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Rehabilitation outcome after acute subarachnoid haemorrhage: the role of early functional predictors and complications

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INTRODUCTION

Non-traumatic subarachnoid haemorrhage (SAH) is a significant cause of morbidity and mortality. While SAH accounts for less than 5% of all strokes, it carries a high disease-specific burden. Half are aged younger than 55 years and long-term disability or cognitive impairment exists in 38%. SAH patients receiving acute inpatient rehabilitation may achieve functional gains comparable to those with stroke or traumatic brain injury.

The objectives of this study were to study; (i) SAH clinical and rehabilitation profiles, (ii) post-ICU neurosurgical and rehabilitation complications, transfer-out from rehabilitation (TOFR) to acute care; and (iii) their respective impacts on rehabilitation functional outcomes.

METHODS

A retrospective cohort study involving the inpatient electronic medical records (EMRs) of patients with non-traumatic acute SAH during rehabilitation was conducted from 1 January 2015 to 31 December 2018. Ethics approvals were granted by the National Healthcare Group Domain Specific Review Boards, and data were anonymized during extraction. (NHG-DSRB 2019/00594, NCT04357626)

The study was conducted in an inpatient rehabilitation centre receiving referrals from acute stroke units. Patients were screened by physiatrists prior to transfer to the multidisciplinary rehabilitation programme.

Consecutive EMRs were screened based on inclusion criteria; (i) spontaneous, first SAH with clinical symptoms of headache, vomiting, neurological symptoms/signs, confirmed by neurosurgeons and CT or MRI neuroimaging; (ii) 21-85 years at onset; (iii) < 180 days post-SAH, and (iv) direct acute hospital admissions.

Exclusion criteria were: (i) radiological absence of SAH; (ii) previous SAH; (iii) traumatic SAH; (iv) non-rehabilitation admissions; (v) incomplete admission or discharge Functional Independence Measure (FIM) scores.[1]

The following data were manually extracted and anonymized: (i) demographics (age, gender, ethnicity); (ii) SAH severity (admission Glasgow Coma Scale (GCS), World Federation of Neurological Societies (WFNS) grading system (I – V)); (iii) SAH etiology, aneurysm location by cerebral angiography, acute management; (iv) acute and rehabilitation length of stay (LOS - days); (v) presence of post-ICU neurosurgical complications prior to rehabilitation; (vi) medical or neurosurgical complications during rehabilitation, which disrupted therapy or needed specific interventions; (vii) major neurological impairments, (number, types); (viii) presence of TOFR > 24 hours; (ix) FIM data (admission and discharge); and discharge destination (home, institution or death). For patients with a TOFR, rehabilitation LOS was computed as: (total rehabilitation LOS [days]) – (post-rehabilitation acute LOS [days]).

For this study, the primary outcome was functional outcome upon discharge from rehabilitation, using total discharge Functional Independence Measure (18–126) (Td-FIM).[1] Total admission FIM (Ta-FIM) scores, total discharge FIM (Td-FIM) scores (18–126), motor FIM (m-FIM) (13–91) and cognitive FIM (c-FIM) sub-scores (5–35), were recorded. Secondary outcomes included, (i) mean FIM gain, [Td-FIM - Ta-FIM] and, (ii) mean FIM efficiency, [FIM-gain]/ [rehabilitation LOS (days)].

Statistical analysis was performed using IBM SPSS® software version 19.0 (IBM Corp, Armonk, NY) and STATA Statistical Software (Release 14, College Station, TX: StataCorp LP). Data are presented as either mean ± standard deviation or median (interquartile range) where appropriate. Differences in Td-FIM and Ta-FIM scores (total and sub-scores) were

analysed using paired sample t-tests. Differences in Td-FIM across clinical variables were explored using independent samples t-tests and Mann-Whitney U tests.

Univariate analysis was used to determine variables associated with Td-FIM. Variables selected included age, WFNS grade, presence of; acute hydrocephalus, cerebral vasospasm, motor weakness, dysphagia requiring nasogastric tubes (NGT), urinary tract infection (UTI), > 2 rehabilitation complications, TOFR and Ta-FIM score. A stepwise method multivariate regression analysis was used in which variables in the univariate analysis displaying a significance level of $P < 0.05$ were included in the model. The level of statistical significance was set at $P < 0.05$ for all tests.

RESULTS

Ninety-six EMRs out of 176 SAH screened EMRs were analysed, and 80 were excluded for reasons of: normal neuroimaging (38), missing FIM data (18), traumatic SAH (9), previous SAH (8), SAH > 180 days (4), and failure to complete rehabilitation (3). Demographic and SAH clinical profiles are presented in Table 1. Td-FIM was significantly higher in endovascularly-treated SAH compared with surgically-treated SAH. (Td-FIM endovascular 99.22 vs Td-FIM surgery 86.1, $P < 0.022$)

Post-ICU neurosurgical complications occurred in 86 patients (89.6%) while 72 (83.7%) had ≥ 2 complications. The majority of complications were neurosurgical, including hydrocephalus (63/96, 65.6%), intraventricular haemorrhage (53/96, 55.2%) and cerebral vasospasm (29/96, 30.2%).

Impairments and complications during rehabilitation are presented in Table II. The prevalence of complications during rehabilitation was lower than that during acute stay (62.5% vs. 89.6%) and medical complications exceeded neurosurgical complications (72.9% vs. 18.8%). Twelve (12.5%) patients experienced at least 1 TOFR, including UTI (6), delayed

hydrocephalus (4), gastrointestinal (3), pneumonia (2), cardiovascular (2), seizures (1) and bacteraemia (1). TOFR patients had significantly longer median (IQR) rehabilitation LOS by 2-fold; and entered rehabilitation with lower mean ± SD Ta-FIM compared to those without TOFR respectively. (Rehabilitation LOS, without TOFR 23 (19) days vs with TOFR 48 (36) days, P < 0.001); (Ta-FIM: without TOFR 66.63 (27.83) vs with TOFR 40.67 (19.37), P = 0.002).

Upon rehabilitation discharge, mean ± SD Td-FIM score was 91.5 ± 28.3 points, representing a significant mean ± SD improvement of 28.1 ± 16.4 points [95% CI, 24.87 to 31.4; P < 0.001] from mean ± SD Ta-FIM score (63.4 ± 28.3). The majority of gains were achieved in m-FIM [mean ± SD Δ = 23.2 ± 13.2 points; 95% CI, 20.5 to 26.0; P < 0.001], compared to c-FIM [mean ± SD Δ = 5.25 ± 5.05 points; 95% CI, 4.21 to 6.28; P < 0.001]. Mean ± SD FIM efficiency was 0.86 ± 0.50.

Univariate analysis showed that Ta-FIM score (P < 0.001), motor weakness (P < 0.001), severe dysphagia needing NGT, (P < 0.001), > 2 rehabilitation complications (P < 0.001), UTI (P = 0.028), TOFR > 24 hours (P < 0.001) and cerebral vasospasm (P = 0.02) were significantly correlated with Td-FIM. TOFR (P < 0.001). Age > 75 years (P = 0.207), poor SAH grade (P = 0.097) and acute hydrocephalus (P = 0.086) were not correlated with Td-FIM (Appendix, Supplementary Table I) Each day in acute wards lowered the Td-FIM by 0.861 points (P < 0.001).

Multivariate analysis for predictors of Td-FIM are presented in table III. Multivariate linear regression identified TOFR as a significant negative factor, reducing total d-FIM by 17.5 points (coefficient −17.541; 95% CI, −26.983 to −8.099; P < 0.001). Higher Ta-FIM (coefficient 0.379; 95% CI, 0.140 to 0.618; P = 0.002) and in particular, admission c-FIM (coefficient 1.264, 95 % CI: 0.598–1.929; P < 0.001) were found to have small positive effects; a unit increase in these factors resulted in Td-FIM gains of 0.379 and 1.264 points, respectively.

Together, these 3 factors accounted for 74.5 % of the variability seen in the multivariate model predicting Td-FIM.

DISCUSSION

Findings from this study show that a month-long inpatient rehabilitation programme significantly improved functional independence, comparable with other reports (Td-FIM, 88.6–91.0 points).[1,2] Upon discharge, ≥ 88% of patients were discharged home, exceeding those by other studies (64.4–87.2%).[3-5] The mean FIM gain of 28.1 paralleled that for strokes (Δ 29 points) (Δ 27.8–33.7 points), smaller c-FIM gains (Δ 5.25 points), compared with m-FIM gains (Δ 23.25 points) reflected the significant and persistent cognitive sequelae from SAH impacting functional progress.[6] These gains far exceeded minimal clinically important difference thresholds referenced at 22 (Δ total FIM), 17 (Δ m-FIM), and 3 (Δ c-FIM) points respectively.[7] The samples' mid-50s peak, female preponderance and predominance of aneurysms concurred with other studies.[3,4,8]

Acute and rehabilitation complications were common in 89.6% and 62.5% of patient respectively, higher than some reports of 40% within 3 months of SAH. [9] Our TOFR of 12.5% concurred with the range of 5.7–19% reported in other studies.[10-12]

While the SAH literature suggests that older age and poorer SAH clinical grade should negatively impact function, in our sample, these variables did not influence Td-FIM.[3,5,13] Possible explanations included: few patients ≥ 75 years (5.2%) with expected poorer response to rehabilitation, small sample size and pre-selection bias.

Each extra day in acute wards lowered Td-FIM by 0.861 points. ($P < 0.001$). Poorer Td-FIM was significantly impacted by secondary neurological damage (vasospasm), motor weakness, dysphagia, aphasia; and medical complications; in particular, TOFR, which reduced

Td-FIM by 17.5 points ($P < 0.001$). Ta-FIM scores were lower by ~26 FIM points in patients with TOFR ($P = 0.002$), implying a poorer admission function regardless of SAH grade.

That Ta-FIM significantly predicted rehabilitation outcome (Td-FIM) was consistent with general stroke studies, accounting for 74% of the variability. (sample's adjusted $R^2 = 0.745$).[5,13] Lower Ta-FIM ($P = 0.002$), in particular c-FIM ($P < 0.001$) and TOFR ($P < 0.001$) significantly predicted poorer Td-FIM on multivariate analyses, possibly related to SAH-related attention, memory and executive dysfunction affecting relearning.[4]

Medical complications have been implicated as independent risk factors for poor functional outcomes at 12–18 months post-SAH.[14] Poorer rehabilitation outcomes at discharge may be explained by TOFR-related interrupted rehabilitation and detrimental effects of medical complications on recovery, delirium and secondary functional decline.[13]

In conclusion, findings from this study unequivocally support the important role of early inpatient rehabilitation following SAH. The high prevalence of complications from ICU through to rehabilitation, and their harmful effects on discharge function underscore the critical need for concerted, effective prevention and management strategies.

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Table I. Demographic, clinical characteristics of SAH patients (N = 96)

Variable	N (%)
Age in years, mean±SD	57.1±11.2
Age group, years	
< 75	91 (94.8)
≥ 75	5 (5.2)
Gender	
Female	72 (75.0)
Male	24 (25.0)
Ethnicity	
Chinese	75 (78.1)
Non-Chinese	21 (21.9)
Initial SAH severity based on GCS score [+]	
Mild (GCS 13 – 15)	54 (56.3)
Moderate (GCS 9 – 12)	16 (16.6)
Severe (GCS 3 – 8)	21 (21.9)
Initial SAH severity based on WFNS grade [+]	
Grade I	28 (29.2)
Grade II	19 (19.8)
Grade III	7 (7.3)
Grade IV	27 (28.1)
Grade V	10 (10.4)
Initial SAH severity based on WFNS grouping [+]	
Good clinical grade (WFNS Grade I – III)	54 (56.25)
Poor clinical grade (WFNS Grade IV– V)	37 (38.54)
SAH aetiology	
Single aneurysm rupture	88 (91.7)
AVM rupture	6 (6.2)
Hypertension (negative angiography)	2 (2.1)
Aneurysm location [‡]	
ACOM/ACA	31 (35.2)
MCA	16 (18.2)
PCA	19 (21.6)
ICA	4 (4.5)
VB	18 (20.5)
Acute management of SAH	
Surgical clipping/Evacuation	51 (53.1)
Endovascular coiling	41 (42.7)
Conservative	4 (4.2)
Length of stay in days, mean±SD	
Intensive Care Unit	9.8±5.7
Acute hospital	32.0±16.8
Rehabilitation	32.8±23.3
Length of stay in days, median (IQR)	
Acute hospital	26.0 (19.0)
Rehabilitation	24.0 (26.0)

GCS, Glasgow Coma Scale; WFNS, World Federation of Neurological Societies; AVM, Arteriovenous Malformation; ACOM, Anterior Communicating Artery; ACA, Anterior Cerebral Artery; MCA, Middle Cerebral Artery; PCA, Posterior Cerebral Artery; ICA; Internal Carotid Artery; VB, Vertebrobasilar Artery. TOFR: transfer-out from rehabilitation

[+] Denominator is 91. [‡] Denominator is 88.

Table II. Impairments and complications during rehabilitation (N = 96)

Types	N (%)
(a) Impairments	
Motor weakness	
Absent	19 (19.8)
Present	77 (80.2)
Hemiparesis/Paraparesis/Monoparesis	49 (63.6)
Tetraparesis	28 (36.4)
Sensory Impairment	34 (35.4)
Dysphagia	63 (65.6)
Dysphagia with NGT	35 (36.5)
Aphasia	18 (18.8)
IDC present	17 (17.7)
(b) Complications (N=96)	
0	36 (37.5)
1	26 (27.1)
≥ 2	34 (35.4)
Total	96 (100.0)
TOFR (N=96)	12 (12.5)
Delayed neurosurgical complications (N=18)	
Hydrocephalus	7 (7.3)
Cerebral haemorrhage	4 (4.2)
Infected VPS/wound	3 (3.1)
Seizures	2 (2.1)
Brain Abscess	1 (1.0)
Trephined Brain Syndrome	1 (1.0)
Medical Complications (N=70)	
Urinary tract infection	29 (30.2)
Mood disorders	14 (14.6)
Gastrointestinal	11 (11.5)
Pulmonary	6 (6.3)
Cardiac	5 (5.2)
Falls	4 (4.2)
Decubitus Ulcers	3 (3.1)
Venous Thromboembolism	1 (1.0)
Discharge Destination (N=96)	
Home	85 (88.5)
Institutional care	10 (10.4)
Death	1 (1.0)
Total	96 (100.0)

VPS, Ventriculo-Peritoneal Shunt; UTI, Urinary Tract Infection; VTE, Venous Thromboembolism; NGT, nasogastric tube; IDC, indwelling catheter; TOFR, transfer-out from rehabilitation

Table III. Regression analyses of factors predicting total discharge FIM score

Variables	Simple Linear Regression			Multiple Linear Regression		
	coef	**95 % CI**	**P-value**	**Adj. coef**	**95 % CI**	**P-value**
Vasospasm[†]	-14.471	-26.658, -2.285	0.020			
Motor weakness [‡] Absent Present	 Ref -26.634	 -40.019, -13.250	 < 0.001			
Dysphagia requiring insertion of NGT [‡] Absent Present	 Ref -29.262	 -39.617, -18.907	 < 0.001			
UTI [§]	-13.730	-25.952, -1.508	0.028			
TOFR [§]	-34.262	-50.198, -18.326	< 0.001	-17.541	-26.983, -8.099	< 0.001
No. of rehabilitation complications [§] 0 – 1 ≥ 2	 Ref -22.693	 -33.800, -11.585	 < 0.001			
Total FIM (admission)	0.833	0.719, 0.947	< 0.001	0.379	0.140, 0.618	0.002
Motor FIM (admission)	1.108	0.923, 1.293	< 0.001			
Cognitive FIM (admission)	2.343	1.996, 2.689	< 0.001	1.264	0.598, 1.929	< 0.001

NGT, Nasogastric Tube; UTI, Urinary Tract Infection; FIM, Functional Independence Measure.
Variable selection stepwise method was used for the multivariate regression analysis; adjusted $R^2 = 0.7448$.
[†] Acute complications. [‡] Impairments during rehabilitation. [§] Complications during rehabilitation.

APPENDIX

Supplementary Table 1. Univariate analysis of factors associated with total discharge FIM score

Factor		Total FIM score at discharge	P-value
Age ‡	< 75 years ≥ 75 years	95.0 (42.0) 108.0 (20.0)	0.207
WFNS grade †	I – III IV – V	96.76 (26.05) 86.97 (29.08)	0.097
Hydrocephalus †, §	Absent Present	98.3 (21.6) 87.9 (30.8)	0.086
Cerebral vasospasm †, §	Absent Present	95.8 (25.6) 81.4 (31.8)	0.020 **
Motor weakness †, ‖	Absent Present	112.8 (10.8) 86.2 (28.8)	< 0.001 **
Dysphagia requiring insertion of NGT†, ‖	Absent Present	102.15 (20.53) 72.89 (30.48)	< 0.001 **
UTI †, ‖	Absent Present	95.6 (28.4) 81.9 (26.0)	0.028 **
No. of rehabilitation complications ‡	0 – 1 ≥ 2	108.5 (27.0) 74.5 (47.0)	< 0.001**
TOFR > 24 hours†	Yes No	95.8 (26.2) 61.5 (24.5)	< 0.001**
Total admission FIM†		0.833 (0.72, 0.95)	<0.001**

WFNS, World Federation of Neurological Societies; NGT, Nasogastric Tube; UTI, Urinary Tract Infection; TOFR: Transfer out from Rehabilitation.

† Values are presented as Mean (SD). Independent samples t-test was performed.

‡ Values are presented as Median (IQR). Mann-Whitney U test was performed.

§ Acute complications

‖ Impairments during rehabilitation.

** indicates significant p-value < 0.05.