Clinical Factors and Perioperative Strategies Associated with Outcome in Preinjury Antiplatelet and Anticoagulation Therapy for Patients with Traumatic Brain Injuries

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Objective: Long-term oral anticoagulation or antiplatelet therapy has been used with increasing frequency in the elderly. These patients are at increased risk of morbidity and mortality from expansion of intracranial hemorrhage. We conducted a single-center retrospective case control study to evaluate risk factors associated with outcomes and to identify the differences in outcome in traumatic brain injury between preinjury anticoagulation use and without anticoagulation.

Methods: A retrospective study of patients who underwent craniotomy or craniectomy for acute traumatic cerebral hemorrhage, between January 2005 and December 2014 was performed.

Results: A consecutive series of 50 patients were evaluated. The factors significantly differed between the two groups were initial Prothrombin Time-International Normalized Ratio, initial platelet count, initial Glasgow Coma Scale score, and postoperative intracranial bleeding. Mean Glasgow Outcome Scale (GOS) score were similar between the two groups. In the patient with low-energy trauma only, no significant differences in GOS score, postoperative bleeding and many other factors were observed. The contributing factors to postoperative bleeding was preinjury anticoagulation and its adjusted odds ratio was 12 [adjusted odds ratio (OR), 12.242; \( p = 0.0070 \)]. The contributing factors to low GOS scores, which mean unfavorable neurological outcomes, were age (adjusted OR, 1.073; \( p = 0.039 \)) and Rotterdam scale score for CT scans (adjusted OR, 3.123; \( p = 0.0020 \)).

Conclusion: Preinjury anticoagulation therapy contributed significantly to the occurrence of postoperative bleeding. However, preinjury anticoagulation therapy in the patients with low-energy trauma did not contribute to the poor clinical outcomes or total hospital stay. Careful attention should be given to older patients and severity of hemorrhage on initial brain CT.

Key Words: Traumatic brain injury · Antiplatelet therapy · Anticoagulation therapy.
MATERIALS AND METHODS

Patients who underwent craniotomy or craniectomy for acute cases of subdural hematoma, epidural hematoma, or intracerebral hemorrhage between January 2005 and December 2014 were included. All of the patients were from a single institute. According to computed tomographic (CT) results, all of the patients had confirmed acute hemorrhage, including acute intracerebral, subdural, and epidural hemorrhages. Patients were considered as anticoagulated if they were taking warfarin, low-molecular-weight heparin, aspirin, nonsteroidal anti-inflammatory agents, clopoidogrel, dipyridamole, pentoxifylline, or naproxen. The control group, which consisted of patients with intracranial injury as defined earlier but without any form of anticoagulation, were matched for mechanism and severity of injury. The number of patients in the control group was set to equal the size of the anticoagulated group. Of the patients, 24 with intracranial injuries were identified to receive prehospital anticoagulation. For comparison, a control group consisting 26 patients with head injury but who were not taking any prehospital anticoagulant or antiplatelet agents were randomly selected based on the hospital records in the same period.

According to the classification by the Committee on Trauma of the American College of Surgeon, high-energy trauma refers to penetrating trauma, trauma from motorcycle crashes, and trauma from falling down from a height of more than 1 m. Meanwhile, low-energy trauma refers to trauma from slipping down and falling down from a height of lower than 1 m.

Statistical analysis was performed to identify differences in age, sex, preoperative Glasgow Coma Scale (GCS) score, Glasgow Outcome Scale (GOS) score, length of hospital stay, preoperative transfusion, intraoperative transfusion, postoperative transfusion, initial INR, initial platelet count, duration of intensive care unit (ICU) stay, length of hospital stay, and postoperative bleeding between the group who had and that who had not received antiplatelet agents or anticoagulants. Postoperative bleeding included postoperative epidural hematoma, postoperative subdural hematoma, and postoperative ICH, all were confirmed by performing an immediate postoperative CT examination within 1 hour after operation.

All of the patients had aggressive transfusion to resolve the abnormality in the prothrombin time-international normalized ratio (PT-INR) and platelet count.

We also performed statistical analysis to identify outcome factors such as neurological outcome, GOS score, and factors attribute to the merge of postoperative acute bleeding. To make statistical analysis easier, GOS scores of 4 and 5 were defined as favorable neurological outcomes, and GOS scores of 1, 2, and 3 were defined as unfavorable neurological outcomes.

Data were statistically analyzed by using the Student t-test, Wilcoxon rank sum test, chi-square test, or Fisher exact test, as appropriate.

RESULTS

Data from a consecutive series of 50 patients were analyzed (Table 1). Of the patients, 24 were given anticoagulants, 7 had atrial fibrillation, 6 underwent operation for valvular heart disease, 4 had angina, 1 had pulmonary thromboembolism, 2 had hypertension, and 7 had a history of cerebral infarction. One patient had both atrial fibrillation and cerebral infarction, another had both angina and valvular heart disease, and one had angina and cerebral infarction.

Among the patients in the preinjury anticoagulated group, 13 were men and 11 were women, with a mean age of the patients was 74.25±10.22 years (range, 55–91 years). Among the patients without anticoagulation, 19 were men and 7 were women, with a mean age of 55.35±16.75 years (range, 18–85 years). The age difference between the two groups was statistically significant (p<0.001).

In general, among the patients who received preinjury anticoagulation or antiplatelet agents, 3 had high-energy trauma and 21 had low-energy trauma. However, in the non-anticoagulated group, 16 had high-energy trauma and 10 had low-energy trauma.

The initial Prothrombin Time-International Normalized Ratio was 2.69±3.5 (range, 0.87–18.38) in the anticoagulated group. Of those patients who did not receive any anticoagulation, the mean PT-INR was 1.1±0.13 (p=0.001).

The initial platelet count was 158.25±54.81 (range, 130–400 /μL) in the anticoagulated group and 232.54±97.13 (range, 80–538) in the non-anticoagulated group (p=0.002). The lengths of ICU stay were 13.71±11.46 days (range, 1–40 days) and 12.46±10.98 days (range, 1–44 days), respectively (p=0.647). The lengths of hospital stay was 32.67±29.71 days (range, 5–135 days) and 30.96±38.45 days (range, 1–171 days), respectively (p=0.403).

The mean initial GCS score was 9.92±3.72 (range, 3–15) in the anticoagulated group and 7.5±3.42 (range, 3–15) in the non-anticoagulated group (p=0.024). The mean GOS scores were 2.69±1.09 and 2.62±1.53, respectively (p=0.660).

In terms of preoperative, intraoperative, and postoperative transfusions, the antithrombotic group received more transfusions of fresh frozen plasma preoperatively. In the preinjury anticoagulated group, 13 patients (54.17%) received transfusion of fresh frozen plasma preoperatively, whereas none received such transfusions in the non-anticoagulated group. In transfusion of red blood cells or platelet concentrates, no significant difference was found between the preinjury anticoagulated and non-anticoagulated groups. Postoperative bleeding was observed in 10 patients (41.67%) in the preinjury anticoagulated group and in 3 patients (11.54%) in the anticoagulated group (p=0.015).

Comparative analysis of patients with low-energy trauma only (Table 2)

Among the patients in the preinjury anticoagulated group with low-energy trauma, 11 were men and 10 were women, with
| Table 1. Baseline characteristics | Anticoagulation (+) | Anticoagulation (-) | p-value |
|----------------------------------|---------------------|---------------------|---------|
|                                  | Total (n=24)        | Low energy (n=21)   | High energy (n=3) | p-value |
| Age                              |                     |                     |                     |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 0.294†  |         |
| Mean±SD                          | 74.25±10.22          | 75.1±9.16           | 68.33±17.39         | 55.35±16.75 | 66.5±13.34 | 48.38±15.04 | 0.005*   | <0.001† |
| Median (min, max)                | 75 (55.91)           | 76 (55.91)          | 62 (55.88)          | 54.5 (18.85) | 70 (45.85)  | 48 (18.75)  |         |         |
| Sex                               |                      |                     |                     |         |         |         |         |         |
| M (%)                            | 13 (54.17)           | 11 (52.38)          | 2 (66.67)           | 19 (73.08) | 6 (60)    | 13 (81.25) | 0.369§   | 0.164‡  |
| F (%)                            | 11 (45.83)           | 10 (47.62)          | 1 (33.33)           | 7 (26.92)  | 4 (40)     | 3 (18.75)  |         |         |
| Rotterdam CT score               |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 0.798*  |         |
| Mean±SD                          | 3.83±1.17            | 3.81±1.21           | 3±1                 | 4.08±1.7  | 3.3±1.77   | 4.56±1.5  | 0.071†   | 0.325§  |
| Median (min, max)                | 4 (1.6)              | 4 (1.6)             | 4 (3.5)             | 4.5 (1.6)  | 3.5 (1.6)  | 5 (1.6)   |         |         |
| Initial GCS score                |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 1.1±0.13 |         |
| Mean±SD                          | 9.92±3.72            | 10±3.69             | 9.93±4.73           | 7.5±3.42  | 9.2±3.82   | 6.44±2.76 | 0.115†   | 0.024‡  |
| Median (min, max)                | 10 (3, 15)           | 10 (3, 15)          | 11 (4, 13)          | 6.5 (3, 15) | 9 (5, 15)  | 6 (3, 13)  |         |         |
| Initial INR                      |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 1.92±0.17 |         |
| Mean±SD                          | 2.69±3.5             | 2.8±3.74            | 1.88±0.17           | 1.1±0.13  | 1.11±0.17  | 1.1±0.11  | 0.959*   | 0.001‡  |
| Median (min, max)                | 1.91 (0.87, 18.38)   | 1.9 (0.87, 18.38)   | 1.92 (1.7, 2.03)    | 1.07 (0.9, 1.4) | 1.07 (0.9, 1.33) | 1.07 (0.96, 1.4) |         |         |
| PLT                              |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 0.073*  |         |
| Mean±SD                          | 158.25±54.81         | 165.81±53.91        | 105.33±26.08        | 232.54±97.13 | 214.8±124.07 | 243.63±78.39 | 0.179‡   | 0.002§  |
| Median (min, max)                | 149.5 (64, 294)      | 156 (64, 294)       | 99 (83, 134)        | 216.5 (80, 538) | 196 (80, 538) | 247 (110, 366) |         |         |
| ICU Stay                          |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 1.1±0.13 |         |
| Mean±SD                          | 13.71±11.46          | 15±11.7             | 4.67±0.58           | 12.46±10.98 | 15±12.81   | 10.88±9.78 | 0.427†   | 0.647‡  |
| Median (min, max)                | 9.5 (1.40)           | 11 (1.40)           | 5 (4.5)             | 9.5 (1.44)  | 13.5 (1.44) | 6.5 (1.33)  |         |         |
| Hospital day                     |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 0.137†  |         |
| Mean±SD                          | 32.67±29.71          | 35.38±30.77         | 13.67±8.08          | 30.96±38.45 | 37±49.15   | 27.19±31.24 | 0.370†   | 0.405‡  |
| Median (min, max)                | 26.5 (5, 135)        | 31 (5, 135)         | 15 (5, 21)          | 20 (1, 171) | 22 (9, 171) | 16.5 (1, 118) |         |         |
| Glasgow Outcome Scale            |                      |                     |                     |         |         |         |         |         |
| n                                | 24                   | 21                  | 3                   | 26      | 10      | 16      | 0.888‡  |         |
| Mean±SD                          | 2.67±1.09            | 2.67±1.06           | 2.67±1.53           | 2.62±1.53 | 3±1.41     | 2.38±1.59 | 0.232‡   | 0.660‡  |
| Median (min, max)                | 3 (1.5)              | 3 (1.5)             | 3 (1.4)             | 2 (1.5)   | 2.5 (1.5)  | 2 (1.5)   |         |         |
| Post OP Bleeding                 |                      |                     |                     |         |         |         |         |         |
| Yes (%)                          | 10 (41.67)           | 9 (42.86)           | 1 (33.33)           | 3 (11.54)  | 2 (20)     | 1 (6.25)  | 0.538§   | 0.015‡  |
| No (%)                           | 14 (58.33)           | 12 (57.14)          | 2 (66.67)           | 23 (88.46) | 8 (80)     | 15 (93.75) |         |         |
| Transfusion pre OP RBC           |                      |                     |                     |         |         |         |         |         |
| Done (%)                         | 1 (4.17)             | 1 (4.76)            | -                   | 1 (3.85)   | -         | 1 (6.25)  | 1.000§   | 1.000§   |
| Not done (%)                     | 23 (95.83)           | 20 (95.24)          | 3 (100)             | 25 (96.15) | 10 (100)   | 15 (93.75) |         |         |
| Transfusion pre OP FFP           |                      |                     |                     |         |         |         |         |         |
| Done (%)                         | 13 (54.17)           | 10 (47.62)          | 3 (100)             | 26 (100)   | 10 (100)   | 16 (100)  |         |         |
| Not done (%)                     | 11 (45.83)           | 11 (52.38)          | -                   | 6 (37.5)   | 7 (40)     | 10 (62.5)  |         |         |

* p-value according to the t-test, † p-value according to the Wilcoxon rank sum test, § p-value according to the chi-square test, ‡ p-value according to the Fisher’s exact test.

ICU : intensive care unit, GCS : Glasgow Outcome Scale, RBC : red blood cell, FFP : fresh frozen plasma.
a mean age of 75.10±9.16 years (range, 55–91 years). Meanwhile, among the patients in the non-anticoagulated group with low-energy trauma only, 6 were men and 4 were women, with a mean age of 66.5±13.34 years (range, 45–85 years; p=0.044).

The initial PT-INR was 2.81±3.74 (range, 0.87–18.38) in the preinjury anticoagulated group with low-energy trauma and 1.11±0.17 (range, 0.87–1.33) in the non-anticoagulated group with low-energy trauma (p=0.029). The initial GCS scores were 10±3.69 (range, 3–15) and 9.2±3.82 (range, 5–15 years), respectively (p=0.640). The mean GOS scores were 2.67±1.06 and 3±1.41, respec-

Table 2. Baseline characteristic in low energy trauma

|                      | Total (n=31) | Anticoagulation (+) (n=21) | Anticoagulation (-) (n=10) | p-value |
|----------------------|-------------|----------------------------|-----------------------------|---------|
| Age                  |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 72.32±11.23 | 75.1±9.16                  | 66.5±13.34                  | 0.044*  |
| Median (min, max)    | 74 (45, 91) | 76 (55, 91)                | 70 (45, 85)                 |         |
| Sex                  |             |                            |                             |         |
| M (%)                | 17 (54.84)  | 11 (52.38)                 | 6 (60)                      | 1.000†  |
| F (%)                | 14 (45.16)  | 10 (47.62)                 | 4 (40)                      |         |
| Rotterdam CT score   |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 3.65±1.4    | 3.81±1.21                  | 3.3±1.77                    | 0.461†  |
| Median (min, max)    | 4 (1, 6)    | 4 (1, 6)                   | 3.5 (1, 6)                  |         |
| Initial GCS score    |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 9.74±3.69   | 10±3.69                    | 9.2±3.82                    | 0.640†  |
| Median (min, max)    | 10 (3, 15)  | 10 (3, 15)                 | 9 (5, 15)                   |         |
| Initial INR          |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 2.26±3.16   | 2.81±3.74                  | 1.11±0.17                   | 0.029†  |
| Median (min, max)    | 1.28 (0.87, 18.38) | 1.9 (0.87, 18.38) | 1.07 (0.9, 1.33)            |         |
| PLT                  |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 181.6±84.25 | 165.8±53.91                | 214.8±124.07                | 0.205†  |
| Median (min, max)    | 168 (64, 538) | 156 (64, 294)              | 196 (80, 538)               |         |
| ICU Stay             |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 15±11.85    | 15±11.7                    | 15±12.81                    | 1.000†  |
| Median (min, max)    | 12 (1, 44)  | 11 (1, 40)                 | 13.5 (1, 44)                |         |
| Hospital day         |             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 35.9±36.83  | 35.38±30.77                | 37±49.15                    | 0.672†  |
| Median (min, max)    | 25 (5, 171) | 31 (5, 135)                | 22 (9, 171)                 |         |
| Glasgow Outcome Scale|             |                            |                             |         |
| n                    | 31          | 21                         | 10                          |         |
| Mean±SD              | 2.77±1.18   | 2.67±1.06                  | 3±1.41                      | 0.660†  |
| Median (min, max)    | 3 (1, 5)    | 3 (1, 5)                   | 2.5 (1, 5)                  |         |
| Post OP intracranial bleeding | | | | |
| Present (%)           | 11 (35.48)  | 9 (42.86)                  | 2 (20)                      | 0.262†  |
| No (%)                | 20 (64.52)  | 12 (57.14)                 | 8 (80)                      |         |
| Transfusion pre OP FFP|             |                            |                             |         |
| Done (%)              | 10 (32.62)  | 10 (47.62)                 | -                           | 0.012†  |
| Not done (%)          | 21 (67.38)  | 11 (52.38)                 | 10 (100)                    |         |
| Transfusion Intra OP FFP|         |                             |                             |         |
| Done (%)              | 14 (45.16)  | 13 (61.9)                  | 1 (10)                      | 0.009†  |
| Not done (%)          | 17 (54.84)  | 8 (38.1)                   | 9 (90)                      |         |

*p-value according to the t-test, †p-value according to the Wilcoxon rank sum test, ‡p-value according to the chi-square test, §p-value according to the Fisher’s exact test.

GCS : Glasgow Coma Scale, PLT : platelet, INR : internal normalized ratio, ICU : intensive care unit, FFP : fresh frozen plasma
tively \((p=0.660)\).

Postoperative bleeding was observed in 9 patients (42.86) in the preinjury anticoagulated group with low-energy trauma and in 2 patients (20\%) in the non-anticoagulated group with low-energy trauma \((p=0.262)\).

The effect of the preinjury anticoagulation and antiplatelet medications

The antiplatelet medications such as aspirin, clopidogrel and cilostazol, and the anticoagulation medications such as warfarin and heparin have different effect. So we conduct comparative analysis to find out differences between the group of preinjury antiplatelet medication, the group of preinjury anticoagulation medication, and the group not having any medication in low energy trauma patients.

Consequently we could find significant differences in the initial INR, pre OP FFP transfusion, intra OP FFP transfusion and intra OP platelet medication between three groups. And other fac-

### Table 3. The effect of preinjury antiplatelet medication and preinjury anticoagulation medications

|                          | Total (n=31) | Antiplatelet (n=7) | Anticoagulation (n=14) | Not having antiplatelet and anticoagulation, both (n=10) | \(p\)-value |
|--------------------------|-------------|-------------------|------------------------|----------------------------------------------------------|-------------|
| Age                      |             |                   |                        |                                                          |             |
| Mean±SD                  | 72.32±11.23 | 72.29±12.84       | 76.5±6.82              | 66.5±13.34                                               | 0.096\*     |
| Median (min, max)        | 74 (45, 91) | 70 (55, 89)       | 76.5 (64, 91)          | 70 (45, 85)                                              |             |
| Sex                      |             |                   |                        |                                                          |             |
| M (%)                    | 17 (54.84)  | 2 (28.57)         | 9 (64.29)              | 6 (60)                                                   | 0.329\†     |
| F (%)                    | 14 (45.16)  | 5 (71.43)         | 5 (35.71)              | 4 (40)                                                   |             |
| Rotterdam CT score       |             |                   |                        |                                                          |             |
| Mean±SD                  | 3.65±1.4    | 4.43±0.53         | 3.5±1.34               | 3.3±1.77                                                 | 0.216\†     |
| Median (min, max)        | 4 (1, 6)    | 4 (4, 5)          | 3.5 (1, 6)             | 3.5 (1, 6)                                               |             |
| Initial INR              |             |                   |                        |                                                          |             |
| Mean±SD                  | 2.26±3.16   | 1.3±0.75          | 3.56±4.41              | 1.1±0.17                                                 | 0.002\‡     |
| Median (min, max)        | 1.28 (0.87, 18.38) | 1.02 (0.87, 2.99) | 2.35 (0.94, 18.38)     | 1.07 (0.9, 1.33)                                        |             |
| PLT                      |             |                   |                        |                                                          |             |
| Mean±SD                  | 81.61±84.25 | 192.57±146.73    | 152.43±53.71           | 214.8±124.07                                            | 0.100\†     |
| Median (min, max)        | 68 (64, 538) | 168 (144, 256)  | 141 (64, 294)          | 196 (80, 538)                                           |             |
| Initial GCS score        |             |                   |                        |                                                          |             |
| Mean±SD                  | 9.74±3.69   | 10.29±3.25        | 9.86±4                 | 9.2±3.82                                                 | 0.836\†     |
| Median (min, max)        | 10 (3, 15)  | 9 (6, 15)         | 10 (3, 15)             | 9 (5, 15)                                                |             |
| Glasgow Outcome Scale    |             |                   |                        |                                                          |             |
| Mean±SD                  | 2.77±1.18   | 3.43±0.79         | 2.29±0.99              | 3±1.4                                                   | 0.090\‡     |
| Median (min, max)        | 3 (5)       | 3 (5)             | 2.5 (1, 4)             | 2.5 (1, 5)                                               |             |
| ICU Stay                 |             |                   |                        |                                                          |             |
| Mean±SD                  | 15±11.85    | 20±11.49          | 12.5±11.39             | 15±12.81                                                 | 0.338\‡     |
| Median (min, max)        | 12 (1, 44)  | 22 (5, 37)        | 8.5 (1, 40)            | 13.5 (1, 44)                                             |             |
| Hospital day             |             |                   |                        |                                                          |             |
| Mean±SD                  | 35.9±36.83  | 55.86±41.19       | 25.14±18.3             | 37±49.15                                                 | 0.108\‡     |
| Median (min, max)        | 25 (5, 171) | 35 (16, 135)      | 21 (5, 54)             | 22 (9, 171)                                              |             |
| Post OP intracranial bleeding |         |                   |                        |                                                          |             |
| Present (%)              | 11 (35.48)  | 3 (42.86)         | 6 (42.86)              | 2 (20)                                                   | 0.558\‡     |
| No (%)                   | 20 (64.52)  | 4 (57.14)         | 8 (57.14)              | 8 (80)                                                   |             |
| Transfusion pre OP FFP   |             |                   |                        |                                                          |             |
| Done (%)                 | 10 (32.26)  | 1 (14.29)         | 9 (64.29)              | -                                                        | 0.001\‡     |
| Not done (%)             | 21 (67.74)  | 6 (85.71)         | 5 (35.71)              | 10 (100)                                                 |             |
| Transfusion intra OP FFP |             |                   |                        |                                                          |             |
| Done (%)                 | 14 (45.16)  | 6 (85.71)         | 7 (30)                 | 1 (10)                                                   | 0.008\‡     |
| Not done (%)             | 17 (54.84)  | 1 (14.29)         | 7 (50)                 | 9 (90)                                                   |             |
| Transfusion intra OP PLT |             |                   |                        |                                                          |             |
| Done (%)                 | 4 (12.9)    | 3 (42.86)         | 1 (7.14)               | -                                                        | 0.034\‡     |
| Not done (%)             | 27 (87.1)   | 4 (57.14)         | 13 (92.86)             | 10 (100)                                                 |             |

* \(p\)-value via ANOVA, \(p\)-value via Wallis test, \(p\)-value via Fisher’s exact test, GCS : Glasgow Coma Scale, PLT : platelet, INR : International Normalized Ratio, ICU : intensive care unit, FFP : fresh frozen plasma
Table 4. p-value corrected for type I error by multiple range test in three groups

|                              | Bonferroni p-value | Hochberg’s p-value |
|------------------------------|--------------------|--------------------|
| Initial INR*                 | 0.037              | 0.025              |
| Antiplatelet vs. anticoagulation | 1.000              | 0.773              |
| Antiplatelet vs. not having antiplatelet, anticoagulation both | 0.004              | 0.004              |
| Anticoagulation vs. not having antiplatelet, anticoagulation both | 0.006              | 0.006              |
| Transfusion pre OP FFP†      | 0.191              | 0.127              |
| Antiplatelet vs. anticoagulation | 1.000              | 0.412              |
| Antiplatelet vs. not having antiplatelet, anticoagulation both | 0.005              | 0.001              |
| Anticoagulation vs. not having antiplatelet, anticoagulation both | 0.237              | 0.158              |
| Transfusion intra OP FFP†     | 0.263              | 0.175              |
| Antiplatelet vs. anticoagulation | 0.011              | 0.011              |
| Antiplatelet vs. not having antiplatelet, anticoagulation both | 0.237              | 0.158              |
| Anticoagulation vs. not having antiplatelet, anticoagulation both | 1.000              | 1.000              |

*Wilcoxon rank sum test, †Fisher’s exact test. INR: International Normalized Ratio, ICU: intensive care unit, FFP: fresh frozen plasma

Clinical factors associated with poor outcomes
Preinjury anticoagulation therapy has been revealed to predict the occurrence of postoperative bleeding (adjusted OR,
12.242; \( p=0.0070 \). Evaluating brain conditions on initial brain CT by using the Rotterdam scale for CT scans has been revealed to predict prognosis of patients with traumatic brain injury. Huang et al.\(^5\) evaluated 127 patients from January 2007 to December 2008 retrospectively and find that higher Rotterdam CT scores were accompanied by higher rates of poor prognosis. In our study, Rotterdam scale scores for CT scans had proven to predict poor neurological outcomes in terms of GOS score. Thus,

### Table 5. Factors associated with post OP intracranial hemorrhage: univariate analysis

|                          | Total (n=50) | Present (n=13) | None (n=37) | Unadjusted OR | 95% CI lower limit | 95% CI upper limit | \( p \)-value |
|--------------------------|-------------|----------------|-------------|---------------|--------------------|--------------------|-------------|
| **Age**                  |             |                |             |               |                    |                    |             |
| Mean±SD                  | 64.4±16.8   | 70.3±11.21     | 62.3±18.07  | 1.033         | 0.988              | 1.080              | 0.148       |
| Median (min, max)        | 67 (18, 91) | 71 (55, 91)    | 66 (18, 89) |               |                    |                    |             |
| **Sex**                  |             |                |             |               |                    |                    |             |
| M (ref) (%)              | 32 (64)     | 6 (46.15)      | 26 (70.27)  | 1.000         |                    |                    |             |
| F (%)                    | 18 (36)     | 7 (53.85)      | 11 (29.73)  | 2.758         | 0.753              | 10.103             | 0.126       |
| **Low vs. high energy**  |             |                |             |               |                    |                    |             |
| Low energy (ref) (%)     | 31 (62)     | 11 (84.62)     | 20 (54.05)  | 1.000         |                    |                    |             |
| High energy (%)          | 19 (38)     | 2 (15.38)      | 17 (45.95)  | 0.214         | 0.042              | 1.102              | 0.065       |
| **Antiplatelet or anticoagulation** |           |                |             |               |                    |                    |             |
| (-) (ref) (%)            | 24 (48)     | 10 (76.92)     | 14 (37.84)  | 1.000         |                    |                    |             |
| 000 (+) (%)              | 26 (52)     | 3 (23.08)      | 23 (62.16)  | 5.475         | 1.283              | 23.369             | 0.022       |
| **Initial GCS**          |             |                |             |               |                    |                    |             |
| Mean±SD                  | 8.66±3.73   | 8.46±2.7       | 8.73±4.07   | 0.980         | 0.826              | 1.164              | 0.822       |
| Median (min, max)        | 8 (3, 15)   | 8 (5, 14)      | 8 (3, 15)   |               |                    |                    |             |
| **Rotterdam CT scale**   |             |                |             |               |                    |                    |             |
| 1–3 (ref) (%)            | 16 (32)     | 4 (30.77)      | 12 (32.43)  | 1.000         |                    |                    |             |
| 4–6 (%)                  | 34 (68)     | 9 (69.23)      | 25 (67.57)  | 1.080         | 0.276              | 4.225              | 0.912       |
| **Initial INR**          |             |                |             |               |                    |                    |             |
| Mean±SD                  | 1.87±2.5    | 2.96±4.7       | 1.48±0.89   | 1.341         | 0.793              | 2.269              | 0.274       |
| Median (min, max)        | 1.17 (0.87,18.38) | 1.32 (0.98,18.38) | 1.1 (0.87,4.58) |               |                     |                    |             |
| **Initial platelet count** |             |                |             |               |                    |                    |             |
| Mean±SD                  | 196.8±87.3  | 179.2±11.2     | 203.0±18.0  | 0.996         | 0.988              | 1.005              | 0.397       |
| Median (min, max)        | 177.5 (64,538) | 168 (64,339)  | 181 (80,538) |               |                     |                    |             |
| **Transfusion intra OP PLT** |           |                |             |               |                    |                    |             |
| Done (%)                 | 41 (82)     | 12 (92.31)     | 29 (78.38)  | 1.000         |                    |                    |             |
| Not done (%)             | 9 (18)      | 1 (7.69)       | 8 (21.62)   | 0.302         | 0.034              | 2.686              | 0.283       |
| **Transfusion post OP FFP** |           |                |             |               |                    |                    |             |
| Done (%)                 | 18 (36)     | 4 (30.77)      | 14 (37.84)  | 1.000         |                    |                    |             |
| Not done (%)             | 32 (64)     | 9 (69.23)      | 23 (62.16)  | 1.370         | 0.354              | 5.295              | 0.649       |

PLT : platelet, FFP : fresh frozen plasma

### Table 6. Factors associated with post OP intracranial hemorrhage: multivariate analysis

|                          | Adjusted OR | 95% CI lower limit | 95% CI upper limit | \( p \)-value |
|--------------------------|-------------|--------------------|--------------------|-------------|
| **Antiplatelet or anticoagulation** |           |                    |                    |             |
| (-) (ref)                | 1.000       |                    |                    |             |
| (+)                      | 12.242      | 1.963              | 76.338             | 0.007       |
| **Transfusion intra OP PLT** |           |                    |                    |             |
| Done                     | 1.000       |                    |                    |             |
| Not done                 | 0.070       | 0.005              | 0.927              | 0.044       |
| **Transfusion post OP PLT** |           |                    |                    |             |
| Done                     | 1.000       |                    |                    |             |
| Not done                 | 8.690       | 1.442              | 52.380             | 0.018       |
### Table 7. Factors associated with Glasgow Outcome Scale: univariate analysis

|                    | Total (n=50) | Favorable (n=12) | Unfavorable (n=38) | Unadjusted OR | 95% CI lower limit | 95% CI upper limit | p-value |
|--------------------|--------------|------------------|--------------------|---------------|---------------------|---------------------|---------|
| **Age**            | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 64.42±16.83      | 52.92±19.96        | 68.05±14.15   | 1.058               | 1.012               | 1.105   | 0.012   |
|                    | Median (min, max) | 67 (18, 91) | 51.5 (18, 82) | 69.5 (36, 91) |                     |                     |         |
| **Sex**            | M(ref) (%)   | 32 (64)          | 8 (66.67)          | 24 (63.16)    | 1.000               |                     |         |
|                    | F (%)        | 18 (36)          | 4 (33.33)          | 14 (36.84)    | 1.167               | 0.297               | 4.588   | 0.825   |
| **Low vs. high energy** |            |                  |                    |               |                     |                     |         |
|                    | Low energy (ref) (%) | 31 (62) | 7 (58.33) | 24 (63.16) | 1.000               |                     |         |
|                    | High energy (%) | 19 (38)          | 5 (41.67)          | 14 (36.84)    | 0.817               | 0.217               | 3.068   | 0.764   |
| **Antiplatlet or anticoagulation** | (-) (ref) (%) | 26 (52)          | 8 (66.67)          | 18 (47.37)    | 1.000               |                     |         |
|                    | (+) (%)      | 24 (48)          | 4 (33.33)          | 20 (52.63)    | 2.222               | 0.571               | 8.647   | 0.249   |
| **Initial GCS**    | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 8.66±3.73        | 10.67±3.75         | 8.03±3.54     | 0.818               | 0.677               | 0.990   | 0.039   |
|                    | Median (min, max) | 8 (3, 15) | 10.5 (3, 15) | 7.5 (3, 15) |                     |                     |         |
| **Rotterdam CT score** | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 3.96±1.46        | 2.5±1.17           | 4.42±1.22     | 3.112               | 1.594               | 6.075   | 0.001   |
|                    | Median (min, max) | 4 (1, 6) | 2.5 (1, 4) | 5 (1, 6) |                     |                     |         |
| **Initial INR**    | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 1.87±2.53        | 2.72±4.96          | 1.6±0.93      | 0.860               | 0.658               | 1.125   | 0.272   |
|                    | Median (min, max) | 1.17 (0.87, 18.38) | 1.11 (0.9, 18.38) | 1.2 (0.87, 4.58) |                     |                     |         |
| **Initial platelet count** | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 196.88±87.34     | 201.08±87.04       | 195.55±88.56  | 0.999               | 0.992               | 1.007   | 0.847   |
|                    | Median (min, max) | 177.5 (64, 538) | 198.5 (80, 366) | 172 (64, 538) |                     |                     |         |
| **ICU Stay**       | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 13.06±11.12      | 7.83±9.61          | 14.71±11.16   | 1.088               | 0.990               | 1.196   | 0.081   |
|                    | Median (min, max) | 9.5 (1, 44) | 5 (1, 37) | 12.5 (1, 44) |                     |                     |         |
| **Hospital day**   | n            | 50               | 12                 | 38            |                     |                     |         |
|                    | Mean±SD      | 31.78±34.2       | 28±34.45           | 32.97±34.49   | 1.005               | 0.984               | 1.027   | 0.660   |
|                    | Median (min, max) | 22 (1, 171) | 18.5 (9, 135) | 24 (1, 171) |                     |                     |         |
| **Post OP intracranial hemorrhage** | None (%) | 37 (74)          | 10 (83.33)         | 27 (71.05)    | 1.000               |                     |         |
|                    | Present (%)  | 13 (26)          | 2 (16.67)          | 11 (28.95)    | 2.037               | 0.383               | 10.845  | 0.404   |

GCS: Glasgow Coma Scale, PLT: platelet, INR: international normalized ratio, ICU: intensive care unit, FFP: fresh frozen plasma

### Table 8. Factors associated with Glasgow Outcome Scale: multivariate analysis

|                    | Adjusted OR | 95% CI lower limit | 95% CI upper limit | p-value |
|--------------------|-------------|--------------------|--------------------|---------|
| **Age**            | 1.073       | 1.004              | 1.148              | 0.039   |
| **Rotterdam CT score** | 3.123    | 1.546              | 6.309              | 0.002   |
when patients with traumatic brain injury arrive at the emergency department, CT must be performed immediately in order to evaluate brain condition and predict patient outcome. Age was a statistically significant predictor of neurological outcome. Thus, older patients require more careful management.

Limitations of the study
The present study had a retrospective design, which typically produces less accurate results than those with a prospective, randomized, multicenter design. And there were only small number of patients in the high-energy trauma group, especially preinjury anticoagulated patients.

CONCLUSION
Preinjury anticoagulation therapy contributed significantly to the occurrence of postoperative bleeding. However, preinjury anticoagulation therapy in the patients with low-energy trauma did not contribute to the poor clinical outcomes. Careful attention should be given to older patients and severity of hemorrhage on initial brain CT because these factors predict poor outcomes. In particular, low Rotterdam scale scores contribute significantly to poor neurological outcomes, with a threefold higher risk than high Rotterdam scale scores.

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