Title:

Therapeutic strategies for pseudoaneurysm following blunt liver and spleen injuries: a multicenter cohort study in the pediatric population.

Short title:

Traumatic pseudoaneurysm in children

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ABSTRACT

Background

Little guidance exists for the treatment of pseudoaneurysm following pediatric blunt liver and/or spleen injuries (BLSI). We aimed to describe the incidence of delayed pseudoaneurysm development and the subsequent clinical course of pseudoaneurysm in pediatric BLSI.

Methods

This multicenter retrospective cohort study from Japan included pediatric patients (≤16 years old) who sustained BLSI from 2008 to 2019. The cohort was divided into four groups based on hemostatic intervention within 48 hours of admission, namely non-operative management (NOM), NOM with interventional radiology (IR), operative management (OM), and combined IR/OM. Descriptive statistics were used to describe the incidence of delayed pseudoaneurysm among the groups and to characterize the clinical course of any pseudoaneurysms.

Results

A total of 1,407 children (median age, 9 years) from 83 institutions were included. The overall number (incidence) of cases of delayed pseudoaneurysm formation was 80 (5.7%), and the number with delayed pseudoaneurysm rupture was 16 (1.1%) cases in the entire cohort. Patients treated with NOM (1056), NOM with IR (276), OM (53), and combined IR/OM (22) developed 43 (4.1%), 32 (12%), 2 (3.8%), and 3 (14%) delayed pseudoaneurysms, respectively. Among patients who developed any pseudoaneurysms, 39% of patients underwent prophylactic IR for unruptured pseudoaneurysm, while 13% required emergency angioembolization for delayed pseudoaneurysm

rupture, with one ruptured case requiring total splenectomy. At least 45% of patients experienced spontaneous resolution of pseudoaneurysm without any interventions.

Conclusion

Our results suggest that the risk of delayed pseudoaneurysm still exists even after acute phase IR as an adjunct to NOM for BLSI in children, indicating the necessity of a period of further observation. While endovascular interventions are usually successful for pseudoaneurysm management, including rupture cases, given the high incidence of spontaneous resolution, the ideal management of pseudoaneurysm remains to be investigated in future studies.

Level of evidence: Level 4; Therapeutic/Care management

Keyword: spleen injury, liver injury, interventional radiology, pseudoaneurysm, children

INTRODUCTION

Appropriate emergency hemostatic intervention is required for children who sustain blunt liver and/or spleen injuries (BLSI), even in an era when non-operative management (NOM) is the mainstay.[1-4] While conservative treatment is applied for most of these injuries in children, a splenic and/or hepatic artery pseudoaneurysm (PA) may develop in a considerable number of patients. These have been reported to occasionally rupture, however, which may result in fatal delayed bleeding with a risk of unexpected circulatory compromise.[5-7]

To address the family burden arising due to late concerns such as re-bleeding from injured organs, treatment indications for PA formation and the prevention of rupture should be investigated, and appropriate guidelines issued. Highly selective use of interventional radiology (IR) has been recommended for pediatric trauma patients as a better balance of risk, benefit, and resource utilization.[3,8] Although angioembolization has been proved as safe in pediatric patients as in adults, with few complications,[1,9-12] its use in children remains controversial due to insufficient evidence on the association between the use of IR and clinical outcomes.[8] In the real world, where there is often

no clear consensus on indications for IR intervention in the acute phase and late phase, individual institutions develop their own empirical indications for hemostatic interventions based primarily on the availability and preferences of the surgeons and interventional radiologists involved.

We previously reported that active contrast extravasation on admission CT was an independent predictor of PA development in pediatric patients with BLSI.[9] In contrast, there is little guidance on therapeutic strategies for PA development as a component of non-operative strategies. Although reports of spontaneous thrombosis and healing of PA have appeared, the actual frequency and subsequent clinical course of PA following BLSI remain unclear.[1,3,5-7,13,14]

Within this context, we conducted a large-scale multicenter cohort study with the two objectives, namely to describe the incidence of delayed PA development based on treatment in the acute phase, and to characterize the clinical manifestations and subsequent clinical course of PA following BLSI in children.

PATIENTS AND METHODS

Study design and setting

This study was conducted under a retrospective, multicenter, cohort design and was sponsored by the Japanese Association for Surgery of Trauma (JAST) Multicenter Trial Committee. Data were accumulated between January 2008 and December 2019 from academic, non-academic, and children's hospitals in Japan. The study protocol was approved by the JAST ethics committee and sequentially by the institutional review board at each participating hospital. As this study was non-interventional and of minimal risk to subjects, the need for informed consent from each patient was waived in all hospitals, but consent could be declined under an opt-out policy. Our study protocol was registered on UMIN-CTR as UMIN000041296.

Inclusion and exclusion criteria

Pediatric trauma patients aged ≤ 16 years who had sustained any BLSI were eligible. Inclusion was limited to patients admitted to an emergency care setting with at least an abbreviated injury scale (AIS) grade ≥I BLSI as detected by any imaging method or operative findings. Inter-hospital transfer patients were eligible for inclusion with the medical record information, such as imaging and laboratory data. To prevent duplicate enrollment of inter-hospital transfer cases from both institutions, data in the database were merged if age, sex, date of birth, date of injury, and facility location matched precisely.

Exclusion criteria were: (1) patient had cardiopulmonary arrest on arrival; (2) patient had an AIS 6 injury of any part of the body; (3) parent or guardian refusal of treatment, or request for limited treatment, due to a severe head injury (head AIS ≥5); and (4) patient transfer to another hospital within five days of admission without required follow-up information.

Data acquisition and management

Study data were collected and managed through the REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN, USA) tool. A standardized data entry guide in line with our research protocols was developed, and web conferences were held to explain the REDCap entry process for all local researchers at participating centers. Anonymized data were entered manually by local researchers. Detailed information on data cleaning and quality control are provided in the **supplemental digital content**.

Study variables and exposure

The following variables were collected: characteristics of participating hospital, patient baseline demographics (age, sex, body weight, pre-existing illness), the circumstances of the injury, physiologic status on arrival (systolic blood pressure [SBP], Shock Index [SI], Pediatric Age-adjusted [SIPA], heart rate [HR], Glasgow coma scale [GCS]), the severity of injuries (injury

severity score [ISS], the highest AIS in each anatomic region, the American Association for Surgery of Trauma [AAST] grade 1994 and 2018 update of splenic and hepatic injury[15]), laboratory data on admission, imaging data on admission and follow-up, treatment data (indications, type, and timing), and outcomes. SIPA was calculated as a parameter of hemodynamic shock (ages 1–6 years [SI > 1.22], age 7–12 years [SI > 1.0], and age 13–16 years [SI > 0.9]).[16,17]

The exposure was the use of IR as emergent or urgent hemostatic intervention[8]. Our study cohort was divided into four groups based on hemostatic intervention within 48 hours of admission: NOM (observed), NOM with IR, operative management (OM), and combined IR/OM. Patients who underwent angiography only or angioembolization were included in the IR intervention group.[8]

Outcome variables and definitions

The outcome of interest was post-traumatic PA formation. The characteristics of all PAs were described, and delayed PA formation, which was detected on or after the second day after injury (but undetectable on CT scan on admission) were evaluated separately.[18] Delayed PA rupture was defined as significant intra-abdominal bleeding from a PA in the splenic or hepatic parenchyma.[9] Spontaneous resolution of PA was defined as a diminishment of PA on follow-up imaging or no event of delayed re-bleeding without follow-up imaging during both the hospitalization and outpatient follow-up periods. This study clearly distinguished between contrast extravasation on CT scan and PA, which appears as an arterial phase-enhancing outpouching from intrasplenic/intrahepatic branches of the splenic/hepatic artery and typically demonstrates delayed phase washout of contrast medium on CT scan.[9,19] Other outcome measures included blood transfusion requirements, in-hospital mortality, and splenic salvage.

Statistical analysis

Descriptive analysis was performed to summarize the baseline characteristics of the entire cohort. Values were reported as mean ± standard deviation (SD) for continuous variables with normal distributions as determined by assessment of skewness and kurtosis. For those continuous variables not possessing a normal distribution, median ± interquartile range (IQR) was used. Categorical variables are expressed as numbers and percentages (%), as appropriate. Inter-group comparisons of continuous variables were performed using the Kruskal-Wallis test, and comparisons of each categorial variable between groups were performed using the chi-squared test. We described the outcomes, including delayed PA formation, by the management group within 48 hours of admission. We performed subgroup analyses according to the injured organ (spleen or liver). In addition, we described the clinical manifestations of PA (date of diagnosis, size, location) based on injury grade and the subsequent clinical course. All statistical analyses were 2-sided, and a p value $\leq$0.05 indicated statistical significance. All analyses were carried out with commercial software, Stata/MP version 17 (Stata Corp, College Station, TX, USA).

RESULTS

Study population and baseline characteristics

A total of 1462 pediatric patients were admitted with a diagnosis of BLSI to 83 participating centers between 2008 and 2019, of whom 1407 met our eligibility criteria. Details of the participating centers are listed in Supplementary Digital Content **Table S1**, while their geographical distribution is shown in **Figure S1**. The data of 18 patients were merged within the master dataset because of inter-hospital transfer with duplicate enrollment from both hospitals. **Figure 1** shows a flow diagram of the participants and reasons for exclusion.

Patient and hospital characteristics of all participants by management group within 48 hours of admission are summarized in **Table 1 and Table S2**. Of the 1407 patients, 821 (58%) had a liver injury, 532 (38%) had a spleen injury, and 54 (4%) had both liver and spleen injuries. Median age

was 9 [IQR 6–13], 67% were male, and median ISS was 10 [6–19] among the overall cohort. The department most commonly in charge of treatment was adult emergency medicine (51%), followed by pediatric surgery (20%), and adult surgery (15%).

Descriptive statistics of endovascular and surgical intervention

A total of 316 patients (22% of the entire cohort) underwent IR treatment, of whom 276 (20% of the entire cohort) underwent IR treatment within 48 hours of admission. Twenty-five patients underwent two or more IR sessions during the same hospitalization. Of the 276 patients who underwent IR within 48 hours of admission, 236 (86%) underwent angioembolization, while 40 patients (14%) underwent diagnostic IR with angiography only. The most common indication for first IR intervention was acute hemorrhage (86%), followed by delayed hemorrhage (6%) and unruptured pseudoaneurysm (6%). A higher proportion of patients in the NOM with IR group and combined IR/OM group had active contrast extravasation and PA detected on admission CT scan, regardless of hemodynamic status (**Table 1**). No patient required IR for arteriovenous or arterioportal shunt in the liver. The commonest location of splenic artery embolization was the distal splenic artery in 85% of cases (selective embolization), while proximal splenic artery embolization was performed in 13% of cases. The commonest location of hepatic artery embolization was distal branches from the right and left hepatic artery branches, in 63% of cases. Endovascular interventions were more frequently performed in those facilities and departments primarily serving adult patients, such as adult trauma centers and emergency medicine departments (**Table S2**).

A total of 79 patients (5.6% of the entire cohort) underwent OM, of whom 53 (3.8% of the whole cohort) underwent OM within 48 hours of admission. Among the overall cohort, 22 patients (1.6%) underwent combined OM and IR intervention within 48 hours of admission, of whom 13 underwent IR intervention followed by OM, while nine patients underwent OM followed by IR. The most common indication for first surgical intervention was acute hemorrhage (90%), followed by

peritonitis (9%). The most common first surgical procedure for spleen injury was total splenectomy (63%) followed by suture repair and/or application of hemostatic agents (28%) and damage control surgery (14%). The most common first surgical procedure for liver injury was damage control surgery (51%) followed by suture repair and/or application of hemostatic agents (40%), and partial hepatectomy (13%).

Outcomes by management group

Overall, 80 of 1407 (5.7%) patients developed delayed PA formation and 14 of 1407 (1.0%) experienced delayed PA rupture. By management group, 12% of patients in the NOM with IR group developed delayed PA, while 4.1% of patients in the NOM group developed delayed PA (**Table 2**). In both the spleen and liver injury subgroups, delayed PA formation occurred approximately 2–4 times more frequently in the NOM with IR group than in the NOM group. (**Table S3**). There was a trend toward an increasing requirement for blood transfusion in the order of NOM group, NOM with IR group, OM group, and combined IR/OM group, at 9.7%, 42%, 83%, and 95%, respectively ($p < 0.001$) (**Table 2**). Similar trends were observed for the frequency of each blood product (packed red blood cell, fresh frozen plasma, and platelets) transfused and for the cumulative total transfusion volume during the entire hospitalization and within 24 hours of admission. No significant differences were found in in-hospital mortality between the NOM group and NOM with IR group on univariate analysis (0.7 % vs. 1.1%, $p = 0.467$). The most common cause of death was traumatic brain injury, which was about twice as common a cause as death due to hemorrhagic shock caused by BLSI.

Clinical manifestations and natural history of pseudoaneurysm based on injury grade

Overall, 104 of 1407 (7%) patients developed PA, including PA detected on the day of injury. Median time to all PA diagnoses and delayed PA diagnoses from injury day was 6 days [IQR 2–10 days] and 7 days [5–10 days], respectively. **Figure 2** illustrates the distribution of PA diagnosis dates

by injury grade. The most common imaging modality that diagnosed PA was CT scan (82%), followed by angiography (11%) and abdominal ultrasound (8%). These imaging tests were performed when symptoms were present, as well as at the attending physician's discretion when symptoms were absent on follow-up imaging tests. Among the overall cohort, follow-up imaging tests with both CT scans and ultrasound were conducted in approximately 72% of patients in situations where the indication was not limited. Follow-up CT scans were also carried out in 84% of patients with an injury grade of III or higher and in 87% with contrast extravasation on the initial CT image. No significant differences were found in the diameter of PA and distance from spleen/liver capsule to PA among the different AAST grades of injury (2018 revision) ($p = 0.515$ and $p = 0.151$, respectively) (**Figure 3**). Similar results were obtained using the AAST grade of injury 1994 version (**Figure S2**). The median diameter of PA was 6.3 mm [4–10 mm] in the ruptured PA group, while it was 6.0 mm [4–10 mm] in the unruptured PA group (**Figure 3**). In addition, the median distance from the spleen/liver capsule to PA was 13 mm [5–17 mm] in the ruptured PA group, while it was 11 mm [6–18 mm] in the unruptured PA group (**Figure 3**). Among the 104 patients who developed PA, PA resolved spontaneously without intervention in 47 (45%) patients (**Table 3**). A total of 41 (39%) patients underwent prophylactic IR intervention for unruptured PA, while 14 (13%) patients underwent emergency angioembolization for PA rupture (**Table 3**). One (1%) patient underwent emergency total splenectomy because of delayed PA rupture. No patient required blood transfusion at the time of delayed PA rupture. Median time to PA rupture from injury day was 9 days [3–13 days].

DISCUSSION

In this retrospective multicenter cohort study, we found that the overall incidence of delayed PA formation was 5.7%. Delayed PA formation was identified in as many as 12% of patients who underwent emergent IR in the acute phase as an adjunct to NOM. Among patients who developed PA, 39% underwent prophylactic IR for unruptured pseudoaneurysm, while 13% underwent

emergent angioembolization for PA rupture and only one required splenectomy due to delayed PA rupture. At least 45% experienced spontaneous resolution of PA without intervention. Given that many of the identified PAs received prophylactic IR treatment, it is conceivable that some of them had a chance of resolving spontaneously. Our findings provide the new perspective that the risk of delayed PA formation still exists even after acute phase IR in pediatric BLSI, and that an accordingly high level of suspicion must be maintained whenever these patients are treated. Further, given the paucity of clear evidence and latent risk of delayed PA rupture, the decision to perform prophylactic angioembolization for PA requires shared decision-making with patients and their families under precisely informed consent.

Some review articles based on the findings of small studies reported no PA was found in AAST grade I or II injuries, and that patients with high-grade (grade IV or V) injuries appeared to have the greatest risk of developing PA.[1,5] Contrary to these reports, however, our study suggests that the risk of PA development should be considered for all injury grades equally, even for low-grade injuries. This is consistent with previous reports in pediatric BLSI[9,20] and adult splenic injury.[18,21,22] Current evidence supporting an association between AAST grade of injury (1994 version) and PA formation or delayed rupture is weak for both pediatric and adult BLSI.[9,18,20-22]

Additionally, many clinicians consider that patients who undergo IR treatment in the acute phase will be less likely to develop delayed PA in the late phase. However, in our study population, patients in the NOM with IR group had a relatively higher incidence of delayed PA development. In the group that received IR intervention as an adjunct to NOM, there was a higher proportion of patients with more complex and severe injury grades and accordingly may have had vascular injuries that were not detected on imaging in the acute post-injury phase. A retrospective study that reviewed adult blunt splenic injuries demonstrated that 10% of patients who underwent admission angiography eventually required either “second-look” angiography or laparotomy to control delayed hemorrhage.[23,24] The following reasons may explain this situation. First, contrast extravasation on

initial CT scan was identified in a higher proportion of patients within the IR group, marking this population as at higher risk for PA development[9]. Second, angiography may fail to identify intermittent active bleeding because of inconsistent timing, and embolization may accordingly be forgone.[21,23] Third, on diagnostic angiography, vasospasm in the damaged artery itself may prevent its opacification, and the tear only becomes obvious later.[21,23]

Whether or not all PA should receive equal intervention at the time of diagnosis is an important clinical question.[9, 25] No data are available to characterize which PAs are susceptible to rupture in pediatric BLSI. Our present study provides little evidence to suggest that the size of the PA or distance from the capsule is associated with PA rupture. Consistent with our findings, a prior retrospective study also found no association between aneurysm size and symptoms.[25] Although larger PAs are more likely to be treated based on the idea that they are more likely to rupture, there is currently no evidence to support this practice. Rather, concerns about PA rupture may apply equally to smaller PAs. Future studies are needed to investigate other predictive factors of PA rupture besides the size and location of the identified PA.

One reason why only one patient in this study required total splenectomy for PA may be related to the very low rate of proximal embolization on admission angiography. In the absence of data regarding the use of IR in children, most of our knowledge on this topic is extrapolated from the adult literature. A recent retrospective evaluation of adult splenic injuries from a level I trauma center in the United States reported that a relatively high proportion of patients who developed PA required subsequent splenectomy.[26] Despite the fact that some patients who undergo distal embolization of the splenic artery experience minor spleen infarcts, the procedure itself rarely results in splenectomy.[24,27] Conversely, if proximal embolization is performed on admission angiography, and then a PA develops in the late phase, vascular access to the splenic artery during "second-look" angiography is limited.[28] Considering late vascular events, distal embolization may be preferable during the initial angiography based on an organ preservation perspective for pediatric patients.

Prospective studies with larger pediatric cohorts are warranted to examine techniques of early angioembolization in preparation for late vascular events.

Our study has several strengths. First, many unique variables not available in the national trauma database were entered from directly reviewed medical records and historical images from trained site researchers, which proved a highly accurate assessment of PA, active bleeding, and AAST injury grade (both 1994 version and 2018 revision). Second, we included inter-hospital transfer cases in this study because pediatric trauma patients are often initially transported to a local emergency hospital, and then transferred to an urban trauma center, or transferred from an adult trauma center to a children's hospital. Third, through repeated data cleaning, we developed a high-quality dataset with few outliers and missing values.

Conversely, our study also has several limitations. First, there was no standardized pediatric trauma protocol used to manage the patients in this study. The variation in management strategies across participating facilities and departments responsible for pediatric trauma patients might therefore have influenced our results and could skewed the findings in favor of practices followed at those sites which contributed more data to the study. The results of this study were obtained in the context of unique Japanese practice patterns that do not adhere to current standard guidelines in the United States, and these practice patterns need to be considered when interpreting the present findings. Second, delayed PA formation is a rare event; even with a large multicenter study, it can be challenging to capture all events. Moreover, some events may have been underreported because routine follow-up CT imaging for pediatric patients was not recommended[1,3]. On the other hand, it is also true that most institutions in Japan do not adhere to the current recommendation for follow-up imaging in the United States, and CT follow-up was likely performed in the majority of cases among the population at risk of pseudoaneurysm formation[9]. In addition, it is unknown what proportion of patients actually underwent imaging follow-up until the pseudoaneurysm was proven to have disappeared. Third, considering the long study period, the influence of advances in imaging

modalities, especially CT scans, on the diagnosis of vascular injuries cannot be excluded. Fourth, the study has a degree of selection bias due to incomplete retrieval because of its retrospective design. In the present study, only data on re-bleeding episodes due to PA rupture were collected, and data on delayed hemorrhage other than PA rupture (e.g., rupture of subcapsular hematoma) were not available. Accordingly, the frequency of other re-bleeding events could not be assessed. Finally, the generalizability of this study is limited by the unique practice patterns in Japan; that is, IR may be aggressively indicated even in pediatric patients as a hemostatic intervention because of fast and easy access to the angiography suite.[29,30]

Notwithstanding these possible limitations, our findings have several important clinical implications for evidence on the natural history and clinical course of PA following BLSI in pediatric patients. These will be essential in establishing standardized recommendations or guidelines. This research may provide an opportunity for countries where standardized guidelines do not exist, such as Japan, to review their own practice. Further, it may improve evidence-based practice with reference to existing guidelines and trigger the establishment of standardized recommendations suited to national circumstances.

CONCLUSION

Endovascular intervention is widely applied to treat acute and delayed hemorrhage as well as to prevent future bleeding from PA rupture following pediatric BLSI in Japan. Our study results suggest that patients undergoing angioembolization for acute hemorrhage are still at risk of delayed PA development and re-bleeding from PA rupture, regardless of injury grade. While endovascular interventions are usually successful for PA management, including ruptured cases, given the high incidence of spontaneous resolution, the ideal management of delayed PA needs further clarification.

Supplemental Digital Content includes data cleaning and quality control methods, geographical distribution and site principal investigators of the participating centers in this study, additional information from Table 1 such as hospital characteristics and primary service, subgroup analysis of Table 2 (spleen injury subgroup and liver injury subgroup) and AAST grade 1994 version of Dotplot Figure 3.

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Figure legends

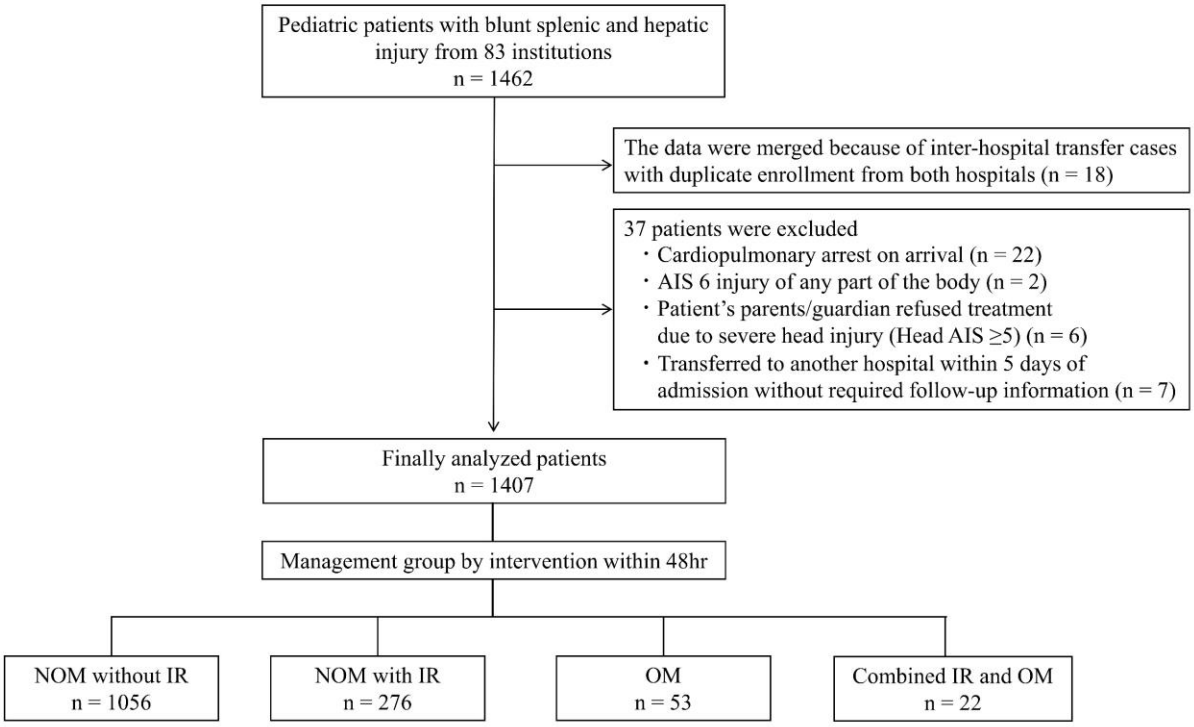

Figure 1. Selection process for the study population

Abbreviations: AIS, abbreviated injury scale; NOM, non-operative management; IR, interventional radiology; OM, operative management

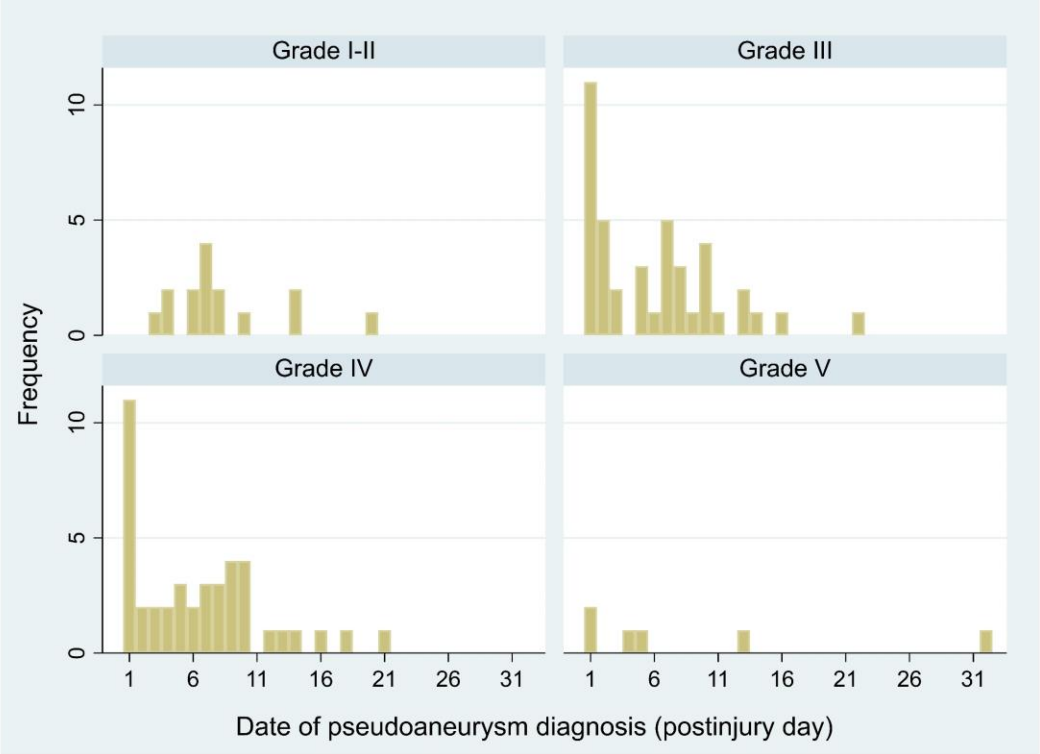

Figure 2. Histogram showing date of pseudoaneurysm diagnosis by AAST grade of spleen/liver injury (2018 revision)

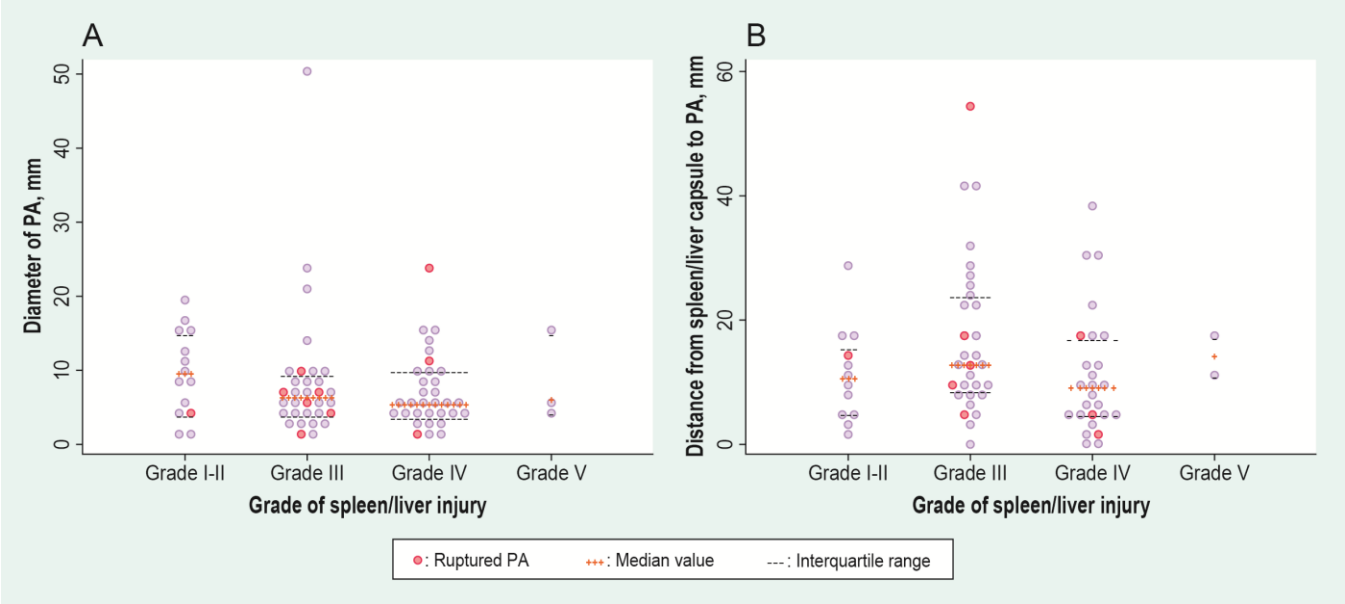

Figure 3. Dotplot showing A) diameter of pseudoaneurysm, and B) distance from spleen/liver capsule to pseudoaneurysm by AAST grade of injury (2018 revision)

Abbreviations: PA, pseudoaneurysm of splenic and/or hepatic artery

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M.K., Y.K., H.Y, S.F., K.M., A.S., A.T., A.K., and S.K. designed the study. M.K and K.M searched the literature. M.K., Y.K., H.Y, A.K., M.G., K.H., N.M., K.S., K.T., and H.Y. collected the data. M.K. and S.F. analyzed the data. M.K. wrote the manuscript. All authors participated in data interpretation, article preparation, and critical revisions, and approved the final article.

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Authors have no conflicts of interest to disclose.

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Supplemental digital content

Supplementary methods. Data cleaning and quality control

Figure S1. Geographical distribution of the participating centers in this study

Table S1. List of the participating centers and site principal investigators in this study

Table S2. Patient and hospital characteristics of all participants by management group within 48 hours of admission (Additional information)

Table S3. Subgroup analysis: univariant comparison of delayed pseudoaneurysm formation by management group within 48 hours of admission

Figure S2. Dotplot showing A) diameter of pseudoaneurysm, and B) distance from spleen/liver capsule to pseudoaneurysm by AAST grade of injury (1994 version)

Supplementary methods. Data cleaning and quality control

Study data were collected and managed through the REDCap (Research Electronic Data Capture, Vanderbilt University, Nashville, TN) tool hosted at Kameda Medical Center, Chiba, Japan. REDCap is a secure, web-based software platform designed to support data capture for research studies. Data registered in REDCap were grouped according to the timing of completed data registration, and data entry errors were checked according to a pre-developed data cleaning logic.[30,31] All facilities were requested to perform this data cleaning process at least twice to crosscheck for inconsistencies, outliers, and missing data by the research investigator per site and correct them. The cleaning logic was updated each time, and the final data cleaning process was conducted simultaneously at all facilities after the data registration of all enrolled cases was completed. This repeated data cleaning for quality control allowed for differences in the quality of data collection between the 83 participating centers to be corrected before data locking.[31,32] All items corrected in the data cleaning process were kept on record.

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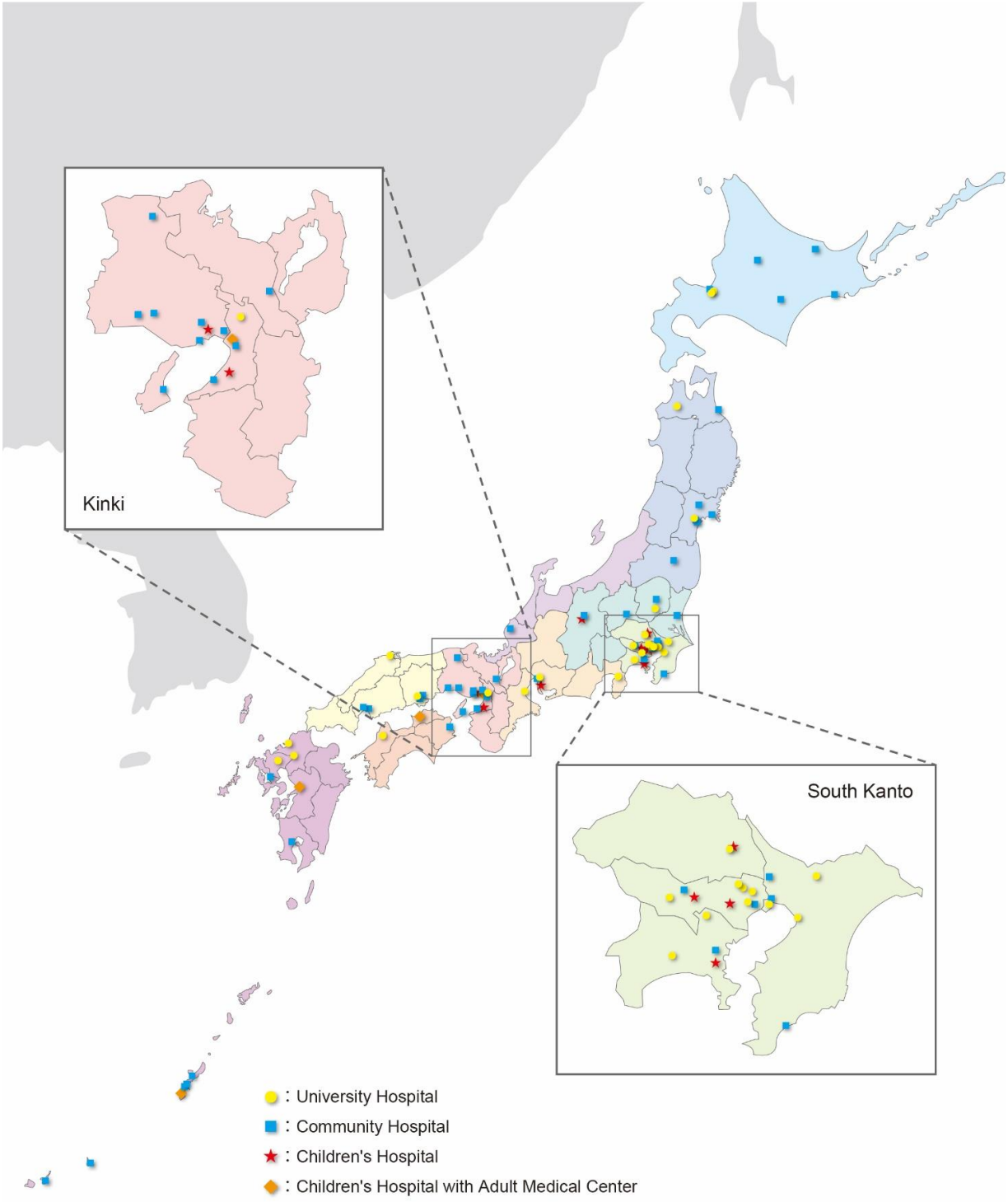

Table S1. A list of the participating centers and site principal investigators in this study (in alphabetical order by site)

No.	Institution name	Site principal investigators	
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3	Asahikawa Red Cross Hospital	Hiroto Manase	
4	Chiba University Hospital	Nozomi Takahashi	
5	Chukyo Hospital	Akinori Osuka	
6	Ehime University Hospital	Suguru Annen	
7	Fukui Prefectural Hospital	Nobuki Ishikawa	
8	Fukuoka University Hospital	Kazushi Takayama	
9	Hachinohe City Hospital	Keita Minowa	
10	Hirosaki University Hospital	Kenichi Hakamada	
11	Hiroshima Prefectural Hospital	Akari Kusaka	
12	Hokkaido university hospital	Mineji Hayakawa	Shota Kawahara
13	Hyogo Emergency Medical Center	Marika Matsumoto	
14	Hyogo Prefectural Amagasaki General Medical Center	Kohei Kusumoto	
15	Hyogo Prefectural Awaji Medical Center	Hiroshi Kodaira	
16	Hyogo Prefectural Kakogawa Medical Center	Chika Kunishige	
17	Hyogo Prefectural Kobe Children's Hospital	Keiichiro Toma	Yusuke Seino
18	Ishinomaki Red Cross Hospital	Michio Kobayashi	
19	JA Hiroshima General Hospital	Masaaki Sakuraya	
20	Jichi Medical University Hospital	Takafumi Shinjo	Shigeru Ono
21	Jichi Medical University Saitama Medical Center	Hideto Yasuda	Haruka Taira
22	Juntendo University Shizuoka Hospital	Kazuhiko Omori	
23	Juntendo University Urayasu Hospital	Yutaka Kondo	
24	Kagoshima City Hospital	Yoshio Kamimura	
25	Kameda Medical Center	Atsushi Shiraishi	Rei Tanaka

26	Kanagawa Children's Medical Center	Yukihiro Tsuzuki	
27	Keio University Hospital	Yukio Sato	
28	Kitami Red Cross Hospital	Noriaki Kyogoku	
29	Kobe City Medical Center General Hospital	Masafumi Onishi	Kaichi Kawai
30	Japanese Red Cross Kumamoto Hospital	Kazuyuki Hayashida	Keiko Terazumi
31	Kurashiki Central Hospital	Akira Kuriyama	Susumu Matsushime
32	Kurume University Hospital	Osamu Takasu	Toshio Morita
33	Kushiro City General Hospital	Nagato Sato	
34	Kyoto Second Red Cross Hospital	Wataru Ishii	Michitaro Miyaguni
35	Maebashi Red Cross Hospital	Yosuke Nakabayashi	Yoshimi Ohtaki
36	Matsudo City General Hospital	Kiyoshi Murata	Masayuki Yagi
37	Mie University Hospital	Tadashi Kaneko	
38	Nagano Children's Hospital	Shigeru Takamizawa	
39	Nagoya University Hospital	Akihiro Yasui	
40	Nakagami Hospital	Yasuaki Mayama	
41	National Center for Child Health and Development	Masafumi Gima	
42	National Hospital Organization Disaster Medical Center	Ichiro Okada	
43	National Hospital Organization Mito Medical Center	Asuka Tsuchiya	Koji Ishigami
44	National Hospital Organization Nagasaki Medical Center	Yukiko Masuda	
45	National Hospital Organization Sendai Medical Center	Yasuo Yamada	
46	Nippon Medical School Chiba Hokusoh Hospital	Hiroshi Yasumatsu	
47	Nippon Medical School Hospital	Kenta Shigeta	
48	Obihiro Kosei Hospital	Kohei Kato	
49	Ohta Nishinouchi Hospital	Fumihito Ito	
50	Okayama Red Cross Hospital	Atsuyoshi Iida	
51	Okayama University Hospital	Tetsuya Yumoto	Hiromichi Naito
52	Okinawa Chubu Hospital	Morihiro Katsura	Yoshitaka Saegusa
53	Okinawa Hokubu Hospital	Tomohiko Azuma	

54	Okinawa Miyako Hospital	Shima Asano	
55	Okinawa Nanbu Medical Center & Children's Medical Center	Takehiro Umemura	Norihiro Goto
56	Okinawa Yaeyama Hospital	Takao Yamamoto	
57	Osaka City General Hospital	Junichi Ishikawa	
58	Osaka Red Cross Hospital	Elena Yukie Uebayashi	
59	Osaka University Hospital	Shunichiro Nakao	
60	Osaka Women's and Children's Hospital	Yuko Ogawa	
61	Osaki Citizen Hospital	Takashi Irinoda	
62	Rinku General Medical Center	Yuki Narumi	
63	Saga University Hospital	Miho Asahi	
64	Saiseikai Utsunomiya Hospital	Takayuki Ogura	Takashi Hazama
65	Saiseikai Yokohamashi Tobu Hospital	Shokei Matsumoto	
66	Saitama Children's Medical Center	Daisuke Miyamoto	
67	Sapporo Medical University Hospital	Keisuke Harada	Narumi Kubota
68	Sendai City Hospital	Yusuke Konda	
69	Shikoku Medical Center for Children and Adults	Takeshi Asai	
70	Shimane University Hospital	Tomohiro Muronoi	
71	St. Luke's International Hospital	Toru Hifumi	Kasumi Shirasaki
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73	Steel Memorial Hirohata Hospital	Makoto Takaoka	
74	Teikyo University Hospital	Kaori Ito	
75	Teine Keijinkai Hospital	Satoshi Nara	
76	Tohoku University Hospital	Shigeki Kushimoto	Atsushi Tanikawa
77	Tokai University Hachioji Hospital	Masato Tsuchikane	
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83	Toyooka Hospital	Tamotsu Gotou	

Table S2. Patient and hospital characteristics of all participants by management group within 48 hours of admission (Additional information)

		Management group by intervention within 48hr				
	Overall cohort (n = 1,407)	NOM without IR (n = 1,056)	NOM with IR (n = 276)	OM (n = 53)	Combined IR/OM (n = 22)	*P* value
Laboratory data on admission						
Hb, median [IQR], g/dL	12.4 [11.3–13.3]	12.5 [11.6–13.4]	12.1 [11.0-13.2]	11.0 [8.8-12.3]	11.3 [9.5-12.1]	<0.001
Hct, median [IQR], %	36.4 [33.5–39.0]	36.7 [34.1–39.2]	35.7 [32.5–38.7]	32.7 [25.7–36.6]	32.9 [26.9–35.6]	<0.001
PLT count, median [IQR], in ten thousands/mcL	27.5 [22.5–33.3]	28.2 [23.1-34.3]	26.0 [22.0-31.1]	22.2 [16.1-28.1]	22.0 [17.1-33.1]	<0.001
INR, median [IQR]	1.10 [1.04–1.19]	1.09 [1.03–1.16]	1.15 [1.07–1.25]	1.25 [1.13–1.70]	1.32 [1.12–1.48]	<0.001
Imaging data on admission						
Hemoperitoneum volume*, n (%)						<0.001
zero	533 (38%)	495 (47%)	37 (13%)	1 (2%)	0 (0%)	
small volume	325 (23%)	257 (24%)	63 (23%)	3 (6%)	2 (9%)	
moderate volume	242 (17%)	164 (16%)	68 (25%)	8 (15%)	2 (9%)	
large volume	307 (22%)	140 (13%)	108 (39%)	41 (77%)	18 (82%)	
Hospital characteristics, n (%)						<0.001
University hospital (adult center)	403 (29%)	274 (26%)	107 (39%)	17 (32%)	5 (23%)	
Community hospital (adult center)	666 (47%)	479 (45%)	148 (54%)	25 (47%)	14 (64%)	
Children's hospital	209 (15%)	190 (18%)	10 (4%)	7 (13%)	2 (9%)	
Mixed adult/pediatric center	129 (9%)	113 (11%)	11 (4%)	4 (8%)	1 (5%)	
Primary service, n (%)						<0.001
Emergency medicine	723 (51%)	490 (46%)	192 (70%)	27 (51%)	14 (64%)	
Pediatric emergency medicine	32 (2%)	31 (3%)	1 (0.4%)	0 (0%)	0 (0%)	
General surgery	218 (15%)	162 (15%)	40 (15%)	11 (21%)	5 (23%)	
Pediatric surgery	278 (20%)	235 (22%)	34 (12%)	8 (15%)	1 (5%)	
Pediatric critical care	131 (9%)	117 (11%)	5 (2%)	7(13%)	2 (9%)	
Others	25 (18%)	21 (2%)	4 (1%)	0 (0%)	0 (0%)	

Abbreviations: NOM, non-operative management; IR, interventional radiology; OM, operative management, Hb, hemoglobin; Hct, hematocrit; PLT, platelet; IQR, interquartile range; INR, International Normalized Ratio.

IQR presents the 25th and 75th percentiles, as appropriate.

P-values of the Table are for four-group comparisons using the Kruskal-Wallis test or chi-squared test.

* Hemoperitoneum volume was estimated by totaling the number of intra-abdominal regions, which were adapted (right upper quadrant, left upper quadrant, right paracolic gutter, left paracolic gutter, and pelvis) when free fluid was identified on initial imaging. The definitions were: small, one region; moderate, two regions; large, three or more regions.

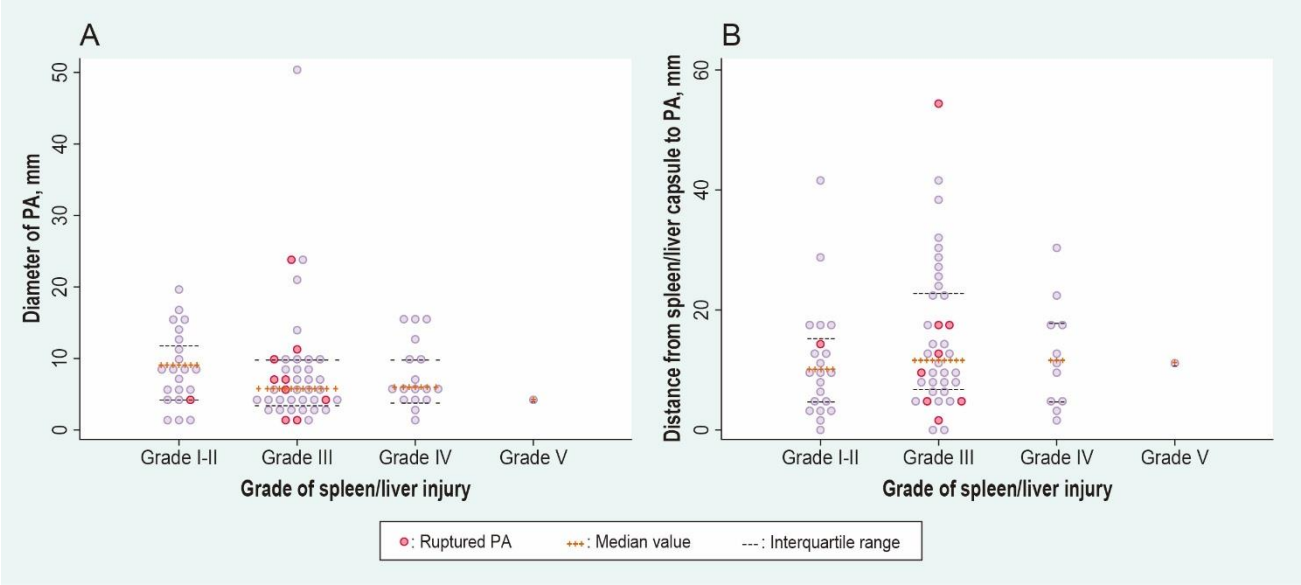
Table S3. Subgroup analysis: univariate comparison of delayed pseudoaneurysm formation by management group within 48 hours of admission

		Management group by intervention within 48hr				
Subgroup Outcome	Overall cohort* (n = 1,353)	NOM without IR (n = 1,031)	NOM with IR (n = 258)	OM (n = 46)	Combined IR/OM (n = 18)	*P* value
Spleen injury						
Delayed PA formation	50/532 (9.4%)	26/345 (7.5%)	22/156 (14%)	2/26 (7.7%)	0/5 (0%)	<0.001
Liver injury						
Delayed PA formation	29/821 (3.5%)	16/686 (2.3%)	10/102 (9.8%)	0/20 (0%)	3/13 (23%)	<0.001

Abbreviations: PA, pseudoaneurysm of splenic/hepatic artery; NOM, non-operative management; IR, interventional radiology; OM, operative management

* Patients who sustained both liver and spleen injuries were excluded from this subgroup analysis because the organ in which the pseudoaneurysm originated could not be determined.

Figure S2. Dotplot showing A) diameter of pseudoaneurysm, and B) distance from spleen/liver capsule to pseudoaneurysm by AAST grade of injury (1994 version)



Abbreviations: PA, pseudoaneurysm of splenic and/or hepatic artery