation, while previous studies looked at functioning at discharge. After discharge further recovery of functioning can take place, but most recovery will take place the first six months after stroke.[20]

On the other hand, there might be some selection bias. A rehabilitation stroke population is always a non-random sample of the total stroke population. It is possible that in different countries the criteria for being admitted for inpatient or outpatient rehabilitation are not the same and that this explains (partially) the difference between our results and the results of the studies described in the introduction.[5–7] We also excluded patients with severe psychiatric disorders and we do not know whether this was equally distributed between both patient groups. In addition, we had no data about the intensity of therapy during the rehabilitation: we therefore do not know if the same therapy effort was used to reach similar recovery and rehabilitation outcomes. More patients with hemorrhagic stroke started with inpatient rehabilitation than patients with ischemic stroke, which could point at differences in intensity of therapy. On the other hand, all patients were treated using the same stroke rehabilitation guidelines[21] and length of inpatient rehabilitation and baseline characteristics was similar for all groups.

Conclusions/clinical implications

Regarding clinical implications, these findings suggest there is no differences in long-term functioning and recovery between hemorrhagic stroke patients and ischemic stroke patients receiving rehabilitation, regardless the hospital treatment they receive.

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Declarations of interest

none.

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