Renal Replacement Therapy

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Functional prognosis following spontaneous intracerebral hemorrhage in patients on hemodialysis: a retrospective study of 100 consecutive cases

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Abstract

Background Recently, discussions have increasingly focused on "withdrawal from dialysis" among patients undergoing dialysis who experience severe brain dysfunction as post-stroke sequelae. In this context, the lack of understanding regarding functional prognosis after spontaneous intracerebral hemorrhage in patients undergoing hemodialysis becomes a particularly important issue. Therefore, we aimed to evaluate the functional prognosis of intracerebral hemorrhage in patients undergoing hemodialysis when life-saving was prioritized and dialysis was not withdrawn. Furthermore, we sought to identify factors influencing life and functional prognosis.

Methods We retrospectively analyzed data of 100 consecutive hemodialysis patients who experienced spontaneous intracerebral hemorrhage between 2012 and 2021. The in-hospital mortality rates and modified Rankin Scale (mRS) and Functional Independence Measure (FIM) scores at discharge and 90 days after onset were examined.

Results The mean age of the patients was 65.7 years, with 29% of them undergoing life-saving brain surgery. The mRS score at discharge was 0, 1, 2, 3, 4, 5, and 6 (indicating death) in 0, 1, 13, 9, 26, 20, and 31 cases, respectively. Among the 69 surviving patients, the median FIM score at discharge was 37 (19–81), with 14 patients having an FIM score of 18 (i.e., complete dependence). Patients who underwent life-saving brain surgery showed a higher median mRS score [5, interquartile range (IQR) 5–6] and a lower FIM score (18, IQR 18–22) at discharge compared with those who did not undergo the surgery. Patients discharged with mRS and FIM scores of 5 and 18, respectively, had the same functional status at 90 days. The Functional Outcome in Patients With Primary Intracerebral Hemorrhage (FUNC) score and intraventricular extension at admission were predictive of a mRS score ≥ 5 (area under the receiver operating characteristic curve = 0.92, $p < 0.0001$) and FIM score at discharge (adjusted $R^2 = 0.3$, $p = 0.0003$).

Conclusion In our single-center study, more than 14% of patients on hemodialysis with cerebral hemorrhage incurred severe, irreversible neurological and functional impairments, necessitating discussions on hemodialysis withdrawal. Moreover, FUNC score and intraventricular extension at admission were highly accurate predictors of functional prognosis.

Keywords Cerebral hemorrhage, End-stage kidney disease, Hemodialysis, Functional prognosis, Withdrawal from dialysis

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Background

Patients with end-stage kidney disease (ESKD) have higher morbidity rates associated with spontaneous intracerebral hemorrhage (ICH). In particular, up to 1.0% of patients undergoing chronic maintenance hemodialysis (HD) develop cerebral hemorrhage annually, which is several times more frequent than that noted in the general population [1–7]. Moreover, spontaneous ICH in patients undergoing HD is associated with a larger hematoma size and higher mortality rate than that in non-dialysis patients, with an overall mortality rate of 27–83% [6, 8]. Wakasugi et al. reported a standardized mortality ratio of 3.8 [95% confidence interval (CI), 3.6–4.1] for ICH in dialysis patients compared with that in the Japanese general population [9].

In recent years, there has been discussion regarding "withdrawal from dialysis" in patients undergoing dialysis who have developed severe brain dysfunction as post-stroke sequelae [10, 11]; however, the functional prognosis of post-spontaneous intracerebral hemorrhage in patients undergoing hemodialysis is not well understood. Therefore, this study aimed to evaluate the life and functional prognoses following spontaneous ICH in patients undergoing HD when life-saving was prioritized and dialysis was not withdrawn; moreover, it aimed to estimate the prognostic factors.

Methods

Study population

This retrospective cohort study was conducted at Saitama Medical University International Medical Center, an academic tertiary referral hospital in Saitama, Japan. A total of 100 consecutive cases of patients undergoing maintenance HD who were diagnosed with spontaneous ICH between 1 January 2012 and 31 December 2021 were identified through electronic medical records. Spontaneous ICH was diagnosed on the basis of neurological examination and head computed tomography findings. We excluded patients with traumatic intracranial hemorrhage and those with subarachnoid hemorrhage.

Ethical approval and consent

This study was conducted in accordance with the principles of the Declaration of Helsinki. Furthermore, this study was reviewed and approved by the Medical Ethical Review Board of Saitama Medical University International Medical Center (approval no.: 2021-021). The requirement for informed consent was waived owing to the retrospective nature of the study.

Data collection

The following clinical and demographic data were collected from individual medical records: age, sex, body weight, height, body mass index, dialysis vintage (length of time on dialysis), cause of ESKD, antithrombotic agent use, Glasgow Coma Scale (GCS) score at admission, bleeding location, presence or absence of intraventricular extension, estimated initial hematoma volume, and details of life-saving brain surgery (craniotomy for hematoma removal and external ventricular drainage). The hematoma volume was estimated as $A \times B \times C/2$, where A, B, and C are the maximum orthogonal diameters of the hematoma, respectively.

Both the ICH score [12] and Functional Outcome in Patients With Primary Intracerebral Hemorrhage (FUNC) score [13] were calculated to validate prognostic ability. The ICH score involves a simple 6-point clinical and radiographic grading scale devised to predict 30-day mortality after ICH. Briefly, the ICH score is determined by adding the score from each of the following components: (1) GCS score at presentation, (2) ICH volume on initial imaging, (3) intraventricular extension of ICH, (4) infratentorial origin of ICH, and (5) age. The ICH score results range from 0 to 6, with higher scores indicating a higher predicted mortality risk.

The FUNC score can help predict prognosis in terms of good functional (neurological) outcomes at 90 days using an 11-point scale. The score takes into account components such as age, ICH volume, ICH location, GCS score, and history of cognitive impairment. The FUNC score results range from 0 to 11, with 0 being the worst and 11 being the best.

Acute treatment

General acute treatment for spontaneous ICH was carried out in accordance with the 2009, 2015, and 2021 Japanese Guidelines for the Management of Stroke [5, 7, 14] as well as with the Guidelines for Management of Cardiovascular Diseases in Patients on Chronic Hemodialysis [6]. Early rehabilitation was performed to maximize functional recovery. During patients' stay at our hospital, life-saving treatment was given top priority, and aggressive treatment was administered; moreover, "withdrawal from dialysis" was not performed even when a poor neurological functional prognosis was predicted.

Indications for surgical treatment

Urgent surgical hematoma evacuation via conventional craniotomy was performed in patients with life-threatening mass effects from the supratentorial ICH. External ventricular drainage was performed as a treatment for acute obstructive hydrocephalus. The patients or their

families were informed about the high probability of serious functional disability if the surgery could save the patients' life.

Renal replacement therapy (RRT) protocol

RRT was performed during the acute phase of cerebral hemorrhage according to the following protocol: RRT was avoided within 24 h of onset, except for severe hyperkalemia (serum K ≥ 6.0 mEq/L) or pulmonary edema. Hemofiltration (HF) was performed during the acute phase of RRT, and replacement fluid (Sublood BSG, Fuso, Tokyo, Japan) for HF was delivered at 20 L/session. Continuous HF was performed in patients with marked hemodynamic instability. Nafamostat mesylate (20–30 mg/h) was used as the anticoagulant. After the acute phase, conventional regular HD was performed three times per week.

Study outcomes

In this study, we examined the following outcomes: in-hospital mortality, GCS score, modified Rankin Scale (mRS) score [15], and Functional Independence Measure (FIM) score at discharge [16]. The mRS, which is the most widely used outcome measure, evaluates functional independence on a 7-grade scale as follows: 0, no symptoms at all; 1, no significant disability despite symptoms; 2, slight disability; 3, moderate disability; 4, moderately severe disability; 5, severe disability; and 6, death. The FIM is an 18-item scale that measures a patient's level of disability, with each item being rated from 1 (requiring total assistance) to 7 (completely independent). The total FIM score ranges from 18 to 126, with 18 indicating complete dependence/total assistance and 126 representing complete independence. Furthermore, we evaluated the mRS and FIM scores at 90 days after onset in patients who were transferred to other facilities with a mRS score of 5 or FIM score of 18 at the time of discharge from our facility.

Statistical analyses

The baseline characteristics of the study participants were analyzed using descriptive statistics. Continuous variables are expressed as either mean ± standard deviation (SD) or as median [interquartile range (IQR)] and were compared using the unpaired *t*-test or Mann–Whitney *U*-test, respectively. Normality of the distribution was verified using the Shapiro–Wilk test. Categorical variables are expressed as percentages and were compared using the chi-squared test or Fisher's exact test. Logistic regression analysis was conducted to evaluate independent predictors of in-hospital mortality and mRS score ≥ 5 at discharge after simultaneous control for potential confounders; variables were selected on the basis of previous literature [12, 13], and factors were identified through univariate regression analysis. Notably, preceding antithrombotic use has been reported to be a poor prognostic factor for ICH [17, 18]. Therefore, we evaluated preceding antithrombotic use as a predictive factor. Multicollinearity was analyzed using Spearman's rank correlation coefficient to assess correlations between covariates. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive performance of the model, and the area under the ROC curve (AUC) was calculated to determine the cutoff value for prediction. Multiple regression analysis was conducted to evaluate the independent predictors of the FIM score at discharge after simultaneous control for potential confounders; the variables were selected on the basis of previous literature [13] and factors identified through univariate regression analysis. The ICH and FUNC scores had similar constructs and were highly correlated with each other. Therefore, we did not simultaneously enter both explanatory variables in the multivariate analysis to prevent multicollinearity. Statistical analyses were performed using JMP Pro version 16 (SAS Institute, Cary, NC, USA), with statistical significance set at $p < 0.05$ (two-sided).

Results

The clinical characteristics of patients are summarized in Table 1. The mean age of the patients was 65.7 years, and 48% of patients showed intraventricular extension. The median GCS score at admission was 13 (IQR 6–14), and the median initial ICH volume was 25 mL (IQR 7.8–64.7 mL). Infratentorial origin of ICH was observed in 19% of patients. The in-hospital mortality rate was 31%. Overall, 14% of patients opted to limit aggressive treatment upon admission due to their low chances of survival, whereas 29% of patients underwent life-saving brain surgery. The mRS score at discharge was 1 in 1 case, 2 in 13 cases, 3 in 9 cases, 4 in 26 cases, 5 in 20 cases, and 6 (i.e., dead) in 31 cases (Fig. 1). Figure 2 shows a histogram of the FIM score at discharge. Notably, 14 patients had a FIM score of 18, indicating complete dependence upon discharge. All patients with a FIM score of 18 also had a mRS score of 5. The mean (± SD) length of hospital stay was 15.4 (± 17.1) days (median 10 days, IQR 3–24 days).

Non-survivors (31 cases) showed a higher frequency of preceding antithrombotic use (59.3% versus 35.3%, $p = 0.03$), lower GCS score at admission (median [IQR]: 4 [3–8] versus 14 [11–15] $p < 0.0001$), higher rate of intraventricular extension (87.1% versus 30.4%, $p < 0.0001$), larger initial ICH volume (53.7 mL [27.8–124.5 mL] versus 15.8 mL [5.4–40.0 mL], $p = 0.0003$), and higher ICH

Table 1 Baseline characteristics of patients

	All patients, *n* = 100
Age, years (mean ± SD)	65.7 ± 11.0
Sex (M/F)	66/34
Body mass index, median (IQR) (kg/m^2)	20.6 (18.6–22.8)
Dialysis vintage, years, median (IQR)	7.8 (3.8–12.2)
Cause of ESKD (%)	DKD, 47; CGN, 19; HTN, 9; ADPKD, 6; others, 19
Preceding antithrombotic use (%)	40
GCS score on admission	13 (6–14)
ICH location (%)	Putamen, 35; thalamus, 27; subcortical, 19; cerebellum, 7; brainstem, 12
Infratentorial origin of ICH (%)	19
Intraventricular extension (%)	48
Initial ICH volume (mL)	25 (7.8–64.7)
ICH score	1 (1–3)
FUNC score	8 (5–10)

Continuous variables are presented as mean (SD) or as median (IQR: first to third quartiles), whereas categorical variables are expressed as numbers or percentages

ESKD end-stage kidney disease, *DKD* diabetic kidney disease, *CGN* chronic glomerulonephritis, *HTN* hypertensive nephrosclerosis, *ADPKD* autosomal dominant polycystic kidney disease, *GCS* Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage

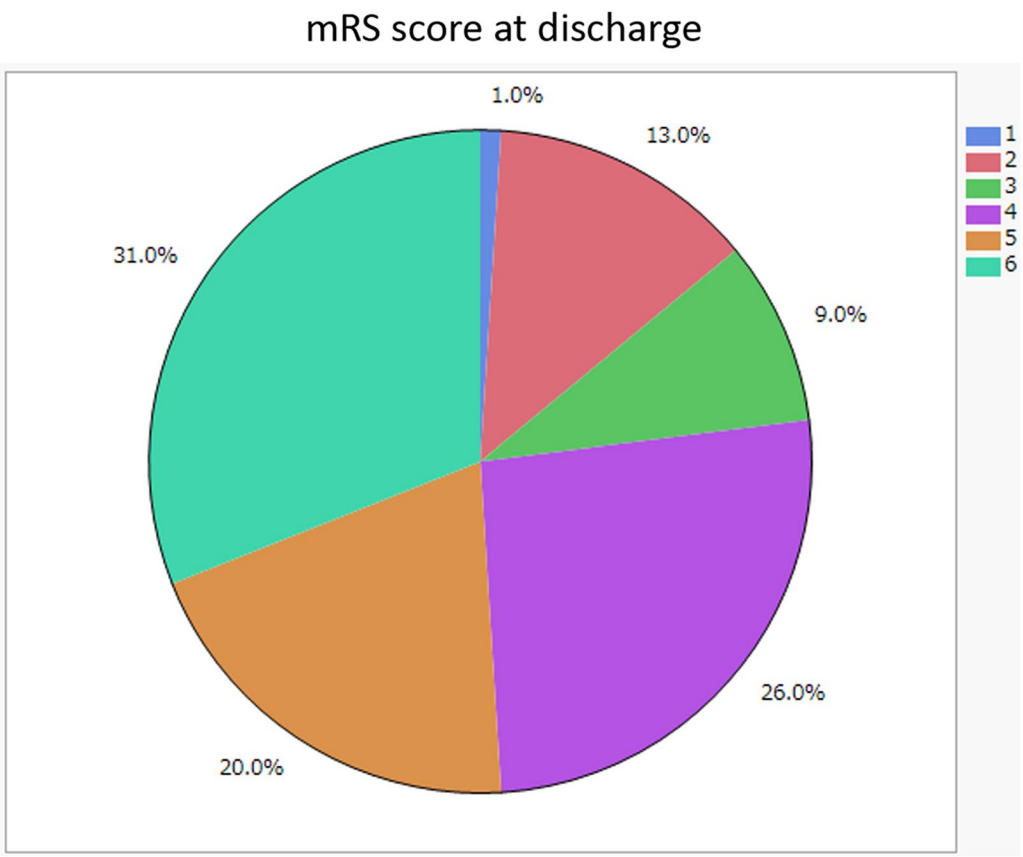

Fig. 1 mRS score at discharge. *mRS* modified Rankin Scale

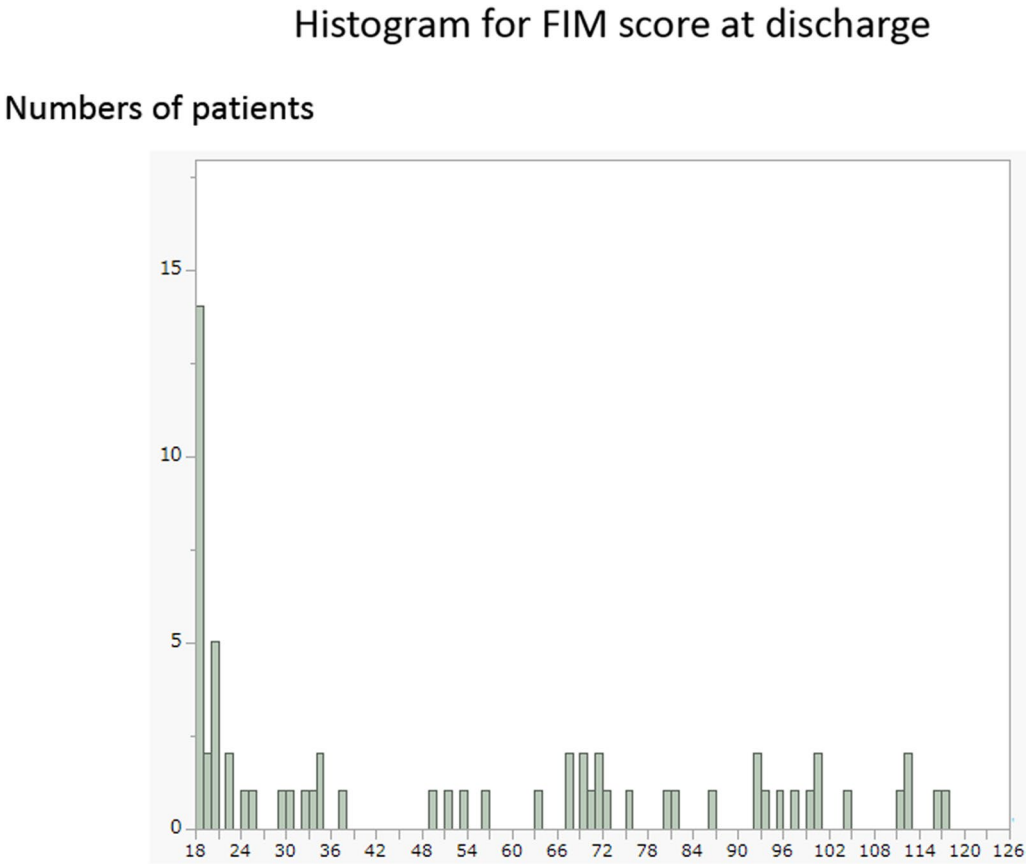

Fig. 2 Histogram for FIM score at discharge. *FIM* Functional Independence Measure

Table 2 Baseline characteristics of patients stratified by life prognosis

	Survivors (69 cases)	Non-survivors (31 cases)	*p*-Value
Age, years (mean ± SD)	66.0 ± 9.5	65.0 ± 13.9	0.7
Sex (M/F)	45/24	21/10	0.8
Dialysis vintage, years, median (IQR)	7.0 (3.7–12.0)	9.2 (3.4–18.3)	0.5
Cause of ESKD (%)	DKD, 47.8; CGN, 17.4; HTN, 8.7; ADPKD, 8.7; others, 17.4	DKD, 45.2; CGN, 22.6; HTN, 9.7; ADPKD, 0; others, 22.6	0.5
Preceding antithrombotic use (%)	35.3	59.3	0.03*
GCS score on admission	14 (11–15)	4 (3–8)	< 0.0001*
ICH location (%)	Putamen, 26; thalamus, 17; subcortical, 16; cerebellum, 6; brainstem, 4	Putamen, 9; thalamus, 10; subcortical, 3; cerebellum, 1; brainstem, 8	0.03*
Infratentorial origin of ICH (%)	14.5	29	0.09
Intraventricular extension (%)	30.4	87.1	< 0.0001*
Initial ICH volume (mL)	15.8 (5.4–40.0)	53.7 (27.8–124.5)	0.0003*
ICH score	1 (0–2)	4 (3–4)	< 0.0001*
FUNC score	9 (7–10)	5 (4–6)	< 0.0001*

ESKD end-stage kidney disease, *GCS* Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage, *IQR* interquartile range, SD, standard deviation

*A *p*-value of < 0.05 was considered statistically significant

score (4 [3, 4] versus 1 [0–2], $p < 0.0001$) than did survivors (69 cases) (Table 2).

Patients with a mRS score of ≥ 5 at discharge (51 cases) had a lower GCS score at admission (6 [3–13] versus 14 [13–15], $p < 0.0001$), higher rate of intraventricular extension (76.5% versus 18.4%, $p < 0.0001$), and larger initial ICH volume (54.5 mL [25.9–122.7 mL] versus 10.9 mL [4.1–20.8 mL], $p < 0.0001$) than did patients with a mRS score of ≤ 4 at discharge (49 cases) (Table 3).

Patients who underwent life-saving brain surgery had a lower GCS score at admission (6 [4–13] versus 14 [13–15], $p < 0.0001$), higher rate of intraventricular extension (82.8% versus 22.8%, $p < 0.0001$), and larger initial ICH volume (98.2 mL [53.6–144 mL] versus 11.0 mL [4.0–20.6 mL], $p < 0.0001$) than did patients who did not undergo surgical treatments. Additionally, patients who underwent life-saving brain surgery showed a lower survival rate and had a lower GCS score (median 10, IQR 8–12.8), higher mRS score (median 5.0, IQR 5.0–6.0), and lower FIM score (median 18, IQR 18–22) at discharge (Table 4) than did patients who did not undergo surgery. In 29 patients who underwent life-saving brain surgery, the mRS score at discharge was 4 in 4 cases, 5 in 14 cases, and 6 (i.e., dead) in 11 cases.

Multivariate logistic regression analysis with clinical indicators at admission showed that ICH score [odds ratio (OR) 4.2, 95% CI 2.4–7.5] and preceding antithrombotic use (OR 5.6, 95% CI 1.4–22.6) were significantly associated with in-hospital mortality. The ROC AUC for the prediction equation, incorporating both the ICH score and preceding antithrombotic use, was 0.91 for in-hospital mortality. In contrast, the ROC AUC of the prediction equation using only the ICH score for in-hospital mortality was 0.9. The cutoff value of the ICH score for predicting in-hospital mortality was 2.

Similarly, we searched for factors associated with mRS score ≥ 5 at discharge and assessed the association of FUNC score, presence of intraventricular extension, and preceding antithrombotic use with mRS score ≥ 5 at discharge. Table 5 presents the ORs and 95% CIs from the multivariate logistic regression analysis. The FUNC score (OR 0.5, 95% CI 0.3–0.7) and presence of intraventricular extension (OR 7.9, 95% CI 2.3–26.8) were significantly associated with mRS score ≥ 5 at discharge. The ROC AUC of the prediction equation was 0.92 using the FUNC score and the presence of intraventricular extension and 0.89 using the FUNC score alone (Fig. 3A, B). The cutoff value of the FUNC score for predicting a mRS score of ≥ 5 was 8.

Furthermore, we searched for clinical indicators correlated with the FIM score at discharge. As a result, we found that the FUNC score showed the strongest correlation. Multiple regression analysis (standard least squares) was performed to search for clinical indicators at admission that could influence the FIM score at discharge, and the FUNC score and presence of intraventricular extension were selected (Table 6). The standardized partial regression coefficients for the FUNC score and intraventricular extension were 0.4 ($p = 0.002$) and 0.3 ($p = 0.03$), respectively.

When we monitored the functional prognosis at 90 days after onset for patients with a mRS score of 5 and FIM score of 18 at discharge from our facility, we observed two distinct outcomes: they either died (4

Table 3 Baseline characteristics of patients stratified by the mRS score at discharge

	mRS score ≤ 4 at discharge (49 cases)	mRS score ≥ 5 at discharge (51 cases)	*p*-Value
Age, years (mean ± SD)	65.1 ± 9.5	66.3 ± 12.3	0.6
Sex (M/F)	32/17	34/17	0.9
Dialysis vintage, years, median (IQR)	7.8 (3.5–11.8)	7.5 (3.9–13.4)	0.8
Cause of ESKD (%)	DKD, 22; CGN, 7; HTN, 5; ADPKD, 5; others, 10	DKD, 25; CGN, 12; HTN, 4; ADPKD, 1; others, 9	0.4
Preceding antithrombotic use (%)	42.9	41.3	0.9
GCS score on admission	14 (13–15)	6 (3–13)	< 0.0001*
ICH location (%)	Putamen, 17; thalamus, 12; subcortical, 11; cerebellum, 6; brainstem, 3	Putamen, 18; thalamus, 15; subcortical, 8; cerebellum, 1; brainstem, 9	0.1
Infratentorial origin of ICH (%)	18.4	19.6	0.9
Intraventricular extension (%)	18.4	76.5	< 0.0001*
Initial ICH volume (mL)	10.9 (4.1–20.8)	54.5 (25.9–122.7)	< 0.0001*
ICH score	1 (0–1)	3 (2–4)	< 0.0001*
FUNC score	10 (8–10)	6 (4–8)	< 0.0001*

ESKD end-stage kidney disease, *mRS* modified Rankin Scale, *GCS* Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage, *IQR* interquartile range, *SD* standard deviation

*A *p*-value of < 0.05 was considered statistically significant (comparison of mRS score ≤ 4 versus ≥ 5).

Table 4 Baseline characteristics of patients stratified by the presence of brain surgery and life and functional prognoses

	Cases of surgery (29 cases)	Cases of non-surgery (57 cases)	*p-Value*
Age, years (mean ± SD)	63.8 ± 11.3	66.7 ± 9.9	0.2
Sex (M/F)	21/8	36/21	0.4
Preceding antithrombotic use (%)	42.9	41.1	0.9
GCS score on admission	6 (4–13)	14 (13–15)	< 0.0001*
ICH location (%)	Putamen, 16; thalamus, 8; subcortical, 5; cerebellum, 0; brainstem, 0	Putamen, 17; thalamus, 16; subcortical, 12; cerebellum, 6; brainstem, 6	0.05
Infratentorial origin of ICH (%)	0	21.1	0.001*
Intraventricular extension (%)	82.8	22.8	< 0.0001*
Initial ICH volume (mL)	98.2 (53.6–144)	11.0 (4.0–20.6)	< 0.0001*
ICH score	3 (2–4)	1 (0–1)	< 0.0001*
FUNC score	5 (4–6)	9 (8–10)	< 0.0001*
Survival, cases (%)	18 (62.1)	51 (89.5)	0.003*
GCS score at discharge	10 (8–12.8)	14 (13.8–15)	< 0.0001*
mRS score at discharge	5 (5–6)	4 (2.5–4)	< 0.0001*
mRS score ≥ 5 at discharge (%)	86.2	21.1	< 0.0001*
FIM at discharge	18 (18–22)	67 (25–93)	< 0.0001*
Tracheostomy at discharge, cases (%)	8 (44.4)	1 (2)	< 0.0001*

Baseline characteristics of patients stratified by the presence or absence of brain surgery (comparison of surgical cases versus non-surgical cases) and life and functional prognoses (except for 14 cases wherein patients opted to limit aggressive treatments upon admission due to their low chances of survival)

mRS modified Rankin Scale, *GCS* Glasgow Coma Scale, *ICH* intracerebral hemorrhage, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage

*A *p*-value of < 0.05 was considered statistically significant

Table 5 Logistic regression analysis of clinical indicators that could affect mRS score ≥ 5 at discharge

Explanatory variable	Odds ratio	95% CI	*p-Value*
FUNC score	0.5	0.3–0.7	< 0.0001*
Intraventricular extension	7.9	2.3–26.8	0.0005*
Preceding antithrombotic use	1.7	0.5–5.9	0.42
($R^2 = 0.47$, $p < 0.0001$*)			

mRS modified Rankin Scale, *CI* confidence interval, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage

*R^2: coefficient of determination; a *p*-value of < 0.05 was considered statistically significant

cases) or remained admitted to a convalescent hospital with a mRS score of 5 or FIM score of 18.

Discussion

In this single-center observational study, we evaluated the life and functional prognoses following spontaneous ICH in patients on chronic maintenance HD. At discharge, 20% of patients had a mRS score of 5, and 14% of patients had a FIM score of 18, with no signs of improvement at 90 days after onset, indicating that > 14% of hemodialysis patients with cerebral hemorrhage had developed severe and irreversible neurological and functional impairments, prompting the need for discussions regarding withdrawal from hemodialysis. In particular, survivors who underwent life-saving surgical treatment exhibited poor functional outcomes at discharge. Additionally, the FUNC score and presence of intraventricular extension at admission proved to be predictors of functional prognosis with high accuracy.

According to previous reports on the general population, the main clinical determinants associated with life prognosis after ICH include increasing age and GCS score at admission, whereas the brain imaging determinants include ICH volume, presence of intraventricular extension, and ICH location [12, 19]. In our study, these factors were significantly different between survivors and non-survivors; furthermore, the ICH score, which could predict the prognosis using the above-mentioned factors, predicted short-term life prognosis with high accuracy, even in patients undergoing HD. Antithrombotic medications were associated with life prognosis. Patients undergoing HD received intravenous anticoagulation during HD performed three times per week to prevent circuit coagulation. Additionally, several patients took oral antithrombotic agents as treatment for cardiovascular diseases. As in previous reports [5, 7, 14], oral antithrombotic medication was a poor prognostic factor for spontaneous ICH in our study.

Similarly, in previous reports on the general population, the major determinants associated with reduced functional recovery after ICH include increasing age, baseline comorbidities, GCS score at admission, ICH

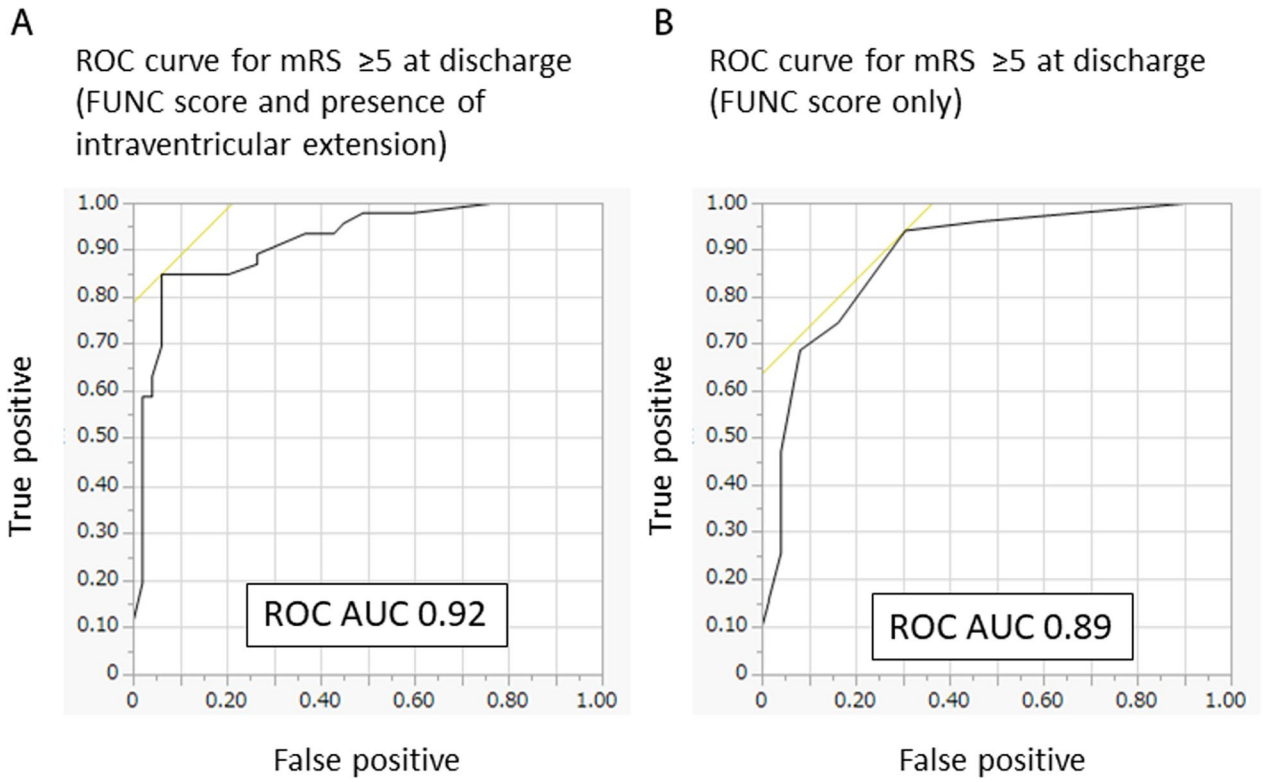

Fig. 3 ROC curves for mRS score ≥ 5 at discharge. **A** mRS score ≥ 5 at discharge constructed using both the FUNC score and the presence of intraventricular extension, and **B** mRS score ≥ 5 at discharge constructed using the FUNC score only. *AUC* area under the curve, *ROC* receiver operating characteristic

Table 6 Multiple regression analysis of clinical indicators that could affect the FIM score at discharge

Explanatory variable	SPRC	PRC (95% CI)	*SE*	*p-Value*
FUNC score	0.4	6.5 (2.6–10.4)	2	0.002*
Intraventricular extension	0.3	9.4 (0.8–18.1)	4.3	0.03*
Preceding antithrombotic use (Adjusted $R^2 = 0.3$, $p = 0.0003$*)	0.2	6.4 (−1.7 to 14.6)	4	0.1

CI confidence interval, *SPRC* standardized partial regression coefficient, *PRC* partial regression coefficient, *SE* standard error, *FUNC* Functional Outcome in Patients With Primary Intracerebral Hemorrhage

*A p-value of < 0.05 was considered statistically significant

volume, presence of intraventricular extension, and ICH location [20]. In our study, FUNC score, including these factors, was significantly associated with a mRS score ≥ 5 and FIM score at discharge. Hence, the results of the present study confirm that ICH and FUNC scores at admission can generally predict the life and functional prognoses of patients undergoing HD with spontaneous ICH.

Surgical treatment for cerebral hemorrhage remains controversial; nevertheless, surgical hematoma evacuation and ventricular drainage in patients with certain conditions can improve life prognoses [7, 21, 22]. At our facility, urgent surgical hematoma evacuation via conventional craniotomy is performed in patients with life-threatening mass effects from supratentorial ICH, whereas external ventricular drainage is conducted for acute hydrocephalus. With such aggressive life-saving surgical interventions and optimal dialysis management, the short-term life prognosis of our patients appears to be better than that previously reported [6, 8].

Currently, ethical issues regarding the treatment of dialysis patients with severe cerebrovascular disorders have arisen [23]. The Renal Physicians Association published the "Clinical Practice Guidelines on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis." This guideline recommends withholding or withdrawing ongoing dialysis in "patients with irreversible, profound neurological impairments such that they lack signs of thought, sensation, purposeful behavior, and awareness of self and environment." [10].

Subsequently, the JSDT published the "Proposal for the Shared Decision-Making Process Regarding Initiation and Continuation of Maintenance Hemodialysis"

[11], which had been recently updated. In this proposal, "Situations when review of forgoing hemodialysis is necessary" are listed. To quote, "When the patient's general condition becomes extremely poor, and the patient's wish regarding the forgoing of hemodialysis have been specifically expressed, or when the family can assume the patient's wish definitely." For instance, when patients experience severe brain dysfunction due to factors such as cerebrovascular diseases or head injuries, making it virtually impossible for them to comprehend crucial information regarding hemodialysis and long-term self-care, and when they reach a point where they can no longer eat or drink by themselves [11].

In terms of functional prognosis after cerebral hemorrhage, a mRS score of 5 or FIM score of 18 represents situations that necessitate a thorough review of whether hemodialysis should be continued. In our study, we observed that patients who survived after undergoing life-saving brain surgery often reached a state where the consideration of discontinuing dialysis was appropriate. The dilemma we faced revolved around deciding whether to pursue aggressive treatments, such as brain surgery, in cases where the functional prognosis was expected to be exceedingly poor, even if the patient were to survive.

Cerebral hemorrhage often occurs in relatively young dialysis patients who show independence in performing activities of daily living and are socially active until the onset of ICH [9]. Currently, advanced directives are not widely used by dialysis patients in Japan, and several of the patients' families often prefer life-saving treatments, even if they have understood that the predicted functional prognosis is poor. In such cases, it would be realistic to provide initial aggressive care, including surgery, for a certain period as a time-limited trial, followed by reevaluation of the patients' condition as well as a discussion with their families regarding the treatment plan. We think that the choice of treatment based on the prediction of functional prognosis using early clinical indicators after the onset of ICH is necessary, and we believe that this study will help in this regard.

This study has several limitations that need to be acknowledged. First, this was a single-center study, and our findings might not be applicable to other samples of patients with different risk profiles. Second, this study had a small sample size and might have been inadequately powered to detect statistically significant differences. Third, potential confounders, such as indications for surgery and subsequent management, were not standardized owing to the retrospective design. Fourth, we evaluated the functional prognosis at 90 days after onset for patients with a mRS score of 5 and FIM score of 18 at discharge; however, we were unable to track long-term functional outcomes beyond 90 days after onset. However, the highest rate of functional recovery after spontaneous ICH has been reported to occur in the first month [24]. Moreover, Yamashita et al. recently investigated the long-term life prognosis of hemodialysis patients with cerebral hemorrhage and reported that many of those discharged from acute care hospitals with a mRS score of 5 died early from aspiration pneumonia or sepsis [25].

Despite these limitations, the present study also has strengths, wherein the distribution of FIM scores in dialysis patients after the onset of a cerebral hemorrhage has been shown for the first time, and the associated predictors have been identified. We believe that the results of our study will provide important information for decision-making regarding treatment strategies.

Conclusions

In this single-center 100-patient study, more than 14% of patients on hemodialysis with cerebral hemorrhage had developed severe irreversible neurological and functional impairments, leading to a need for discussions regarding withdrawal from hemodialysis. Furthermore, FUNC score and intraventricular extension at admission proved to be predictors of functional prognosis with high accuracy.

Abbreviations

AUC	Area under the ROC curve
BP	Blood pressure
CI	Confidence interval
GCS	Glasgow Coma Scale
ESKD	End-stage kidney disease
ESO	European Stroke Organisation
FIM	Functional Independence Measure
FUNC	Functional Outcome in Patients with Primary Intracerebral Hemorrhage
HD	Hemodialysis
HF	Hemofiltration
ICH	Intracerebral hemorrhage
IQR	Interquartile range
mRS	Modified Rankin scale
OR	Odds ratios
ROC	Receiver operating characteristic
RRT	Renal replacement therapy
SD	Standard deviation

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Author contributions

Y.W. and H.O. contributed to the study concept and design, were involved in data analysis, and wrote the first draft of the manuscript. T.I., K.S., and H.K. conducted the data analysis and critically reviewed the manuscript. Y.W., T.I., K.S., H.K., and H.O. read and approved the final manuscript.

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Availability of data and materials
The data supporting the findings of this study are not publicly available because they contain information that could compromise the privacy of research participants. However, they are available from the corresponding author H.O. (email: hirookda@saitama-med.ac.jp) upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the principles embodied in the Declaration of Helsinki. Furthermore, this study was reviewed and approved by the Medical Ethical Review Board of Saitama Medical University International Medical Center (approval no.: 2021-021). The requirement for informed consent was waived owing to the retrospective nature of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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