The Incidence, Clinical Outcomes, and Risk Factors of Thrombocytopenia in Intra-Abdominal Infection Patients: A Retrospective Cohort Study

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Abstract

Background

Studies on the incidence and risk factors of thrombocytopenia among intra-abdominal infection patients remain absent, hindering efficacy assessments regarding thrombocytopenia prevention strategies.

Methods

We retrospectively studied 267 consecutively enrolled patients with intra-abdominal infections. Occurrence of thrombocytopenia was scanned for all patients. All-cause 28-day mortality was recorded. Variables from univariate analyses that were associated with occurrence of hospital-acquired thrombocytopenia were included in a multivariable logistic regression analysis to determine thrombocytopenia predictors.

Results

Median APACHE II score and SOFA score of the whole cohort was 12 and 3 respectively. The overall ICU mortality was 7.87% and the 28-day mortality was 8.98%. The incidence of thrombocytopenia among intra-abdominal infection patients was 21.73%. Regardless of pre-existing or hospital-acquired one, thrombocytopenia is associated with an increased ICU mortality and 28-day mortality as well as length of ICU or hospital stay. A higher SOFA and ISTH score at admission were significant hospital-acquired thrombocytopenia risk factors.

Conclusions

This is the first study to identify a high incidence of thrombocytopenia in patients with intra-abdominal infections. Our findings suggest that the inflammatory milieu of intra-abdominal infections may uniquely predispose those patients to thrombocytopenia. More effective thrombocytopenia prevention strategies are necessary in intra-abdominal infection patients.
Introduction

Intra-abdominal infections (IAIs), defined as infections occurring within an abdominal organ or in the abdominal cavity, are a frequent and dangerous entity in the treatment of critically illness patients.[1] Although the therapeutic techniques including pharmaceutical and radiographic interventions develop a lot, the overall mortality in patients with IAIs remains to exceed 10% and IAI brings a substantial burden for patients, surgeons, and the healthcare system.[2, 3]

Independent of the cause, patients with IAIs are at high risk of severe complications. Thrombocytopenia is one of the very common laboratory abnormalities among IAI patients.[4, 5] The underlying pathogenesis of thrombocytopenia in IAI remains incompletely understood, but is thought to be the result of multiple factors, including immobility, activation of thrombo-inflammatory pathways, disseminated intravascular coagulation (DIC), and venous stasis.[5–7]

Recently, the epidemiology of thrombocytopenia has been investigated by several studies as well as the impact of thrombocytopenia on outcomes among critically illness patients[8]. However, depending on its definition and the category of patients in which it was studied, the prevalence and incidence of thrombocytopenia in ICU varied a lot.[5, 9] Most of those well-conducted studies were performed in more heterogeneous groups of critically illness patients. [5, 10] To date, there remain no studies investigating thrombocytopenia incidence, clinical outcome and risk factors specifically in IAI patients. This absence of data limits advances in the prevention of thrombocytopenia among these IAIs patients. Thus, identification of the incidence, the impact on the outcome and risk factors of thrombocytopenia in IAI patients remains paramount. The purpose of this study was to retrospectively determine the incidence, clinical characteristics, outcomes and predictors of thrombocytopenia in a large cohort of IAI patients.

Method

Study Population

This retrospective database cohort study was conducted at Jinling Hospital, Nanjing, China. The Jinling Hospital is a national tertiary academic medical center for the treatment of gastrointestinal fistula. The study was approved by the Institutional Review Board of Jinling Hospital and informed consent was not required because of the anonymous and the observational nature of the study. Consecutive adult admissions from January 1, 2013 to December 31, 2014 were identified from a prospectively collected hospital database via individual chart review. Patient database information at our hospital is either collected automatically by computer or is entered by physicians. Specialized software (Haitai Software, Nanjing Haitai Medical Information System Company, Nanjing, China) is used to monitor integrity of the data.

Study Protocol

All patients admitted during the study period were scanned for the diagnosis of IAI according to the medical records. IAI in this study was defined as: (1) Patient has organisms cultured from purulent material from intra-abdominal space obtained during a surgical operation or needle aspiration; (2) Patient has abscess or other evidence of intra-abdominal infection seen during a surgical operation or histopathologic examination; (3) Patient has at least two of the following signs or symptoms with no other recognized cause: fever, nausea, vomiting, abdominal pain, or jaundice and at least one of the following: (a) Organisms cultured from drainage from surgically placed drain; (b) Organisms seen on Gram stain of drainage or tissue obtained during surgical operation or needle aspiration; (c) Organisms cultured from blood and radiographic evidence of infection. [11]
For patients with IAI, the occurrence of thrombocytopenia is determined. In this study, thrombocytopenia was defined as a peripheral platelet count < 100×10^9/L, or a relative platelet count drop of > 50% from baseline. Patients whose age were less than 18 years at admission were excluded.

Based on platelet counts at admission, patients were divided into a preexisting thrombocytopenia group and a non-preexisting thrombocytopenia group. For patients without thrombocytopenia at admission, records of platelet counts during hospitalization were reviewed to identify any episodes of thrombocytopenia. According to the platelet count during hospitalization, patients without preexisting thrombocytopenia were further categorized as hospital-acquired thrombocytopenia group and non-hospital-acquired thrombocytopenia group.

To explore the risk factor of thrombocytopenia, database records of patients were reviewed. Using the DIC scoring system of the Japanese Association for Acute Medicine DIC scoring system (JAAM score) and the DIC score of the International Society of Thrombosis and Haemostasis (ISTH score), we determined if any episodes of DIC occurred during thrombocytopenia in our department.

**Data collection**

In our hospital, laboratory test, including routine analysis of blood would be done within 4 h after admission for all patients to establish the baseline. Data recorded routinely on admission also included age, gender, primary and secondary admission diagnoses, and surgical procedures preceding admission. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, the JAAM score and the ISTH score were calculated by the attending physician who was in charge of the patient. After admission, venous blood for all laboratory tests, including platelet counts would be drawn whenever required, according to the judgment of the attending physician (available 24 hrs/day). Usually, laboratory values were calculated at least once per day during ICU stay or at least every other day during hospital stay. After obtaining the blood sample, laboratory values were calculated within 2 hours of blood collection. To be specific, platelet counts were measured with the Beckman Coulter LH 750 (Beckman Coulter, Miami, FL, USA). Other laboratory parameters at admission and during hospitalization were collected, including white red blood cell counts, C-reactive protein, blood cell counts, international normalized ratio, pro-thrombin time, activated partial thromboplastin time, fibrinogen, Alkaline Phosphatase, Alanine aminotransferase, Aspartate amino Transferase, gamma-glutamyl transpeptidase, blood urea nitrogen and electrolytes. Records of bleeding events, mechanical ventilation events, and renal replacement therapy event during hospitalization were extracted.

**Statistical Analyses**

Data were analyzed with SPSS Statistics 17 (SPSS Software, Chicago, IL, USA), Origin software (version 3.78; Microcal Software Inc., Northampton, MA) and GraphPad Prism (GraphPad Software, San Diego, CA, USA). Discrete variables are expressed as counts (percentage) and continuous variables as means ± SD or median and interquartile range (IQR) unless stated otherwise. The Kolmogorov—Smirnov test was used to verify the normality of distribution of continuous variables. Categorical variables were compared with the chi-squared test. Continuous variables conforming to a normal distribution were compared using analysis of variance and Student’s t test; otherwise the Kruskal—Wallis and Mann—Whitney U test was applied. Cumulative survival curves were constructed with the Kaplan-Meier method; the log-rank test was used to assess statistical differences between survival curves. To assess the risk factors for hospital-acquired thrombocytopenia and to determine if preexisting or hospital-acquired
thrombocytopenia were independent predictors of mortality, multivariate analyses were performed with logistic regression. The level of significance was set at 0.05.

**Results**

A total of 1,026 consecutive patients admitted to our department during the study period were included in. Among them, 17 were excluded because of age was less than 18 year at admission. For the remaining 1,009 patients, 267 patients who admitted as IAI were enrolled in (Fig 1). Table 1 summarized the baseline characteristics of the study population. Accompanied by a male predominance, the mean ages of the whole cohort were 49.45. Surgical complication and traffic accident were the most common primary disease that caused the IAI. The median APACHE II score and SOFA score was 12 and 3, respectively. More than half of the patients were admitted into ICU. The overall ICU mortality was 7.87% and the 28-day mortality was 8.98%. The median ICU length of stay (LOS) was 7 days and the hospital LOS was 29 days. The average platelet counts in enrolled patients within 28 days after admission was demonstrated in Fig 2.

**Preexisting thrombocytopenia at hospital admission**

Fig 3 showed the distribution of platelet counts of all patients on admission. The incidence of preexisting thrombocytopenia at hospital admission among IAI patients were 8.99% (24 out of 267, Fig 1) while only 1.62% (12/742) non-IAI patients admitted to hospital with preexisting thrombocytopenia. Demographic data of the patients with pre-existing thrombocytopenia had no significant differences compared with those without preexisting thrombocytopenia (Table 2). Fig 4 demonstrated the changing trend of platelet counts in patients with or without preexisting thrombocytopenia after admission. The platelet counts in preexisting thrombocytopenia patients were significantly lower than those without preexisting thrombocytopenia.
Table 1. Demographics, Clinical and Outcome data of all enrolled patients.

| Parameters                                  | All enrolled patients (n = 267) |
|---------------------------------------------|---------------------------------|
| Demographic Data                            |                                 |
| Age, mean (SD),y                            | 49.45 (15.89)                   |
| Male, n (%)                                 | 193 (72.28)                     |
| BMI, mean (SD),                             | 20.56 (3.69)                    |
| Primary Disease, n (%)                      |                                 |
| Traffic accident                            | 38 (14.23)                      |
| Injury a                                     | 34 (12.73)                      |
| Surgical complication b                     | 161 (60.30)                     |
| Others                                      | 34 (12.73)                      |
| Fistula location, n (%)                     |                                 |
| Small bowel                                 | 74 (27.72)                      |
| Colon                                       | 56 (20.97)                      |
| Duodenum                                    | 31 (11.61)                      |
| Pancreas                                    | 12 (4.49)                       |
| Stomach                                     | 18 (6.74)                       |
| Multiple viscera c                          | 76 (28.46)                      |
| Clinical Data (at admission)                |                                 |
| APACHE II Score, median (SD)                | 12 (4)                          |
| SOFA score, median (SD)                     | 3 (1)                           |
| ISTH, median (SD)                           | 0 (0)                           |
| JAAM, median (SD)                           | 1 (1)                           |
| WBC, mean (SD),×10⁹/L                       | 10.31 (6.79)                    |
| RBC, mean (SD),×10⁹/L                       | 3.52 (0.76)                     |
| PC, mean (SD),×10⁹/L                        | 260.88 (146.76)                 |
| CRP, mean (SD), mg/L                        | 67.85 (65.21)                   |
| PCT, mean (SD), ng/mL                       | 3.40 (11.29)                    |
| INR, mean (SD)                              | 1.18 (0.15)                     |
| PT, mean (SD), s                            | 13.60 (1.82)                    |
| APTT, mean (SD), s                          | 34.29 (7.45)                    |
| Fib, mean (SD), g/L                         | 3.71 (1.25)                     |
| Serum albumin, mean (SD),g/L                | 34.11 (6.18)                    |
| ALP, mean (SD),U/L                          | 129.55 (101.78)                 |
| ALT, mean (SD),U/L                          | 51.21 (180.55)                  |
| AST, mean (SD),U/L                          | 52.73 (184.28)                  |
| GG, mean (SD),U/L                           | 118.54 (141.92)                 |
| Bilirubin, mean (SD),umol/L                 | 31.23 (41.57)                   |
| Creatinine, mean (SD),umol/L                | 71.44 (70.62)                   |
| BUN, mean (SD), mmol/L                      | 7.16 (6.76)                     |
| Serum sodium, mean (SD),mmol/L              | 138.10 (5.73)                   |
| Serum potassium, mean (SD),mmol/L           | 4.13 (0.70)                     |
| Serum chloride, mean (SD),mmol/L            | 101.76 (5.78)                   |
| Serum calcium, mean (SD),mmol/L             | 2.11 (0.20)                     |
| Serum phosphorus, mean (SD),mmol/L          | 1.30 (0.36)                     |
| Mechanical ventilation, n (%)               | 26 (9.73)                       |
| Renal replacement therapy, n (%)            | 12 (4.49)                       |
| Incidence of preexisting thrombocytopenia, n (%) | 24 (8.99)                     |
| Incidence of hospital-acquired thrombocytopenia, n (%) | 34 (13.99)                     |

(Continued)
within 7 days after admission. For the outcome data, patients with preexisting thrombocytopenia at admission had higher ICU and 28-day mortality rates, as well as a longer ICU LOS compared with patients without preexisting thrombocytopenia (Table 2). The survival analysis showed the significant difference in 28-day mortality in patients with or without preexisting thrombocytopenia (S1 Fig). In a multivariable logistic regression analysis, occurrence of pre-existing thrombocytopenia was independently associated with a greater risk of 28-day death (OR 4.739; 95% CI 1.038–16.280; p = 0.013, Table 3).

Hospital-Acquired Thrombocytopenia

For patients without preexisting thrombocytopenia, at least one episode of hospital-acquired thrombocytopenia was occurred in 13.99% (34/243) of the cohort (Fig 1) while only 3.23% (24/742) of non-IAI patients experienced hospital-Acquired Thrombocytopenia. Fig 5 showed the distribution of the nadir of the platelet count during hospitalization in patients without pre-existing thrombocytopenia. The changing trend of platelet counts in hospital-acquired and non-

| Parameters | All enrolled patients (n = 267) |
|------------|---------------------------------|
| Incidence of ICU administration, n (%) | 144 (53.92) |
| Reasons for ICU administration, n (%) | |
| Organ dysfunction | 16 (5.99) |
| Unstable hemodynamic status | 15 (5.62) |
| Post damage control surgery | 43 (16.10) |
| Others | 6 (2.25) |
| Undetermined | 64 (23.97) |
| Outcome Data | |
| Hospital mortality, n (%) | 35 (13.11) |
| 28-day mortality, n (%) | 24 (8.98) |
| ICU mortality, n (%) | 21 (7.87) |
| ICU LOS d, median (IQR),d | 7 (9) |
| ICU LOS e, median (IQR),d | 6 (11) |
| Hospital LOS f, median (IQR),d | 29 (30) |
| Hospital LOS g, median (IQR),d | 32 (31) |
| Hospital cost, median (IQR), dollar | 30,837.33 (29,501) |

BMI: Body Mass Index; APACHE: Acute Physiology and Chronic Health Evaluation; WBC: white blood cell; RBC: red blood cell; PC: platelet count; CRP: C-reactive protein; INR: International Normalized Ratio; PT: prothrombin time; APTT: activated partial thromboplastin time; Fib: fibrinogen; ALP: Alkaline Phosphatase; ALT: Alanine aminotransferase; AST: Aspartate amino Transferase; GGT: gamma-glutamyl transpeptidase; BUN: blood urea nitrogen; LOS: length of stay; IQR: interquartile range;

a Injury includes gunshot, falling, cuts, bruising
b Patients who developed into intra-abdominal infection after elective surgery were categorized as surgical complication
c For all ICU patients Includes appendicitis, ileus, several nonmalignant processes, pancreatitis, cholecystitis, and vascular disease
d For all ICU patients
e For ICU survivors
f For all patients
g For all survivors

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hospital-acquired thrombocytopenic patients during hospitalizations was demonstrated in Fig 6. Patients with hospital-acquired thrombocytopenia had higher severity scores at admission (Table 4). During hospitalization, platelet counts in hospital-acquired thrombocytopenic patients were significantly lower than those with non-hospital-acquired thrombocytopenic patients. The ICU and 28-day mortality rates in hospital-acquired thrombocytopenic patients were significantly higher and a longer ICU LOS was demonstrated compared to those who did not experience thrombocytopenia throughout their hospital stay. The survival analysis showed the significant difference in 28-day mortality in patients with or without hospital-acquired thrombocytopenia (S2 Fig). In a multivariable logistic regression analysis, the occurrence of hospital-acquired thrombocytopenia was independently associated with 28-day mortality (OR 41.236; 95% CI 11.138–152.669; p < 0.001, Table 5).

In order to predict the occurrence of hospital-acquired thrombocytopenia in patients without preexisting thrombocytopenia at admission, we used logistic regression analysis to determine the risk factors for hospital-acquired thrombocytopenia (Table 6). In particular, SOFA score and ISTH score at admission is associated with the occurrence of hospital-acquired thrombocytopenia.
Discussion

In this study, we retrospectively investigated thrombocytopenia incidence, outcomes, and risk factors in intra-abdominal infection patients. The principal findings were that both preexisting and hospital-acquired thrombocytopenia were common among patients diagnosed as intra-abdominal infection. The occurrence of thrombocytopenia, regardless the preexisting or the hospital-acquired one, was associated with worse outcomes and a longer hospital or ICU LOS. Risk factor analysis indicated SOFA score and ISTH score at admission could be a predictor of hospital-acquired thrombocytopenia for patients without preexisting thrombocytopenia.

Although some other studies have investigated the epidemiology of thrombocytopenia in surgical critical care patients[12], to our knowledge, this is the first study to investigate the epidemiology of thrombocytopenia and its possible impact on adverse outcomes in a large cohort of IAI patients.

IAIs are frequent and dangerous entity in ICU. Mortality and morbidity of IAIs are high, causes are numerous, and treatment options are varied.[3, 11] The intensivist is challenged to recognize and treat IAIs in a timely fashion to prevent complications including thrombocytopenia. Thrombocytopenia, which is one of the most commonly observed laboratory abnormalities in ICU population, has an incidence ranging from 13.0% to 44.1%, depending on the study.

![Distribution of platelet counts at admission for all enrolled patients. 24 IAI patients were admitted with preexisting thrombocytopenia.](https://example.com/platelet-counts)
Table 2. Characteristics and Outcome of the Study Cohort According to the platelet count at Admission.

| Parameters                        | Preexisting Thrombocytic patients (n = 24) | Non-preexisting thrombocytic patients (n = 243) | P    |
|-----------------------------------|--------------------------------------------|-----------------------------------------------|------|
| **Demographic Data**              |                                            |                                               |      |
| Age, mean (SD), y                 | 55.71 (16.99)                              | 48.84 (15.68)                                 | 0.063|
| Male, n (%)                       | 17 (70.83)                                 | 176 (72.43)                                   | 0.947|
| BMI, mean (SD),                   | 19.55 (4.55)                               | 20.65 (3.61)                                  | 0.236|
| **Primary Disease, n (%)**        |                                            |                                               | 0.237|
| Traffic accident                  | 1 (4.17)                                   | 37 (15.22)                                    |      |
| Injury a                          | 2 (8.33)                                   | 32 (13.17)                                    |      |
| Surgical complication b           | 19 (79.17)                                 | 142 (58.44)                                   |      |
| Others                            | 2 (8.33)                                   | 32 (13.17)                                    |      |
| **Clinical Data (at admission)**  |                                            |                                               |      |
| APACHE II Score, median (SD)      | 13 (4.5)                                   | 12 (4)                                        | 0.142|
| SOFA score, median (SD)           | 4.5 (3)                                    | 3 (1)                                         | <0.001|
| ISTH score, median (SD)           | 0 (0)                                      | 0 (0)                                         | 0.124|
| JAAM score, median (SD)           | 1 (1)                                      | 1 (1)                                         | 0.126|
| WBC, mean (SD),×10^9/L            | 10.35 (7.79)                               | 10.30 (6.70)                                  | 0.971|
| RBC, mean (SD),×10^9/L            | 3.05 (0.73)                                | 3.57 (0.74)                                   | 0.003|
| PC, mean (SD),×10^9/L             | 59.16 (24.48)                              | 281.32 (138.25)                               | <0.001|
| CRP, mean (SD), mg/L              | 100.84 (68.62)                             | 64.47 (64.05)                                 | 0.022|
| PCT, mean (SD), ng/mL             | 17.64 (22.64)                              | 1.55 (5.17)                                   | <0.001|
| INR, mean (SD)                    | 1.28 (0.17)                                | 1.17 (0.15)                                   | 0.004|
| PT, mean (SD), s                  | 14.86 (1.94)                               | 13.47 (1.77)                                  | 0.003|
| APTT, mean (SD), s                | 36.90 (7.77)                               | 34.04 (7.40)                                  | 0.128|
| Fib, mean (SD), g/L               | 2.94 (1.36)                                | 3.79 (1.21)                                   | 0.039|
| Serum albumin, mean (SD), g/L     | 38.21 (4.67)                               | 34.71 (6.00)                                  | <0.001|
| ALP, mean (SD), U/L               | 123.25 (87.21)                             | 130.19 (103.33)                               | 0.722|
| ALT, mean (SD), U/L               | 44.91 (33.62)                              | 51.88 (189.73)                                | 0.864|
| AST, mean (SD), U/L               | 52.10 (44.87)                              | 52.79 (192.47)                                | 0.971|
| GGT, mean (SD), U/L               | 112.35 (137.22)                            | 119.19 (142.74)                               | 0.838|
| Bilirubin, mean (SD), umol/L       | 66.99 (69.78)                              | 27.22 (35.19)                                 | 0.018|
| Creatinine, mean (SD), umol/L      | 79.72 (65.34)                              | 70.57 (71.24)                                 | 0.584|
| BUN, mean (SD), mmol/L             | 13.81 (10.75)                              | 6.46 (5.81)                                   | <0.001|
| Serum sodium, mean (SD), mmol/L    | 141.68 (6.65)                              | 137.73 (5.51)                                 | 0.013|
| Serum potassium, mean (SD), mmol/L | 3.73 (0.54)                                | 4.17 (0.70)                                   | 0.005|
| Serum chloride, mean (SD), mmol/L  | 105.84 (8.41)                              | 101.39 (5.34)                                 | 0.042|
| Serum calcium, mean (SD), mmol/L   | 1.98 (0.21)                                | 2.12 (0.19)                                   | 0.010|
| Serum phosphorus, mean (SD), mmol/L| 1.08 (0.28)                                | 1.32 (0.35)                                   | 0.001|
| Mechanical ventilation, n (%)      | 3 (33.33)                                  | 23 (33.74)                                    | 0.632|
| Renal replacement therapy, n (%)   | 2 (29.17)                                  | 2 (31.28)                                     | 0.341|
| Incidence of ICU administration, n (%)| 17 (53.92)                               | 127 (53.92)                                   | 0.082|
| **Outcome Data**                  |                                            |                                               |      |
| Hospital mortality, n (%)          | 24 (100.00%)                               | 11 (6.99)                                     | <0.001|
| 28-day mortality, n (%)            | 16 (66.67)                                 | 8 (3.29)                                      | <0.001|
| ICU mortality, n (%)               | 11 (45.83)                                 | 10 (4.11)                                     | <0.001|
| ICU LOS c, median (IQR), d         | 12 (22.75)                                 | 6 (10)                                        | 0.030|
| ICU LOS d, median (IQR), d         | 15.5 (64.5)                                | 6 (8)                                         | <0.001|

(Continued)
Table 2. (Continued)

| Parameters                              | Preexisting Thrombocypenic patients (n = 24) | Non-preexisting thrombocypenic patients (n = 243) | P     |
|-----------------------------------------|---------------------------------------------|--------------------------------------------------|-------|
| Hospital LOS <sup>a</sup>, median (IQR),d | 29 (33)                                     | 29 (30)                                          | 0.226 |
| Hospital LOS <sup>1</sup>, median (IQR),d | 39 (32.5)                                    | 31 (32)                                          | 0.859 |
| Hospital cost, median (IQR), dollar     | 49,850 (48,650.62)                          | 29,753.37 (27,272.6)                            | <0.001|

BMI: Body Mass Index; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sepsis-related Organ Failure Assessment; ISTH: international society of thrombosis and haemostasis; JAAM: Japanese Association for Acute Medicine DIC scoring system; WBC: white blood cell; RBC: red blood cell; PC: platelet count; CRP: C-reaction protein; PCT: procalcitonine; INR: International Normalized Ratio; PT: prothrombin time; APTT: activated partial thromboplastin time; Fib: fibrinogen; ALP: Alkaline Phosphatase; ALT: Alanine aminotransferase; AST: Aspartate amino Transferase; GGT: gamma-glutamyl transpeptidase; BUN: blood urea nitrogen; LOS: length of stay; IQR: interquartile range;

<sup>a</sup> Injury includes gunshot, falling, cuts, bruising
<sup>b</sup> Patients who developed into intra-abdominal infection due to elective surgery were categorized as surgical complication
<sup>c</sup> For all ICU patients
<sup>d</sup> For ICU survivors
<sup>e</sup> For all patients
<sup>f</sup> For all survivors

Fig 4. Changing trend of platelet counts in preexisting thrombocypenic and non-preexisting thrombocypenic patients after admission over time. A statistically significant difference was exhibited between preexisting thrombocypenia group and non-preexisting group after admission. * p<0.05.

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population, the timing and frequency of platelet monitoring, and the definition of thrombocytope-

Table 3. Multivariate analysis of preexisting thrombocytopenia and other covariates associated with 28-day mortality.

| Variables                              | Odds Ratio | 95% CI  | P value |
|----------------------------------------|------------|---------|---------|
|                                        | lower      | upper   |         |
| Age                                    |            |         |         |
| <49                                    | 1.000      | -       | -       |
| >=49                                   | 1.566      | 0.616   | 3.982   | 0.346   |
| Gender                                 |            |         |         |
| Female                                 | 1.000      | -       | -       |
| Male                                   | 1.451      | 0.526   | 4.002   | 0.472   |
| BMI                                    |            |         |         |
| <20.5                                  | 1.008      | 0.417   | 2.437   | 0.986   |
| >=20.5                                 | 1.000      | -       | -       |
| Primary diagnosis                      |            |         |         |
| Surgical complication                  | 0.983      | 0.368   | 2.629   | 0.973   |
| Non-surgical complication              | 1.000      | -       | -       |
| APACHE II score at admission           |            |         |         |
| <12                                    | 2.113      | 0.813   | 5.488   | 0.125   |
| >=12                                   | 1.000      | -       | -       |
| SOFA score at admission                |            |         |         |
| <4                                     | 0.832      | 0.340   | 2.034   | 0.686   |
| >=4                                    | 1.000      | -       | -       |
| ISTH score at admission                |            |         |         |
| <1                                     | 0.370      | 0.074   | 1.848   | 0.225   |
| >=1                                    | 1.000      | -       | -       |
| JAAM score at admission                |            |         |         |
| <1                                     | 0.892      | 0.360   | 2.207   | 0.804   |
| >=1                                    | 1.000      | -       | -       |
| Occurrence of preexisting thrombocytope-

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thrombocytopenia may be related to the expectedly lower severity of illness in IAI patients than other surgical ICU patients.

Our data characterize demographic data associated with preexisting thrombocytopenia and hospital acquired thrombocytopenia in IAI patient population. Preexisting thrombocytopenic patients had higher severity scores and more likely elder compared to those without preexisting thrombocytopenia. Anemia and disorder of electrolytes are significantly prevalent among pre-existing thrombocytopenic patients, with a higher CRP and PCT level. It indicates that platelet may have a complex interaction with the immune system during infection. For hospital-acquired thrombocytopenia patients, they have a higher SOFA score and also more likely elder compared to others. The disorders of coagulation at admission are significantly more common in hospital-acquired thrombocytopenia patients. It raises the possibility that most of the hospital-acquired thrombocytopenia is not really “hospital acquired” but is derived from implicit coagulation disorders at admission. Still, more studies are needed to confirm our speculation.

We found that either preexisting thrombocytopenia or hospital-acquired thrombocytopenia is associated with mortality. The association between thrombocytopenia and mortality has been well established in mixed critical illness patients. We confirmed the associations in IAI patients. Moreover, our multivariate analysis indicates that the hospital-acquired
Fig 6. Changing trend of platelet counts in hospital-acquired thrombocytopenic and non-hospital-acquired thrombocytopenic patients after admission over time. A statistically significantly difference was exhibited between hospital-acquired thrombocytopenia group and non-hospital-acquired group after admission. * p<0.05.

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Table 4. Characteristics and Outcome of the Study Cohort According to the platelet count at Admission.

| Parameters                                | Hospital-acquired Thrombocytopenic patients (n = 34) | Non-Hospital-acquired Thrombocytopenic patients (n = 209) | P     |
|-------------------------------------------|-----------------------------------------------------|-----------------------------------------------------------|-------|
| Demographic Data                          |                                                     |                                                           |       |
| Age, mean (SD), y                         | 53.23 (14.85)                                       | 48.12 (15.73)                                             | 0.078 |
| Male, n (%)                               | 24 (70.59)                                          | 152 (72.73)                                               | 0.796 |
| BMI, mean (SD),                           | 20.23 (3.24)                                        | 20.72 (3.67)                                              | 0.502 |
| Primary Disease, n (%)                    |                                                     |                                                           | 0.548 |
| Traffic accident                          | 7 (20.59)                                           | 30 (14.35)                                                |       |
| Injury a                                   | 6 (17.65)                                           | 26 (12.44)                                                |       |
| Surgical complication b                   | 18 (52.94)                                          | 124 (59.33)                                               |       |
| Others                                    | 3 (8.82)                                            | 29 (13.88)                                                |       |
| Clinical Data (at admission)              |                                                     |                                                           |       |
| APACHE II Score, median (SD)              | 12 (4)                                              | 12 (2.5)                                                  | 0.780 |
| SOFA score, median (SD)                   | 4 (3)                                               | 3 (1)                                                     | <0.001|
| ISTH score, median (SD)                   | 0 (0)                                               | 0 (0)                                                     | 0.059 |
| JAAM score, median (SD)                   | 0 (1)                                               | 1 (1)                                                     | 0.623 |

(Continued)
### Table 4. (Continued)

| Parameters | Hospital-acquired Thrombocypenic patients (n = 34) | Non- Hospital-acquired Thrombocypenic patients (n = 209) | P |
|------------|--------------------------------------------------|--------------------------------------------------------|---|
| WBC, mean (SD),×10⁹/L | 9.99 (5.73) | 10.35 (6.86) | 0.777 |
| RBC, mean (SD),×10⁹/L | 2.92 (0.69) | 3.68 (0.70) | <0.001 |
| PC, mean (SD),×10⁹/L | 190.00 (114.76) | 296.08 (136.27) | <0.001 |
| CRP, mean (SD), mg/L | 84.39 (62.87) | 61.03 (63.78) | 0.053 |
| PCT, mean (SD),ng/mL | 2.29 (3.61) | 1.42 (5.42) | 0.471 |
| INR, mean (SD) | 1.27 (0.16) | 1.15 (0.14) | <0.001 |
| PT, mean (SD), s | 14.69 (1.87) | 13.26 (1.66) | <0.001 |
| APTT, mean (SD), s | 38.03 (11.57) | 33.29 (6.09) | <0.001 |
| Fib, mean (SD), g/L | 3.15 (1.08) | 3.90 (1.20) | <0.001 |
| Serum albumin, mean (SD),g/L | 32.34 (6.43) | 35.15 (5.84) | 0.013 |
| ALP, mean (SD),U/L | 132.61 (133.97) | 129.72 (96.74) | 0.885 |
| ALT, mean (SD),U/L | 34.50 (27.56) | 55.10 (206.13) | 0.574 |
| AST, mean (SD),U/L | 38.14 (23.32) | 56.45 (215.00) | 0.699 |
| GGT, mean (SD),U/L | 29.13 (23.32) | 123.92 (145.98) | 0.296 |
| Bilirubin, mean (SD),umol/L | 29.34 (41.94) | 24.99 (33.49) | 0.043 |
| Creatinine, mean (SD),umol/L | 116.93 (150.54) | 61.93 (37.79) | <0.001 |
| BUN, mean (SD), mmol/L | 9.12 (8.64) | 5.97 (5.00) | 0.004 |
| Serum sodium, mean (SD),mmol/L | 137.13 (5.69) | 137.84 (5.49) | 0.469 |
| Serum potassium, mean (SD),mmol/L | 3.99 (0.78) | 4.20 (0.68) | 0.974 |
| Serum chloride, mean (SD),mmol/L | 101.36 (5.92) | 101.39 (5.25) | 0.042 |
| Serum calcium, mean (SD),mmol/L | 2.14 (0.17) | 2.14 (0.19) | 0.030 |
| Serum phosphorus, mean (SD),mmol/L | 1.19 (0.44) | 1.35 (0.33) | 0.020 |
| Mechanical ventilation, n (%) | 2 (8.33) | 20 (9.57) | 0.845 |
| Renal replacement therapy, n (%) | 2 (8.33) | 8 (3.83) | 0.302 |
| Incidence of ICU administration, n (%) | 30 (88.24) | 97 (47.55) | <0.001 |
| **Outcome Data** | | | |
| Hospital mortality, n (%) | 24 (100.00%) | 11 (6.99) | <0.001 |
| 28-day mortality, n (%) | 10 (29.41) | 6 (2.87) | <0.001 |
| ICU mortality, n (%) | 11 (45.83) | 4 (1.91) | <0.001 |
| ICU LOS a, median (IQR),d | 13 (21.25) | 5 (7) | 0.030 |
| ICU LOS b, median (IQR),d | 12.5 (28.25) | 5 (6) | <0.001 |
| Hospital LOS a, median (IQR),d | 30 (42.5) | 29 (30) | 0.226 |
| Hospital LOS b, median (IQR),d | 47 (56) | 30 (30) | 0.859 |
| Hospital cost, median (IQR), dollar | 54,497.55 (33,022.63) | 33,183.67 (23,037.21) | <0.001 |

BMI: Body Mass Index; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sepsis-related Organ Failure Assessment; ISTH: international society of thrombosis and haemostasis; JAAM: Japanese Association for Acute Medicine DIC scoring system; WBC: white blood cell; RBC: red blood cell; PC: platelet count; CRP: C-reaction protein; PCT: procalcitonin; INR: International Normalized Ratio; PT: prothrombin time; APTT: activated partial thromboplastin time; Fib: fibrinogen; ALP: Alkaline Phosphatase; ALT: Alanine aminotransferase; AST: Aspartate amino Transferase; GGT: gamma-glutamyl transpeptidase; BUN: blood urea nitrogen; LOS: length of stay; IQR: interquartile range;

a Injury includes gunshot, falling, cuts, bruising
b Patients who developed into intra-abdominal infection due to elective surgery were categorized as surgical complication
c For all ICU patients
d For ICU survivors
e For all patients
f For all survivors

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Thrombocytopenia has a more severe negative impact on the mortality compared with the pre-existing thrombocytopenia. Since the occurrence of preexisting thrombocytopenia can hardly be interrupted, hospital-acquired thrombocytopenia may be more clinically important than the preexisting one. The future study should focus on the intervention to prevent the hospital-acquired thrombocytopenia, which may bring a direct improvement of mortality in IAI patients.

The risk factor for developing hospital-acquired thrombocytopenia has been evaluated in our study. A higher SOFA score and ISTH score at admission are associated the occurrence of hospital-acquired thrombocytopenia, which may bring a direct effect on platelet count. This finding indicates that various factors were involved in the process.

This study has several important limitations. In our study cohort, we only investigated the platelet count within 28 days after admission. In 2013, we had conducted a prospective study to evaluate the efficiency of recombinant human thrombopoietin, which has a direct effect on platelet count.[17] Confounding factors may bring in although administration of thrombopoietin in IAI patients has a limited impact on the occurrence of thrombocytopenia. Because of

### Table 5. Multivariate analysis of hospital acquired thrombocytopenia and other covariates associated with mortality.

| Variables                          | Odds Ratio | 95% CI     | P value |
|-----------------------------------|------------|------------|---------|
|                                   | lower      | upper      |         |
| Age                               |            |            |         |
| <49                               | 0.773      | 0.235      | 2.524   | 0.671   |
| >=49                              | 1.000      | -          | -       |         |
| Gender                            |            |            |         |
| Female                            | 1.000      | -          | -       |         |
| Male                              | 1.202      | 0.294      | 4.908   | 0.798   |
| BMI                               |            |            |         |
| <20.5                             | 0.634      | 0.185      | 2.178   | 0.469   |
| >=20.5                            | 1.000      | -          | -       |         |
| Primary diagnosis                 |            |            |         |
| Surgical complication             | 1.954      | 0.178      | 21.510  | 0.584   |
| Non-surgical complication         | 1.000      | -          | -       |         |
| APACHE II score at admission      |            |            |         |
| <12                               | 1.000      | -          | -       |         |
| >=12                              | 3.161      | 0.929      | 10.754  | 0.065   |
| SOFA score at admission           |            |            |         |
| <4                                | 1.000      | -          | -       |         |
| >=4                               | 1.055      | 0.305      | 3.656   | 0.932   |
| ISTH score at admission           |            |            |         |
| <1                                | 1.000      | -          | -       |         |
| >=1                               | 1.387      | 0.291      | 4.241   | 0.801   |
| JAAM score at admission           |            |            |         |
| <1                                | 1.000      | -          | -       |         |
| >=1                               | 2.360      | 0.694      | 8.019   | 0.169   |
| Occurrence of hospital-acquired thrombocytopenia | 41.236      | 11.138     | 152.669 | <0.001 |
| No                                | 1.000      | -          | -       |         |

95% CI: 95% confidence interval

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the study design, making a diagnosis of the cause of thrombocytopenia is extremely challenging and the causes of thrombocytopenia were not fully determined. We did not elaborate on relevant therapeutics, such as antibiotics administration, because of the retrospective nature of the study. As with all retrospective database studies, there are concerns about observation bias. Despite these weaknesses, this study does provide an important and novel evaluation of thrombocytopenia in IAI patients.

Supporting Information

S1 Fig. Survival Analysis. A significant difference in mortality was observed between preexisting thrombocytopenia patients and non-preexisting thrombocytopenia patients. (TIF)

S2 Fig. Survival Analysis. A significant difference in mortality was observed between hospital-acquired thrombocytopenia patients and non-hospital-acquired thrombocytopenia patients. (TIF)

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Author Contributions

Conceived and designed the experiments: QW JR JL. Performed the experiments: QW GL YZ. Analyzed the data: QW GL. Contributed reagents/materials/analysis tools: GW XW GG JC. Wrote the paper: XW YL.

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| Table 6. Logistic regression analysis of risk factors for developing hospital-acquired thrombocytopenia in patients without preexisting thrombocytopenia. |
|-----------------|-----------------|-----------------|-----------------|
| Variables       | Odds Ratio      | 95% CI          | P value         |
|                 | lower           | upper           |                 |
| Age             | 0.919           | 0.315           | 2.683           | 0.877 |
| Gender          | 1.021           | 0.988           | 1.055           | 0.210 |
| BMI             | 0.955           | 0.849           | 1.074           | 0.440 |
| Primary diagnosis | 0.796           | 0.481           | 1.317           | 0.374 |
| APACHE II score at admission | 0.925 | 0.779 | 1.099 | 0.376 |
| SOFA score at admission | 1.754 | 1.160 | 2.651 | 0.008 |
| ISTH score at admission | 6.209 | 1.563 | 24.663 | 0.009 |
| JAAM score at admission | 0.669 | 0.275 | 1.624 | 0.374 |

Primary diagnoses were categorized as trauma, surgical complication, IBD and others. 95% CI: 95% confidence interval

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