ORIGINAL ARTICLE

Does Early Rehabilitation Admission Improve Functional Outcomes of Stroke Patients after a Short Hospital Stay? A Thai Retrospective Study on 596 Patients

Witsanu Kumthornthip, MD[1], Supitcha Tassatarn, MD[1], Chayaporn Chotiyarnwong, MD[1]

[1] Department of Rehabilitation Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: It remains unknown whether inpatient rehabilitation lasting three weeks or less, following one or two weeks of acute-phase treatment for stroke patients at Siriraj Hospital, Mahidol University (SH-MU), Thailand, is effective, especially when the beginning is deferred.

Objective: To examine functional outcomes (FO) of short hospitalized rehabilitation (SHR) for stroke patients with three different stroke onsets to rehabilitation admission intervals (SOTRAI), and to determine whether there are any differences in FO regarding SOTRAI.

Materials and Methods: The investigators conducted a retrospective cohort study of medical records on inpatient rehabilitated at the Department of Rehabilitation Medicine, SH-MU. The investigators enrolled a cohort of stroke patients who underwent SHR at a Thai university-based, quaternary-care medical center between 2015 and 2019. The predictor variable was SOTRAI, categorized as early, which is 30 days or less, early-late, which is 31 to 90 days, and late, which is more than 90 days. The FO variables were the modified Barthel Index (MBI) score change, rehabilitation efficiency, and effectiveness, and percentages of responders. Appropriate statistics were computerized with the significant level at p-value less than 0.05.

Results: Five hundred ninety-six patients, with 44.8% females and 45.8% early SOTRAI, with the mean age of 65.3±13.4 years (range of 19 to 94) were included. Early SOTRAI was associated with the highest FO parameters (p<0.001).

Conclusion: Stroke survivors should be apt to SHR within 30 days after the symptoms begin. In other words, early SOTRAI could help improve FO, compared with late SOTRAI.

Keywords: Stroke; Rehabilitation; Hospital admission; Outcome; Inpatient

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The World Health Organization (WHO) defines stroke as "rapidly developing clinical signs of focal or generalized disturbance of cerebral functions, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular causes"[1]. This condition poses a significant challenge to global public health. Annually, over 13.7 million new stroke cases are estimated worldwide, with more than 300,000 treated in Thailand every year[2,3].

Correspondence to:

Chotiyarnwong C.

Department of Rehabilitation Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand.

Phone: +66-2-4197508

Email: hedhom2000@hotmail.com, chayaporn.cho@gmail.com

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Poor neurological recovery post-stroke inevitably diminishes the patient's quality of life. This recovery process relies on mechanisms including the reduction of cerebral oedema and the restoration of vascular perfusion to penumbral tissue[4,5]. Additionally, damaged neurons have the capacity to repair and reorganize themselves over time. This phenomenon has been known as "neural plasticity", which can be enhanced with timely and appropriate rehabilitation interventions (RI)[6]. Previous studies have indicated that RI during the first month after stroke yields optimal neurological recovery[7-9]. Typically, the recovery process spans three to six months before reaching a plateau phase[9-11].

However, akin to other middle- and low-income countries, the Thai healthcare system faces challenges such as budgetary constraints, shortages of beds and personnel, and often restrictive government policies. Although Siriraj Hospital, Mahidol University (SH-MU) boasts 2,154 beds and serves over 3.8 million outpatients annually, and it is among the top-ranking hospitals in the country, the length of hospital stay (LOS) for stroke RI in this university hospital has been limited to three weeks following acute stroke patient care for one or two weeks. In the present study, the investigators termed "short hospitalized rehabilitation (SHR)" because this duration is notably shorter than that reported in other countries or hospitals, which is ranging between 40 and 70 days[12,13]. Furthermore, significant obstacles to stroke patient care quality in Thailand include delayed referral systems and a scarce of hospitals with available RI, medical personnel, and devices.

Yet, it remains unclear whether the SHR approach for stroke patients utilized at SH-MU is effective, particularly when its initiation is delayed. The present study aimed to examine the functional outcomes (FO) of stroke survivors admitted to RI as a part of SHR with varying stroke onset to rehabilitation admission intervals (SOTRAI). Additionally, the investigators aimed to ascertain whether any differences in FO exist among patients with different SOTRAI. The investigators hypothesized that early SOTRAI, compared to early-late and late SOTRAI, would be associated with better FO. The specific objectives of the present study were 1) to conduct a retrospective cohort study on stroke patients treated at SH-MU, 2) to assess the FO of SHR for stroke patients, and 3) to evaluate the association between SOTRAI and FO of SHR for this patient group.

Materials and Methods

Study design and sample description

The study was structured as a retrospective cohort study, utilizing data from hospitalized stroke patients treated at the Department of Rehabilitation Medicine, SH-MU, Thailand, between January 1, 2015 and December 31, 2019. The chosen study period aligned with the prevailing medical care protocol preceding the global healthcare disruption caused by the COVID-19 pandemic.

The stroke service at SH-MU comprised 20 acute stroke beds, and 25 beds dedicated to RI. The RI was multidisciplinary, overseen by a team consisting of physiatrists, rehabilitation nurses, physiotherapists, occupational and speech therapists, clinical psychologists, and social workers. Admission criteria for SHR included stable general health, capability for compliance and memory retention exceeding 24 hours, and ability to maintain an upright position for over two hours during RI sessions. Patients initially received treatments in acute stroke units during the first two weeks post-stroke, before transitioning to RI program. Upon achieving RI goals or the predetermined LOS, patients were discharged and continued treatments on an outpatient basis. Prior to discharge, supportive interventions were implemented to facilitate the transition from hospital to home, as they had been shown to enhance FO and other treatment outcomes[14].

Inclusion criteria for the present study cohort were 1) adult patients defined as age 18 years or older, 2) diagnosed with first-time stroke, and 3) deemed suitable for SHR at the SH-MU. Subjects were excluded from the study cohort if they had 1) unstable general health, including neurologic complications such as cervical myelopathy, 2) modified Barthel Index (MBI) scores upon hospital admission exceeding 18 out of 20 to mitigate the ceiling effect[15,16], 3) premature discharge due to treatment denial, or 4) incomplete medical documentation.

The present study adhered to ethical guidelines outlined in the Helsinki Declaration and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The study protocol received approval from the Institutional Review Board (Certificate of Approval no. Si 618/2020, SIRB Protocol no. 530/2563(IRB4).

Study variables

The predictor variable in the present study was SOTRAI, categorized as early for 30 days or less, early-late for 31 to 90 days, and late for more than 90 days. Notably, neurological recovery within the first month post-stroke demonstrated significant improvement, while recovery tended to plateau after three months[7-11]. Throughout their hospital stay, patients received physical and occupational therapies for one hour per session, with one or two sessions conducted daily. Additionally, speech therapy, psychotherapy, and robot-assisted training (RAT) utilizing devices such as the Gait Trainer GT1, Lokomat®, Armeo®Spring (Hocoma AG, Volketswil, Switzerland) and/or Bi-Manu-Track® (Reha-Stim MedTec AG, Berlin, Germany) were administered on an individual basis.

The primary outcome variables included 1) MBI change, defined as the difference between MBI scores upon hospital admission and before discharge, evaluated by a physiatrist[17,18], 2) rehabilitation efficiency, denoting the daily average increase in MBI scores, calculated as the MBI change divided by LOS[19], 3) rehabilitation effectiveness, indicating the potential improvement in patient's daily activities, computed as (MBI change × 100) ÷ (20 – MBI score on admission score)[19], and 4) percentage of responders with minimally clinically important differences in daily activities, defined as MBI improvement of 1.85 or more[20]. The MBI change was assessed as an interval scale, while the other outcome variables were considered ratio parameters.

Additional study variables encompassed relevant risk factors associated with poor FO following stroke RI[21-23]. These variables were categorized into the following groups, demographics including age, and biological gender at birth, patient-specific factors such as body mass index (BMI), highest education level, tobacco use for current smokers, alcohol use, underlying diseases, communication disorders, and presence of dysphagia; and clinical/therapeutic parameters such as British Medical Research Council (MRC) scales of muscle strength on affected proximal upper, distal upper, proximal lower, and distal lower extremities[24], readmission due to the same stroke event, interventions, LOS, and living arrangement.

Age, BMI, and LOS were recorded as ratio scales, while gender, tobacco and alcohol uses, presence of chronic conditions, communication disorders and/or dysphagia, readmission, treatment methods, and living at home after discharge were noted as binary such as female or male, and yes or no. Dysphagia screening was conducted early post-stroke onset to mitigate potential health complications such as pneumonia, mortality, dependency, and prolonged LOS[25]. The highest education level was categorized into no formal education, primary, which is grade 1 to 6, secondary, which is grade 7 to 12, and tertiary education, which is university. The MRC scales of muscle strength were adjusted into binary categories as grade 0 to 3 versus grade 4 and 5 due to the method's inherent variability within the good, which is grade 4, to normal range, which is grade 5, leading to inconsistent results between examiners[26]. Grade 4 and 5 on the MRC scale indicate muscle ability against gravity, potentially influencing FO.

Data collection, management, and statistical analyses

Patient data were extracted from the hospital database by one of investigators (ST) and subsequently recorded in a Microsoft Excel Spreadsheet (Microsoft Co., Redmond, WA, USA). Quantitative data was represented by mean ± standard deviation (SD) whereas qualitative data was represented by number and percentage. Data in each group were compared by One-way ANOVA with post hoc analysis by Bonferroni and Games-Howell method for continuous data or either chi-square or Fisher's exact test for categorical data. All statistical analyses were performed by PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA). A significance level of p-value less than 0.05 was predetermined for statistical significance.

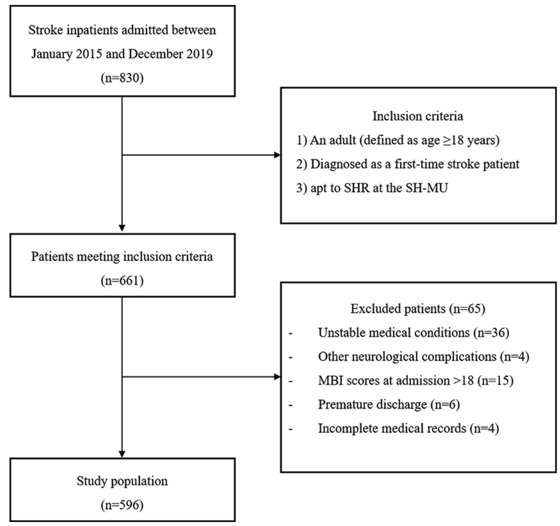

Figure 1. Flow chart of patient enrollment.

Results

During the study period spanning from January 1, 2015 through December 31, 2019, 830 stroke patients received treatment in the present study RI ward. Following the application of inclusion and exclusion criteria, the final study sample comprised of 596 subjects (Figure 1). The cohort had a mean age of 65.3±13.4 years (range of 19 to 94), and with 44.8% being females.

Of the included patients, 45.8% were early admitted to the investigators RI ward within 30 days after stroke onset, particularly prevalent among young individuals (p=0.03) and those with higher body weight (p<0.001). Educational levels and underlying diseases were not identified as risk factors for delay SOTRAI. As the investigators expectations, both early-late and late SOTRAI were significantly associated with poorer MRC scales of muscle strength such as grade 3 or lower, more communication disorders on arrival, and higher readmission rates due to the same stroke event (Table 1).

Patients with early-late or late SOTRAI, compared to those with early SOTRAI, tended to be older, and less overweight, and more frequently presented with hemorrhagic stroke requiring surgical

Table 1. Study variables grouped by stroke onset to rehabilitation admission interval (SOTRAI)

Study variables	SOTRAI (n=596)			p-value
	≤30 days (n=273)	31 to 90 days (n=143)	>90 day (n=180)	
Demographics				
Age (year); mean±SD (range)	63.7±12.8^{a} (19 to 94)	66.8±13.9^{b} (20 to 90)	66.3±13.6^{b} (28 to 93)	0.03*
Female; n (%)	130 (47.6)	65 (45.5)	72 (40.0)	0.28
Body mass index (BMI); mean±SD (range)	24.3±4.1^{a} (14.20 to 36.51)	22.2±4^{b} (15.38 to 35.16)	21.8±3.3^{b} (15.50 to 33.23)	<0.001*
Highest education level#; n (%)				0.45
No formal education	10 (3.8)	7 (5.0)	4 (2.3)	
Primary education	103 (39.2)	63 (44.7)	82 (46.6)	
Secondary education	71 (27.0)	31 (22.0)	40 (22.7)	
Tertiary education	79 (30.0)	40 (28.4)	50 (28.4)	
Underlying disease/condition; n (%)				
Diabetes mellitus	100 (36.6)	54 (37.8)	57 (31.7)	0.44
Hypertension	239 (87.5)	124 (86.7)	158 (87.8)	0.96
Dyslipidemia	191 (70.0)	95 (66.4)	117 (65.0)	0.5
Atrial fibrillation	27 (9.9)	25 (17.5)	26 (14.4)	0.08
Coronary artery disease	13 (4.8)	9 (6.3)	16 (8.9)	0.2
Peripheral artery disease	1 (0.4)	0 (0.0)	0 (0.0)	0.55
Carotid artery disease	0 (0.0)	0 (0.0)	2 (1.1)	0.1
Active smoking	40 (14.7)^{a}	26 (18.2)^{a}	12 (6.7)^{b}	0.006*
Chronic alcoholic consumption	65 (23.8)^{a}	37 (25.9)^{a}	24 (13.3)^{b}	0.008*
Muscle strength on affected side#: grade ≤3; n (%)				
Proximal upper extremities	153 (57.3)^{a}	101 (74.3)^{b}	133 (76.9)^{b}	<0.001*
Distal upper extremities	185 (69.3)^{a}	108 (80.0)^{a,c}	144 (83.2)^{b,c}	0.002*
Proximal lower extremities	155 (57.8)^{a}	105 (77.2)^{b}	125 (71.8)^{b}	<0.001*
Distal lower extremities	180 (67.2)^{a}	108 (79.4)^{b}	135 (78.0)^{b}	0.008*
Associated condition; n (%)				
Communication disorders	56 (20.5)^{a}	52 (36.4)^{b,c}	54 (30.0)^{a,c}	0.002*
Dysphagia	131(48.0)	76 (53.1)	80 (44.4)	0.3
Readmission; n (%)	2 (0.7)^{a}	11 (7.7)^{b}	89 (49.4)^{c}	<0.001*
The modified Barthel Index score on admission; mean±SD (range)	7.6±4.3^{a} (0 to 18)	6.1±5.2^{b} (0 to 18)	7.9±5.1^{a} (0 to 18)	0.003*
Ischaemic stroke; n (%)				
Sample size	230 (84.2)^{a}	104 (72.7)^{b}	109 (60.6)^{b}	<0.001*
Intervention†				
• Thrombolysis	40 (17.4)	19 (18.3)	14 (12.8)	0.49
• Embolectomy	18 (7.8)	8 (7.7)	10 (9.2)	0.9
• Surgery	2 (0.9)^{a}	6 (5.8)^{b}	11(10.1)^{b}	<0.001*
• Conservative treatments	185 (80.4)	75 (72.1)	82 (75.2)	0.2
Hemorrhagic stroke; n (%)				
Sample size	43 (15.8)^{a}	39 (27.3)^{b}	71 (39.4)^{b}	<0.001*
Intervention†				
• Surgery	4 (9.3)^{a}	16 (41.0)^{b}	32 (45.1)^{b}	<0.001*
• Embolisation	1 (2.3)	0 (0.0)	3 (4.2)	0.4
• Conservative treatments	39 (90.7)^{a}	23 (59.0)^{b}	36 (50.7)^{b}	<0.001*
Length of hospital stay; mean±SD	21.3±7.9^{a}	20.8±7^{a,c}	19.4±6.8^{b,c}	0.02*
Rehabilitation interventions; n (%)				
Physical therapy	273 (100)	143 (100)	180 (100)	N/A
Occupational therapy	269 (98.5)	143 (100)	177 (98.3)	0.3
Robot-assisted training				
• Gait trainer GT1	45 (16.5)^{a}	7 (4.9)^{b}	9 (5.0)^{b}	<0.001*
• Lokomat®	102 (37.4)^{a}	48 (33.6)^{a}	37 (20.6)^{b}	0.001*
• Armeo®Spring	22 (8.1)^{a,c}	8 (5.6)^{b,d}	0 (0.0)^{c,d}	0.001*
• Bi-manu-track®	47 (17.2)^{a}	15 (10.5)^{a,c}	13 (7.2)^{b,c}	0.005*
Living at home; n (%)	249 (91.2)	120 (83.9)	160 (88.9)	0.08

N/A=not available

Continuous measurements are listed as mean ± standard deviation (SD) and range; categorical measurements are listed as number (percentage).

Missing data were excluded, † ≥1 interventions per patient were possible

* Statistically significant p-values, different superscript letters within the same row indicate statistically significant differences (p<0.05), identical superscript letters within the same row indicate insignificant differences.

Table 2. Primary outcomes grouped by Stroke onset to rehabilitation admission interval (SOTRAI)

Outcome measures	Overall (n=596)	SOTRAI			p-value
		≤30 days (n=273)	31 to 90 days (n=143)	>90 day (n=180)	
The modified Barthel Index (MBI) change; mean±SD (range)	4.7±3.5	6.6±3.4[a] (0 to 15)	3.8±3[b] (–2 to 13)	2.5±2.5[c] (0 to 10)	<0.001*
Rehabilitation interventions: Efficiency; mean±SD	0.2±0.09	0.3±0.01[a] (0 to 1.4)	0.2±0.01[b] (–0.1 to 1)	0.1±0.01[c] (0 to 0.7)	<0.001*
Rehabilitation interventions: Effectiveness; mean±SD (range)	42.7±32.4	58.9±29.7[a] (0 to 100)	34.4±30[b] (–12.5 to 100)	24.8±25.6[c] (0 to 100)	<0.001*
Responders; n (%)	442 (74.2)	247 (90.5)[a]	103 (72.0)[b]	92 (51.1)[c]	<0.001*

Continuous measurements are listed as mean ± standard deviation (SD) and range; categorical measurements are listed as number (percentage).

* Statistically significant p-values, different superscript letters within the same row indicate statistically significant differences (p<0.05), identical superscript letters within the same row indicate insignificant differences.

intervention. Conversely patients with early SOTRAI were often successfully managed with conservative measures and had shorter LOS, regardless of stroke type (Table 1).

Table 2 provided multiple significant insights. Firstly, early SOTRAI was associated with the highest FO measured in the present study. After adjusting responders' percentage into binary categories, early SOTRAI significantly increased the percentage of responders for SOTRAI of 30 days or less versus more than 30 days (relative risk 0.24, 95% confidence interval [CI] 0.16 to 0.35, p<0.0001), absolute risk reduction of 30.1% (95% CI 23.7 to 36.5), and the number needed to treat (NNT) was 3.3 (95% CI 2.7 to 4.3). Secondly, upon completion of the investigators' 3-week SHR program, stroke survivors exhibited an overall MBI change, RI efficiency and effectiveness, and responder percentages of 4.7±3.5, 0.2±0.1, 42.7±32.4, and 74.2%, respectively.

Discussion

The aim of the present study was to explore the relationship between SOTRAI and FO in stroke patients after SHR at a large-volume university hospital in Thailand. The results revealed a clear association between SOTRAI and FO. Specifically, the early SOTRAI group demonstrated the best FO, while early-late and late SOTRAI were associated with a 24% increased risks of non-responsiveness. The NNT of 3.3 suggests that approximately one in every three patients would benefit from early SOTRAI, defined as achieving an MBI improvement of 1.85 or greater. These findings corroborate previous research, suggesting that early initiation of SHR within 30 days after stroke onset leads to superior treatment outcomes(12), consistent with the belief that neurological recovery is most rapid during the acute/subacute phase(27).

The brain recovery usually continues for three months(9-11). The observed poor FO in patients with late SOTRAI may be attributed to delayed initiation of rehabilitation, as supported by a recent meta-analysis indicating the benefits of rehabilitation within the first three months post-stroke in terms of increased muscle strength, grip strength, and pinch strength, and decreased muscle thickness(28). Advanced age was found to be associated with early-late and late SOTRAI, due to prolonged pre-RI treatments and complications requiring surgical interventions, leading to delayed entry into the SHR program(29). This delay could also result from the ineffective referral system and bed shortage coupled with medical negligence among stroke patients with an advanced age, which have been noted as challenges in stroke patient care in Thailand(30). Access to stroke patient care is beyond the present study's scope and requires further investigations.

Interestingly, despite higher body weight, which is within the normal range according to the WHO's BMI classification for Asians(31), the present study patients in the early SOTRAI group exhibited better FO, due to prompt and effective treatments, as well as fewer degrees of physical impairment. The investigators' findings regarding the absence of the effect of obesity on FO in stroke survivors are consistent with recent meta-analytic data(32). Additionally, reductions in tobacco and alcohol use among patients with early-late and late SOTRAI reflect lifestyle modifications after the stroke event, potentially affecting the effectiveness of RI. In contrast, patients in the early SOTRAI group tended to continue consuming tobacco and/or alcohol. It may be due to the fact that their early SOTRAI treatments deemed simpler and faster until health behaviors remained unchanged.

The present study 3-week SHR program demonstrated notable improvement in FO, comparable to previous studies that reported longer LOS of a mean of 60 days(12). According to the WHO, RI programs help maximize FO and minimize limitations in daily activities through neuro-facilitation, functional, and compensatory training strategies. If the patient was medically stable, RI can be initiated in the acute care facility within approximately 72 hours. A systematic review demonstrated that patients who underwent hospitalization for RI had significantly higher functional independence measure scores (effect size 0.10, 95% CI 0.01 to 0.2) and shorter LOS with a range of 9 to 76 days (effect size 0.14, 95% CI 0.03 to 0.2)[33].

Because patients in the early SOTRAI group received RAT more frequently than those in the other two groups, incorporating RAT into interventions aimed at supporting the transition to home could potentially enhance the FO of these patients[14]. Previously, systematic reviews have underscored the importance of RAT to functional rehabilitation in stroke survivors[34,35]. In another recent meta-analysis, Loro et al.[35] analyzed 19 studies and found that about half of them demonstrated the superiority of RAT over conventional RIs in the Berg Balance Scale (BBS) or Timed Up and Go test (TUG). However, these findings should be interpreted cautiously due to several aspects. For instance, there are various RAT techniques and devices, along with different treatment protocols, such as treatment durations ranging from 2 to 20 weeks, and each session lasting from 30 to 120 minutes. RAT devices are still under investigation. Therefore, RAT should be considered as an adjunctive treatment rather than a standalone therapeutic method. At the investigators' institution, RAT is frequently combined with conventional RI.

Strengths of the present study include a large patient cohort treated by a group of healthcare providers following an identical, or nearly identical, treatment protocol, data collection conducted by one observer, and limited confounding factors such as no significant differences in patients' gender, education levels, chronic diseases, given physical and occupational therapies provided, and interventions to support the transition home after acute stroke.

However, the results of the present study should be interpreted within the context of its limitations. These include being a single-center study with a retrospective design, the lack of baseline neurological and cognitive data and a control group, and the probability of variations in MBI rating by different practitioners despite the excellent reliability of the MBI scoring with a weighted kappa of 0.93[36]. Moreover, selection bias cannot be ruled out since patients in the early SOTRAI group were younger and had fewer degrees of neurological impairment, and almost 10% of the patients treated at SH-MU during the study period were excluded. The present study results may also be limited in terms of accuracy and reliability due to the categorization and measurement of variables such as SOTRAI and MRC scales of muscle strength. Additionally, the findings may have limited generalizability to other hospitals in different world regions because the study design was a single-center study, and the sample cohort was limited to otherwise healthy individuals with the exclusion criteria of persons with unstable health status and high MBI scores. Nonetheless, early SOTRAI should be emphasized and supported, particularly in the hospital setting similar to SH-MU, which has a short length of stay. Future research considerations should include prospective controlled trials in larger and diverse populations that may provide evidence of the results and minimize the possible confounders, such as no or low number of excluded patients, inclusion of baseline neurological status, and analysis of the effects of different LOS and admission criteria on patient outcomes.

Conclusion

Despite the abovementioned limitations, the present study has demonstrated that early SOTRAI is recommended for all stroke survivors because it is significantly associated with better FO. In other words, hospitalized stroke patients submitted to early RI could reach the optimal treatment goals with three weeks LOS.

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Conflicts of interest

The authors report there are no competing interests to declare.

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