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ARTICLE



## In spontaneous intracerebral hematoma patients, prediction of the hematoma expansion risk and mortality risk using radiological and clinical markers and a newly developed scale

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### ABSTRACT

**Objective:** In patients with spontaneous intracerebral hematoma (ICH), early-stage hematoma expansion has been associated with poor prognosis in literature. This study aimed to develop predictive parameter(s) as well as a new scale to define hematoma expansion and short-term prognosis in patients with ICH.

**Methods:** In 46 patients with ICH, Glasgow Coma Scale (GCS) scores, non-contrast CT (NCCT) markers (hematoma volume on admission and follow-up, hypodensity, intraventricular hemorrhage, blend and island sign, BAT score), and modified Rankin Scale scores were evaluated for predicting the hematoma expansion risk and mortality risk. Furthermore, a newly developed scale called the 'HEMRICH scale' was constituted using the GCS score, hematoma volumes, and some NCCT markers.

**Results:** *Roc-Curve* and *Logistic Regression* test results revealed that GCS score, initial hematoma volume value, hypodensity, intraventricular haemorrhage, BAT score, and HEMRICH scale score could be the best markers in predicting hematoma expansion risk whereas GCS score, intraventricular haemorrhage, BAT score, hematoma expansion, and HEMRICH scale score could be the best markers in predicting mortality risk ( $p = 0.01$ ). Moreover, *Factor analysis* and *Reliability* test results showed that HEMRICH scale score could predict both hematoma expansion and mortality risks validly (Kaiser-Meyer-Olkin test value = 0.729) and reliably (Cronbach's alpha = 0.564).

**Conclusion:** It was concluded that the GCS score, intraventricular haemorrhage, and BAT score could predict both hematoma expansion risk and mortality risk in the early stage in patients with ICH. Furthermore, it was suggested that the newly produced HEMRICH scale could be a valid and reliable scale for predicting both hematoma expansion and mortality risk.

### ARTICLE HISTORY

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### KEYWORDS

Spontaneous intracerebral hematoma; hematoma expansion; hypodensity; intraventricular haemorrhage; blend sign; island sign; bat score; mortality

## Introduction

Although the clinical course can change by the location and size of the spontaneous intracerebral hematoma (ICH) and consciousness of the patients, approximately 35–50% of the patients die within the first month [1,2]. Patients who survive one year later continue in their lives with serious neurological deficits [3]. Studies reported a strong relationship between the 30-day mortality rate and age, GCS score on admission, presence of bleeding into the ventricle, location, and size of the hematoma [4,5].

Today, most of the treatment strategies in ICH are focused on preventing secondary damage and preventing the increase in hematoma size. Besides this, in stroke patients with intracerebral hematoma, the hematoma enlargement in early-stage has been associated with poor prognosis, and therefore, many findings and scoring systems in literature have been proposed to predict the hematoma enlargement [6]. Among these, scoring systems based on radiological

findings such as BAT score, hypodensity, blend sign, and island sign on unenhanced brain-computed tomography images, and spot sign on computed tomography angiography images is available in the literature [2,6–8].

In literature, the non-contrast CT markers (NCCT) also have been investigated for predicting the hematoma expansion risk and mortality risk of the patients with spontaneous ICH not developed secondary to the stroke. Those studies reported that such markers can predict the hematoma expansion risk as well as mortality risk, and they argued that the NCCT markers can consistent as much as CT angiography markers. However, to easily and simply evaluate both the risk of hematoma growth and mortality risk, a few scales produced using these CT findings have been found in the literature [9,10].

This retrospective study was constructed with two aims as follows: The first aim was to evaluate the predictive properties of some parameters described in the literature before in predicting the possibility of

hematoma expansion and/or mortality risk in patients with spontaneous ICH. The second aim was to create a valid and reliable scale that can predict the hematoma expansion risk and mortality risk simply and easily in these patients using these mentioned parameters.

## Materials and methods

Approval for this single-centre, retrospective study was granted by the Local Clinical Research Ethics Committee (Approval number: 2020.04.06).

### Patients groups

Forty-six patients who were diagnosed with spontaneous ICH using NCCT images, and treated medically in neurology or neurosurgery clinics or their intensive care units between 2015 and 2020 were included in this study.

Patients whose ICH spread into the ventricle on admission to the hospital, patients who underwent emergency surgery before follow-up NCCT, patients who underwent surgery due to the spontaneous ICH while they stayed in the hospital, patients with hemorrhagic transformation due to ischemic stroke, patients whose had ICH due to either aneurysm, arteriovenous malformation, head trauma, cerebral aneurysm or brain tumour, and pediatric patients (<18-year-old) were excluded from the study.

Patients were divided into three groups according to hematoma location as follows:

- LOBAR group (patients with lobar located hematoma, n = 17),
- DEEP group (patients with deep-seated hematoma, n = 23)
- CEREBELLUM group (patients with posterior fossa located hematoma, n = 6)

In addition, they were divided into two groups according to whether hematoma volume increased or not as follows:

- Patients without hematoma expansion (consisted of the patients whose last measured hematoma volume did not increase more than 3 mm<sup>3</sup> from the initial hematoma volume, n = 18)
- Patients with hematoma expansion (consisted of the patients whose last measured hematoma volume increased more than 3 mm<sup>3</sup> from the initial hematoma volume, n = 28)

In addition, patients were grouped according to mortality rate as follows:

- SURVIVED group (patients discharged from hospital, n = 25)
- NON-SURVIVED group (patients who deceased in hospital, n = 21)

Patients were also divided into two groups according to gender and their findings were analyzed.

### Materials

Patients' data included age, gender, Glasgow Coma Scale (GCS) scores, systolic blood pressures (SBF) and diastolic blood pressure (DBP) values determined on admission to hospital, 'time from onset to brain NCCT scan', 'hematoma volume measured in the initial NCCT images (called "initial hematoma volume")', 'hematoma volume measured in last NCCT images during the stay in hospital (called "last hematoma volume")', 'the presence of hematoma spread into the ventricle during the stay in hospital (called intraventricular haemorrhage)', 'NCCT related markers (called 'hypodensity', 'blend sign', 'island sign' (Figure 1)), 'BAT score', previously used drugs (acetylsalicylic acid/warfarin), presence of the comorbidity (essential hypertension (HT), diabetes mellitus (DM)), blood biochemistry findings on admission to hospital, and modified Rankin Scale (mRS) scores were evaluated.

The scales and scores used in this study were described below:



**Figure 1.** In non-contrast CT images of patients with spontaneous intracerebral hematoma, it can be seen the hypodensity (1A), island sign (1B), and blend sign (1C) findings.

- **Glasgow Coma Scale (GCS):** This scale was used to determine and simply describe the patient's level of consciousness and neurological level. The scale consists of three subareas (eye findings, speech content, motor response) and is evaluated over 15 points [11].
- **Modified Rankin's Scale (mRS):** This scale is composed of six sub-dimensions and is used to simply describe the neurological level and consciousness of the patients when they are discharged from the hospital [12].
- **Blend sign:** The hematoma blend sign has been defined as blending of relatively hypoattenuating area with adjacent hyperattenuating field within a hematoma; a well-defined margin between these two areas. Furthermore, the hematoma should have at least 18 Hounsfield unit difference between the 2 density regions and the relatively hypoattenuating area was not encapsulated by the hyperattenuating region. The hematoma has to meet the 4 criteria mentioned above to be defined as blend sign [7].
- **Island sign:** It has been described as  $\geq 3$  scattered small round or oval hematomas all separate from the main hematoma or  $\geq 4$  small hematomas some or all of which may connect with the main hematoma [8].
- **BAT score:** It can be obtained as following: 1 point for blend sign, 2 points for any hypodensity, and 2 points for time from onset to NCCT  $< 2.5$  hours (2).

### Scale development

First, the predictive forces of all study parameters were determined using *Spearman's rho Correlation* test, *ROC-Curve* test, *Logistic Regression* test, and *Odds ratio* test, and those parameters were selected to develop a scale. Then, those selected parameters were analyzed for their validity using the *Factor analysis* test. The validity test results demonstrated that scale could be constituted by the 'GCS score', 'initial hematoma volume', 'last hematoma volume', 'intraventricular haemorrhage', 'island sign', and 'BAT score'. Finally, this scale was called HEMRICH scale (Using the initials of the phrase '*Hematoma Expansion and Mortality Risk in Intracerebral Hematoma*'), and it was evaluated over 6 points. It was assumed that the higher the score, the high risk of hematoma expansion and the worse the prognosis of the patient (Table 1).

### Biochemical analysis

Blood biochemistry findings were obtained from the evaluation of the venous blood samples of the patients on admission to the hospital. Serum glucose (reference

**Table 1.** The table demonstrates the components of the HEMRICH scale developed in this study using the study variables.

| Prediction              | Variable                    | Cut-off value       | Scale Score | Patient's score |
|-------------------------|-----------------------------|---------------------|-------------|-----------------|
| Hematoma expansion risk | Initial hematoma volume     | $> 19 \text{ cm}^3$ | 1           |                 |
|                         | Last hematoma volume        | $> 44 \text{ cm}^3$ | 1           |                 |
|                         | Intraventricular hemorrhage | +                   | 1           |                 |
| Mortality risk          | GCS score                   | $< 10$              | 1           |                 |
|                         | Island sign                 | +                   | 1           |                 |
|                         | BAT score                   | $> 1$               | 1           |                 |
| <b>TOTAL SCORE</b>      |                             |                     |             |                 |

range 74–109 mg/dL), C-reactive protein (CRP) (reference range 0.15–5 mg/dL) blood urea nitrogen (BUN) (reference range 17–43 mg/dL) and creatinine (reference range: 0.84–1.24 mg/dL) level values were measured using an analyzer device (Roche Diagnostic COBAS c501). The haemoglobin level (reference range 10–18 g/dL), leukocyte (reference range 4400–11,300/uL) and neutrophil (reference range 1,100–9600/uL) count values were determined using an analyzer device (Mindray BC-6800, Shenzhen, China).

### Statistical analysis

The categorical variables were analyzed using the *Pearson's chi-square* test ( $p < 0.05$ ). Non-parametric study findings were statistically analyzed using the *Kruskall Wallis* test ( $p < 0.05$ ). *Mann-Whitney U* test was used in paired group comparisons ( $p < 0.05$ ).

The parametric study findings were analyzed using the *Independent Samples t* test and *One Way Analysis of Variance (ANOVA)* test ( $p < 0.05$ ). In paired group comparisons, *Tukey Multiple Comparisons* test was used ( $p < 0.05$ ).

In addition, *Spearman's rho Correlation* test was used to determine the presence of correlation between parameters belonging to patients ( $p < 0.05$ ).

The *ROC-Curve* test was used to determine which study parameters predict the hematoma expansion and the mortality risk, and the sensitivity and specificity rates of the parameters were determined by obtaining 'cut-off' values. In addition, *Logistic Regression* test and *Likelihood Ratio* test were used to determine the 'best parameter' ( $p < 0.05$ ).

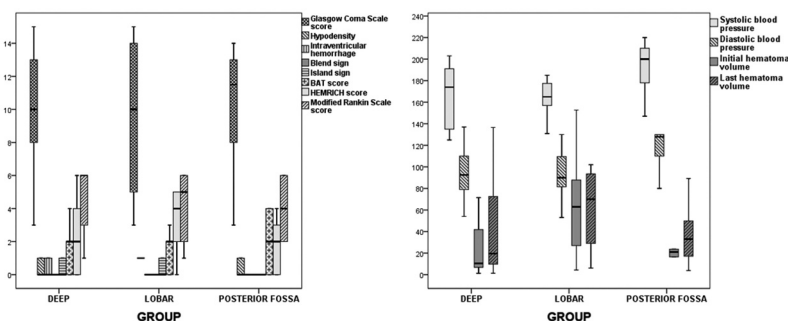
The direction and strength of the association between NCCT markers and hematoma expansion risk and mortality risk was quantified using *Odds Ratio* (OR) and their corresponding 95% confidence intervals (95%CI).

Finally, *Factor analysis* (i.e. *Principal Component Analysis*) test and *Reliability analysis* test was applied to evaluate the validity and reliability of the HEMRICH scale.

**Table 2.** Descriptive table shows the demographic, radiological and biochemical findings of the groups by location of spontaneous intracerebral hematoma. *One Way Analysis of Variance (ANOVA) test; Kruskal Wallis test; and Pearson's chi-square test, p < 0.05.*

| Variable                                   | LOCALIZATION OF HEMATOMA                 |  |  | F/X <sup>2</sup> | p            |              |
|--|--|--|--|------------------|--------------|--------------|
|  | DEEP                                     | LOBAR                                    | CEREBELLUM                               |                  |              |              |
|  | Mean ± SD/<br>Median (min-max)/<br>N (%) | Mean ± SD/<br>Median (min-max)/<br>N (%) | Mean ± SD/<br>Median (min-max)/<br>N (%) |                  |              |              |
| Age (year)                                 | 71.87 ± 16.84                            | 78.59 ± 8.89                             | 73.83 ± 13.29                            | 1.142*           | 0.329        |              |
| Gender                                     | Female                                   | 11 (23.9%)                               | 6 (13.0%)                                | 4 (8.7%)         | 1.847‡       | 0.397        |
|  | Male                                     | 12 (26.1%)                               | 11 (23.9%)                               | 2 (4.3%)         |              |              |
| Comorbidity                                | No                                       | 12 (26.1%)                               | 11 (23.9%)                               | 0 (0.0%)         | 7.514‡       | <b>0.023</b> |
|  | Yes                                      | 11 (23.9%)                               | 6 (13.0%)                                | 6 (13.0%)        |              |              |
| Medication                                 | No                                       | 21 (45.7%)                               | 14 (30.4%)                               | 2 (4.3%)         | 11.648‡      | <b>0.020</b> |
|  | ASA                                      | 2 (4.3%)                                 | 1 (2.2%)                                 | 2 (4.3%)         |              |              |
|  | Warfarin                                 | 0 (0.0%)                                 | 2 (4.3%)                                 | 2 (4.3%)         |              |              |
| GCS score                                  | 10 (3–15)                                | 10 (3–15)                                | 11.50 (3–14)                             | 0.112†           | 0.946        |              |
| SBP (mmHg)                                 | 166.43 ± 29.10                           | 167.18 ± 33.51                           | 191.00 ± 29.10                           | 1.292*           | 0.291        |              |
| DBP (mmHg)                                 | 93.29 ± 24.79                            | 96.91 ± 30.32                            | 115.60 ± 21.61                           | 1.325*           | 0.283        |              |
| Time from onset to NCCT scan (hour)        | 2 (1–2)                                  | 2 (2–2)                                  | 1 (1–2)                                  | 9.173†           | <b>0.010</b> |              |
| Initial hematoma volume (cm <sup>3</sup> ) | 16.80 (1.20–176)                         | 64 (4.30–305)                            | 18.75 (1.80–40)                          | 9.262†           | <b>0.010</b> |              |
| Follow-up CT time (hour)                   | 20 (2.50–240)                            | 20 (1–72)                                | 16 (2.50–47)                             | 0.590†           | 0.744        |              |
| Last hematoma volume (cm <sup>3</sup> )    | 36.10 (1.30–249.60)                      | 84.40 (6.05–347.70)                      | 25.05 (1.95–89.20)                       | 6.069†           | <b>0.048</b> |              |
| Hypodensity                                | No                                       | 12 (26.1%)                               | 4 (8.7%)                                 | 4 (8.7%)         | 4.773‡       | 0.092        |
|  | Yes                                      | 11 (23.9%)                               | 13 (28.3%)                               | 2 (4.3%)         |              |              |
| IV hemorrhage                              | No                                       | 13 (28.3%)                               | 14 (30.4%)                               | 6 (13.0%)        | 5.935‡       | 0.051        |
|  | Yes                                      | 10 (21.7%)                               | 3 (6.5%)                                 | 0 (0.0%)         |              |              |
| Blend sign                                 | No                                       | 23 (50.0%)                               | 15 (32.6%)                               | 6 (13.0%)        | 3.567‡       | 0.168        |
|  | Yes                                      | 0 (0.0%)                                 | 2 (4.3%)                                 | 0 (0.0%)         |              |              |
| Island sign                                | No                                       | 15 (32.6%)                               | 12 (26.1%)                               | 6 (13.0%)        | 2.857‡       | 0.240        |
|  | Yes                                      | 8 (17.4%)                                | 5 (10.9%)                                | 0 (0.0%)         |              |              |
| BAT Score                                  | 1  | 10 (21.7%)                               | 5 (10.9%)                                | 2 (4.3%)         | 9.464‡       | 0.149        |
|  | 2  | 9 (19.6%)                                | 10 (21.7%)                               | 2 (4.3%)         |              |              |
|  | 3  | 0 (0.0%)                                 | 2 (4.3%)                                 | 0 (0.0%)         |              |              |
|  | 4  | 4 (8.7%)                                 | 0 (0.0%)                                 | 2 (4.3%)         |              |              |
| Hematoma expansion                         | No                                       | 6 (13.0%)                                | 9 (19.6%)                                | 3 (6.5%)         | 0.403‡       | 0.818        |
|  | Yes                                      | 11 (23.9%)                               | 14 (30.4%)                               | 3 (6.5%)         |              |              |
| HEMRICH score                              | 3 (0–6)                                  | 4 (0–5)                                  | 2 (0–4)                                  | 2.088†           | 0.352        |              |
| Hemoglobin (g/dL)                          | 14.00 ± 2.26                             | 12.91 ± 2.37                             | 13.22 ± 1.05                             | 1.132*           | 0.333        |              |
| Leukocyte count (/uL)                      | 10,449 ± 3.69                            | 9984 ± 3.60                              | 11,600 ± 2.95                            | 0.430*           | 0.653        |              |
| Neutrophil count (/uL)                     | 7943 ± 3.68                              | 7892 ± 3.79                              | 7617 ± 2.69                              | 0.019*           | 0.981        |              |
| Glucose (mg/dL)                            | 161.63 ± 55.98                           | 140.74 ± 23.21                           | 164.75 ± 62.76                           | 0.923*           | 0.406        |              |
| C-reactive protein (mg/dL)                 | 15.30 (1–164)                            | 12.60 (0.180)                            | 7.05 (0.7–17)                            | 1.503†           | 0.472        |              |
| Blood urea nitrogen (mg/dL)                | 38.52 (20.50–106)                        | 46.98 (17.82–107)                        | 44.35 (28.50–57.20)                      | 1.405†           | 0.495        |              |
| Creatinine (mg/dL)                         | 0.90 (0.58–10.20)                        | 0.88 (0.52–1.50)                         | 1.30 (1.04–4.50)                         | 5.401†           | 0.067        |              |
| mRS  | 6 (0–6)                                  | 3 (0–6)                                  | 4 (2–6)                                  | 0.674†           | 0.714        |              |
| Mortality rate                             | Survived                                 | 11 (23.9%)                               | 11 (23.9%)                               | 3 (6.5%)         | 1.175‡       | 0.556        |
|  | Dead                                     | 6 (13.0%)                                | 12 (26.1%)                               | 3 (6.5%)         |              |              |

(\*) F value of the *One Way Analysis of Variance (ANOVA) test*; (†) X<sup>2</sup> value of the *Kruskal Wallis test*; (‡) X<sup>2</sup> value of the *Pearson's chi-square test* (SD: standart deviation, min: minimum, max: maximum, N: number of participants, F: F score, X<sup>2</sup>: Chi-Square value, IV: intraventricular, GCS: Glasgow Coma Scale, SBP: systolic blood pressure, DBP: diastolic blood pressure, ASA: acetylsalicylic acid, mRS: modified Rankin's Scale)



**Figure 2.** Each error bar shows the clinical and radiological findings of the groups by location of spontaneous intracerebral hematoma.



**Table 3.** Descriptive table demonstrates the demographic, radiological and biochemical findings of the groups with and without hematoma expansion. *Independent Samples t test; Mann Whitney U test; and Pearson's chi-square test, p < 0.05.*

| Variable                                   | HEMATOMA EXPANSION                       |  | t/Z/X <sup>2</sup> | p       |        |
|--|--|--|--------------------|---------|--------|
|  | No                                       | Yes                                      |                    |         |        |
|  | Mean ± SD/<br>Median (min-max)/<br>N (%) | Mean ± SD/<br>Median (min-max)/<br>N (%) |                    |         |        |
| Age (year)                                 | 73.39 ± 11.85                            | 75.39 ± 15.39                            | -0.469*            | 0.641   |        |
| Gender                                     | Female                                   | 7 (15.2%)                                | 14 (30.4%)         | 0.545‡  | 0.460  |
|  | Male                                     | 11 (23.9%)                               | 14 (30.4%)         |         |        |
| Comorbidity                                | No                                       | 7 (15.2%)                                | 16 (34.8%)         | 1.460‡  | 0.227  |
|  | Yes                                      | 11 (23.9%)                               | 12 (26.1%)         |         |        |
| Medication                                 | No                                       | 14 (30.4%)                               | 23 (50.0%)         | 1.276‡  | 0.528  |
|  | ASA                                      | 3 (6.5%)                                 | 2 (4.3%)           |         |        |
|  | Warfarin                                 | 1 (2.2%)                                 | 3 (6.5%)           |         |        |
| GCS score                                  | 13 (9–15)                                | 7.5 (3–15)                               | -4.204†            | <0.001  |        |
| SBP (mmHg)                                 | 166.77 ± 29.81                           | 173.88 ± 32.63                           | -0.614*            | 0.544   |        |
| DBP (mmHg)                                 | 94.31 ± 26.64                            | 101.41 ± 27.42                           | -0.712*            | 0.483   |        |
| Localization                               | Deep                                     | 9 (19.6%)                                | 14 (30.4%)         | 0.403‡  | 0.818  |
|  | Lobar                                    | 6 (13.0%)                                | 11 (23.9%)         |         |        |
|  | Cerebellum                               | 3 (6.5%)                                 | 3 (6.5%)           |         |        |
| Time from onset to NCCT scan (hour)        | 2 (1–2)                                  | 2 (1–2)                                  | -2.072†            | 0.038   |        |
| Initial hematoma volume (cm <sup>3</sup> ) | 13.65 (1.20–100.80)                      | 40.75 (1.70–305)                         | -2.375†            | 0.018   |        |
| Follow-up CT scan time (hour)              | 12 (1–160)                               | 24.50 (2.50–240)                         | -2.073†            | 0.038   |        |
| Last hematoma volume (cm <sup>3</sup> )    | 14.40 (1.30–102)                         | 78.45 (6.80–347.70)                      | -3.703†            | <0.001  |        |
| Hypodensity                                | No                                       | 12 (26.1%)                               | 8 (17.4%)          | 6.470‡  | 0.011  |
|  | Yes                                      | 6 (13.0%)                                | 20 (43.5%)         |         |        |
| IV hemorrhage                              | No                                       | 17 (37.0%)                               | 16 (34.8%)         | 7.519‡  | 0.006  |
|  | Yes                                      | 1 (2.2%)                                 | 12 (26.1%)         |         |        |
| Blend sign                                 | No                                       | 17 (37.0%)                               | 27 (58.7%)         | 0.104‡  | 0.747  |
|  | Yes                                      | 1 (2.2%)                                 | 1 (2.2%)           |         |        |
| Island sign                                | No                                       | 16 (34.8%)                               | 17 (37.0%)         | 4.290‡  | 0.038  |
|  | Yes                                      | 2 (4.3%)                                 | 11 (23.9%)         |         |        |
| BAT Score                                  | 1  | 12 (26.1%)                               | 5 (10.9%)          | 13.089‡ | 0.004  |
|  | 2  | 5 (10.9%)                                | 16 (34.8%)         |         |        |
|  | 3  | 1 (2.2%)                                 | 1 (2.2%)           |         |        |
|  | 4  | 0 (0.0%)                                 | 6 (13.0%)          |         |        |
| HEMRICH score                              | 0.5 (0–5)                                | 4 (0–6)                                  | -3.826†            | <0.001  |        |
| Hemoglobin (g/dL)                          | 14.21 ± 1.64                             | 13.03 ± 2.41                             | 1.748*             | 0.088   |        |
| Leukocyte count (/uL)                      | 11.51 ± 3.29                             | 9.71 ± 3.55                              | 1.642*             | 0.109   |        |
| Neutrophil count (/uL)                     | 8.81 ± 3.59                              | 7.22 ± 3.39                              | 1.454*             | 0.154   |        |
| Glucose (mg/dL)                            | 147.39 ± 44.73                           | 160.31 ± 51.09                           | -0.839*            | 0.406   |        |
| C-reactive protein (mg/dL)                 | 6 (0–80)                                 | 15 (0–164)                               | -1.059†            | 0.290   |        |
| Blood urea nitrogen (mg/dL)                | 39.80 (17.82–62.20)                      | 44.10 (24–107)                           | -1.059†            | 0.290   |        |
| Creatinine (mg/dL)                         | 0.88 (0.55–9.87)                         | 0.95 (0.52–10.20)                        | -0.344†            | 0.731   |        |
| mRS  | 2 (0–6)                                  | 6 (0–6)                                  | -4.663†            | <0.001  |        |
| Mortality                                  | No                                       | 17 (37%)                                 | 8 (17.4%)          | 19.162‡ | <0.001 |
|  | Yes                                      | 1 (2.2%)                                 | 20 (43.5%)         |         |        |

(\*) t value of the *Independent Samples t test*; (†) Z value of the *Mann Whitney U test*; (‡) X<sup>2</sup> value of the *Pearson's chi-square test*

(SD: standart deviation, min: minimum, max: maximum, N: number of participants, t: t score, Z: Z score, X<sup>2</sup>: Chi-Square value, IV: intraventricular, GCS: Glasgow Coma Scale, SBP: systolic blood pressure, DBP: diastolic blood pressure ASA: acetylsalicylic acid, mRS: modified Rankin's Scale)

## Results

When patients were divided into three groups according to the hematoma location, comorbidity (X<sup>2</sup> = 7.514, p = 0.023), anticoagulant/antiaggregan drug use (X<sup>2</sup> = 11.648, p = 0.020) and time from onset to NCCT scan (X<sup>2</sup> = 9.173, p = 0.010), the initial hematoma volume values (X<sup>2</sup> = 9.262, p = 0.010), and last hematoma volume values (X<sup>2</sup> = 6.069, p = 0.048) were found different among the groups (Table 2, Figure 2). It was observed that the time from onset to NCCT scan was different between LOBAR/DEEP groups (Z = -2.271, p = 0.023) and between LOBAR/CEREBELLUM groups (Z = -3.117, p = 0.002). Initial hematoma volume values were different between the LOBAR/DEEP groups (Z = -2.449, p = 0.014) and between the LOBAR/CEREBELLUM groups (Z = -2.801, p = 0.005). Last hematoma

volume values were different between LOBAR/CEREBELLUM groups (Z = -2.011, p = 0.044), and between DEEP/CEREBELLUM groups (Z = -2.66, p = 0.039).

When the patients were divided into two groups according to hematoma expansion, GCS score (Z = -4.204, p < 0.001), time from onset to NCCT scan (Z = -2.072, p = 0.038), initial hematoma volume value (Z = -2.375, p = 0.018), hypodensity (X<sup>2</sup> = 6.470, p = 0.011), intraventricular hemorrhage (X<sup>2</sup> = 7.519, p = 0.006), island sign (X<sup>2</sup> = 4.290, p = 0.038), BAT score (X<sup>2</sup> = 13.089, p = 0.004), last hematoma volume value (Z = -3.703, p < 0.001), HEMRICH score (Z = -3.826, p < 0.001), mRS score values (Z = -5.021, p < 0.001), and mortality rate (X<sup>2</sup> = 19.162, p < 0.001) were found different between these groups (Table 3, Figure 3).G

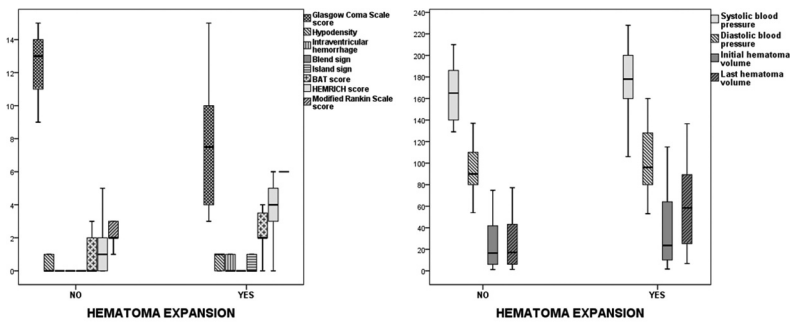


Figure 3. Each error bar shows the clinical and radiological findings of the patients with or without hematoma expansion.

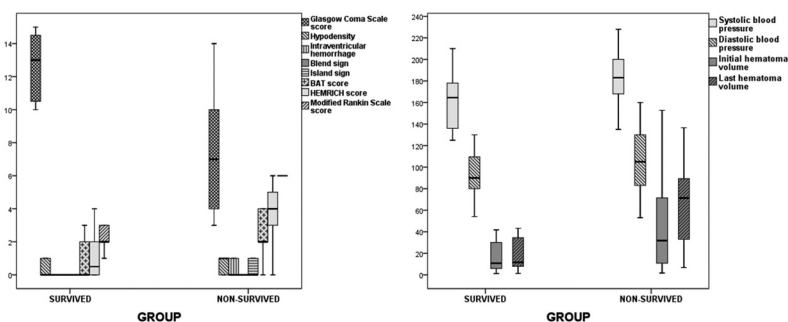
Table 4. Descriptive table reveals the demographic, radiological, and biochemical findings of the SURVIVED and NON-SURVIVED groups. Independent Samples t test; Mann Whitney U test; and Pearson’s chi-square test, p < 0.05.

| Variable                                   | SURVIVED                               |  | NON-SURVIVED                           |  | t/Z/X <sup>2</sup> | p |
|--|--|--|--|--|--------------------|---|
|  | Mean±SD/<br>Median (min-max)/<br>N (%) | Mean±SD/<br>Median (min-max)/<br>N (%) | Mean±SD/<br>Median (min-max)/<br>N (%) | Mean±SD/<br>Median (min-max)/<br>N (%) |                    |   |
| Age (year)                                 | 72.76 ± 15.92                          | 76.81 ± 11.31                          | -0.976*                                | 0.334                                  |                    |   |
| Gender                                     | Female                                 | 12 (26.1%)                             | 9 (19.6%)                              | 0.122‡                                 | 0.727              |   |
|  | Male                                   | 13 (28.3%)                             | 12 (26.1%)                             |  |                    |   |
| Comorbidity                                | No                                     | 15 (32.6%)                             | 8 (17.4%)                              | 2.190‡                                 | 0.139              |   |
|  | Yes                                    | 10 (21.7%)                             | 13 (28.3%)                             |  |                    |   |
| Medication                                 | No                                     | 21 (45.7%)                             | 16 (34.8%)                             | 1.539‡                                 | 0.463              |   |
|  | ASA                                    | 3 (6.5%)                               | 2 (4.3%)                               |  |                    |   |
|  | Warfarin                               | 1 (2.2%)                               | 3 (6.5%)                               |  |                    |   |
| GCS score                                  | 13 (4–15)                              | 7 (3–14)                               | -4.314†                                | <0.001                                 |                    |   |
| SBP (mmHg)                                 | 162.00 ± 28.44                         | 180.86 ± 31.97                         | -1.710*                                | 0.098                                  |                    |   |
| DBP (mmHg)                                 | 90.56 ± 21.83                          | 107.21 ± 30.01                         | -1.754*                                | 0.090                                  |                    |   |
| Localization                               | Deep                                   | 11 (23.9%)                             | 12 (26.1%)                             | 1.175‡                                 | 0.556              |   |
|  | Lobar                                  | 11 (23.9%)                             | 6 (13.0%)                              |  |                    |   |
|  | Cerebellum                             | 3 (6.5%)                               | 3 (6.5%)                               |  |                    |   |
| Time from onset to NCCT scan (hour)        | 2 (1–2)                                | 1 (1–2)                                | -3.278†                                | 0.001                                  |                    |   |
| Initial hematoma volume (cm <sup>3</sup> ) | 16.80 (1.20–202)                       | 41.50 (1.70–305)                       | -2.040†                                | 0.041                                  |                    |   |
| Follow-up CT time (hour)                   | 16 (1–160)                             | 24 (2.50–240)                          | -1.733†                                | 0.083                                  |                    |   |
| Last hematoma volume (cm <sup>3</sup> )    | 18 (1.30–240)                          | 76.90 (6.80–347.70)                    | -3.154†                                | 0.002                                  |                    |   |
| Hypodensity                                | No                                     | 14 (30.4%)                             | 6 (13.0%)                              | 3.494‡                                 | 0.062              |   |
|  | Yes                                    | 11 (23.9%)                             | 15 (32.6%)                             |  |                    |   |
| IV hemorrhage                              | No                                     | 22 (47.8%)                             | 11 (23.9%)                             | 7.142‡                                 | 0.008              |   |
|  | Yes                                    | 3 (6.5%)                               | 10 (21.7%)                             |  |                    |   |
| Blend sign                                 | No                                     | 24 (52.2%)                             | 20 (43.5%)                             | 0.016‡                                 | 0.900              |   |
|  | Yes                                    | 1 (2.2%)                               | 1 (2.2%)                               |  |                    |   |
| Island sign                                | No                                     | 19 (41.3%)                             | 14 (30.4%)                             | 0.490‡                                 | 0.484              |   |
|  | Yes                                    | 6 (13.0%)                              | 7 (15.2%)                              |  |                    |   |
| BAT Score                                  | 1                                      | 14 (30.4%)                             | 3 (6.5%)                               | 12.915‡                                | 0.005              |   |
|  | 2                                      | 10 (21.7%)                             | 11 (23.9%)                             |  |                    |   |
|  | 3                                      | 1 (2.2%)                               | 1 (2.2%)                               |  |                    |   |
|  | 4                                      | 0 (0.0%)                               | 6 (13.0%)                              |  |                    |   |
| Hematoma expansion                         | No                                     | 17 (37.0%)                             | 1 (2.2%)                               | 19.162‡                                | <0.001             |   |
|  | Yes                                    | 8 (17.4%)                              | 20 (43.5%)                             |  |                    |   |
| HEMRICH score                              | 1 (0–6)                                | 4 (0–6)                                | -3.715†                                | <0.001                                 |                    |   |
| Hemoglobin (g/dL)                          | 14.10 ± 1.80                           | 12.95 ± 2.41                           | 1.730*                                 | 0.092                                  |                    |   |
| Leukocyte count (/uL)                      | 11.08 ± 3.24                           | 9.87 ± 3.75                            | 1.107*                                 | 0.275                                  |                    |   |
| Neutrophil count (/uL)                     | 8.67 ± 3.66                            | 7.13 ± 3.29                            | 1.420*                                 | 0.164                                  |                    |   |
| Glucose (mg/dL)                            | 142.65 ± 42.84                         | 166.67 ± 51.45                         | -1.620*                                | 0.113                                  |                    |   |
| C-reactive protein (mg/dL)                 | 7.05 (0–80)                            | 13 (0.04–164)                          | -1.070†                                | 0.285                                  |                    |   |
| Blood urea nitrogen (mg/dL)                | 39.90 (17.82–62.20)                    | 45 (24–107)                            | -0.900†                                | 0.368                                  |                    |   |
| Creatinine (mg/dL)                         | 0.94 (0.52–9.87)                       | 0.95 (0.70–10.20)                      | -0.365†                                | 0.715                                  |                    |   |
| mRS  | 2 (1–5)                                | 6 (6–6)                                | -                                      | -                                      |                    |   |

(\*) t value of the Independent Samples t test; (†) Z value of the Mann Whitney U test; (‡) X<sup>2</sup> value of the Pearson’s chi square test (SD: standard deviation, min: minimum, max: maximum, N: number of participants, t: t score, Z: Z score, X<sup>2</sup>: Chi-Square value, IV: intraventricular, GCS: Glasgow Coma Scale, SBP: systolic blood pressure, DBP: diastolic blood pressure, ASA: acetylsalicylic acid, mRS: modified Rankin’s Scale)

When the patients were divided into two groups according to mortality rate, GCS score (Z = -4.314, p < 0.001), time from onset to NCCT scan (Z = -3.278, p = 0.001), initial hematoma volume value (Z = -2.040, p = 0.041), last hematoma volume value (Z = -3.154,

p = 0.002), intraventricular hemorrhage (X<sup>2</sup> = 7.142, p = 0.008), BAT score (X<sup>2</sup> = 12.915, p = 0.005), hematoma expansion (X<sup>2</sup> = 19.162, p < 0.001), and HEMRICH score values (Z = -3.715, p < 0.001) were found different between these groups (Table 4, Figure 4).



**Figure 4.** Each error bar shows the clinical and radiological findings of the SURVIVED and NON-SURVIVED groups.

When patients were divided into two groups according to gender, no statistical difference was found between the groups in terms of all variable values.

### Correlation analysis

The correlation analysis applied to the data of all patients revealed a positive correlation between the GCS scores and time from onset to NCCT scan ( $r = 0.415$ ,  $p = 0.018$ ) and a negative correlation between the GCS scores and initial hematoma volume values ( $r = -0.550$ ,  $p < 0.001$ ), last hematoma volume values ( $r = -0.621$ ,  $p < 0.001$ ), hypodensity ( $r = -0.511$ ,  $p = 0.001$ ), intraventricular hemorrhage ( $r = -0.484$ ,  $p = 0.001$ ), island sign ( $r = -0.427$ ,  $p = 0.005$ ), BAT score ( $r = -0.616$ ,  $p < 0.001$ ), hematoma expansion ( $r = -0.665$ ,  $p < 0.001$ ), mRS scores ( $r = -0.736$ ,  $p < 0.001$ ) and mortality rates ( $r = 0.682$ ,  $p < 0.001$ ).

A positive correlation was seen between the SBP values and hypodensity ( $r = 0.739$ ,  $p < 0.001$ ), intraventricular hemorrhage ( $r = 0.616$ ,  $p < 0.001$ ), island sign ( $r = 0.633$ ,  $p < 0.001$ ), BAT score ( $r = 0.777$ ,  $p < 0.001$ ), initial hematoma volume ( $r = 0.839$ ,  $p < 0.001$ ), last hematoma volume ( $r = 0.869$ ,  $p < 0.001$ ), hematoma expansion ( $r = 0.570$ ,  $p < 0.001$ ), mRS scores ( $r = 0.598$ ,  $p < 0.001$ ) and mortality rates ( $r = 0.554$ ,  $p < 0.001$ ). SBP values were negatively correlated with the NCCT scan ( $r = -0.423$ ,  $p = 0.011$ ), and GCS scores ( $r = -0.760$ ,  $p < 0.001$ ). DBP values were negatively correlated with the BAT scores ( $r = -0.380$ ,  $p = 0.039$ ),

A negative correlation was found between the time from onset to NCCT scan and hematoma expansion ( $r = -0.355$ ,  $p = 0.036$ ), mRS scores ( $r = -0.494$ ,  $p = 0.004$ ), and mortality rates ( $r = -0.562$ ,  $p < 0.001$ ). A positive correlation was found between the hematoma location and comorbidity ( $r = 0.338$ ,  $p = 0.022$ ), and a negative correlation was found between the hematoma location and

time from onset to NCCT scan ( $r = -0.519$ ,  $p = 0.001$ ), initial hematoma volume values ( $r = -0.449$ ,  $p = 0.002$ ), last hematoma volume values ( $r = -0.366$ ,  $p = 0.012$ ), and hypodensity ( $r = -0.320$ ,  $p = 0.030$ ).

A positive correlation was found between initial hematoma volume values and last hematoma volume values ( $r = 0.917$ ,  $p < 0.001$ ), hypodensity ( $r = 0.677$ ,  $p < 0.001$ ), intraventricular hemorrhage ( $r = 0.387$ ,  $p = 0.008$ ), island sign ( $r = 0.507$ ,  $p < 0.001$ ), BAT scores ( $r = 0.565$ ,  $p < 0.001$ ), hematoma expansion ( $r = 0.354$ ,  $p = 0.016$ ), mRS scores ( $r = 0.463$ ,  $p = 0.002$ ) and mortality rates ( $r = 0.304$ ,  $p = 0.040$ ). In addition, a positive correlation was found between the last hematoma volume values and hypodensity ( $r = 0.707$ ,  $p < 0.001$ ), intraventricular hemorrhage ( $r = 0.489$ ,  $p = 0.001$ ), island sign ( $r = 0.456$ ,  $p = 0.001$ ), BAT scores ( $r = 0.661$ ,  $p < 0.001$ ), hematoma expansion ( $r = 0.552$ ,  $p < 0.001$ ), mRS scores ( $r = 0.636$ ,  $p < 0.001$ ) and mortality rates ( $r = 0.470$ ,  $p = 0.001$ ). Finally, a positive correlation was found between the hematoma expansion and hypodensity ( $r = 0.375$ ,  $p = 0.010$ ), intraventricular hemorrhage ( $r = 0.404$ ,  $p = 0.005$ ), island sign ( $r = 0.305$ ,  $p = 0.039$ ), BAT scores ( $r = 0.492$ ,  $p = 0.001$ ), the mRS scores ( $r = 0.794$ ,  $p < 0.001$ ), and mortality rates ( $r = 0.645$ ,  $p < 0.001$ ).

A positive correlation was found between mRS scores and hypodensity ( $r = 0.489$ ,  $p = 0.001$ ), intraventricular hemorrhage ( $r = 0.473$ ,  $p = 0.002$ ), island sign ( $r = 0.311$ ,  $p = 0.048$ ), BAT scores ( $r = 0.637$ ,  $p < 0.001$ ) and HEMRICH scores ( $r = 0.598$ ,  $p < 0.001$ ). A positive correlation was found between the mortality rates and intraventricular haemorrhage ( $r = 0.394$ ,  $p = 0.007$ ), and BAT scores ( $r = 0.506$ ,  $p < 0.001$ ).

On the other hand, a positive correlation was found between hypodensity and intraventricular hemorrhage ( $r = 0.356$ ,  $p = 0.015$ ), island sign ( $r = 0.550$ ,  $p < 0.001$ ), and BAT scores ( $r = 0.766$ ,  $p < 0.001$ ). Moreover, a positive correlation was found between the intraventricular hemorrhage and island sign



**Table 5.** The table shows the parameters that can predict the hematoma expansion risk and mortality risk in patients with spontaneous intracerebral hematoma. *ROC-Curve test, and Logistic Regression test, p < 0.05.*

| Prediction                  | Variable                    | ROC-Curve test |        |                        |             |             |  |
|-----------------------------|-----------------------------|----------------|--------|------------------------|-------------|-------------|--|
|                             |                             | Area           | p      | Cut-off value          | Sensitivity | Specificity |  |
| Hematoma expansion risk     | GCS score                   | 0.113          | <0.001 | <10                    | 83%         | 82%         |  |
|                             | Initial hematoma volume     | 0.709          | 0.018  | >19.17 cm <sup>3</sup> | 61%         | 75%         |  |
|                             | Hypodensity                 | 0.690          | 0.031  | >0                     | 71%         | 67%         |  |
|                             | Intraventricular hemorrhage | 0.687          | 0.034  | >0                     | 43%         | 94%         |  |
|                             | BAT score                   | 0.769          | 0.002  | >1                     | 82%         | 67%         |  |
|                             | Last hematoma volume        | 0.826          | <0.001 | 44.55 cm <sup>3</sup>  | 71%         | 78%         |  |
| Mortality risk              | HEMRICH scale score         | 0.830          | <0.001 | ≥3                     | 82%         | 72%         |  |
|                             | GCS score                   | 0.108          | <0.001 | <10                    | 86%         | 75%         |  |
|                             | Initial hematoma volume     | 0.676          | 0.003  | >19.17 cm <sup>3</sup> | 81%         | 54%         |  |
|                             | Hypodensity                 | 0.682          | 0.046  | >0                     | 71%         | 56%         |  |
|                             | Intraventricular hemorrhage | 0.678          | 0.039  | >0                     | 48%         | 88%         |  |
|                             | BAT score                   | 0.770          | 0.002  | >1                     | 86%         | 56%         |  |
| Mortality risk              | Last hematoma volume        | 0.772          | 0.002  | >44.55 cm <sup>3</sup> | 81%         | 72%         |  |
|                             | Hematoma expansion          | 0.816          | <0.001 | >0                     | 95%         | 72%         |  |
|                             | HEMRICH scale score         | 0.814          | <0.001 | ≥3                     | 86%         | 68%         |  |
|                             | Logistic Regression test    |                |        |                        |             |             |  |
|                             | Prediction                  | Variable       | B      | Wald                   | p           |             |  |
|                             | Hematoma expansion risk     | GCS score      | 0.591  | 10.209                 | 0.001       |             |  |
| Initial hematoma volume     |                             | 0.019          | 4.152  | 0.042                  |             |             |  |
| Hypodensity                 |                             | 1.609          | 6.095  | 0.014                  |             |             |  |
| Intraventricular hemorrhage |                             | 2.546          | 5.379  | 0.020                  |             |             |  |
| BAT score                   |                             | 0.943          | 9.528  | 0.002                  |             |             |  |
| Mortality risk              | HEMRICH scale               | 0.728          | 12.423 | <0.001                 |             |             |  |
|                             | GCS score                   | -0.542         | 10.901 | 0.001                  |             |             |  |
|                             | Intraventricular hemorrhage | 1.897          | 6.318  | 0.012                  |             |             |  |
|                             | BAT score                   | 0.953          | 6.318  | 0.002                  |             |             |  |
|                             | Last hematoma volume        | 0.012          | 5.219  | 0.022                  |             |             |  |
| Mortality risk              | Hematoma expansion          | 3.750          | 11.394 | 0.001                  |             |             |  |
|                             | HEMRICH scale               | 0.661          | 11.164 | 0.001                  |             |             |  |

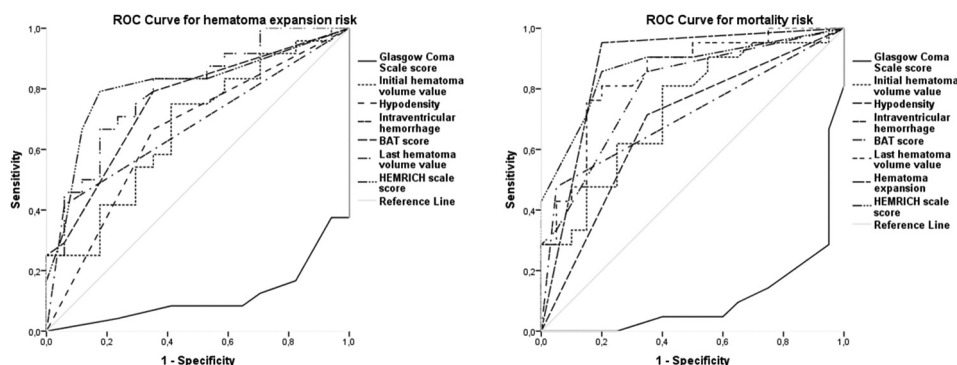
(GCS: Glasgow Coma Scale, B: B score)

( $r = 0.357$ ,  $p = 0.015$ ), and BAT scores ( $r = 0.445$ ,  $p = 0.002$ ). Island sign was positively correlated with the BAT scores ( $r = 0.414$ ,  $p = 0.004$ ).

**ROC-curve and regression analysis**

ROC-Curve test results revealed that the hematoma expansion risk of the patient could be high if GCS score was <10 (area = 0.113,  $p < 0.001$ , cut-off value<10, 83% sensitivity, 82% specificity), if the initial hematoma volume value was >19 cm<sup>3</sup> (area = 0.709,  $p = 0.018$ , cut-off value>19.17, 61% sensitivity, 75% specificity), if hypodensity was found (area = 0.690,  $p = 0.031$ , cut-off value>0, 71% sensitivity, 67%

specificity), if intraventricular hemorrhage was observed (area = 0.687,  $p = 0.034$ , cut-off value>0, 43% sensitivity, 94% specificity), if BAT score was >1 (area = 0.769,  $p = 0.002$ , cut-off value>1, 82% sensitivity, 67% specificity), if last hematoma volume value was >44.55 cm<sup>3</sup> (area = 0.826,  $p < 0.001$ , cut-off value>44.55, 71% sensitivity, 78% specificity), and if HEMRICH scale score was ≥3 (area = 0.830,  $p < 0.001$ , cut-off value ≥3, 82% sensitivity, 72% specificity) (Table 5, Figure 2). Logistic Regression analysis revealed that GCS score (B = -0.591, Wald = 10.209,  $p = 0.001$ ), initial hematoma volume (B = 0.019, Wald = 4.152,  $p = 0.042$ ), hypodensity (B = 1.609, Wald = 6.095,  $p = 0.014$ ), intraventricular hemorrhage



**Figure 5.** The ROC-Curve plot shows the parameters that can predict the hematoma expansion risk and mortality risk in patients with spontaneous intracerebral hematoma.

( $B = 2.546$ ,  $Wald = 5.379$ ,  $p = 0.020$ ), BAT score ( $B = 0.943$ ,  $Wald = 9.528$ ,  $p = 0.002$ ), and HEMRICH scale score ( $B = 0.728$ ,  $Wald = 12.423$ ,  $p < 0.001$ ) could be the best markers in predicting the hematoma expansion risk (Table 5, Figure 5).

ROC-Curve analysis revealed that the mortality risk of the patient could be high if GCS score was  $<10$  (area = 0.108,  $p < 0.001$ , cut-off value  $<10$ , 86% sensitivity, 75% specificity), if initial hematoma volume value was  $>19 \text{ cm}^3$  (area = 0.676,  $p = 0.003$ , cut-off value  $>19.17$ , 81% sensitivity, 54% specificity), if hypodensity was detected (area = 0.682,  $p = 0.046$ , cut-off value  $>0$ , 71% sensitivity, 56% specificity), if intraventricular hemorrhage developed (area = 0.678,  $p = 0.039$ , cut-off value  $>0$ , 48% sensitivity, 88% specificity), if BAT score was  $>1$  (area = 0.770,  $p = 0.002$ , cut-off value  $>1$ , 86% sensitivity, 56% specificity), if last hematoma volume value was  $>44.55 \text{ cm}^3$  (area = 0.772,  $p = 0.002$ , cut-off value  $>44.55$ , 81% sensitivity, 72% specificity), if an hematoma expansion was detected

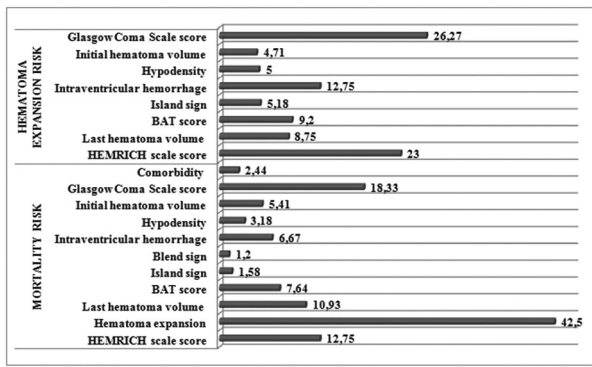
(area = 0.816,  $p < 0.001$ , cut-off value  $>0$ , 95% sensitivity, 72% specificity), and if HEMRICH scale score was  $\geq 3$  (area = 0.814,  $p < 0.001$ , cut-off value  $\geq 3$ , 86% sensitivity, 68% specificity) (Table 5, Figure 2). However, Logistic Regression test results revealed that GCS score ( $B = -0.542$ ,  $Wald = 10.901$ ,  $p = 0.001$ ), intraventricular hemorrhage ( $B = 1.897$ ,  $Wald = 6.318$ ,  $p = 0.012$ ), BAT score ( $B = 0.953$ ,  $Wald = 6.318$ ,  $p = 0.002$ ), last hematoma volume ( $B = 0.012$ ,  $Wald = 5.219$ ,  $p = 0.022$ ), hematoma expansion ( $B = 3.750$ ,  $Wald = 11.394$ ,  $p = 0.001$ ), and HEMRICH scale score ( $B = 0.661$ ,  $Wald = 11.164$ ,  $p = 0.001$ ) could be the best predictors of mortality risk (Table 5, Figure 5).

On the other hand, the Likelihood Ratio test performed to mRS score revealed that the GCS score ( $X^2 = 17.282$ ,  $p = 0.002$ ), comorbidity ( $X^2 = 18.477$ ,  $p = 0.002$ ), initial hematoma volume value ( $X^2 = 25.040$ ,  $p < 0.001$ ), last hematoma volume ( $X^2 = 32.214$ ,  $p < 0.001$ ), and hematoma expansion

**Table 6.** The table shows the Odds Ratio test results and its corresponding 95% confidence intervals for the direction and strength of the association between the patients's data and hematoma expansion risk and mortality risk.

| Variable                    |                           | HEMATOMA EXPANSION RISK |            | Odds Ratio value | 95% CI |        |
|-----------------------------|---------------------------|-------------------------|------------|------------------|--------|--------|
|                             |                           | No                      | Yes        |                  | Lower  | Upper  |
| GCS score                   | $\geq 10$                 | 17 (37.0%)              | 11 (23.9%) | 26.27            | 3.05   | 226.60 |
|                             | $< 10$                    | 1 (2.2%)                | 17 (37.0%) |                  |        |        |
| Initial hematoma volume     | $\leq 19.17 \text{ cm}^3$ | 11 (23.9%)              | 7 (15.2%)  | 4.71             | 1.32   | 16.90  |
|                             | $> 19.17 \text{ cm}^3$    | 7 (15.2%)               | 21 (45.7%) |                  |        |        |
| Hypodensity                 | No                        | 12 (26.1%)              | 8 (17.4%)  | 5.00             | 1.39   | 17.94  |
|                             | Yes                       | 6 (13.0%)               | 20 (43.5%) |                  |        |        |
| Intraventricular hemorrhage | No                        | 17 (37.0%)              | 16 (34.8%) | 12.75            | 1.48   | 109.59 |
|                             | Yes                       | 1 (2.2%)                | 12 (26.1%) |                  |        |        |
| Island sign                 | No                        | 16 (34.8%)              | 17 (37.0%) | 5.18             | 0.99   | 27.06  |
|                             | Yes                       | 2 (4.3%)                | 11 (23.9%) |                  |        |        |
| BAT score                   | $< 1$                     | 12 (26.7%)              | 4 (8.9%)   | 9.20             | 2.32   | 36.45  |
|                             | $\geq 1$                  | 6 (13.3%)               | 23 (51.1%) |                  |        |        |
| Last hematoma volume        | $\leq 44.55 \text{ cm}^3$ | 14 (30.4%)              | 8 (17.4%)  | 8.75             | 2.20   | 34.81  |
|                             | $> 44.55 \text{ cm}^3$    | 4 (8.7%)                | 20 (43.5%) |                  |        |        |
| HEMRICH scale score         | $< 3$                     | 15 (32.6%)              | 5 (10.9%)  | 23.00            | 4.77   | 110.80 |
|                             | $\geq 3$                  | 3 (6.5%)                | 23 (50.0%) |                  |        |        |
| Variable                    |                           | MORTALITY RISK          |            | Odds Ratio value | 95% CI |        |
|                             |                           | No                      | Yes        |                  | Lower  | Upper  |
| Comorbidity                 | No                        | 15 (32.6%)              | 8 (17.4%)  | 2.44             | 0.74   | 8.01   |
|                             | Yes                       | 10 (21.7%)              | 13 (28.3%) |                  |        |        |
| GCS score                   | $\geq 10$                 | 22 (47.8%)              | 6 (13.0%)  | 18.33            | 3.96   | 84.96  |
|                             | $< 10$                    | 3 (6.5%)                | 15 (32.6%) |                  |        |        |
| Initial hematoma volume     | $\leq 19.17 \text{ cm}^3$ | 14 (30.4%)              | 4 (8.7%)   | 5.41             | 1.41   | 20.77  |
|                             | $> 19.17 \text{ cm}^3$    | 11 (23.9%)              | 17 (37.0%) |                  |        |        |
| Hypodensity                 | No                        | 14 (30.4%)              | 6 (13.0%)  | 3.18             | 0.93   | 10.92  |
|                             | Yes                       | 11 (23.9%)              | 15 (32.6%) |                  |        |        |
| Intraventricular hemorrhage | No                        | 22 (47.8%)              | 11 (23.9%) | 6.67             | 1.52   | 29.27  |
|                             | Yes                       | 3 (6.5%)                | 10 (21.7%) |                  |        |        |
| Blend sign                  | No                        | 24 (52.2%)              | 20 (43.5%) | 1.20             | 0.07   | 20.43  |
|                             | Yes                       | 1 (2.2%)                | 1 (2.2%)   |                  |        |        |
| Island sign                 | No                        | 19 (41.3%)              | 14 (30.4%) | 1.58             | 0.44   | 5.76   |
|                             | Yes                       | 6 (13.0%)               | 7 (15.2%)  |                  |        |        |
| BAT score                   | $< 1$                     | 14 (30.4%)              | 3 (6.5%)   | 7.64             | 1.78   | 32.72  |
|                             | $\geq 1$                  | 11 (23.9%)              | 18 (39.1%) |                  |        |        |
| Last hematoma volume        | $\leq 44.55 \text{ cm}^3$ | 18 (39.1%)              | 4 (8.7%)   | 10.93            | 2.71   | 44.14  |
|                             | $> 44.55 \text{ cm}^3$    | 7 (15.2%)               | 17 (37.0%) |                  |        |        |
| Hematoma expansion          | No                        | 17 (37.0%)              | 1 (2.2%)   | 42.50            | 4.82   | 374.87 |
|                             | Yes                       | 8 (17.4%)               | 20 (43.5%) |                  |        |        |
| HEMRICH scale score         | $< 3$                     | 17 (37.0%)              | 3 (6.5%)   | 12.75            | 2.89   | 56.19  |
|                             | $\geq 3$                  | 8 (17.4%)               | 18 (39.1%) |                  |        |        |

(GCS: Glasgow Coma Scale; CI: confidence intervals)



**Figure 6.** The Odds Ratio test plot shows the parameters that can be associated with the hematoma expansion risk and mortality risk in patients with spontaneous intracerebral hematoma.

( $X^2 = 26.305$ ,  $p < 0.001$ ) could be the markers in predicting the short-term prognosis of the patients.

**Odds ratio and 95% confidence intervals**

Odds Ratio test results revealed that if GCS score was  $<10$ , it was associated with more than 20 six-fold risk of hematoma expansion (OR = 26.27; 95% CI = 3.05–226.60). If initial hematoma volume value was  $>19.17 \text{ cm}^3$ , it was associated with more than four-fold risk of hematoma expansion (OR = 4.71; 95% CI = 1.32–16.90). If hypodensity and island sign were found, they were associated with more than five-fold risk of hematoma expansion (OR = 5.00; 95% CI = 1.39–17.94 and OR = 5.18; 95% CI = 0.99–27.06, respectively). If intraventricular haemorrhage was observed, it was associated with more than twelve-fold risk of hematoma expansion (OR = 12.75; 95% CI = 1.48–109.59). If BAT score was  $>1$ , it was associated with more than nine-fold risk of

hematoma expansion (OR = 9.20; 95% CI = 2.32–36.45). If last hematoma volume value was  $>44.55 \text{ cm}^3$ , it was associated with more than eight-fold risk of hematoma expansion (OR = 8.75; 95% CI = 2.20–34.81). If HEMRICH scale score was  $\geq 3$ , it was associated with more than 20 three-fold risk of hematoma expansion (OR = 23.00; 95% CI = 4.77–110.80) (Table 6, Figure 6).

If comorbidity was found, it was associated with more than two-fold risk of mortality (OR = 2.44; 95% CI = 0.74–8.01). If GCS score was  $<10$ , it was associated with more than eighteen-fold risk of hematoma expansion (OR = 18.33; 95% CI = 3.96–84.96). If initial hematoma volume value was  $>19.17 \text{ cm}^3$ , it was associated with more than five-fold risk of hematoma expansion (OR = 5.41; 95% CI = 1.41–20.77). If hypodensity was found, it was associated with more than three-fold risk of mortality (OR = 3.18; 95% CI = 0.93–10.92). If intraventricular haemorrhage was observed, it was associated with more than the six-fold risk of mortality (OR = 6.67; 95% CI = 1.52–29.27). If blend sign and island sign were seen, they were associated with more than one-fold risk of mortality (OR = 1.20; 95% CI = 0.07–20.43 and OR = 1.58; 95% CI = 0.44–5.76, respectively). If BAT score was  $>1$ , it was associated with more than seven-fold risk of mortality (OR = 7.64; 95% CI = 1.78–32.72). If last hematoma volume value was  $>44.55 \text{ cm}^3$ , it was associated with more than ten-fold risk of hematoma expansion (OR = 10.93; 95% CI = 2.71–44.14). If hematoma expansion was found, it was associated with more than 40 two-fold risk of mortality (OR = 42.50; 95% CI = 4.82–374.87). If HEMRICH scale score was  $\geq 3$ , it was associated with more than twelve-fold

**Table 7.** The table reveals the validity and reliability of the HEMRICH scale. Factor analysis test and Reliability test,  $p < 0.05$ .

| Factor analysis test          |                  |                                       |             |                              |       |        |          |
|-------------------------------|------------------|---------------------------------------|-------------|------------------------------|-------|--------|----------|
|                               |                  | Factor 1<br>(Hematoma expansion risk) |             | Factor 2<br>(Mortality risk) |       |        |          |
| Initial hematoma volume       |                  | 0.94                                  |             | 0.16                         |       |        |          |
| Last hematoma volume          |                  | 0.93                                  |             | 0.29                         |       |        |          |
| Intraventricular hemorrhage   |                  | 0.60                                  |             | 0.42                         |       |        |          |
| Island sign                   |                  | 0.09                                  |             | 0.80                         |       |        |          |
| BAT Score                     |                  | 0.31                                  |             | 0.77                         |       |        |          |
| GCS score                     |                  | -0.45                                 |             | -0.70                        |       |        |          |
| Eigenvalues                   |                  | 2.40                                  |             | 2.00                         |       |        |          |
| Explained variance (%)        |                  | 40.10                                 |             | 40.10                        |       |        |          |
| Cumulative Variance (%)       |                  | 33.37                                 |             | 73.47                        |       |        |          |
| Kaiser-Meyer-Olkin test       |                  |                                       |             | 0.729                        |       |        |          |
| Bartlett's test of Sphericity |                  |                                       |             | 153.443 ( $p < 0.001$ )      |       |        |          |
| Reliability test              |                  |                                       |             |                              |       |        |          |
| 95% CI                        |                  |                                       |             |                              |       |        |          |
| Variable                      | Cronbach's Alpha | Intraclass Correlation                | Lower Bound | Upper Bound                  | F     | F Test | p        |
| HEMRICH scale                 | 0.564            | 0.564                                 | 0.319       | 0.642                        | 2.295 |        | $<0.001$ |

(CI: confidence intervals)

risk of mortality (OR = 12.75; 95% CI = 2.89–56.19) (Table 6, Figure 6).

### Validity and reliability analysis of the HEMRICH scale

The *Factor analysis* test results revealed that the sample size of this study was found adequate (*Kaiser-Meyer-Olkin* test value = 0.729). Test results based on the correlation matrix table suggested that only GCS score, initial hematoma volume, last hematoma volume, intraventricular haemorrhage, island sign, and BAT score values could be the component of the HEMRICH scale (*Bartlett's Test of Sphericity* value = 153.443,  $p < 0.001$ ). Furthermore, analysis results showed that HEMRICH scale scores were uniformly distributed under two separate factors (with an explained variance of 73.47%). The variance explained by the Factor 1 (i.e. hematoma expansion risk) scores was higher than the explained variance for the Factor 2 (i.e. mortality risk) scores (40.10% vs. 33.37%, respectively). The 2-factor differentiation in *Factor analysis* showed that this scale could predict both hematoma expansion risk and mortality risk in patients with spontaneous ICH (Eigenvalues = 2.40 and 2.00) (Table 7).

The *Reliability analysis* test showed that this scale had *slightly* low reliability because Cronbach's alpha value was between 0.40 and 0.60 (Cronbach's alpha = 0.564, intraclass correlation = 0.564, 95% CI = 0.319–0.742). However, *F* test revealed that there was no similarity among the parameters forming this scale ( $F = 2.295$ ,  $p < 0.001$ ) (Table 7).

### Discussion

Wada et al [13] reported that hyperdense areas within the hematoma, called 'spot sign', are associated with hematoma expansion in brain CT angiography taken within 3 hours after the symptom onset. However, Morotti et al [1] showed that several NCCT markers (i.e. 'black hole sign', 'blend sign', 'heterogeneous density', 'hypodensity', 'swirl sign', 'irregular shape' and 'island sign') can associate with the hematoma expansion, and they recommended that NCCT is a promising tool for prediction of hematoma expansion and unfavourable prognosis. They also concluded that their complementary diagnostic yield could be adequate, when used in combination with clinical variables. Additionally, some studies reported the accuracy of 'blend sign', 'black hole sign', 'swirl sign' and 'island sign' as predictors of early hematoma expansion on NCCT images with low incidence, limited sensitivity, and high specificity [14,15].

In the present study, it was found that in patients in the LOBAR group, time from onset to NCCT scan was earlier, the initial and last hematoma volume values

were higher, and most of the patients did not use any medication. Comorbidity was mostly found in deeply located and posterior fossa-located ICH patients (in the DEEP group 9 patients had HT and 2 patients had DM; in the LOBAR group 5 patients had HT and 2 patients had DM; in the CEREBELLUM group 5 patients had HT and 3 patients had DM). In patients with hematoma expansion, the GCS scores were lower, time from onset to NCCT scan was earlier, initial and last hematoma volume values were higher, intraventricular haemorrhage, and/or island sign was observed more common. Furthermore, BAT scores, HEMRICH scale scores, mRS scores and mortality rates were found high in these patients. In the NON-SURVIVED group, GCS scores were lower, time from onset to NCCT scan was earlier, initial and last hematoma volume values were higher, intraventricular haemorrhage and/or hematoma expansion was observed more common, and BAT scores, and HEMRICH scale scores were found high.

The correlation analysis applied to all patients' data demonstrated that if GCS score was low, the initial and/or last hematoma volume values, and BAT score might be found high. Furthermore, if GCS score was low, hypodensity, intraventricular haemorrhage, island sign, and/or hematoma expansion might be detected commonly in these patients. Additionally, if SBP value was measured higher, in these patients BAT score, initial and last hematoma volumes might be measured high and hypodensity, intraventricular haemorrhage, island sign, and/or hematoma expansion might be detected commonly. Furthermore, these patients might have low GCS scores and high mRS scores and thus their prognosis might be poor. When the initial hematoma volume was measured to be high, it was thought that the possibility of developing hypodensity, intraventricular haemorrhage, island sign, and/or high BAT score values, and consequently, the risk of hematoma expansion might be high during the stay in hospital, and it was considered that these patients' mRS scores might increase, and thus their prognosis might be poor. Moreover, it was predicted that if hypodensity was observed, intraventricular haemorrhage and/or island sign might be seen, and high BAT score and/or hematoma expansion might be observed. On the other hand, it was concluded that in patients with hematoma expansion, the GCS scores could be lower, the initial and last hematoma volume values could be higher, intraventricular haemorrhage, hypodensity, island sign, and high BAT score could be found more common, and in these patients, it was considered that the mRS scores and mortality risk could be higher, and thus, their prognosis could be worse. Additionally, it was thought that the island sign,



BAT scores and mRS scores could be higher in patients with intraventricular haemorrhage. It also was observed that BAT scores of the patients with island sign could be high.

Both the *ROC-Curve* analysis and *Logistic Regression* analysis results revealed that if GCS scores were <10, if the initial hematoma volume value was >19.17 cm<sup>3</sup>, if the hypodensity, and development of the intraventricular haemorrhage was observed on NCCT images, if the BAT score was >1, if HEMRICH score ≥3, it was determined that these parameters could indicate the high possibility of hematoma expansion. However, initial systolic and/or diastolic blood pressure values could not predict the hematoma expansion risk. Briefly, it could be said that hematoma expansion risk might be high in patients with low GCS score, high initial hematoma volume value, high BAT score, high HEMRICH score, and/or developed the hypodensity and/or intraventricular haemorrhage. Interestingly, the *Odds Ratio* test results revealed that GCS scores, initial and last hematoma volume values, hypodensity, intraventricular haemorrhage, island sign, BAT score, and HEMRICH scale score could be associated with the high risk of hematoma expansion.

Accurate diagnosis and prediction of outcome after ICH are important for treatment regimens and the setting of rehabilitation goals. It has been documented in literature that age, initial level of consciousness, hematoma volume, intraventricular spread of the haemorrhage, and hydrocephalus are predicting factors of long-term survival and functional outcome after ICH [4,5,16,17]. Additionally, some studies revealed that NCCT markers such as blend sign, black hole sign, heterogeneous density, hypodensity, island sign, spot sign, swirl sign, irregular shape, hematoma volume, intraventricular haemorrhage, and early hematoma expansion can predict the poor outcome in the patients with ICH [1,18].

In present study, in the surviving patients, the mRS score was determined 1 point in 4 (8.7%) patients, 2 points in 10 (21.7%) patients, 3 points in 7 (15.2%) patients, 4 points in 1 (2.2%), and 5 points in 3 (6.5%) patients. Based on correlation analysis results, if the patient's GCS score was found low; if the time from onset to brain NCCT scan was earlier; if initial and last hematoma volume was measured high; if the hypodensity and/or island sign was detected on initial NCCT; if the hematoma expansion and/or hematoma spread into the ventricle was observed on follow-up NCCT; if the BAT score value was >1, the mRS scores could be found high and the short-term prognosis of these patients could be worse. Besides this, the *Likelihood Ratio* test revealed that the GCS score, comorbidity, initial and last hematoma volume value, and hematoma expansion could be the best predictors for short-term prognosis of the patients.

In the present study, almost all patients who died in the hospital had low GCS score, time from onset to NCCT scan was early, the initial hematoma volume and last hematoma volume values were found high, BAT score was found 2 points or above, HEMRICH scale score was high, an increase in hematoma volume was detected and it was commonly seen that hematoma spread into the ventricle. However, *ROC-Curve* analysis and *Logistic Regression* analysis revealed that if GCS score was found <10, if development of the intraventricular haemorrhage was observed on follow-up NCCT; if the BAT score was >1; if last hematoma volume was measured >44.55 cm<sup>3</sup>, if hematoma expansion was detected on follow-up NCCT images, and if HEMRICH score was found ≥3, it was thought that these parameters could indicate an increase in mortality risk. However, initial systolic and/or diastolic blood pressure values could not predict the mortality risk. Additionally, *Odds ratio* test results showed that comorbidity, GCS scores, initial and last hematoma volume values, hypodensity, intraventricular haemorrhage, blend sign, island sign, BAT score, hematoma expansion, and HEMRICH scale scores were associated with the high mortality risk.

At the end of this study, it was seen that a new and simple scale was needed to easily predict the hematoma expansion risk and mortality risk in spontaneous ICH patients. Therefore, to fulfill this need, a scale called the HEMRICH scale was developed using the parameters of this study. In this scale, it was considered that the parameters called 'initial hematoma volume', 'last hematoma volume' and 'intraventricular haemorrhage' could predict hematoma expansion risk whereas 'BAT score', 'island sign', and 'GCS score' could predict the mortality risk. Interestingly, it was found that if this scale score was ≥3 points, both hematoma expansion risk and mortality risk might be strongly high. Based on these findings, the scoring of this scale and the interpretation of the scores could be as follows: In this scale, if GCS value, initial hematoma volume value, and any of the other scale parameters (except the last hematoma volume value) are scored on admission to the hospital, it can be said that both hematoma volume may increase and patient's risk of death may be increase. If more than four parameters are scored on this scale, it can be concluded that the hematoma expansion risk and mortality risk in this patient may be almost certain.

Finally, the *Factor analysis* test results demonstrated that this scale could be accepted a valid scale. However, the *Reliability* test results showed that this scale had low reliability. It was thought that the reason for the low-reliability of this scale may be that randomly selected low number individuals were evaluated by different observers and the correlation value was calculated by taking the average of these evaluations. Furthermore, the small



number of the parameters of the scale and some of the test factors which are negatively related to each other also may reduce this reliability. However, the BAT score, one of the components of this scale, contains three sub-scores called 'hypodensity', 'blend sign', and 'time from onset to NCCT scan'. Therefore, it can be said that these sub-scores can increase the reliability of this scale. In addition, it is known that a reliable scale may not always be valid. Sometimes even the purpose of making the scale reliable can conflict with the purpose of validating the scale. For this reason, it can be concluded that this measurement tool, which has high validity, may have a high degree of reliability. Therefore, it was considered that this newly produced scale could be a valid and reliable scale for safely and easily predicting both hematoma expansion risk and mortality risk in patients with spontaneous ICH. However, it also was recognized that re-testing was necessary for the reliability and validity of this scale in larger patient samples.

### Limitations

There were some limitations to this study. *Primarily* this study was conducted in a single-centre without a surgically treated group and it was retrospective in design corresponding to a low level of evidence. Furthermore, the low number of patients and the inequality of the patient groups might have caused a statistical power loss. *Secondly*, intracranial pressure monitoring that can show the possibility of the hematoma expansion in early-stage could not be administered to any patient because of the financial restriction. *Finally*, the patients' long-term follow-up results were not included in this study because they were outside the study scope.

### Conclusion

At the end of this study, it was concluded that the GCS score, BAT score, HEMRICH scale score, and intraventricular haemorrhage observed on NCCT images could be the powerful indicators of both the hematoma expansion risk and mortality risk in early stage in patients with spontaneous ICH.

Moreover, it was considered that the GCS score, presence of the comorbidity, the initial and last hematoma volume value measured on NCCT images, and the presence of the hematoma expansion could be the predictors for short-term prognosis.

Finally, it can be said that the HEMRICH scale developed in this study may aid in the rapid identification and management of patients with spontaneous ICH who had a high risk of hematoma expansion and/or mortality risk.

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### Disclosure statement

The authors declare that they have no conflict of interests.

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### Informed consent

Since the study had a retrospective character, the patients were informed that their information could be used in the study on the condition of protecting their personal information, and consent was obtained, so no additional consent was obtained.

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