The Journal of Physical Therapy Science

Original Article

Outcome prediction in patients with putaminal hemorrhage at admission to a convalescent rehabilitation ward based on hemorrhage volume assessed with computed tomography during acute care

Toshiki Yasukawa, MD[1]*, Tetsuo Koyama, MD, PhD[1, 2], Yuki Uchiyama, MD, PhD[1],
Saya Iwasa, MD[1], Jun Saito, MD, PhD[3], Jun Takahashi, MD, PhD[3],
Naoko Kiritani, MD[3], Kazuhisa Domen, MD, PhD[1]

[1] Department of Rehabilitation Medicine, Hyogo College of Medicine: 1-1 Mukogawa-cho, Nishinomiya,
    Hyogo 663-8501, Japan
[2] Department of Rehabilitation Medicine, Nishinomiya Kyoritsu Neurosurgical Hospital, Japan
[3] Department of Rehabilitation Medicine, Rakusai Shimizu Hospital, Japan

Abstract. [Purpose] The aim of this study was to assess the usefulness of computed tomography for outcome prediction in patients with putaminal hemorrhage at admission to a convalescent rehabilitation ward. [Participants and Methods] Patients admitted to our convalescent rehabilitation ward after transfer from acute care hospitals were included in this study. Multiple regression analyses were performed using the score in the motor component of the Functional Independence Measure at discharge as the target value. Hemorrhage volume assessed with computed tomography during acute care and age were set as the explanatory variables. The motor component of the Functional Independence Measure score at admission and the time (days) from onset were also recorded. Correlation analyses between all the possible pairs of explanatory variables were then performed. [Results] Hemorrhage volume and age were both significant contributors to the motor component of the Functional Independence Measure score at discharge. However, the contribution of hemorrhage volume disappeared when the time from onset and motor component of the Functional Independence Measure score at admission were added. Hemorrhage volume significantly correlated with the time from onset and motor component of the Functional Independence Measure score at admission. [Conclusion] The present findings suggest that computed tomography may be useful for outcome prediction from the acute stage in stroke patients with putaminal hemorrhage. However, because of multicollinearity, its predictive power was reduced when the patients were transferred to a convalescent rehabilitation ward.
Key words: Acute-care, Imaging, Prognosis

INTRODUCTION

Outcome prediction is critically important for scheduling appropriate rehabilitative treatment for patients after stroke[1]. Several prediction methods have been proposed. For example, initial clinical severity was reported to be critical for prediction of long-term outcome[2, 3]. Age was also found to be one of the most powerful predictors for outcome[4, 5]. Further, several new technologies were reported to have utility for outcome prediction[6], including transcranial magnetic stimulation (TMS)

*Corresponding author: Toshiki Yasukawa (E-mail: toshytoshytosyu@gmail.com)

combined with motor evoked potential[7, 8]. However, clinical examination using TMS is not yet widely available in Japan because the equipment is expensive and interpretation of motor evoked potential data is difficult[9]. Alternatively, diffusion-tensor imaging, which allows assessment of neural fiber integrity *in vivo*, has been used for outcome prediction[10, 11], although this application is not widely used because of the complexity of image analysis procedures and their interpretation[12].

Computed tomography (CT) is a conventional neuroimaging technique used for diagnosis of stroke, particularly in hemorrhagic cases. For example, the hemorrhage volume assessed by CT is a powerful predictor of mortality[13, 14], but a less accurate predictor of functional outcome[15, 16]. Nevertheless, CT is widely used in daily clinical practice for assessing neurological stroke biomarkers. In the present study, we examined the utility of CT in combination with age and clinical severity, measured in our convalescent rehabilitation ward in Japan, for predicting functional outcome. To avoid confounders related to different types of stroke and lesion sites, we focused on patients with putaminal hemorrhage.

PARTICPANTS AND METHODS

We included patients admitted into our convalescent rehabilitation ward in Rakusai Shimizu Hospital between April 2016 and May 2019. The study protocol was approved by the Hyogo College of Medicine Ethics Committee (No. 3522). Patient consent was obtained by the opt-out method. Patients were typically transferred to our convalescent rehabilitation ward from local community acute care hospitals where they were diagnosed with a stroke. During acute care, patients were managed conservatively with anti-hypertensives and, when necessary, surgical evacuation of hematoma. In line with Japanese health insurance procedures, patients were referred from acute care hospitals to our convalescent rehabilitation facility within 60 days after stroke, where they subsequently received in-patient rehabilitation. During hospitalization, patients received physical, occupational, and speech therapy for up to 180 min (combined daily total) in accordance with the Japanese Guidelines for the Management of Stroke standard recommendations[17].

To minimize variability related to different types of stroke and lesion sites, we limited our analytical database inclusion criteria to patients with putaminal hemorrhage. To avoid confounders related to variability of pre-stroke functional status, we also limited inclusion criteria to first-ever stroke patients who could walk unaided and who had been functionally independent in their activities of daily living. To minimize potential confounders related to surgical invasiveness, we excluded patients who underwent surgery. Patients who required subsequently acute medical services (e.g., for recurrence of stroke, angina pectoris, or other coincidental condition) were also excluded.

On arrival at an acute care hospital, the patients in the study population underwent head CT scanning. The volume of the intracerebral hemorrhage was estimated via a conventional method, as follows[13, 14]. First, the CT slice that contained the largest area of hemorrhage was identified and the largest hemorrhage diameter was measured (value A; in cm). Next, the largest hemorrhage diameter perpendicular to A was measured (value B; in cm). Finally, the height of the hemorrhage was measured (value C; in cm). The hemorrhage volume (in mL) was estimated using following equation: $(A \times B \times C)/2$[18].

For outcome assessment, we used the Functional Independence Measure (FIM), a common tool in stroke rehabilitation[19]. FIM comprises motor and cognition components. In the present study, we focused on the motor component (FIM-motor), which comprises 13 items: eating, grooming, bathing, dressing the upper body, dressing the lower body, toileting, bladder control, bowel control, transfer to bed, chair, or wheelchair, transfer to toilet, transfer to tub or shower, walking or wheelchair propulsion, and stair climbing. Each item is scored on a seven-point scale (1=total assistance; 7=complete independence) and the sum of FIM-motor (scale range, 13–91) is used to evaluate functional independence in activities in daily living for stroke rehabilitation. FIM scores were assessed at admission to our convalescent rehabilitation ward, then monthly and finally at discharge. Patients were typically discharged from our facility when the growth of the FIM-motor score plateaued over a 1-month period. The total length of hospital stay (LOS) was recorded for each patient[20].

Multivariate regression was used for all analyses. The target values were FIM-motor at discharge and LOS. For both target values we performed two types of multivariate regression analyses. For two-factor modeling, two factors determined at onset (age and hemorrhage volume assessed by CT) were used as explanatory variables. For four-factor modeling, days after onset and FIM-motor scores at admission (assessed when patients were transfer to our convalescent rehabilitation ward) were also added as explanatory variables. The rationale for use of these additional explanatory variables was previously described[21, 22]. The multicollinearity relationships between the four explanatory variables were examined using a Spearman's correlation test for all possible pairs. All statistical analyses were performed using statistical software (JMP software package; SAS Institute, Cary, NC, USA). A p-value ≤0.05 was considered statistically significant.

RESULTS

A total of 67 patients were initially included in this study. Of these, 13 patients received surgical removal of the hematoma and two patients required acute medical services during hospitalization. Based on our inclusion criteria, these 15 patients were excluded from the final analytical database. Thus, 52 patients were entered into the final study. The demographics of the patients are shown in Table 1. There were 33 male and 19 female cases, with 19 having right hemisphere lesions and 33 having left hemisphere lesions.

The results of two-factor modeling and multivariate regressions for FIM-motor at discharge and LOS are shown in Table 2.

J. Phys. Ther. Sci. Vol. 33, No. 1, 2021

28

The estimated *f*-values for the explanatory values indicated that both age and hemorrhage volume assessed by CT were equally powerful predictors of FIM-motor at discharge. Conversely, only hemorrhage volume was significantly associated with LOS.

The results of four-factor modeling and multivariate regressions for FIM-motor at discharge and LOS are shown in Table 3. Age, days from onset, and FIM-motor at admission were significantly associated with FIM-motor at discharge. By contrast, only age and FIM-motor at admission were significantly associated with LOS. Hematoma volume assessed by CT was not significant for FIM-motor at discharge or LOS in the four-factor models.

The results obtained from correlation analyses between the explanatory variables are shown in Table 4. The hemorrhage

Table 1. Patients' demographics

Age (years)	64.5 ± 13.0
Lesion hemisphere (right/left)	19/33
Gender (males/females)	33/19
Volume of hemorrhage (mL)	25.4 ± 21.7
Days from onset	22.8 ± 9.0
FIM-motor score at admission	38.3 ± 19.6
FIM-motor score at discharge	71.3 ± 19.7
LOS (days)	128.9 ± 49.2

FIM-motor: motor component of the Functional Independence Measure; LOS: length of hospital stay.
Data are presented as mean ± standard deviation unless otherwise stated.

Table 2. Two-factor multivariate regression analyses

	FIM-motor at discharge				LOS			
	Estimate	SE	*f*-value	p-value	Estimate	SE	*f*-value	p-value
Age	−0.956	0.161	35.240	<0.001	−0.112	0.467	0.057	0.813
Volume of hemorrhage	−0.416	0.096	18.670	<0.001	1.209	0.279	18.754	<0.001
Intercept	143.478	11.355	-	<0.001	105.317	35.934	-	0.002
Adjusted r^2	0.456	-	-	<0.001	0.264	-	-	<0.001

FIM-motor: motor component of the Functional Independence Measure; LOS: length of hospital stay; SE: standard error.

Table 3. Four-factor multivariate regression analyses

	FIM-motor at discharge				LOS			
	Estimate	SE	*f*-value	p-value	Estimate	SE	*f*-value	p-value
Age	−0.596	0.124	22.979	<0.001	−0.895	0.431	4.318	0.043
Volume of hemorrhage	−0.026	0.089	0.092	0.763	0.392	0.306	1.640	0.207
FIM-motor at admission	0.418	0.066	39.917	<0.001	−1.023	0.229	19.985	<0.001
Day from onset	−0.580	0.185	9.816	0.003	0.778	0.641	1.478	0.230
Intercept	99.512	11.223	-	<0.001	218.028	38.877	-	<0.001
Adjusted r^2	0.728	-	-	<0.001	0.476	-	-	<0.001

FIM-motor: motor component of the Functional Independence Measure; LOS: length of hospital stay; SE: standard error.

Table 4. Correlations between explanatory variables

	Age	Volume of hemorrhage	FIM-motor at admission
Age	-	-	-
Volume of hemorrhage assessed by CT	−0.276 (p=0.046)	-	-
FIM-motor at admission	−0.154 (p=0.277)	−0.474 (p<0.001)	-
Day from onset	0.098 (p=0.490)	0.273 (p=0.050)	−0.276 (p=0.048)

FIM-motor: motor component of the Functional Independence Measure; LOS: length of hospital stay; SE: standard error.

volume was significantly correlated with FIM-motor at admission, days from onset, and age, indicating that there were multiple collinearities between these factors.

DISCUSSION

To evaluate the utility of CT during acute care for outcome prediction in stroke patients, we examined the association between long-term outcome and hemorrhage volume assessed by CT in combination with established predictive factors including age and clinical severity assessed by FIM-motor. Data for age and hemorrhage volume were collected at stroke onset. Analysis using these two factors revealed that hemorrhage volume significantly contributed to final outcome assessed by FIM-motor and LOS. However, hemorrhage volume was not significant when days from onset and FIM-motor at admission into a long-term rehabilitative facility were added into the analysis. Finally, correlation analyses revealed that hemorrhage volumes were significantly correlated with days from onset and FIM-motor at admission, suggesting that multiple collinearities diminished the predictive power of hemorrhage volume when the patients were transferred to long-term rehabilitative settings.

CT is a conventional imaging technique used worldwide for diagnosis of stroke. It is less expensive and more convenient than modern biomarkers such as magnetic resonance imaging or TMS. However, previous studies suggest that CT can only be applied for prediction of mortality but not functional outcome[13–16]. Nevertheless, although we limited inclusion to patients with putaminal hemorrhage, our data indicate that CT obtained at stroke onset may provide predictive value for functional outcome.

Parameter estimates from multivariate regression analysis for functional outcome (four-factor models; Table 3) indicated that CT data did not contribute to outcome prediction when patients were transferred to long-term rehabilitative settings. However, the hemorrhage volume assessed by CT correlated with clinical severity assessed by FIM-motor at admission and days from onset (Table 4); this is expected given the relationship between pathology and clinical manifestation of the disease. Thus, these correlations undermine the relative importance of hemorrhage volume assessed by CT when patients were transferred to a convalescent rehabilitation ward.

Our findings suggest that CT data may be useful for outcome prediction for a certain type of stroke. In our preliminary stages of data collection and analyses, we included a broader range of hemorrhagic strokes including thalamic hemorrhage. However, although the severity of clinical symptoms were similar between thalamic cases and putaminal cases, the hemorrhage volumes tended to be smaller for the thalamic cases[23]. Thus, we limited our study to patients with putaminal hemorrhage.

CT is a diagnostic tool used mainly in acute care hospitals where early and accurate prediction of stroke patients is required. Although the relative contribution was lower than for the four-factor models (Table 3), the two-factor models comprising age and CT data (Table 2) may be useful for predicting long-term outcome. Further, because clinical severity during acute care is another important outcome determinant, the addition of the severity of stroke symptoms in the acute stage may improve outcome prediction. Indeed, for ischemic stroke cases, we reported that scores of National Institute of Health Stroke Scale during the acute phase can predict the relative independence of FIM-motor items[24]. This study was conducted in a convalescent rehabilitation ward. However, we could not collect systematic data on clinical severity scores during the acute phase. Further studies are needed to clarify this issue.

This study has several limitations. First, the outcome measurements were limited as we only sampled FIM-motor score and LOS data. Patients with stroke exhibit a variety of symptoms including dysphagia, hemiparesis, and higher brain dysfunction. Thus, we may have overlooked some important parameters related to functional outcomes. Second, we omitted the analysis for confirmation of the model derived from multiple regression analysis[25]. Using our strict inclusion criteria over a 37-month study period, only 52 samples were entered into the final analytical database. The aim of this study was to assess the potential utility of conventional CT data for outcome prediction. Because of the small number of participants, we only focused on model development. Future studies are required to assess the applicability of the derived model using a larger number of patients. Third, we limited our inclusion criteria to patients who were functionally independent before stroke, which may have contributed to the relatively good recovery in our cohort[26]. Thus, care should be taken when applying our findings to the more generalized population. Nevertheless, our data suggest the potential utility of conventional CT in combination with established parameters such as age for outcome prediction in stroke patients. Thus, conventional CT can be used for outcome prediction for some types of strokes.

Conflict of interest
The authors declare that there are no conflicts of interest.

REFERENCES

1) Veerbeek JM, Kwakkel G, van Wegen EE, et al.: Early prediction of outcome of activities of daily living after stroke: a systematic review. Stroke, 2011, 42: 1482–1488. [Medline] [CrossRef]

J. Phys. Ther. Sci. Vol. 33, No. 1, 2021

30

2) Counsell C, Dennis M, McDowall M, et al.: Predicting outcome after acute and subacute stroke: development and validation of new prognostic models. Stroke, 2002, 33: 1041–1047. [Medline] [CrossRef]

3) Harvey RL: Predictors of functional outcome following stroke. Phys Med Rehabil Clin N Am, 2015, 26: 583–598. [Medline] [CrossRef]

4) Duarte E, Marco E, Muniesa JM, et al.: Early detection of non-ambulatory survivors six months after stroke. NeuroRehabilitation, 2010, 26: 317–323. [Medline] [CrossRef]

5) Kwakkel G, Kollen BJ: Predicting activities after stroke: what is clinically relevant? Int J Stroke, 2013, 8: 25–32. [Medline] [CrossRef]

6) Boyd LA, Hayward KS, Ward NS, et al.: Biomarkers of stroke recovery: consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. Int J Stroke, 2017, 12: 480–493. [Medline] [CrossRef]

7) Stinear CM: Prediction of motor recovery after stroke: advances in biomarkers. Lancet Neurol, 2017, 16: 826–836. [Medline] [CrossRef]

8) Connell LA, Smith MC, Byblow WD, et al.: Implementing biomarkers to predict motor recovery after stroke. NeuroRehabilitation, 2018, 43: 41–50. [Medline] [CrossRef]

9) Rossini PM, Burke D, Chen R, et al.: Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol, 2015, 126: 1071–1107. [Medline] [CrossRef]

10) Puig J, Blasco G, Schlaug G, et al.: Diffusion tensor imaging as a prognostic biomarker for motor recovery and rehabilitation after stroke. Neuroradiology, 2017, 59: 343–351. [Medline] [CrossRef]

11) Lin LY, Ramsey L, Metcalf NV, et al.: Stronger prediction of motor recovery and outcome post-stroke by cortico-spinal tract integrity than functional connectivity. PLoS One, 2018, 13: e0202504. [Medline] [CrossRef]

12) Koyama T, Uchiyama Y, Domen K: Comparison of fractional anisotropy from tract-based spatial statistics with and without lesion masking in patients with intracerebral hemorrhage: a technical note. J Stroke Cerebrovasc Dis, 2019, 28: 104376. [Medline] [CrossRef]

13) Broderick JP, Brott TG, Duldner JE, et al.: Volume of intracerebral hemorrhage. A powerful and easy-to-use predictor of 30-day mortality. Stroke, 1993, 24: 987–993. [Medline] [CrossRef]

14) Kothari RU, Brott T, Broderick JP, et al.: The ABCs of measuring intracerebral hemorrhage volumes. Stroke, 1996, 27: 1304–1305. [Medline] [CrossRef]

15) Reid JM, Gubitz GJ, Dai D, et al.: Predicting functional outcome after stroke by modelling baseline clinical and CT variables. Age Ageing, 2010, 39: 360–366. [Medline] [CrossRef]

16) Kim B, Winstein C: Can neurological biomarkers of brain impairment be used to predict poststroke motor recovery? A systematic review. Neurorehabil Neural Repair, 2017, 31: 3–24. [Medline] [CrossRef]

17) Shinohara Y, Yanagihara T, Abe K, et al.: VII. Rehabilitation. J Stroke Cerebrovasc Dis, 2011, 20: S145–S180. [Medline] [CrossRef]

18) Koyama T, Tsuji M, Miyake H, et al.: Motor outcome for patients with acute intracerebral hemorrhage predicted using diffusion tensor imaging: an application of ordinal logistic modeling. J Stroke Cerebrovasc Dis, 2012, 21: 704–711. [Medline] [CrossRef]

19) Heinemann AW, Linacre JM, Wright BD, et al.: Relationships between impairment and physical disability as measured by the functional independence measure. Arch Phys Med Rehabil, 1993, 74: 566–573. [Medline] [CrossRef]

20) Koyama T, Uchiyama Y, Domen K: Associations of diffusion-tensor fractional anisotropy and FIM outcome assessments after intracerebral hemorrhage. J Stroke Cerebrovasc Dis, 2018, 27: 2869–2876. [Medline] [CrossRef]

21) Liu M, Domen K, Chino N: Comorbidity measures for stroke outcome research: a preliminary study. Arch Phys Med Rehabil, 1997, 78: 166–172. [Medline] [CrossRef]

22) Inouye M: Predicting outcomes of patients in Japan after first acute stroke using a simple model. Am J Phys Med Rehabil, 2001, 80: 645–649. [Medline] [CrossRef]

23) Koyama T, Tsuji M, Nishimura H, et al.: Diffusion tensor imaging for intracerebral hemorrhage outcome prediction: comparison using data from the corona radiata/internal capsule and the cerebral peduncle. J Stroke Cerebrovasc Dis, 2013, 22: 72–79. [Medline] [CrossRef]

24) Saito J, Koyama T, Domen K: Long-term outcomes of FIM motor items predicted from acute stage NIHSS of patients with middle cerebral artery infarct. Ann Rehabil Med, 2018, 42: 670–681. [Medline] [CrossRef]

25) Koyama T, Uchiyama Y, Domen K: Outcome in stroke patients is associated with age and fractional anisotropy in the cerebral peduncles: a multivariate regression study. Prog Rehabil Med, 2020, 5: 20200006. [Medline] [CrossRef]

26) Koyama T, Marumoto K, Miyake H, et al.: Relationship between diffusion tensor fractional anisotropy and long-term motor outcome in patients with hemiparesis after middle cerebral artery infarction. J Stroke Cerebrovasc Dis, 2014, 23: 2397–2404. [Medline] [CrossRef]