Aspirin Does Not Increase the Need for Hemostatic Interventions in Blunt Liver and Spleen Injuries.

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Research article

Keywords: Blunt trauma, hepatic, splenic, aspirin, transarterial angioembolization, surgeries, non-operative management

Posted Date: June 22nd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-36501/v1>

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Abstract

Background: The prohemorrhagic effect of aspirin may cause concern about worse prognoses when treating blunt hepatic or splenic injuries. This study investigated whether preinjury aspirin yields an increasing need for hemostatic interventions.

Methods: Admission and outpatient records were extracted from the Taiwan National Health Insurance Research Database (NHIRD) from 2003 to 2015. Patients with splenic or hepatic injuries were identified. Patients with preinjury nonaspirin APAC or with penetrating injuries were excluded. The primary outcome measurement was the necessity of invasive procedures to stop bleeding, including transarterial embolization (TAE) and surgeries. One-to-two propensity score matching (PSM) was used to minimize selection bias. Multilogistic regression (MLR) analysis was used to identify factors associated with hemostatic interventions.

Results: 20,470 (60.6%) had blunt hepatic injuries, and 15,235 (45.1%) had blunt splenic injuries, of whom 691 (3.4%) and 667 (4.4%) used preinjury aspirin, respectively. In the blunt hepatic injury cohort, there was no significant difference in the need for hemostatic procedures (TAE (6.1% vs 6.1%, $p=1.000$), exploratory laparotomy (6.1% vs 6.1%, $p=1.000$), hepatectomy (3.0% vs 2.7%, $p=0.694$) or hepatorrhaphy (14.3% vs 15.0%, $p=0.681$)). MLR analysis showed that preinjury aspirin did not increase the need for hemostatic interventions (OR 0.92, 95% CI 0.73-1.16, $p=0.473$). Regarding the blunt splenic injury cohort, there was no significant difference in the need for hemostatic procedures (TAE (11.5% vs 10.6%, $p=0.547$), splenectomy (43.5% vs 41.4%, $p=0.407$) or splenorhaphy (3.0% vs 3.3%, $p=0.698$)). An MLR analysis showed that preinjury aspirin did not increase the need for hemostatic interventions (OR 1.12, 95% CI 0.91-1.38, $p=0.290$).

Conclusions: Preinjury aspirin use is not associated with increased hemostatic procedures in blunt hepatic or splenic injuries.

Introduction

With the aging population, the use of antiplatelet agents or anticoagulants (APAC) is increasing rapidly.(1) Aspirin is effective in preventing thromboembolic events and is commonly used.(2, 3) There are approximately 18 million annual prescriptions for aspirin in the United States.(4) However, the adverse effect of bleeding can be a great concern.(5) Once trauma is encountered with concomitant aspirin use, the inability to achieve hemostasis can have disastrous results. Moreover, the underlying diseases of such patients and the prohemorrhagic effect of aspirin may result in worse prognosis and bring an additional burden to the medical care system.

Understanding the impact of aspirin on trauma patients is essential. In the management of patients with blunt hepatic or splenic injuries, it is important to achieve effective hemostasis. Although most blunt hepatic or splenic injuries can be managed conservatively, there are still patients who need hemostatic interventions, either surgical treatment or transarterial embolization (TAE). The role of preinjury aspirin should be determined in the management of patients with blunt hepatic or splenic injuries. To our knowledge, most studies have focused on overall mortality, blood transfusion requirements and hospital stay instead of treatment algorithm alterations.(1, 6, 7) Few reports have addressed the impact of preinjury aspirin on hemostatic procedures.

In the current investigation, the hypothesis was that preinjury aspirin use may result in an increasing need for hemostatic interventions. Accordingly, the failure rate of conservative treatment was expected to be higher among patients using aspirin and lead to more surgeries than those in patients without preinjury aspirin. A retrospective study using a nationwide population-based dataset was performed.

Materials And Methods

Data source

Admission and outpatient records were extracted from the Taiwan National Health Insurance Research Database (NHIRD). The National Health Insurance (NHI) program has covered more than 99.9% of the Taiwan population since March 1995. Nearly all medical institutes in Taiwan are covered in the NHI program. The NHI program includes inpatient and outpatient medical costs for nearly all therapeutic indications. All medications, examinations, and therapeutic procedures are recorded as NHI-specific order

codes and are the source for an insurance claim. The claims from the institutions are reviewed by an expert peer review system to verify the justifiability. The NHIRD has been maintained since 2000 and continues updating each year. All privacy-related information is encrypted and deidentified in the database. Each diagnosis is recorded and coded as the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Although there is no detailed registry of the injury severity score (ISS), major trauma with an ISS exceeding 16 is defined as a catastrophic disease and can be identified in the catastrophic illness database.

Study population and design

Patients with splenic injuries (ICD-9-CM 865.xx) or hepatic injuries (ICD-9-CM 864.xx) presenting between Jan 2003 and Dec 2015 were identified. Penetrating injuries (ICD-9-CM 864.1, 865.1, 866.1) were excluded. Per the regulation of the NHI of Taiwan, a three-month prescription for chronic diseases could be allowed. Therefore, we reviewed patients' preinjury APAC use within 92 days of index trauma admission, which was documented in the outpatient clinic and inpatient admission record; the drugs included aspirin, clopidogrel, cilostazol, warfarin, dabigatran, apixaban, edoxaban and rivaroxaban. Patients with preinjury intake of nonaspirin APAC were excluded. The study population and protocol of the current study are shown in Fig. 1.

Definition of comorbidities and associated injuries

The basic demographic information, comorbidities, and associated injuries were identified using the ICD-9-CM codes recorded before and during the index trauma admission (supplementary table 1). Pre-existing comorbidities related to possible long-term aspirin usage, including atrial fibrillation, hypertension, ischemic heart disease, congestive heart failure, valvular heart disease, peripheral vascular disease, hemorrhagic stroke, ischemic stroke, and sequelae of cerebral vascular disease, were identified. The associated injuries of index trauma episodes with possible bleeding complications, including intracranial hemorrhage (ICH), hemothorax, liver injury, kidney injury, spleen injury, pelvic fracture, and femoral fracture, were recorded. An ISS exceeding 16 was recognized from the catastrophic illness database from the NHI. All procedures performed during the index trauma emergency room visit and admission were analyzed (supplementary table 2).

Outcome measurement

The primary outcome measurement of this study was the necessity of invasive procedures to stop bleeding. TAE was treated as an invasive procedure to stop bleeding for all cohorts.(8–12) Additionally, other surgical procedures, including splenectomy, splenorrhaphy, exploratory laparotomy, hepatectomy and hepatorrhaphy, were characterized as hemostatic interventions in each target organ cohort. The secondary outcome measurement included blood product consumption, ventilator support days, intensive care unit (ICU) length of stay, ward length of stay, and in-hospital mortality.

Statistical analysis

The studied patients were separated into liver and spleen cohorts to analyze the influence of pre-existing aspirin on specific organs. Patients with blunt splenic or hepatic injuries were evaluated using the same statistical analyses. In the current study, we used two analytic approaches to evaluate the effect of aspirin on outcomes. First, a one-to-two propensity score matching (PSM) methodology was used to minimize the selection bias between the aspirin group and the control group, and pairs of these two groups were constructed with the greedy neighbor approach.(13) Covariables that may have affected the need for hemostatic interventions clinically were considered for PSM. These covariables included age, gender, year of injury, comorbidities, and associated injuries. A caliper setting of 0.1 was utilized.(13) Standardized mean differences (SMDs) were used to confirm a balanced matching result. When the SMD was less than 0.1, the matching result could be considered balanced.(14) After well-balanced matching, outcomes between aspirin groups and control groups patients were compared. Second, adjusted multivariate logistic regression (MLR) models were performed to evaluate the effect of aspirin on the requirements for hemostatic interventions in patients with blunt hepatic or splenic injury. The independent risk factors and the associated odds ratios for the necessity of hemostatic interventions were analyzed accordingly.

All statistical analyses were performed using SAS (version 9.4). The comparison of continuous variables was performed using a t test. Categorical variables were analyzed using the Chi-square test and Fisher's exact test. The risk factor analysis for outcome was performed with MLR. For each statistical analysis, a *p* value < 0.05 was considered statistically significant.

Results

During the study period, 38,660 patients had hepatic or splenic injuries. A total of 4,496 patients were excluded due to penetrating injuries, 34,184 patients sustained blunt hepatic or splenic injuries, and another 388 patients treated with nonaspirin APAC were excluded. A total of 33,796 patients were enrolled in the study (Supplementary Table 3). There were 20,470 (60.6%) patients with blunt hepatic injuries and 15,235 (45.1%) patients with blunt splenic injuries. Among the patients with blunt hepatic ($N = 20,470$) or splenic injuries ($N = 15,235$), 691 (3.4%) and 667 (4.4%) patients used preinjury aspirin, respectively. The study design and patient distribution are illustrated in Fig. 1.

Effect of preinjury aspirin on blunt hepatic injury

Compared with blunt hepatic injury patients who did not take aspirin before injury, the corresponding patients with preinjury aspirin had significantly more requirements for packed red blood cell (PRBC) transfusion (7.8 ± 12.5 vs. 6.5 ± 13.7 units, $p = 0.011$), more ventilator days (4.3 ± 10.0 vs. 2.6 ± 16.0 days, $p < 0.001$), longer ICU stays (6.6 ± 11.1 vs. 4.0 ± 8.0 days, $p < 0.001$) and more days in the ward (26.9 ± 36.5 vs. 15.5 ± 33.9 days, $p < 0.001$). There was no significant difference in the need for TAE (5.6% vs. 7.0%, $p = 0.165$), exploratory laparotomy (3.2% vs. 4.1%, $p = 0.252$), hepatectomy (3.2% vs. 3.5%, $p = 0.698$) or hepatorrhaphy (14.9% vs. 13.8%, $p = 0.416$) between patients with and without preinjury aspirin. However, after a 1:2 well-balanced PSM, there was no significant difference in the need for hemostatic procedures (TAE (6.1% vs 6.1%, $p = 1.000$), exploratory laparotomy (6.1% vs 6.1%, $p = 1.000$), hepatectomy (3.0% vs 2.7%, $p = 0.694$) or hepatorrhaphy (14.3% vs 15.0%, $p = 0.681$)); number of transfusions (whole blood (WB) (0.8 ± 12.5 vs. 0.6 ± 2.5 units, $p = 0.306$), PRBCs (7.8 ± 12.9 vs. 6.9 ± 12.4 units, $p = 0.145$), frozen fresh plasma (FFP) (6.6 ± 17.1 vs. 6.0 ± 24.6 units, $p = 0.545$) or platelets (3.1 ± 12.4 vs. 4.0 ± 17.4 units, $p = 0.179$)); length of hospital stay (ventilator days (4.3 ± 10.1 vs. 6.4 ± 54.4 days, $p = 0.189$), ICU days (6.5 ± 10.9 vs. 6.1 ± 12.9 days, $p = 0.545$) or ward days (26.1 ± 36.4 vs. 26.0 ± 77.1 days, $p = 0.980$)); or mortality (9.0% vs 7.5%, $p = 0.256$) between patients with and without preinjury aspirin. (Table 1) The details of comparisons before and after PSM are shown in Supplementary Table 4. In addition to PSM, an MLR analysis showed that in 20,675 blunt hepatic injury patients, preinjury aspirin did not increase the need for hemostatic interventions after adjusting for age, gender, comorbidities and associated injuries (OR 0.92, 95% CI 0.73–1.16, $p = 0.473$) (Table 2).

Table 1

Comparisons between patients with and without aspirin use, after 1:2 propensity score matching in patients with liver injuries (N = 1,905)

	With Aspirin (N = 635)	Without Aspirin (N = 1,270)	SMD *	p value
Interventions and surgeries				
TAE (N, %)	39 (6.1%)	78 (6.1%)	0.00	1.000 [†]
Exploratory laparotomy (N, %)	21 (3.3%)	54 (4.3%)	0.05	0.318 [†]
Hepatectomy (N, %)	19 (3.0%)	34 (2.7%)	0.02	0.694 [†]
Hepatorrhaphy (N, %)	91 (14.3%)	191 (15.0%)	0.02	0.681 [†]
All (N, %)	153 (24.1%)	313 (24.7%)	0.01	0.792 [†]
Transfusions				
WB (units) §	0.8 ± 4.0	0.6 ± 2.5	0.05	0.306 [‡]
PRBCs (units) §	7.8 ± 12.9	6.9 ± 12.4	0.07	0.145 [‡]
FFP (units) §	6.6 ± 17.1	6.0 ± 24.6	0.03	0.545 [‡]
Platelets (units) §	3.1 ± 12.4	4.0 ± 17.4	0.06	0.179 [‡]
Hospital length of stay				
Ventilator (days)	4.3 ± 10.1	6.4 ± 54.4	0.05	0.189 [‡]
ICU (days)	6.5 ± 10.9	6.1 ± 12.9	0.03	0.545 [‡]
Ward (days)	26.1 ± 36.4	26.0 ± 77.1	0.00	0.980 [‡]
Outcome				
Mortality (N, %)	57 (9.0%)	95 (7.5%)	0.05	0.256 [†]
Numerical data: mean ± standard deviation, Nominal data: N (percentage)				
* SMD (SMD ≥ 0.1 was considered statistically significant)				
[†] Chi-square test ($p < 0.05$ was considered statistically significant)				
[‡] Student's t test ($p < 0.05$ was considered statistically significant)				
§ Taiwan unit: blood products separated from 250 ml of whole blood				
SMD = standard mean difference, TAE: transarterial embolization, WB = whole blood, PRBC = packed red blood cell, FFP = fresh frozen plasma, ICU = intensive care unit				

Table 2
Multivariate logistic regression analysis for the predictors of
hemostatic interventions

	Liver			
	OR	95% CI	<i>p</i> value	
Age	1.01	0.99	1.01	0.070
Sex	1.33	1.06	1.67	0.014
Atrial fibrillation	0.93	0.55	1.58	0.790
Hypertension	1.09	0.79	1.52	0.590
Ischemic heart disease	0.80	0.63	1.01	0.061
Congestive heart failure	1.19	0.89	1.58	0.241
Valvular heart disease	0.90	0.64	1.26	0.537
Peripheral vascular disease	1.09	0.79	1.51	0.604
Hemorrhagic stroke	1.08	0.71	1.65	0.724
Ischemic stroke	0.90	0.70	1.17	0.435
Sequelae of CVA	1.34	0.94	1.91	0.110
Liver				
Spleen	2.60	1.85	3.66	<.001
Kidney	0.61	0.37	1.02	0.061
Intracranial hemorrhage	0.75	0.53	1.08	0.125
Hemothorax	0.77	0.59	1.01	0.061
Pelvic fracture	1.07	0.68	1.68	0.770
Femur fracture	0.92	0.56	1.50	0.725
ISS over 16	2.62	1.98	3.47	<.001
Preinjury aspirin	0.92	0.73	1.16	0.473
CVA: cerebrovascular accident; ISS: injury severity score				

Effect of preinjury aspirin on blunt splenic injury

Regarding blunt splenic injury, patients with preinjury aspirin had significantly more requirements for PRBCs (10.8 ± 12.9 vs. 8.0 ± 12.6 units, $p < 0.001$), FFP (8.6 ± 22.9 vs. 6.1 ± 18.0 units, $p = 0.004$) and platelet concentrates (4.5 ± 15.8 vs. 3.1 ± 14.7 units, $p = 0.024$). The preinjury aspirin group had longer ventilator use (7.6 ± 23.7 vs. 3.0 ± 34.9 days, $p < 0.001$) and hospital stays (ICU 8.9 ± 14.3 vs. 4.3 ± 8.9 days, $p < 0.001$, ward 30.3 ± 46.0 vs. 16.5 ± 44.0 days, $p < 0.001$). There was no significant difference in the need for TAE (11.8% vs. 10.5%, $p = 0.253$) or splenorrhaphy (3.2% vs. 3.9%, $p = 0.342$) between patients with and without preinjury aspirin. The splenectomy rate was higher in the preinjury aspirin group (42.9% vs. 36.2%, $p < 0.001$). However, after a 1:2 well-balanced PSM, there was no significant difference in the need for hemostatic procedures (TAE (11.5% vs 10.6%, $p = 0.547$), splenectomy (43.5% vs 41.4%, $p = 0.407$) or splenorrhaphy (3.0% vs 3.3%, $p = 0.698$); number of transfusions (WB (1.0 ± 3.4 vs. 1.0 ± 3.3 units, $p = 0.984$), PRBCs (11.0 ± 13.4 vs. 10.0 ± 13.2 units, $p = 0.164$), frozen fresh plasma (FFP) (8.6 ± 23.2 vs. 7.8 ± 15.6 units, $p = 0.475$) or platelets (4.3 ± 15.6 vs. 5.0 ± 18.4 units, $p = 0.411$)); or mortality (8.6% vs 7.8%, $p = 0.572$) between patients with and without preinjury aspirin. The preinjury aspirin group had a longer ICU stay (8.5 ± 13.2 vs. 7.1 ± 11.7 days, $p = 0.032$) but did not remain longer on the ventilator (7.2 ± 24.1 vs. 5.4 ± 22.5 days, $p = 0.120$) or in the ward (29.3 ± 46.8 vs. 26.6 ± 46.9 days, $p = 0.260$) (Table 3). The details of the comparisons before and after PSM are shown in Supplementary Table 5. In addition to PSM,

an MLR analysis showed that in 15,235 patients with blunt splenic injury, preinjury aspirin did not increase the need for hemostatic interventions after adjusting for age, gender, comorbidities and associated injuries (OR 1.12, 95% CI 0.91–1.38, $p = 0.290$) (Table 4).

Table 3

Comparisons between patients with and without aspirin after 1:2 propensity score matching in patients with spleen injuries (N = 1,716)

	With Aspirin (N = 572)	Without Aspirin (N = 1,144)	SMD *	<i>p</i> value
Interventions and surgeries				
TAE (N, %)	66 (11.5%)	121 (10.6%)	0.03	0.547 [†]
Splenectomy (N, %)	249 (43.5%)	474 (41.4%)	0.04	0.407 [†]
Splenorrhaphy (N, %)	17 (3.0%)	38 (3.3%)	0.02	0.698 [†]
All (N, %)	322 (56.3%)	616 (53.9%)	0.05	0.337 [†]
Transfusions				
WB (units) §	1.0 ± 3.4	1.0 ± 3.3	0.00	0.984 [‡]
PRBCs (units) §	11.0 ± 13.4	10.0 ± 13.2	0.07	0.164 [‡]
FFP (units) §	8.6 ± 23.2	7.8 ± 15.6	0.04	0.475 [‡]
Platelets (units) §	4.3 ± 15.6	5.0 ± 18.4	0.04	0.411 [‡]
Hospital stay				
Ventilator (days)	7.2 ± 24.1	5.4 ± 22.5	0.08	0.120 [‡]
ICU (days)	8.5 ± 13.2	7.1 ± 11.7	0.11	0.032 [‡]
Ward (days)	29.3 ± 46.8	26.6 ± 46.9	0.06	0.260 [‡]
Outcome				
Mortality (N, %)	49 (8.6%)	89 (7.8%)	0.03	0.572 [†]
Numerical data: mean ± standard deviation; Nominal data: N (percentage)				
* SMD (SMD ≥ 0.1 was considered statistically significant)				
[†] Chi-square test ($p < 0.05$ was considered statistically significant)				
[‡] Student's t test ($p < 0.05$ was considered statistically significant)				
§ Taiwan unit: blood products separated from 250 ml of whole blood				
SMD = standard mean difference, TAE = transarterial embolization, WB = whole blood, PRBC = packed red blood cell, FFP = fresh frozen plasma, ICU = intensive care unit				

Table 4
Multivariate logistic regression analysis for the predictors of hemostatic interventions in blunt splenic injury

Spleen				
	OR	95% CI		<i>p</i> value
Age	1.01	0.99	1.01	0.143
Sex	1.08	0.88	1.34	0.466
Atrial fibrillation	0.88	0.58	1.34	0.540
Hypertension	0.79	0.58	1.07	0.124
Ischemic heart disease	0.81	0.64	1.01	0.065
Congestive heart failure	1.17	0.91	1.52	0.226
Valvular heart disease	1.34	0.97	1.84	0.073
Peripheral vascular disease	1.25	0.90	1.73	0.189
Hemorrhagic stroke	0.73	0.50	1.07	0.104
Ischemic stroke	1.14	0.90	1.44	0.277
Sequelae of CVA	0.81	0.58	1.13	0.204
Liver	0.83	0.59	1.17	0.283
Spleen				
Kidney	0.78	0.54	1.11	0.165
Intracranial hemorrhage	1.04	0.74	1.48	0.809
Hemothorax	0.61	0.47	0.79	<.001
Pelvic fracture	0.70	0.41	1.19	0.187
Femur fracture	1.67	0.99	2.79	0.054
ISS over 16	3.38	2.61	4.38	<.001
Preinjury aspirin	1.12	0.91	1.38	0.290
ICD-9-CM				
Blunt hepatic or splenic injuries				
Hepatic injury	864.xx, not 864.1			

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen	
Splenic injury	865.xx, not 865.1
Associated injuries	
Intracranial hemorrhage	852.0, 852.2, 852.4, 853.0
Hemothorax	860.2, 860.4
Kidney injury	866.xx, not 866.1
Pelvic fracture	808.x
Femoral fracture	820, 821
Comorbidities	
Atrial fibrillation	427.31
Hypertension	401, 402
Ischemic heart disease	410–414
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x
Valvular heart disease	394, 395, 396, 424, V43.3
Peripheral vascular disease	440, 443, 557, V43.4
Hemorrhagic stroke	430.x–432.x
Ischemic stroke	433.x–437.x
Sequelae of CVA	438.x
Catastrophic illness	
ISS over 16	959.99

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen

ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification;
CVA: cerebrovascular accident;
ISS: injury severity score

Supplementary Table 2. National Health Insurance codes for interventions, blood transfusions and hospital stay.

code

Hemostatic interventions

Exploratory laparotomy	75805B
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Hepatectomy	75002B, 75003B, 75004B, 75005B, 75015B, 75016B, 75017B, 75018B
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Hepatorrhaphy	75007B, 75008B, 75009B
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Hepatic artery ligation	75010B
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Splenectomy	70001B, 70003B, 70006B
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Splenorrhaphy	70002B
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TAE	33075A, 33075B
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Blood transfusions

Whole blood (WB)	93013C
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Packed RBCs (PRBCs)	93001C, 93002C, 93003C, 93019C
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Frozen fresh plasma (FFP)	93010C
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Platelet concentrate	93004C
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Cryoprecipitate	93012C
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Hospital stay	
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CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen		
ICU	02011K, 02012A, 02013B	
Ward	02006K, 02007A, 02008B, 02014K, 02015A, 02016B	
Ventilator	57001B	
TAE: transarterial embolization; ICU: intensive care unit.		
Supplementary Table 3. Overview of the study population		
	Liver (N = 20,675)	Spleen (N = 15,418)
Age	35.9 ± 18.3	37.6 ± 19.1
Sex		
Male	13,381 (64.7%)	10,865 (70.5%)
Female	7,294 (35.3%)	4,553 (29.5%)
Comorbidities		
Atrial fibrillation	200 (1.0%)	276 (1.8%)
Hypertension	4,697 (22.7%)	4,079 (26.5%)
Ischemic heart disease	1,989 (9.6%)	1,712 (11.1%)
Congestive heart failure	858 (4.2%)	853 (5.5%)
Valvular heart disease	834 (4.0%)	677 (4.4%)
Peripheral vascular disease	638 (3.1%)	523 (3.4%)
Hemorrhagic stroke	776 (3.8%)	592 (3.8%)
Ischemic stroke	1,345 (6.5%)	1,260 (8.2%)
Sequalae of CVA	589 (2.9%)	543 (3.5%)
CVA: cerebrovascular accident; ISS: injury severity score		
Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities		

Spleen		
Medications		
Aspirin	743 (3.59%)	712 (4.62%)
Clopidogrel	99 (0.48%)	109 (0.71%)
Cilostazol	36 (0.17%)	24 (0.16%)
Warfarin	115 (0.56%)	90 (0.58%)
Dabigatran	0	0
Rivaroxaban	7 (0.03%)	6 (0.04%)
Edoxaban	0	0
Apixaban	0	0
Associated Injuries		
Liver	–	1,909 (12.4%)
Spleen	1,909 (9.2%)	–
Kidney	1,869 (9.0%)	1,658 (10.8%)
Intracranial hemorrhage	1,960 (9.5%)	1,247 (8.1%)
Hemothorax	3,688 (17.8%)	2,585 (16.8%)
Pelvic circle	1,316 (6.4%)	711 (4.6%)
Femur fracture	1,480 (7.2%)	767 (5.0%)
Interventions		
TAE	1,452 (7.0%)	1,632 (10.6%)
Operations		
Any	5,337 (25.8%)	7,896 (51.2%)
Exploratory laparotomy	845 (4.1%)	499 (3.2%)
Hepatectomy	717 (3.5%)	147 (1.0%)
Hepatorrhaphy	2,881 (13.9%)	689 (4.5%)
CVA: cerebrovascular accident; ISS: injury severity score		
Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities		

Spleen		
Splenectomy	800 (3.9%)	5,629 (36.5%)
Splenorrhaphy	130 (0.6%)	594 (3.9%)
Blood Transfusion		
WB	0.8 ± 3.5	0.9 ± 3.2
PRBCs	6.7 ± 13.9	8.2 ± 12.8
FFP	5.6 ± 17.3	6.2 ± 18.5
Platelets	3.2 ± 15.5	3.2 ± 15.1
Hospital Stay		
Ventilator	2.8 ± 20.5	3.3 ± 34.9
ICU	4.2 ± 9.1	4.6 ± 9.5
Ward	16.1 ± 35.5	17.4 ± 44.3
Severity and Outcome		
ISS over 16	4,004 (19.4%)	3,281 (21.3%)
Mortality	1,714 (8.3%)	1,069 (6.9%)

Numerical data: mean ± standard deviation

Nominal data: N (percentage)

CVA: cerebrovascular accident; TAE: transarterial embolization; WB: whole blood; PRBC: packed red blood cell; FFP: fresh frozen plasma; ICU: intensive care unit; ISS: injury severity score

Supplementary Table 4. Comparisons between patients with and without aspirin in liver injuries and the results after propensity score matching

Original					Propensity Score Matched, 1:2			
With Aspirin (N = 691)	Without Aspirin (N = 19779)	SMD *	<i>p</i> value		With Aspirin (N = 635)	Without Aspirin (N = 1270)	SMD *	<i>p</i> value

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen								
Age	59.8 ± 17.0	34.9 ± 17.6	1.44	< .001 ‡	58.3 ± 16.9	58.7 ± 17.0	0.02	0.622 ‡
Sex			0.05	0.224 †			0.08	0.121 †
Male	432 (62.5%)	12810 (64.8%)			395 (62.2%)	743 (58.5%)		
Female	259 (37.5%)	6969 (35.2%)			240 (37.8%)	527 (41.5%)		
Comorbidities								
Atrial fibrillation	51 (7.4%)	121 (0.6%)	0.35	< .001 †	36 (5.7%)	52 (4.1%)	0.07	0.123 †
Hypertension	573 (82.9%)	4004 (20.2%)	1.61	< .001 †	517 (81.4%)	1041 (82.0%)	0.01	0.769 †
Ischemic heart disease	403 (58.3%)	1490 (7.5%)	1.28	< .001 †	347 (54.7%)	684 (53.9%)	0.02	0.745 †
Congestive heart failure	171 (24.8%)	621 (3.1%)	0.66	< .001 †	137 (21.6%)	236 (18.6%)	0.07	0.121 †
Valvular heart disease	120 (17.4%)	672 (3.4%)	0.47	< .001 †	94 (14.8%)	157 (12.4%)	0.07	0.138 †
Peripheral vascular disease	101 (14.6%)	509 (2.6%)	0.44	< .001 †	77 (12.1%)	158 (12.4%)	0.01	0.844 †
Hemorrhagic stroke	54 (7.8%)	713 (3.6%)	0.18	< .001 †	44 (6.9%)	102 (8.0%)	0.04	0.394 †
Ischemic stroke	261 (37.8%)	1013 (5.1%)	0.87	< .001 †	207 (32.6%)	408 (32.1%)	0.01	0.835 †
Sequelae of CVA	117 (16.9%)	439 (2.2%)	0.52	< .001 †	81 (12.8%)	154 (12.1%)	0.02	0.694 †
Associated Injuries and Severity								
Spleen	62 (9.0%)	1847 (9.3%)	0.01	0.745 †	59 (9.3%)	105 (8.3%)	0.04	0.453 †
Kidney	39 (5.6%)	1830 (9.3%)	0.14	0.001 †	36 (5.7%)	72 (5.7%)	0.00	1.000 †
Intracranial hemorrhage	83 (12.0%)	1853 (9.4%)	0.09	0.020 †	79 (12.4%)	140 (11.0%)	0.04	0.361 †
Hemothorax	170 (24.6%)	3467 (17.5%)	0.17	< .001 †	151 (23.8%)	275 (21.7%)	0.05	0.294 †

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen								
Pelvic fracture	46 (6.7%)	1256 (6.4%)	0.01	0.745 †	43 (6.8%)	71 (5.6%)	0.05	0.306 †
Femur fracture	38 (5.5%)	1419 (7.2%)	0.07	0.092 †	37 (5.8%)	64 (5.0%)	0.03	0.470 †
ISS over 16	132 (19.1%)	3817 (19.3%)	0.01	0.898 †	124 (19.5%)	202 (15.9%)	0.10	0.048 †
Interventions and Operations								
TAE	39 (5.6%)	1387 (7.0%)	0.06	0.165 †	39 (6.1%)	78 (6.1%)	0.00	1.000 †
Exploratory laparotomy	22 (3.2%)	802 (4.1%)	0.05	0.252 †	21 (3.3%)	54 (4.3%)	0.05	0.318 †
Hepatectomy	22 (3.2%)	684 (3.5%)	0.02	0.698 †	19 (3.0%)	34 (2.7%)	0.02	0.694 †
Hepatorrhaphy	103 (14.9%)	2733 (13.8%)	0.03	0.416 †	91 (14.3%)	191 (15.0%)	0.02	0.681 †
Any	169 (24.5%)	4804 (24.3%)	0.01	0.919 †	153 (24.1%)	313 (24.7%)	0.01	0.792 †
Transfusions								
WB (unit) §	0.8 ± 3.8	0.8 ± 3.4	0.01	0.943 ‡	0.8 ± 4.0	0.6 ± 2.5	0.05	0.306 ‡
PRBCs (unit) §	7.8 ± 12.5	6.5 ± 13.7	0.10	0.011 ‡	7.8 ± 12.9	6.9 ± 12.4	0.07	0.145 ‡
FFP (unit) §	6.4 ± 16.5	5.5 ± 17.3	0.05	0.176 ‡	6.6 ± 17.1	6.0 ± 24.6	0.03	0.545 ‡
Platelets (unit) §	3.2 ± 12.8	3.1 ± 15.4	0.01	0.869 ‡	3.1 ± 12.4	4.0 ± 17.4	0.06	0.179 ‡
Hospital Stay								
Ventilator (day)	4.3 ± 10.0	2.6 ± 16.0	0.13	< .001 ‡	4.3 ± 10.1	6.4 ± 54.4	0.05	0.189 ‡
ICU (day)	6.6 ± 11.1	4.0 ± 8.0	0.28	< .001 ‡	6.5 ± 10.9	6.1 ± 12.9	0.03	0.545 ‡
Ward (day)	26.9 ± 36.5	15.5 ± 33.9	0.32	< .001 ‡	26.1 ± 36.4	26.0 ± 77.1	0.01	0.980 ‡
Outcome								
Mortality	59 (8.5%)	1633 (8.3%)	0.01	0.791 †	57 (9.0%)	95 (7.5%)	0.05	0.256 †
Numerical data: mean ± standard deviation; Nominal data: N (percentage)								

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen								
* SMD (SMD ≥ 0.1 was considered statistically significant)								
† Chi-square test ($p < 0.05$ was considered statistically significant)								
‡ Student's t test ($p < 0.05$ was considered statistically significant)								
§ Taiwan unit: blood products separated from 250 ml of whole blood								
SMD = standard mean difference, TAE = transarterial embolization, WB = whole blood, PRBC = packed red blood cell, FFP = fresh frozen plasma, ICU = intensive care unit								
Supplementary Table 5. Comparisons between patients with and without aspirin in spleen injury and the results after propensity score matching.								
Original					Propensity Score Matched, 1:2			
	With Aspirin (N = 667)	Without Aspirin (N = 14568)	SMD *	p value	With Aspirin (N = 572)	Without Aspirin (N = 1144)	SMD *	p value
Age	60.2 $\pm$ 17.3	36.3 $\pm$ 18.3	1.34	< .001 ‡	57.8 $\pm$ 17.3	57.7 $\pm$ 17.7	0.00	0.930 ‡
Sex			0.09	0.023 †			0.00	0.971 †
Male	444 (66.6%)	10296 (70.7%)			379 (66.3%)	757 (66.2%)		
Female	223 (33.4%)	4272 (29.3%)			193 (33.7%)	387 (33.8%)		
Comorbidities								
Atrial fibrillation	78 (11.7%)	162 (1.1%)	0.44	< .001 †	44 (7.7%)	65 (5.7%)	0.08	0.108 †
Hypertension	551 (82.6%)	3403 (23.4%)	1.48	< .001 †	456 (79.7%)	920 (80.4%)	0.02	0.732 †
Ischemic heart disease	379 (56.8%)	1237 (8.5%)	1.20	< .001 †	284 (49.7%)	577 (50.4%)	0.02	0.759 †
Congestive heart failure	192 (28.8%)	596 (4.1%)	0.71	< .001 †	133 (23.3%)	266 (23.3%)	0.00	1.000 †
Valvular heart disease	104 (15.6%)	536 (3.7%)	0.41	< .001 †	77 (13.5%)	136 (11.9%)	0.05	0.351 †
Peripheral vascular disease	83 (12.4%)	415 (2.9%)	0.37	< .001 †	64 (11.2%)	117 (10.2%)	0.03	0.541 †
Hemorrhagic stroke	55 (8.3%)	523 (3.6%)	0.20	< .001 †	43 (7.5%)	95 (8.3%)	0.03	0.572 †

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen								
Ischemic stroke	280 (42.0%)	903 (6.2%)	0.92	< .001 †	190 (33.2%)	371 (32.4%)	0.02	0.743 †
Sequelae of CVA	132 (19.8%)	364 (2.5%)	0.57	< .001 †	69 (12.1%)	136 (11.9%)	0.01	0.916 †
Associated Injuries and Severity								
Liver	62 (9.3%)	1847 (12.7%)	0.11	0.010 †	57 (10.0%)	114 (10.0%)	0.00	1.000 †
Kidney	52 (7.8%)	1606 (11.0%)	0.11	0.009 †	47 (8.2%)	94 (8.2%)	0.00	1.000 †
Intracranial hemorrhage	76 (11.4%)	1152 (7.9%)	0.12	0.001 †	65 (11.4%)	109 (9.5%)	0.06	0.235 †
Hemothorax	147 (22.0%)	2405 (16.5%)	0.14	< .001 †	131 (22.9%)	228 (19.9%)	0.07	0.154 †
Pelvic fracture	26 (3.9%)	678 (4.7%)	0.04	0.363 †	24 (4.2%)	41 (3.6%)	0.03	0.531 †
Femur fracture	30 (4.5%)	722 (5.0%)	0.02	0.593 †	29 (5.1%)	51 (4.5%)	0.03	0.571 †
ISS over 16	183 (27.4%)	3050 (20.9%)	0.15	< .001 †	153 (26.8%)	312 (27.3%)	0.01	0.818 †
Interventions and Operations								
TAE	79 (11.8%)	1523 (10.5%)	0.04	0.253 †	66 (11.5%)	121 (10.6%)	0.03	0.547 †
Splenectomy	286 (42.9%)	5271 (36.2%)	0.14	< .001 †	249 (43.5%)	474 (41.4%)	0.04	0.407 †
Splenorrhaphy	21 (3.2%)	564 (3.9%)	0.04	0.342 †	17 (3.0%)	38 (3.3%)	0.02	0.698 †
All	373 (55.9%)	7134 (49.0%)	0.14	< .001 †	322 (56.3%)	616 (53.9%)	0.05	0.337 †
Transfusions								
WB (unit) §	1.0 ± 3.5	0.9 ± 3.2	0.06	0.173 ‡	1.0 ± 3.4	1.0 ± 3.3	0.00	0.984 ‡
PRBCs (unit) §	10.8 ± 12.9	8.0 ± 12.6	0.22	< .001 ‡	11.0 ± 13.4	10.0 ± 13.2	0.07	0.164 ‡
FFP (unit) §	8.6 ± 22.9	6.0 ± 18.0	0.12	0.004 ‡	8.6 ± 23.2	7.8 ± 15.6	0.04	0.475 ‡
Platelets (unit) §	4.5 ± 15.8	3.1 ± 14.7	0.09	0.024 ‡	4.3 ± 15.6	5.0 ± 18.4	0.04	0.411 ‡

CVA: cerebrovascular accident; ISS: injury severity score

Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities

Spleen								
Hospital Stay								
Ventilator (day)	7.6 ± 23.7	3.0 ± 34.9	0.15	< .001 [‡]	7.2 ± 24.1	5.4 ± 22.5	0.08	0.120 [‡]
ICU (day)	8.9 ± 14.3	4.3 ± 8.9	0.39	< .001 [‡]	8.5 ± 13.2	7.1 ± 11.7	0.11	0.032 [‡]
Ward (day)	30.3 ± 46.0	16.5 ± 44.0	0.31	< .001 [‡]	29.3 ± 46.8	26.6 ± 46.9	0.06	0.260 [‡]
Outcome								
Mortality (N)	57 (8.6%)	1001 (6.9%)	0.06 [†]	0.096	49 (8.6%)	89 (7.8%)	0.03	0.572 [†]
Numerical data: mean ± standard deviation; Nominal data: N (percentage)								
* SMD (SMD ≥ 0.1 was considered statistically significant)								
† Chi-square test ($p < 0.05$ was considered statistically significant)								
‡ Student's t test ($p < 0.05$ was considered statistically significant)								
§ Taiwan Unit: blood products separated from 250 ml of whole blood								
SMD = standard mean difference, TAE = transarterial embolization, WB = whole blood, PRBC = packed red blood cell, FFP = fresh frozen plasma, ICU = intensive care unit								
CVA: cerebrovascular accident; ISS: injury severity score								
Supplementary Table 1. ICD-9-CM codes for blunt abdominal solid organ injuries, associated injuries, and comorbidities								

Discussion

Aspirin is of great value in preventing cardiovascular events and is commonly used.(2, 4) In the management of trauma patients, the bleeding tendency related to aspirin should be a major concern. However, if the injury patterns or injured organs are not specified, the evaluation of the effect of preinjury aspirin intake on bleeding risk would be fuzzy. The treatment modalities are somewhat diverse among various target organs in trauma. Careful reviews for specific body regions are necessary. For instance, it is difficult to manage ICH in the presence of platelet dysfunction or coagulopathy since one can neither use packing to apply pressure to the brain parenchyma nor employ angioembolization. Thus, the influence of aspirin on brain injury would not be the same as that on blunt abdominal trauma.

Literature reviews have reported that patients with preinjury aspirin have mortality rates comparable to those of nonaspirin controls.(15–17) Ferraris et al. reported that bleeding risk is not increased in antiplatelet-treated patients presenting with trauma. The researchers regarded the result as less potent platelet inhibition while using aspirin monotherapy.(1) For patients with head injury, aspirin monotherapy would not influence the risk of ICH, the need for surgical interventions or the mortality rate.(18–20) There is no strong evidence showing the benefit of reversing platelet function by transfusion in traumatic ICH patients.(21–24) Regarding non-head injuries, the available studies have reported that aspirin does not increase overall mortality or the need for blood transfusions.(15–17, 25) Regarding chest trauma, one series demonstrated that antiplatelet or anticoagulation drugs did not increase the complications of hemothorax in blunt chest wall trauma.(26) On the other hand, regarding pelvic fractures, Christy et al. found that antiplatelet therapy was associated with increased blood transfusions but not mortality or morbidity.(27) Therefore, it remains controversial whether preinjury aspirin might increase the difficulty of hemostasis.

Practically, patients sustaining trauma insults are relatively younger and healthy. The incidence of APAC use is low, which yields insufficient case numbers to conduct such research. Therefore, to date, most studies that address the impact of APAC on trauma are small case series. In the current population-based study, liver or spleen injuries were focused upon in a nationwide patient population, which can reflect the real-world situation. In addition, the current study excluded all other APAC drugs and dealt with aspirin only. Thus, the influence of aspirin could be clearly evaluated. The current study revealed that preinjury aspirin use does not increase the need for hemostatic interventions for blunt hepatic or splenic injuries. Indeed, multiple abdominal organ involvement and severity of trauma per se may be the major determinants for angioembolizations or operations. Regarding surgical treatments specifically, patients with preinjury aspirin intake did not require more operations than the PSM control group. It seems that nonoperative management can be safely performed in these patients. Furthermore, the amount of blood transfusion was similar between the preinjury aspirin and control groups without affecting the prognosis. Though not direct evidence, this has suggested that aggressive reversal of functional platelets by transfusions would not be beneficial in blunt abdominal trauma. Based on this study, the current treatment algorithm for blunt hepatic or splenic injuries would be applicable to patients with preinjury aspirin use, and this could be fundamental evidence for trauma treatment in the growing population of individuals taking aspirin.

In patients with chronic diseases, each APAC drug has its own characteristics, and combination use is also common. A large diversity exists among the selections of APAC drugs, including APAC monotherapy only or combination prescription. Understanding the features of each drug and each combination may be valuable for daily practice. Aspirin plays a fundamental role in such medications. Measurement of platelet and coagulation function could be a method. Attempts have been made to utilize laboratory examinations to quantify platelet function and predict clinical outcomes for trauma patients. However, the ability of various assays to detect preinjury aspirin use or predict clinical outcomes has remained controversial.(6, 28, 29)

There were several limitations of the study. First, information on patient compliance with the medication was not accessible in the database. Second, the dosage of aspirin and the degree of platelet inhibition were not assessed. Further investigation can be carried out to determine the effects of dosage and the degree of platelet inhibition. Last, the current study did not evaluate all intra-abdominal organs. The liver and spleen were the most commonly involved organs in blunt abdominal trauma and presented with hemorrhage. Injuries to the pancreas, bowel and mesentery, bladder, and diaphragm would pose problems other than bleeding. Kidneys are retroperitoneal structures and should be discussed separately.

Conclusion

Preinjury aspirin use was not associated with increased hemostatic procedures in blunt hepatic or splenic injuries. The associated multiple organ injury and severity of trauma were the major determinants for interventions.

Declarations

Ethics approval

This study was exempt from full review by the Ethics Institutional Review Board of Chang Gung Memorial Hospital (IRB No. 201801580B1).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the National Health Insurance research database but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was financially supported by grants CMRPG3H1531 from Chang Gung Memorial Hospital.

Authors' contributions

JFH and CYF designed the study. JFH, CPH and CTC analyzed the data. JFH wrote the paper with input from all authors. All authors discussed the results and contributed to the final manuscript.

Acknowledgements

The authors thank the statistical assistance and wish to acknowledge the support of the Maintenance Project of the Center for Big Data Analytics and Statistics (Grant CLRPG3D0046) at Chang Gung Memorial Hospital for study design and monitor, data analysis and interpretation.

This study is based in part on data from the National Health Insurance research database provided by the National Health Insurance Administration and managed by Health and Welfare Data Science Center, Ministry of Health and Welfare. However, the interpretation and conclusions contained herein do not represent the position of Chang Gung Memorial Hospital, National Health Insurance Administration and Ministry of Health and Welfare.

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Abbreviations

APAC, antiplatelet agents or anticoagulants

FFP, frozen fresh plasma

ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification

ICH, intracranial hemorrhage

ICU, intensive care unit

ISS, injury severity score

MLR, multivariate logistic regression

NHI, National Health Insurance

NHIRD, National Health Insurance Research Database

PRBC, packed red blood cell

PSM, propensity score matching

SMDs, Standardized mean differences

TAE, transarterial embolization

Figures

APAC = antiplatelet or anticoagulant

*Non-aspirin APAC = clopidogrel, cilostazol, warfarin, dabigatran, apixaban, edoxaban or rivaroxaban

Each patient could have had both liver and splenic injuries. Thus, the total number of blunt liver injuries and blunt splenic injuries exceeds the total number of patients

Figure 1

Study population and protocol of the current study.