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Original Research

Is strict adherence to the nonoperative management protocol associated with better outcome in patients with blunt splenic injuries?: A retrospective comparative cross-sectional study

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ABSTRACT

Background: The nonoperative management (NOM) protocol with angioembolization (AE) presents a trend in dealing with trauma patients with blunt splenic injury (BSI). This study was designed to explore the adverse events and associated risk factors before and after protocol-based NOM of BSI over a 12-year period.

Methods: A retrospective study was performed on adult trauma patients with BSI who were admitted from 2005 to 2016. The patients were divided into before cohort (2005–2010) and after cohort (2011–2016). Multivariate logistic regression analysis was performed to identify risk factors associated with the morbidity. The primary outcomes are NOM-related mortality and total number of complications, the secondary outcome is the incidence of each complication.

Results: The before cohort was composed of 209 patients, and the after cohort had 190 patients. There was a significant increase in the use of AE (from 18.1% to 47.5%, $p < 0.001$) with a higher incidence of patients who had a shock episode before AE (from 4.2% to 16.5%, $p < 0.001$). Regarding the outcomes, there were no significant differences in the incidences of NOM-related mortality between the after than before cohorts. However, there were 190 complications in 71 patients in the before cohort but 289 complications in 73 patients in the after cohort. The incidence of complications was significantly higher in the group of after cohort than the group of before cohort. Regarding the complications, the patients in the after cohort were significantly more likely to have adverse events of coagulopathy, acidosis, hyperbilirubinemia, respiratory failure, and acute kidney injury than those in the before cohort.

Conclusion: Strict adherence to the NOM protocol in treating patients with BSI without adequate patient selection increased not only the use of NOM but also the possibility of complications and failed to significantly improve the clinical outcomes.

1. Introduction

The high success rate of nonoperative management (NOM) of blunt splenic injuries (BSIs) was mainly attributed to the liberal use of angioembolization (AE) particularly in patients with high grades of injuries (grades III–V) that was associated with high risk of failure [1–6]. However, despite the wide use of AE, the NOM in BSI continues to be controversial with regard to the selection of optimal patients [7]. In the past, an unstable hemodynamic status was an absolute contraindication to NOM [8]; meanwhile, with the evolution of damage control resuscitation as an adjunct to NOM, the contraindication seems to move from absolute to controversial [9]. Implementation of the permissive hypotension strategy had further extended the application of NOM to hemodynamically unstable patients with blunt visceral organ injury [10,11]. Furthermore, mandatory AE was proposed in addition to a protocol to help increase the NOM success rate in high-grade BSI [1,4,12]. In a prospective study with a developed protocol with AE for 168 hemodynamically stable patients with BSI grades III–V, the NOM failure rate was only 5% as compared to their historic failure rate of 15% [4]. A retrospective analysis of a 16-year experience in BSI

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concluded that utilizing AE in the standardized protocol was correlated with an increased rate of attempted NOM (61%–88%) and successful NOM (77%–97%) [5]. Previously, we had published our experience with the NOM protocol with AE in high-grade blunt hepatosplenic trauma in a cohort of 150 patients and revealed an overall NOM success rate of 95% [12].

These published researches had pushed the NOM in a trend to be the gold standard strategy in dealing with BSI regardless of injury severity. Currently, trauma surgeons are more willing to accept the NOM to preserve the spleen as much as possible. However, NOM still has potential drawbacks. The fact that NOM failure increased resource use and may be associated with a higher rate of morbidity was overlooked [8]. A meta-analysis that included 15 retrospective studies with 479 patients revealed that the overall failure rate of AE was 10.2%, with rebleeding being the most common cause [3]. In a multi-institutional study on 140 patients who underwent AE, 20% of the patients had major complications, including 11% with rebleeding, 4% with splenic abscess, 3% with missed injuries, and 1% with vascular injury [13]. In a retrospective study of 91 patients who underwent AE, 14% had major complications, including 6.8% with splenic abscess, 2.3% with splenic infarction, 2.3% with splenic cyst, and 2.3% with contrast-induced acute kidney injury [14]. Therefore, this study was designed to explore the adverse events and associated risk factors before and after protocol-based NOM of BSI over a 12-year period in our institution. The primary outcome of interest in this study would be the associated complications and mortality.

2. Methods

2.1. Study population

This was a retrospective study and the work has been reported with the STROCSS criteria [15]. Trauma patients with BSI admitted to the hospital from January 2005 to December 2016 were retrospectively identified from the registered trauma database in a 2686-bed facility and Level I regional trauma center that provides primary care to trauma patients primarily from southern Taiwan [16–18]. Patients younger than 16 years or those who died in the emergency department (ED) were excluded. The severity of splenic injury was determined by a grading system developed by the American Association for the Surgery of Trauma, according to the finding on the CT scan, operative, or autopsy [19]. There are five grades of splenic injury. Generally, grades I (laceration < 1 cm or subcapsular hematoma $< 10\%$ of surface area) and II (laceration between 1 and 3 cm or subcapsular hematoma between 10% and 50% of surface area) are considered as minor injuries, grade III (laceration > 3 cm, subcapsular hematoma $> 50\%$ of surface area, or ruptured subcapsular or parenchymal hematoma) as a moderate injury, and grades IV (segmental or hilar vascular injury or devascularization $> 25\%$ of spleen) and V (hilar injury or shattered spleen) as severe injuries [19]. All patients with BSI at the ED were initially considered as candidates for NOM. They were first assessed and resuscitated at the ED according to the guidelines of Acute Trauma Life Support. The selection of patients for NOM was based on a formal NOM protocol with AE in patients with BSI since 2004 in our institution [20]. The inclusion criteria of patients for NOM were as follows: (1) hemodynamic stability at admission or shortly after initial resuscitation; (2) no obvious peritoneal signs of acute surgical abdomen; and (3) no associated major trauma requiring immediate laparotomy. According to the protocol, AE was performed in patients who had one or more of the following presentations: significant hemoperitoneum (bloody ascites in any of the compartments including bilateral subphrenic, bilateral paracolic, or pelvic cavity) or contrast extravasation over peri-splenic or intra-splenic parenchyma on computed tomography (CT) scan, persisted hypotension despite fluid resuscitation, grade IV or V splenic injury, and decreased hemoglobin or hematocrit level that require ongoing blood transfusions. If the above criteria were met, AE would be performed as early as possible after initial stabilization of the vital signs. In the case of rapid clinical deterioration or if the patient had received massive blood transfusions, administration of 10 U or more of packed red blood cells (pRBC) or whole blood within 24 h, the procedure was abandoned and the patient underwent immediate emergency laparotomy. Before the introduction of the NOM protocol, the decisions to transfuse and to proceed to splenectomy or angioembolization did not depend on a clinical pathway but rather were made by the attending trauma surgeon. The NOM protocol with AE was recognized and accepted after our previous study reported in 2004 [20], and the protocol of NOM became more aggressively and strictly adhered to since 2011 [12]. Hence, in this study, the patients over a 12-year period were divided into patient cohorts before (2005–2010, before cohort) and after (2011–2016, after cohort) the implementation of the protocol. The comparisons regarding patient characteristics, management modality, and clinical outcomes were made between the before and after cohorts.

2.2. Angiography and embolization technique

Angiography was performed after placing a 4- to 6-F diagnostic catheter in the splenic artery via femoral artery puncture. Selective coaxial microcoil was mainly performed and sometimes small pledgets of gelform were applied or a combination of both methods for occlusion of bleeding vessels. The nature of the embolization (i.e., proximal splenic artery, distal selective embolization, or both) was per the judgment of the interventional radiologist at the time of the study. For suspicious bleeder, an attempt was made to embolize the focal distal branches of the splenic artery with gelform. The dose of intravenous contrast medium Iohexol (OMNIPAQUE) used for abdominal CECT and intra-arterial angiography was 60–120 cc and 100–150 cc, respectively, depending on the weight of the patient. The upper limit of overall contrast dose was 1.5 mL/kg for abdominal CECT and 3 mL/kg for angiography.

2.3. Definitions of complications

Complications were categorized into serious adverse events or simple adverse events. Serious adverse events were defined as direct or indirect adverse effects believed to be associated with management from blunt splenic injuries that were potential fatal or resulted in disability. Simple adverse events were considered as adverse effects that were not critical or life-threatening. The following were considered to be serious adverse events: respiratory failure, acute kidney injury, pneumonia, sepsis, empyema, re-bleeding, miss injury, hemodialysis, inotropic agent use, adult respiratory distress syndrome (ARDS), and use of *Extracorporeal Membrane Oxygenation* (ECMO). Coagulopathy, acidosis, hyperbilirubinemia, pleural effusion, urinary tract infection, intraabdominal infection, and negative laparotomy were considered to be simple adverse events. Re-bleeding was defined as any bleeding from the spleen, occurring after initial management, necessitating unplanned surgical or radiologic intervention. Miss injury was defined as returning to operative room due to hollow organ perforation after receiving non-operative management for BSI. Pneumonia, urinary tract infection, intraabdominal infection, empyema, and sepsis were categorized into infectious complications and accordance with established guidelines [18]. Intraabdominal infection included both splenic abscess and abscess from a non-splenic source after confirmation from radiologic or surgical evidence. Pleural effusion was considered complications when they occurred days and weeks and were not attributable to rib fractures. Coagulopathy was defined as a prothrombin time > 14 s or partial thromboplastin time > 35 s. Acidosis was defined as pH < 7.25. Hyperbilirubinemia was defined as total bilirubin level > 2.0 mg/dL. Acute kidney injury was diagnosed according to the KDIGO criteria [21].

2.4. Definition of the outcomes

Shock before waiting AE was defined as the patients had sustained episodes with systolic blood pressure less than 90 mm Hg before sent to angio-suit after decision-making to receive angioembolization. Morbidity was defined as at least one above-mentioned adverse event occurs in a patient. Overall mortality was defined as in-hospital death from any cause. Spleen-related mortality was death directly due to acute ongoing bleeding from BSI that was not controlled, whereas NOM-related mortality was caused by complications in patients receiving NOM. Successful NOM was defined as the combination of splenic salvage without the need for any delayed laparotomy including splenectomy or peritonitis during index admission. Failure of NOM was defined as any delayed laparotomy in patients initially managed non-operatively, including those who had AE converted to operation or observation converted to operation.

2.5. Data collection

This study had been registered with UIN as NCT03943355. https://clinicaltrials.gov/show/NCT03943355. From the registered trauma database as well as the electric and paper medical records, we collected the patients' data, including age, sex, mechanism of injury, vital signs upon arrival at the ED, splenic injury grade (SIG), Injury Severity Score (ISS), traumatic brain injury, defined as head abbreviated injury scale (AIS) ≥ 3 [22,23], blood products used at the ED, within 24 h, and overall requirement during hospitalization, treatment modality by AE, observation alone, or laparotomy, hospital length of stay (LOS), ICU LOS, occurrence of adverse events and morbidities, and mortality.

2.6. Statistical analysis

Comparisons were performed with Student's t-test for continuous variables with the data presented as mean ± standard deviation. The categorical variables were analyzed with chi-square analysis or Fisher's exact analysis and presented as odds ratios (OR) with corresponding 95% confidence intervals (CI). All statistical tests were two-tailed. Comparisons between groups were performed using univariate analysis with purposeful variable selection for the multivariate logistic regression modeling to evaluate the risk factors for the development of morbidities. A P-value < 0.05 was considered statistically significant. Kaplan-Meier curves were plotted to compare morbidity of these patients with BSI in the before and after cohorts, with the log-rank test to assess the difference in morbidity curves between these two groups. In this study, the primary outcomes are NOM-related mortality and total number of complications, the secondary outcome is the incidence of each complication.

3. Results

3.1. Demographics and clinical outcomes of patients

After exclusion of 29 patients aged less than 16 years and 6 patients who died at the ED, there were 399 patients enrolled into the final analysis, including 209 patients in the before cohort and 190 in the after cohort (Fig. 1). As shown in Table 1, there were no significant difference in age, sex, and trauma mechanisms, ED vital signs, and level of hemoglobin (Hb) between the before and after cohorts. Injury severity as ISS (20.8 ± 10.6 vs. 16.7 ± 10.1, 95% CI of the difference: 2.10–6.71, p < 0.001) and SIG (3.11 ± 1.08 vs. 2.88 ± 1.15, 95% CI of the difference: 0.01–0.46, p = 0.037) was significantly higher in after cohort than before cohort. Compared to the patients in the before cohort, there were significantly fewer patients who sustained a SIG I + II, but more patients with a SIG III in the after cohort. The incidence of traumatic brain injury was significantly higher in the group of after cohort than that in the group of before cohort (17.9% vs. 8.1%, p = 0.004). The requirement for a blood transfusion at ED was higher in the group of after cohort than the group of before cohort (60.0% vs. 36.8%, p < 0.001), with the units of blood transfused significantly higher in the group of after cohort than the group of before cohort (2.45 ± 3.17 vs. 1.44 ± 2.35 U, p < 0.001). There was no significant difference in the units of blood transfused within 24 h, incidences of massive and hospital transfusions, and units of blood transfused upon hospitalization between the after and before cohorts. Regarding the outcomes, there were no significant differences in the incidences of morbidities, hospital LOS in those with or without morbidity, spleen-related mortality, NOM-related mortality, and overall mortality between the after than before cohorts. The ICU LOS was significantly longer in the after than before cohort (5.91 ± 7.57 days vs. 4.49 ± 4.21 days, p = 0.023).

3.2. Management of the patients with splenic injury and concomitant internal organ injury

In the before cohort, there were 29 patients with splenic injury with concomitant liver injury (4 splenectomies and 2 splenorrhaphies were performed), 20 splenic injury with concomitant renal injury (one splenorrhaphy), 4 splenic injury with concomitant liver and renal injury (3 splenorrhaphies), 5 splenic injury with concomitant pancreatic injury (all NOM), 4 splenic injury with concomitant bowel perforation (3 splenectomies), and one splenic injury with concomitant mesentery artery tear (one splenectomy). In the after cohort, there were 23 patients with splenic injury with concomitant liver injury (5 splenectomies), 19 splenic injury with concomitant renal injury (4 splenectomies), 2 splenic injury with concomitant liver and renal injury (all NOM), 3 splenic injury with concomitant pancreatic injury (2 splenectomies), 5 splenic injury with concomitant bowel perforation (2 splenectomies and 1 splenorrhaphy), and one splenic injury with concomitant mesentery artery tear (one splenectomy).

3.3. Patients initially treated with NOM

As shown in Table 2, there were 324 (81.2%) patients who had undergone initial treatment with NOM, with 166 patients in the before cohort and 158 in the after cohort. The incidence of patient receiving initial AE was significantly higher in the group of after cohort compared with that in the group of before cohort (47.5% vs. 18.1%, p < 0.001). A significantly higher SIG (2.97 ± 1.06 vs. 2.57 ± 1.01, p < 0.001) and incidence of patients who had shock episode before AE (16.5% vs. 4.2%, p < 0.001) was found in the after cohort than the before cohort. However, there was no significant difference in the average time to the procedure between the after and before cohorts, albeit there was a short time spent in the after cohort owing to that these caring staff were more familiar with the refined process in the after cohort. In addition, there was no significant difference in the rate of conversion between the after and before cohorts. The reason for the conversion to AE or operation was attributed to a re-bleeding in most of the cases. Additionally, there were 3 cases in the after cohort initially received AE and then received delayed laparotomy due to missed bowel injury, whereas there was only one case in the before cohort initially received observation and then received delayed laparotomy due to missed bowel injury. Likewise, there was only one case in the after cohort initially received observation and then converted to laparotomy due to intra-abdominal abscess.

3.4. Complication of patients treated with NOM

There were 190 complications in 71 patients in the before cohort but 289 complications in 73 patients in the after cohort (Table 3). Regarding the complications, the patients in the after cohort were significantly more likely to have adverse events of coagulopathy, acidosis, and hyperbilirubinemia than those in the before cohort. The after

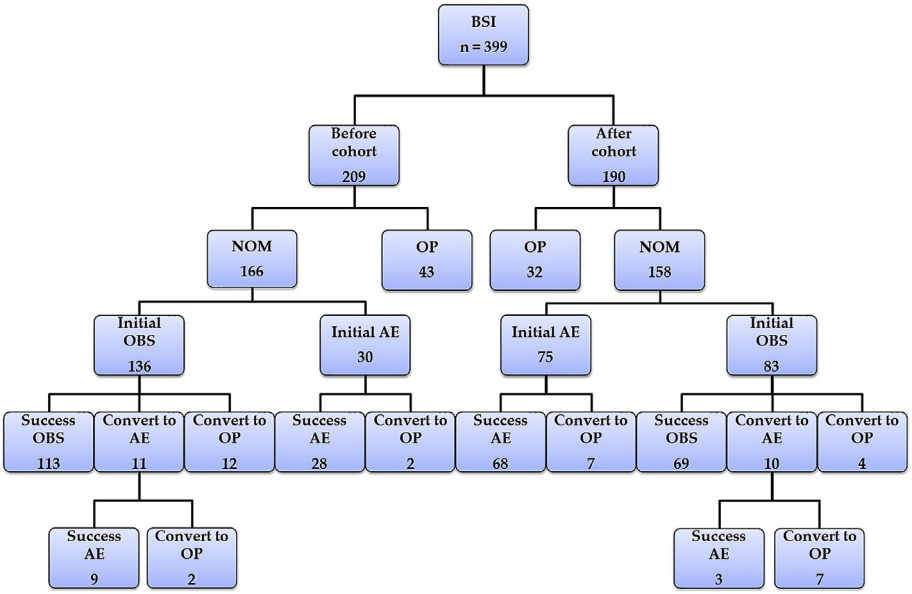

Fig. 1. Treatment modalities performed for the study population. BSI, blunt splenic injury; NOM, nonoperative management, OP, operation, AE, angioembolization, OBS, observation.

cohort also had a significantly higher incidence of respiratory failure (50.7% vs. 33.8%, p = 0.040) and acute kidney injury (47.9% vs. 25.4%, p = 0.005). However, there were significantly fewer patients who had urinary tract infection in the after cohort than the before cohort (4.1% vs. 14.1%, p = 0.037). As shown in Fig. 2, a significant difference in morbidity curves between these patients with BSI in the before and after cohorts was identified in the plotted Kaplan-Meier curves (p = 0.035).

3.5. Risk factors for morbidities

The multivariate logistic regression model revealed that units of blood transfused upon hospitalization and ICU admission was a risk factor for the development of morbidities, while successful NOM was a protective factor for the morbidities in both before and after cohorts. Notably, the multivariate model identified “shock before waiting AE” and “observation converted to AE” as independent risk factors with 37.71 and 30.66 odds of risk, respectively, for the development of morbidities in the after cohort (Table 4). However, the two variables were not significant risk factors for morbidities in the before cohort. In contrast, units of blood transfused at the ED, within 24 h, and on hospitalization was a significant independent risk factor for morbidities only in the before cohort but not in the after cohort.

4. Discussion

In the present study, this number of initial AE of patients receiving NOM had significantly increased from 18.1% in the before cohort to 47.5% in the after cohort. The time from ED arrival to the angio-suite was reduced from 301 ± 148 min in the before cohort to 244 ± 79 min in the after cohort, albeit the time discrepancy was not significant. These findings indicated that the management was better fit to the protocol implemented in the after cohort. In addition, the success rate of NOM was 91.6% in the before cohort and 93% in the after cohort; this is comparable to rates reported by other meta-analysis reviews (Requarth et al., 91.7%; Crichton et al., 91.8%) [2,3] and our previous report with an overall NOM failure rate of 5% [12]. However, although many trauma centers considered that strict follow-up protocols are critical to the high success rate of NOM [1,4], based on this current study, the strict adherence to the NOM protocol is not associated with better outcomes and lower morbidity. These findings are consistent with a recent meta-analysis review, which included 23 studies in 6684 patients and revealed that AE was not associated with any improvements in mortality with NOM but increased the morbidity compared with NOM alone [2]. Additionally, Sabe et al. [5] had reported that the standardized protocol use of initial AE in patients determined to be at high risk of failure was not associated with significant improved success rate of NOM or clinical outcomes compared to patients who used AE in a discretionary manner. In a retrospective study that involved assessment of 154 patients with BSI who presented with contrast extravasation on CT scan over 5 years, Duchesne and colleagues [24] reported that, for patients with high-grade BSI, patients who underwent splenectomy had similar mortality rate compared to patients who underwent proximal AE, but there was a significantly higher incidence of ARDS and sepsis in patients undergoing proximal AE. Indeed, NOM with AE does not contribute to a higher number of spleen salvage. In this study, the rate of spleen salvage was about 75–78% and was not different in both groups. These aforementioned studies [2,5,24] also agree with that a more aggressive attempt for NOM was potentially at the expense of increased morbidity, but may not increase the rate of organ salvage.

In this study, although there was significantly higher mean SIG in patients in the after cohort than those in the before cohort, the incidence of SIG grades 4 and 5 was similar in both groups. Notably, the success of NOM primarily relies on those achievements in the patients with SIG grades 4 and 5 injuries [1,3,20]. A meta-analysis published by Requarth et al. [3] reported that the NOM failure rate estimate for grade 3 injuries did not depend on embolization and suggested that AE does not contribute to the success of NOM in grade 3 injuries. Another meta-analysis study suggested that splenic angioembolization significantly improved the success of NOM of grades 4 and 5, but had no demonstrable benefit for grades 1, 2 and 3 [2]. Bhullar et al. [1] reported similar findings regarding grade 3 injuries and proposed that AE is associated with significantly higher splenic salvage rates in grade 4 and 5 injuries. Apart from SIG 3, a Delphi study by Olthof et al. [25] also proposed that ISS does not influence the management strategy of BSI. Another aspect controversial in NOM indication refers to patients with severe traumatic brain injury (TBI). Eastern Association for the Surgery of Trauma (EAST) noted that the level of consciousness is not a contraindication for NOM of BSI [26]. Dhillon and colleagues [27] from National Trauma Data Bank recently reported their results on 47,713 patients with BSI. Their findings indicate that the presence of TBI

Table 1
Demographics and clinical outcomes of the patients.

	Before cohort (2005–2010)	After cohort (2011–2016)	P-value
Patient number	209	190	
Age (years)	37.1 ± 17.8	34.8 ± 17.1	0.199
Male sex, n (%)	150 (71.8)	138 (72.6)	0.848
Mechanisms, n (%)			
Motorcycle accidents	149 (71.3)	143 (75.3)	0371
Car accidents	26 (12.4)	14 (7.4)	0.092
Others	34 (16.3)	33 (17.3)	0.769
ISS	16.7 ± 10.1	20.8 ± 10.6	< 0.001
Splenic injury grade (SIG)	2.88 ± 1.15	3.11 ± 1.08	0.037
Grade I + II, n (%)	82 (39.2)	52 (27.4)	0.012
Grade III, n (%)	64 (30.6)	78 (41.1)	0.030
Grade VI + V, n (%)	63 (30.2)	60 (31.6)	0.756
Traumatic brain injury, n (%)	17 (8.1)	34 (17.9)	0.004
ED vital signs			
HR (beat/min)	97.5 ± 21.3	99.9 ± 23.7	0.289
SBP (mmHg)	113.0 ± 26.1	118.2 ± 30.1	0.063
Shock (SBP < 90 mmHg), n (%)	37 (17.7)	32 (16.8)	0.820
Hb (mg/dL)	11.8 ± 2.4	12.1 ± 2.5	0.202
Blood transfusion			
Blood transfusion at ED, n (%)	77 (36.8)	114 (60)	< 0.001
Blood transfusion at ED (U)	1.44 ± 2.35	2.45 ± 3.17	< 0.001
Blood transfusion within 24 h (U)	4.35 ± 6.41	5.22 ± 8.36	0.241
Massive transfusion, n (%)	31 (14.8)	26 (14.2)	0.860
Hospital transfusion, n (%)	122 (58.4)	107 (56.3)	0.678
Hospital transfusion (U)	5.11 ± 8.8	4.97 ± 10.27	0.886
Managements			
Initial NOM, n (%)	166 (79.4)	158 (83.2)	0.341
Initial laparotomy, n (%)	43 (20.6)	35 (16.8)	0.341
Spleen salvage, n (%)	158 (75.6)	149 (78.4)	0.504
Outcomes			
Morbidity, n (%)	71 (34.0)	73 (38.4)	0.355
Hospital LOS (days)	14.15 ± 10.14	16.02 ± 12.33	0.102
with morbidity	20.15 ± 13.48	22.53 ± 14.71	0.314
without morbidity	11.07 ± 5.91	11.95 ± 8.36	0.339
ICU LOS (days)	4.49 ± 4.21	5.91 ± 7.57	0.023
Spleen-related mortality, n (%)	8 (3.8)	6 (3.2)	0.716
NOM-related mortality, n (%)	1 (0.5)	4 (2.1)	0.145
Overall mortality, n (%)	12 (5.7)	13 (6.8)	0.651

ISS, Injury Severity Score; ED, emergency department, SBP, systolic blood pressure; HR, heart rate; Hb, hemoglobin; ICU, intensive care unit; LOS, length of stay; NOM, nonoperative management.

should not preclude the implementation of the principles of NOM of BSI. According to the results of this study, we recommended that although ISS, SIG, and TBI does not preclude the use of NOM in managing the patients with BSI, such parameters may be associated with NOM failure and therefore such patients must be closely followed in order to treat the failures." Thank you for your meticulous reading and professional recommendation.

One of the potential drawbacks of NOM is the higher amounts of blood transfusion that are often required. Worries about increased transfusion requirements with NOM have been presented [28]. During the period of after cohort, a more aggressive NOM with strict adherence to the protocol was implemented. This could be explained why there were significantly higher amounts of blood products and rates of transfused patents at ED in the after cohort (2.45 ± 3.17 U vs. 1.44 ± 2.35 U, p < 0.001) (60% vs. 36.8%, p < 0.001). In addition, the period of after cohort also had a trend toward an increase in transfusion amounts with initial 24 h (5.22 ± 8.36 U vs. 4.35 ± 6.41 U, p = 0.241). In fact, the blood volume in NOM implementation is still not clear [26]. Although some experts agreed on the importance of the volume of transfused blood in the first 24 h for NOM of BSI, they did not reach a consensus as to the volume that contraindicates NOM [29]. Currently, the timing and indication for blood transfusion in patients with BSI is controversial and there is no consensus on blood transfusion protocol in patients with BSI in our institution. Furthermore, in this study, although the associated higher ISS may be suspected as the cause of more blood transfusions in the after cohort, the higher ISS was associated with significantly higher incidences of brain injury, and in such condition a largely-increased blood transfusion generally was not necessary for the concomitant brain injury.

In the effort to pursue organ salvage, there was significantly higher incidence of "shock episode before AE" in the after cohort than that in the before cohort (16.5% vs 4.2%, p < 0.001). These greater units of blood transfusions and prolonged shock for the purpose of AE are expected to contribute to the higher complication rate. This could explain why the multivariate analysis revealed that patients in the after cohort with status of "observation converted to angiography" and "shock episode before angiography" were highly associated with the occurrence of morbidity. In contrast, these two factors are not significantly different for the morbidity in patients of the before cohort. There is a tendency that the trauma surgeons are willing to accept the NOM and further the preservation of the spleen as possible. In order to achieve the organ preserving, surgeons might resuscitate the high-grade splenic injury patients with maintenance of the borderline systolic blood pressure despite of episodes with unstable hemodynamics before angiosuite. The prolonged states of hypoperfusion may lead to a significant higher rate of acidosis and subsequent coagulopathy. This may also be the reason for a significant longer ICU LOS in patients in the after cohort than that in the before cohort, because a longer time would be required for critical care and resuscitation in the ICU.

Furthermore, there is concern regarding the risk of missing hollow organ injury in the attempt to avoid untherapeutic laparotomy in NOM in patients with BSI. The hollow organ injuries were found in only 0.3% of blunt abdominal trauma from an analysis of 275,557 trauma admissions [30]. However, in this study, accompanied by a reduction in initial laparotomy rate from 20.6% to 16.8%, there was an increased rate of missed injury from 1.4% to 4.1%. The rate of hollow organ injuries in our study was higher than that in the above report, regardless of before or after cohort. Moreover, the NOM-related or spleen-related mortality rate in this study is higher than those patients with overwhelming post-splenectomy infection, which has a mortality rate of around 50–70% but develops in only 0.5% of trauma patients with splenectomies [31]. Velmahos et al. [6] evaluated 388 adult patients with a grade 4 or 5 BSI and proposed that the generalization of NOM should not represent severe BSI. Peitzman et al. [7] described the dangers of attempting NOM in hemodynamically unstable patients by reporting a mortality of 37% in this group of patients. Bhullar et al. [1] suggested that blood transfusion in an effort to stabilize hemodynamically unstable patients of possible AE was prohibited in their protocol of NOM for high-grade BSI. Coincidentally, they both thought that, as for NOM in BSI, the indication may be applied too extensive for severely-injured patients. Accordingly, the issue of pursuing organ salvage by NOM is worth further investigation, particularly for those borderline candidates.

4.1. Limitations

There are some limitations in our study. It is limited by its dependence on retrospective data and small size, with the attendant issues of a nonrandomized single-center study evaluating outcomes over a 12-year period. The decision on which management strategy is selected was mostly based on the protocol; therefore, the selection bias could be reduced as much as possible. Additionally, it was not possible to evaluate long-term results of the reported complications. Moreover,

Table 2
Treatments and final strategy in patients initially managed nonoperatively.

	Before cohort (2005–2010)	After cohort (2011–2016)	P-value
Patient number	166	158	
Initial AE, n (%)	30 (18.1)	75 (47.5)	< 0.001
Average time from ED arrival to AE (min)	301.35 ± 148.04[a]	244.72 ± 79.04[b]	0.075
Average time from ED arrival to AE with CT had been performed (min)	155.50 ± 49.82[c]	145.36 ± 59.42[d]	0.761
Average time from observation to delay AE (h)	106.18 ± 127.08	46.80 ± 37.83	0.165
Average time from ED arrival to NOM failure (h)	108.07 ± 124.75[e]	139.42 ± 246.96[f]	0.620
Shock before waiting AE, n (%)	7 (4.2)	26 (16.5)	< 0.001
Observation convert to AE, n (%)	11 (8.1)	10 (12.0)	0.334
AE convert to operation, n (%)	2 (6.7)	7 (9.3)	1.000
Observation convert to operation, n (%)	12 (8.8)	4 (4.8)	0.269
Success NOM, n (%)	152 (91.6)	147 (93.0)	0.620

AE, angioembolization; CT, computed tomography; ED, emergency department; NOM, nonoperative management.
[a] 26 cases.
[b] 61 cases.
[c] 4 cases.
[d] 14 cases.
[e] 14 cases.
[f] 11 cases.

Table 3
Complications of the patients during the management.

	Before cohort (2005–2010)	After cohort (2011–2016)	P-value
Patient number	71	73	
Number of complications	190	289	
Coagulopathy, n (%)	38 (53.5)	53 (72.6)	0.018
Acidosis, n (%)	13 (18.3)	34 (46.6)	< 0.001
Hyperbilirubinemia, n (%)	15 (21.1)	32 (43.8)	0.004
Pleural effusion, n (%)	3 (4.2)	7 (9.6)	0.327
ECMO use, n (%)	1 (1.4)	2 (2.7)	0.576
Respiratory failure, n (%)	24 (33.8)	37 (50.7)	0.040
Pneumonia, n (%)	9 (12.7)	15 (20.5)	0.205
ARDS, n (%)	3 (4.2)	6 (8.2)	0.494
Acute kidney injury, n (%)	18 (25.4)	35 (47.9)	0.005
Hemodialysis, n (%)	0 (0)	3 (4.1)	0.245
Urinary tract infection, n (%)	10 (14.1)	3 (4.1)	0.037
Intraabdominal infection, n (%)	9 (12.7)	6 (8.2)	0.381
Empyema, n (%)	2 (2.8)	2 (2.7)	0.978
Sepsis, n (%)	5 (7.0)	11 (15.1)	0.125
Rebleeding, n (%)	21 (29.6)	21 (28.8)	0.915
Missing injury, n (%)	1 (1.4)	3 (4.1)	0.62
Negative laparotomy, n (%)	6 (8.5)	1 (1.4)	0.061

ARDS, adult respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation.

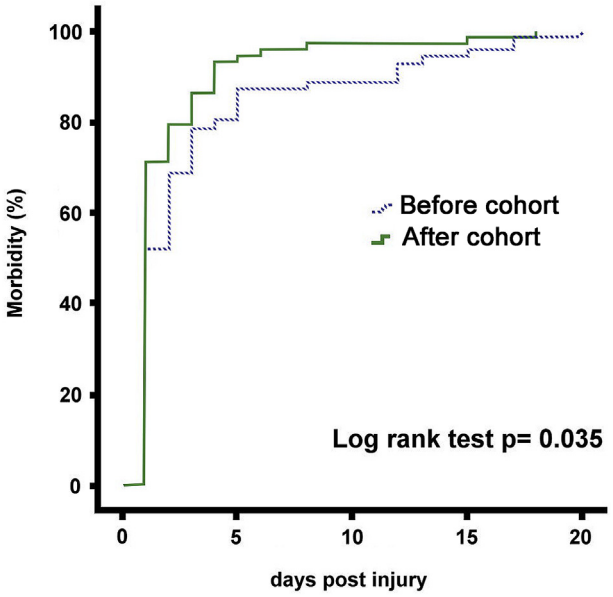

Fig. 2. Kaplan-Meier curves plotting the associated morbidities of the patients in the before and after cohorts.

although our institution had adopted a policy of damage control resuscitation in the after cohort, we did not elaborate on a resuscitation strategy or record the amount of resuscitation fluid including crystal, fresh frozen plasma, and platelet; therefore, our study cannot present the shift in resuscitation strategy completely in the after cohort. Furthermore, associated abdominal internal organs injuries might influence the treatment or even the choice of treatment; however, such consideration could not be identified from this study designed in retrospective character, thus might lead to a selection bias. In addition, analysis of the success rate according to the grade of injury of the spleen is impeded by compromised power of statistical analysis in stratifying the relatively few patients in this study. Furthermore, in this study, the embolization in distal or proximal splenic artery was judged by the radiologist at the time of invention. Because the complications related to distal or proximal splenic artery embolization were different, such selection of embolization may lead to a bias in the outcome of the patients. At last, we did not record the detailed information on angioembolization of the splenic artery, such as embolization location and dimension. Therefore, potential adverse events resulting from AE cannot further be identified.

5. Conclusion

We concluded that a strict adherence to protocol of NOM for patients with BSI without adequate patient selection increased the use of NOM but also increased the possibility of complications and failed to have a significant improvement in clinical outcomes. In our opinion in the future, we should set up a transfusion mechanism with a cutoff that would contraindicate AE. This should be taken into consideration in the treatment algorithm. As soon as the patient presented recurrent hypotension after blood resuscitation over the upper limit of a critical point, the patient should be proceeded to operation without hesitation. However, prospective studies are needed to validate these findings and to assess the utility of this clinical paradigm.

Ethical approval

This study was approved by the institutional review board of the

Table 4
The multivariate logistic regression of morbidities development before and after cohorts.

Variables	Before cohort (2005–2010)		After cohort (2011–2016)	
	OR (95% CI)	p	OR (95% CI)	P-value
Age (years)	1.00 (0.97–1.03)	0.612	0.99 (0.96–1.03)	0.910
ISS	1.00 (0.94–1.05)	0.936	1.01 (0.93–1.08)	0.791
Splenic injury grade 4, 5	1.85 (0.47–7.29)	0.375	0.39 (0.06–2.23)	0.292
Units of blood transfused at ED (U)	1.60 (1.16–2.20)	0.004	1.54 (0.98–2.43)	0.059
Units of blood transfused within 24 h (U)	0.68 (0.51–0.92)	0.012	0.71 (0.45–1.11)	0.138
Units of blood transfused in hospitalization (U)	1.63 (1.24–2.16)	< 0.001	1.82 (1.21–2.75)	0.004
Massive transfusion	0.79 (0.14–4.44)	0.791	0.54 (0.05–5.47)	0.603
Shock before waiting AE	2.11 (0.17–25.33)	0.555	37.71 (5.85–243.01)	< 0.001
Observation convert to AE	1.74 (0.24–12.64)	0.580	30.66 (2.48–378.87)	0.008
ICU admission	1.36 (1.14–1.63)	0.001	1.36 (1.08–1.72)	0.009
Successful NOM	0.24 (0.07–0.75)	0.015	0.08 (0.01–0.42)	0.002

CI, confidence interval; ED, emergency department; ICU, intensive care unit; ISS, Injury Severity Score; NOM, nonoperative management; OR, odds ratio.

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Author contribution

TMH wrote the manuscript, CTL edited the tables, BYW performed the statistical analyses, CHH contributed to the analysis and interpretation of data. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no competing interests.

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CRediT authorship contribution statement

Ting-Min Hsieh: Conceptualization, Writing - original draft, Writing - review & editing. **Chun-Ting Liu:** Data curation. **Bei-Yu Wu:** Formal analysis. **Ching-Hua Hsieh:** Funding acquisition, Supervision, Validation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2019.07.033.

References

[1] I.S. Bhullar, J.J. Tepas 3rd, D. Siragusa, T. Loper, A. Kerwin, E.R. Frykberg, To nearly come full circle: nonoperative management of high-grade IV-V blunt splenic trauma is safe using a protocol with routine angioembolization, J. Trauma. Acute. Care. Surg. 82 (4) (2017) 657–664.

[2] J.C.I. Crichton, K. Naidoo, B. Yet, S.I. Brundage, Z. Perkins, The role of splenic angioembolization as an adjunct to nonoperative management of blunt splenic injuries: a systematic review and meta-analysis, J. Trauma. Acute. Care. Surg. 83 (5) (2017) 934–943.

[3] J.A. Requarth, R.B. D'Agostino Jr., P.R. Miller, Nonoperative management of adult blunt splenic injury with and without splenic artery embolotherapy: a meta-analysis, J. Trauma 71 (4) (2011) 898–903 discussion 903.

[4] P.R. Miller, M.C. Chang, J.J. Hoth, N.T. Mowery, A.N. Hildreth, R.S. Martin, J.H. Holmes, J.W. Meredith, J.A. Requarth, Prospective trial of angiography and embolization for all grade III to V blunt splenic injuries: nonoperative management success rate is significantly improved, J. Am. Coll. Surg. 218 (4) (2014) 644–648.

[5] A.A. Sabe, J.A. Claridge, D.I. Rosenblum, K. Lie, M.A. Malangoni, The effects of splenic artery embolization on nonoperative management of blunt splenic injury: a 16-year experience, J. Trauma 67 (3) (2009) 565–572 discussion 571-562.

[6] G.C. Velmahos, N. Zacharias, T.A. Emhoff, J.M. Feeney, J.M. Hurst, B.A. Crookes, D.T. Harrington, S.C. Gregg, S. Brotman, P.A. Burke, et al., Management of the most severely injured spleen: a multicenter study of the research consortium of new england centers for trauma (ReCONECT), Arch. Surg.(Chicago, Ill) 145 (5) (1960) 456–460 2010.

[7] A.B. Peitzman, B.G. Harbrecht, L. Rivera, B. Heil, Failure of observation of blunt splenic injury in adults: variability in practice and adverse consequences, J. Am. Coll. Surg. 201 (2) (2005) 179–187.

[8] G.C. Velmahos, L.S. Chan, E. Kamel, J.A. Murray, N. Yassa, D. Kahaku, T.V. Berne, D. Demetriades, Nonoperative management of splenic injuries: have we gone too far? 2000, Arch. Surg.(Chicago, Ill) 135 (6) (1960) 674–679 discussion 679-681.

[9] N. Curry, P.W. Davis, What's new in resuscitation strategies for the patient with multiple trauma? Injury 43 (7) (2012) 1021–1028.

[10] M. Mitsusada, Y. Nakajima, M. Shirokawa, T. Takeda, H. Honda, Non-operative management of blunt liver injury: a new protocol for selected hemodynamically unstable patients under hypotensive resuscitation, J. Hepato-Biliary-Pancreatic Sci. 21 (3) (2014) 205–211.

[11] A. Hagiwara, H. Fukushima, A. Murata, H. Matsuda, S. Shimazaki, Blunt splenic injury: usefulness of transcatheter arterial embolization in patients with a transient response to fluid resuscitation, Radiology 235 (1) (2005) 57–64.

[12] T.M. Hsieh, T. Cheng Tsai, J.L. Liang, C. Che Lin, Non-operative management attempted for selective high grade blunt hepatosplenic trauma is a feasible strategy, World J. Emerg. Surg. : WJES 9 (1) (2014) 51.

[13] F.A. Moore, J.W. Davis, E.E. Moore Jr., C.S. Cocanour, M.A. West, R.C. McIntyre Jr., Western Trauma Association (WTA) critical decisions in trauma: management of adult blunt splenic trauma, J. Trauma 65 (5) (2008) 1007–1011.

[14] A.P. Ekeh, S. Khalaf, S. Ilyas, S. Kauffman, M. Walusimbi, M.C. McCarthy, Complications arising from splenic artery embolization: a review of an 11-year experience, Am. J. Surg. 205 (3) (2013) 250–254 discussion 254.

[15] R.A. Agha, M.R. Borrelli, M. Vella-Baldacchino, R. Thavayogan, D.P. Orgill, The STROCSS statement: strengthening the reporting of cohort studies in Surgery, Int. J. Surg. 46 (2017) 198–202.

[16] C.H. Hsieh, S.Y. Hsu, H.Y. Hsieh, Y.C. Chen, Differences between the sexes in motorcycle-related injuries and fatalities at a Taiwanese level I trauma center, Biomed. J. 40 (2) (2017) 113–120.

[17] C.H. Hsieh, H.T. Liu, S.Y. Hsu, H.Y. Hsieh, Y.C. Chen, Motorcycle-related hospitalizations of the elderly, Biomed. J. 40 (2) (2017) 121–128.

[18] C.H. Hsieh, Y.C. Chen, S.Y. Hsu, H.Y. Hsieh, P.C. Chien, Defining polytrauma by abbreviated injury scale > /= 3 for a least two body regions is insufficient in terms of short-term outcome: a cross-sectional study at a level I trauma center, Biomed. J. 41 (5) (2018) 321–327.

[19] E.E. Moore, T.H. Cogbill, G.J. Jurkovich, S.R. Shackford, M.A. Malangoni,

H.R. Champion, Organ injury scaling: spleen and liver (1994 revision), J. Trauma 38 (3) (1995) 323–324.
[20] P.P. Liu, W.C. Lee, Y.F. Cheng, P.M. Hsieh, Y.M. Hsieh, B.L. Tan, F.C. Chen, T.C. Huang, C.C. Tung, Use of splenic artery embolization as an adjunct to non-surgical management of blunt splenic injury, J. Trauma 56 (4) (2004) 768–772 discussion 773.
[21] M.E. Thomas, C. Blaine, A. Dawnay, M.A. Devonald, S. Ftouh, C. Laing, S. Latchem, A. Lewington, D.V. Milford, M. Ostermann, The definition of acute kidney injury and its use in practice, Kidney Int. 87 (1) (2015) 62–73.
[22] C.S. Rau, S.C. Wu, Y.C. Chen, P.C. Chien, H.Y. Hsieh, P.J. Kuo, C.H. Hsieh, Stress-induced hyperglycemia, but not diabetic hyperglycemia, is associated with higher mortality in patients with isolated moderate and severe traumatic brain injury: analysis of a propensity score-matched population, Int. J. Environ. Res. Public Health 14 (11) (2017).
[23] C.S. Rau, S.C. Wu, Y.C. Chen, P.C. Chien, H.Y. Hsieh, P.J. Kuo, C.H. Hsieh, Effect of age on glasgow coma scale in patients with moderate and severe traumatic brain injury: an approach with propensity score-matched population, Int. J. Environ. Res. Public Health 14 (11) (2017).
[24] J.C. Duchesne, J.D. Simmons, R.E. Schmieg Jr., N.E. McSwain Jr., C.F. Bellows, Proximal splenic angioembolization does not improve outcomes in treating blunt splenic injuries compared with splenectomy: a cohort analysis, J. Trauma 65 (6) (2008) 1346–1351 discussion 1351-1343.
[25] D.C. Olthof, C.H. van der Vlies, P. Joosse, O.M. van Delden, G.J. Jurkovich, J.C. Goslings, Consensus strategies for the nonoperative management of patients with blunt splenic injury: a Delphi study, J. Trauma. Acute. Care. Surg. 74 (6) (2013) 1567–1574.
[26] N.A. Stassen, I. Bhullar, J.D. Cheng, M.L. Crandall, R.S. Friese, O.D. Guillamondegui, R.S. Jawa, A.A. Maung, T.J. Rohs Jr., A. Sangosanya, et al., Selective nonoperative management of blunt splenic injury: an Eastern Association for the Surgery of Trauma practice management guideline, J. Trauma. Acute. Care. Surg. 73 (5 Suppl 4) (2012) S294–S300.
[27] N.K. Dhillon, G. Barmparas, G.M. Thomsen, K.A. Patel, N.T. Linaval, E. Gillette, D.R. Margulies, E.J. Ley, Nonoperative management of blunt splenic trauma in patients with traumatic brain injury: feasibility and outcomes, World J. Surg. 42 (8) (2018) 2404–2411.
[28] C. Gaarder, J.B. Dormagen, T. Eken, N.O. Skaga, N.E. Klow, J. Pillgram-Larsen, T. Buanes, P.A. Naess, Nonoperative management of splenic injuries: improved results with angioembolization, J. Trauma 61 (1) (2006) 192–198.
[29] D. Gomez, B. Haas, K. Al-Ali, O. Monneuse, A.B. Nathens, N. Ahmed, Controversies in the management of splenic trauma, Injury 43 (1) (2012) 55–61.
[30] D.D. Watts, S.M. Fakhry, Incidence of hollow viscus injury in blunt trauma: an analysis from 275,557 trauma admissions from the East multi-institutional trial, J. Trauma 54 (2) (2003) 289–294.
[31] S. Uranus, J. Pfeifer, Nonoperative treatment of blunt splenic injury, World J. Surg. 25 (11) (2001) 1405–1407.