

Original Article

Relationship between in-hospital mortality and abdominal angiography among patients with blunt liver injuries: a propensity score-matching from a nationwide trauma registry of Japan

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Aim: To assess relationships between abdominal angiography and outcomes in adults with blunt liver injuries.

Methods: A retrospective observational study carried out from January 2004 to December 2018. Adult blunt-trauma patients with AAST grade III–V were analyzed with in-hospital mortality as the primary outcome using propensity-score-(PS) matching to seek associations with abdominal angiography findings.

Results: A total of 1,821 patients were included, of which 854 had available abdominal angiography data (AA+) and 967 did not (AA–). From these, 562 patients were selected from each group by propensity score matching. In-hospital mortality was found to be lower in the AA+ than in the AA– group (15.1% [87/562] versus 25.4% [143/562]; odds ratio 0.544, 95% confidence interval 0.398–0.739).

Conclusion: Abdominal angiography is shown to be of benefit for adult patients with blunt liver injury in terms of their lower in-hospital mortality.

Key words: Abdominal angiography, in-hospital mortality, liver injury, propensity score-matching

INTRODUCTION

ABDOMINAL TRAUMA IS potentially fatal. Liver injury is commonly associated with hemorrhagic death; therefore, appropriate management is essential. In the past, surgery was the primary treatment, but managing liver injuries without resorting to surgery has recently emerged as the treatment of choice.^{1–3} Abdominal angiography (AA)

and arterial embolization are particularly useful measures. Previous observational studies using transarterial embolization (TAE) to treat severe liver injury indicated that this could be carried out in a safe, feasible, and effective manner.⁴ In practice, conservative management, TAE, and surgery are selected after angiography. The Eastern Association for the Surgery of Trauma (EAST) and World Society of Emergency Surgery (WSES) guidelines state that AA is indicated for adults whose hemodynamics are stable.^{5,6} We reported earlier that AA for blunt hepatosplenic injury resulted in lower in-hospital pediatric mortality in Japan.⁷ In adults, observational studies have suggested that AA performed following abdominal surgery for severe liver injuries

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Received 25 Jul, 2021; accepted 14 Dec, 2021

is associated with reduced hospital mortality.⁸ Several reports have indicated that nonoperative management, including TAE, is possible even when a severe blunt liver injury is accompanied by hemodynamic instability.

The Japan Trauma Data Bank (JTDB) is a nationwide hospital-based multicenter trauma registry. Here, using JTDB data, we compared in-hospital mortality of adults hospitalized with blunt liver injury who did or did not receive AA.

METHODS

Study design and data set

THIS WAS A retrospective, nationwide multicenter observational study of adult trauma patients registered in the JTDB over 15 years (2004–2018). This work followed the guidelines of the “Strengthening the Reporting of Observational Studies in Epidemiology” on cohort and cross-sectional studies.⁹

The Japan Trauma Data Bank

The JTDB is a nationwide hospital-based multicenter trauma registry under the auspices of the Japanese Association for the Surgery of Trauma (Trauma Surgery Committee) and the Japanese Association for Acute Medicine.¹⁰ Over the study period reviewed here, data from 280 certified tertiary hospital emergency medical centers in Japan were extracted for analysis via internet access. In most cases, patient data had been entered by physicians and medical assistants who had completed the Abbreviated Injury Scale (AIS) coding course. The JTDB captures 92 data elements including pre-hospital and hospital information on age, sex, the reason for the injury, the mode of transportation to hospital, vital signs, AIS codes (version 1998) for all bodily regions, the injury severity score (ISS), in-hospital procedures such as interventional radiology and surgery, and discharge information.

Participants

We included patients aged ≥ 18 years with severe blunt liver injuries (American Association for the Surgery of Trauma–Organ Injury Scale [AAST-OIS] grades III–V). Patients were identified using AIS codes (version 1998) consistent with liver injury (AIS PREDOT code 541810–541899).¹¹ Liver injury was graded on the basis of liver AIS scoring.¹² We excluded patients who were transported between hospitals, or experienced cardiopulmonary arrest on arrival, whose ISS could not be calculated, or where the data on vital signs at the time of hospital admission and discharge were not available. A systolic blood pressure (BP) of 0 mmHg or a heart rate

(HR) of 0 bpm on admission was taken as unequivocal cardiopulmonary arrest.¹³ Within the JTDB, the liver, spleen, and kidneys cannot be distinguished for AA. Therefore, to exclude patients who underwent AA for other intra-abdominal organs, patients with spleen or kidney injuries were also excluded (spleen AIS PREDOT code 544299–544240, kidney AIS PREDOT code 541699–541640).¹¹ Other intra-abdominal organ injuries (such as pancreas, gastrointestinal injuries) were not excluded.

Variables

We extracted data from the JTDB on age, sex, hospital admission year, cause of injury, systolic BP and HR on admission to hospital, Japan Coma Scale (JCS) score at that time, the Focused Assessment with Sonography for Trauma (FAST), computed tomography (CT) of the abdomen, emergency intubation, liver AAST-OIS grade, whether the liver injury was isolated or not, concomitant extra-abdominal injuries (number of head, thorax, and lower extremity [including pelvic fracture] injuries of AIS grades >2), intra-abdominal (pancreas, gastrointestinal) injury, the ISS, the use of AA, or abdominal surgery. Within the JTDB, AA, pelvic angiography, and angiography for the spine were distinguished. Patients were identified based on AIS scores consistent with injury to the pancreas and gastrointestinal tract, including the mesentery. Consciousness level was evaluated using the JCS score¹⁴ on admission. According to this scale, awareness is assessed in terms of three classifications, and agrees quite well with the Glasgow Coma Scale (GCS; a JCS score of 100 points corresponds to a GCS score of 6–9). Patients were stratified into four groups based on the JCS score as follows: 0, alert; 1–3, delirious; 10–30, somnolent; and 100–300, in a coma.^{15,16} We calculated the frequency of AA imaging for liver injury at each hospital by dividing the total number of patients so evaluated by the total number of liver injury patients in that hospital.¹⁷ Missing covariates were labeled “Unknown.”

Outcome

The main outcome was in-hospital mortality. The need for TAE was a secondary outcome.

Statistical analysis

We dichotomized all patients based on whether emergency AA was or was not conducted (AA+ versus AA–). We present the medians with interquartile ranges (IQRs) of continuous variables and the frequencies and percentages of categorical variables. Mann–Whitney testing was used to

compare continuous variables, whereas the chi-square test was used for categorical variables.

Propensity score (PS) matching^{18,19} was carried out to compensate for potential confounding factors that might have otherwise differed between the AA+ and AA− groups. PSs were calculated on the basis of multiple logistic regression accounting for the following 19 variables (prior to AA): age, sex, admission year (2004–2006, 2007–2009, 2010–2012, 2013–2015, or 2016–2018), cause of injury, systolic BP on arrival, HR on arrival, JCS score (alert, delirious, somnolent, in a coma, or unknown), FAST, CT of the abdomen, emergency intubation, liver AAST-OIS grade (III, IV, or V), isolated liver injury, any concomitant non-intra-abdominal injury with an AIS score >2 at any site, any concomitant intra-abdominal injury to the pancreas or gastrointestinal tract including the mesentery, the ISS, and the frequency of performance of AA for liver injury at each hospital.

The model fit was evaluated by deriving the c-statistic using the area under the receiver-operating characteristic curve. The AA+ and AA− groups were then paired 1:1 based on these propensity scores using one-to-one nearest-neighbor matching without replacement. A standard caliper size of $0.1 \times \log [\text{SD of the propensity score}]$ was used. The standardized mean difference (SMD) of the variables used for PS estimation was used to assess goodness of match between groups. An SMD <0.1 indicates a good match between two groups.²⁰ We used the McNemar test to determine differences in in-hospital mortality between the two groups after PS matching.

To verify the acceptability of PS matching, an inverse probability of treatment weighting (IPTW) estimation based on the PS was used.^{18,19} Data are depicted as odds ratios (ORs) and 95% confidence intervals (CIs).

We divided patients by age (≥ 65 or <65 years), shock status on arrival (in shock or not), AAST liver injury grade (III, IV, or V), AIS head score >2 (yes or no), ISS (≥ 25 or <25), and abdominal surgery (yes or no). The patient was considered to be in shock when systolic BP was <80 mmHg on admission.²¹ We used linear regression to calculate the ORs for in-hospital mortality in the AA+ and AA− groups and the interactions between subgroups. In addition, we performed a subgroup analysis by shock status on hospital arrival. Statistical analyses were performed using R version 4.0.2 (The R Foundation for Statistical Computing, Vienna, Austria). $P < 0.05$ was accepted as significant (two-sided).

RESULTS

THIS STUDY INCLUDED 354,608 patients hospitalized between 2004 and 2018 who were registered in the JTDB database. Of these patients, 3,798 had hepatic injuries

of AAST-OIS grades III–V. Of these, 3,318 (87.4%) were ≥ 18 years of age (Fig. 1). We excluded 567 patients transported from other hospitals, 250 who experienced cardiopulmonary arrest on arrival, 502 who had injuries to the spleen or kidney, 107 for whom discharge data were lacking, 3 for whom ISSs could not be calculated, and 68 for whom vital sign data on hospital admission were missing. We finally included 1,821 patients of whom 854 had undergone AA and 967 had not.

The background of all patients is summarized in Table 1. Prior to PS matching, the median age was 45 years (IQR 30–63 years) in the AA+ group and 43 years (IQR 29–63 years) in the AA− group. There were 525 (61.5%) FAST-positive patients in the AA+ group and 483 (49.9%) in the AA− group. In total, 774 (90.6%) and 810 (83.8%) patients in the AA+ and AA− groups, respectively, underwent CT. The median ISS was 26 (IQR 17–34) and 26 (IQR 17–38) in the AA+ and AA− groups, respectively. The median frequency of performing AA for liver injury per hospital was 0.55 (IQR 0.40–0.67) for the AA+ group and 0.38 (IQR 0.26–0.50) for the AA− group. In the former, 57 (6.7%) underwent abdominal surgery, whereas this figure was 41 (4.2%) in the latter. Following matching by PS, a comparison of 562 AA+ and the same number of AA− patients yielded a c-statistic indicating goodness of fit of 0.778. The SMD revealed a well-balanced distribution of covariates between AA+ and AA− PS-matched patients (SMD < 0.1).

Table 2 shows the association between the use of AA and in-hospital mortality. Among all patients (i.e., prior to PS matching), in-hospital mortality was lower in AA+ than AA− patients (14.8% [126/854] versus 25.7% [249/967]; OR 0.499, 95% CI 0.392–0.631). A total of 511 patients (59.8%) underwent TAE in the AA+ group. After PS matching, the in-hospital mortality rate remained lower in AA+ patients (15.1% [87/562] versus 25.4% [143/562]; OR 0.544, 95% CI 0.398–0.739). A total of 321 patients (57.1%) underwent abdominal TAE in the AA+ group. These results were confirmed using an IPTW model (OR 0.562, 95% CI 0.426–0.741; Fig. 2).

Subgroup analyses depicted in Figure 3 stratified patients by age, shock on arrival, liver injury AAST grade, head injury, ISS, and abdominal surgery. In the context of age, there was a significant relationship between receiving AA and experiencing less in-hospital mortality (≥ 65 years: OR 0.493, 95% CI 0.323–0.745; <65 years: OR 0.491, 95% CI 0.364–0.658). Regarding AAST-OIS liver injury grades, a similar benefit of receiving AA was seen (grade III: OR 0.673, 95% CI 0.477–0.941; grade IV: OR 0.372,

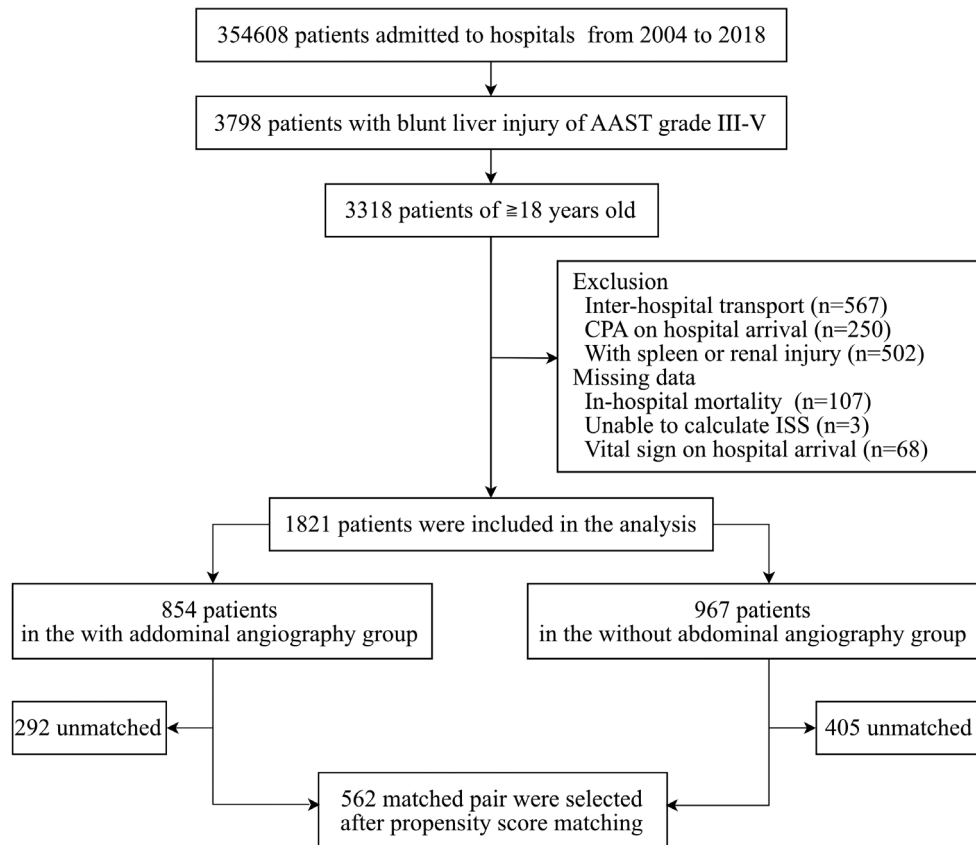


Fig. 1. Flowchart of patient selection from the Japan Trauma Data Bank (JTDB). AAST, American Association for the Surgery of Trauma; CPA, cardiopulmonary arrest; ISS, injury severity score

95% CI 0.233–0.588; grade V: OR 0.217, 95% CI 0.111–0.412). Only in patients with an ISS ≥ 25 but not in those with an ISS of < 25 was AA significantly associated with less in-hospital mortality (OR 0.401, 95% CI 0.305–0.525 versus OR 0.996, 95% CI 0.533–1.847, respectively). Regardless of abdominal surgery, having received AA was similarly beneficial (surgery performed: OR 0.410, 95% CI 0.174–0.944; surgery not performed: OR 0.487, 95% CI 0.378–0.625). Significant interactions were found in the analysis for additional effect modification related to concomitant shock status on arrival, AAST-OIS liver injury grade, and ISS subgroup (P for interaction 0.012, 0.005, and < 0.001 , respectively). Regarding the subgroup analysis in shock patients, 59.4% of patients with shock on hospital arrival who underwent AA had TAE, and 12.1% had abdominal surgery (Table S1).

DISCUSSION

WE USED JTDB data to investigate whether adult patients with blunt liver injury who had been

examined by AA had significantly lower in-hospital mortality than patients who had not received AA. Clearly, there is no direct causal connection with the use of angiography alone (without embolization of active hemorrhage) so this would not be expected to have any beneficial influence as such. However, the relationship between the application of AA in hepatic injury and the lower in-hospital mortality documented here may have been useful for selecting treatment strategies for these patients and thus had an indirect beneficial effect. Nevertheless, we found that AA+ adult patients with blunt liver injury exhibited significantly lower in-hospital mortality than AA– patients. The EAST and WSES guidelines suggest that contrast-enhanced CT should be used to assess liver injury.^{5,6,22} Abdominal CT was performed for 87% of all patients. However, the detection rates of contrast extravasation with contrast-enhanced CT and angiography for patients with abdominal parenchymal organ injuries did not always match in a previous study.²³ The data can vary according to the imaging protocol.^{24,25} If the source of bleeding can be identified angiographically, embolization is possible. In the present study, the frequency of performing

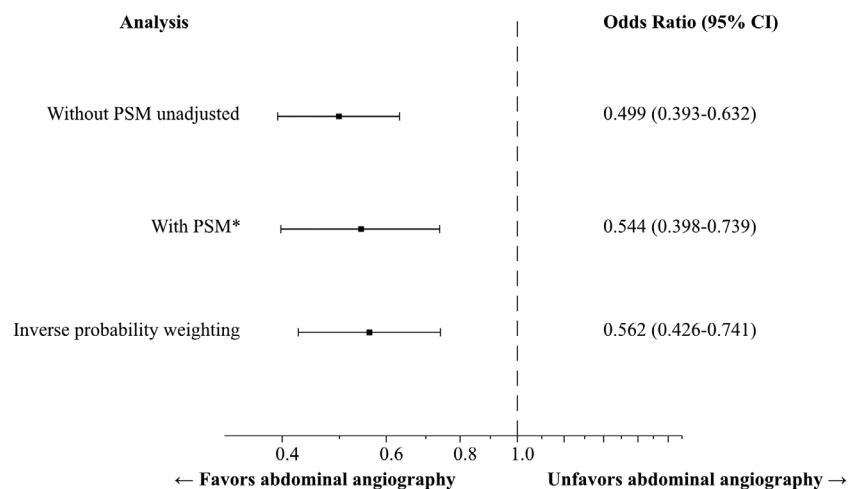
Table 1. Comparisons of the covariates before and after propensity score matching

Variables	All patients			Propensity score-matched patients		
	Abdominal angiography (-) N = 967	Abdominal angiography (+) N = 854	SMD	Abdominal angiography (-) N = 562	Abdominal angiography (+) N = 562	SMD
Age, median (IQR)	43 (29–63)	45 (30–63)	0.052	44 (28–63)	45 (30–62)	0.004
Male, sex, n (%)	677 (70.0)	575 (67.3)	0.058	384 (68.3)	380 (67.6)	0.015
Admission year, n (%)						
2004–2006	67 (6.9)	24 (2.8)	0.244	22 (3.9)	23 (4.1)	0.033
2007–2009	165 (17.1)	111 (13.0)		84 (14.9)	87 (15.5)	
2010–2012	246 (25.4)	227 (26.6)		152 (27.0)	149 (26.5)	
2013–2015	263 (27.2)	283 (33.1)		170 (30.2)	164 (29.2)	
2016–2018	226 (23.4)	209 (24.5)		134 (23.8)	139 (24.7)	
Mechanism of injury, n (%)						
Traffic accident	677 (70.0)	609 (71.3)	0.053	393 (69.9)	404 (71.9)	0.058
Fall from an elevation	107 (11.1)	81 (9.5)		59 (10.5)	59 (10.5)	
Fall down	77 (8.0)	67 (7.8)		48 (8.5)	40 (7.1)	
Other	106 (11.0)	97 (11.4)		62 (11.0)	59 (10.5)	
Systolic BP on arrival (mmHg), median (IQR)	111 (84–133)	110 (87–132.3)	0.005	112 (85–133)	110 (88–134)	0.024
Heart rate on arrival (bpm), median (IQR)	93 (78–113)	92 (78–110)	0.074	91 (76–111)	94 (79–112)	0.021
Japan coma scale, n (%)						
0-Alert	381 (39.4)	356 (41.7)	0.173	231 (41.1)	229 (40.7)	0.035
1-Delirium	279 (28.9)	280 (32.8)		176 (31.3)	180 (32.0)	
2-Somnolence	109 (11.3)	97 (11.4)		61 (10.9)	63 (11.2)	
3-Coma	190 (19.6)	115 (13.5)		90 (16.0)	85 (15.1)	
4-Unknown	8 (0.8)	6 (0.7)		4 (0.7)	5 (0.9)	
FAST, n (%)						
Negative	394 (40.7)	259 (30.3)	0.238	190 (33.8)	194 (34.5)	0.021
Positive	483 (49.9)	525 (61.5)		326 (58.0)	324 (57.7)	
Undone	52 (5.4)	39 (4.6)		28 (5.0)	26 (4.6)	
Unknown	38 (3.9)	31 (3.6)		18 (3.2)	18 (3.2)	
Abdominal CT, n (%)	810 (83.8)	774 (90.6)	0.207	500 (89.0)	502 (89.3)	0.011
Emergency endotracheal intubation, n (%)	350 (36.2)	323 (37.8)	0.034	203 (36.1)	209 (37.2)	0.022
Liver AAST-OIS grade, n (%)						
Grade III	672 (69.5)	531 (62.2)	0.251	365 (64.9)	369 (65.7)	0.019
Grade IV	187 (19.3)	254 (29.7)		138 (24.6)	137 (24.4)	
Grade V	108 (11.2)	69 (8.1)		59 (10.5)	56 (10.0)	
Isolated liver injury, n (%)	268 (27.7)	239 (28.0)	0.006	163 (29.0)	158 (28.1)	0.020
Concomitant extra-abdominal injury, n (%)						
AIS head >2	193 (20.0)	142 (16.6)	0.086	98 (17.4)	100 (17.8)	0.009
AIS chest >2	554 (57.3)	496 (58.1)	0.016	319 (56.8)	325 (57.8)	0.022
AIS lower extremity injury including pelvis >2	207 (21.4)	167 (19.6)	0.046	114 (20.3)	117 (20.8)	0.013
Concomitant intra-abdominal injury, n (%)						
Pancreas injury	31 (3.2)	18 (2.1)	0.068	16 (2.8)	15 (2.7)	0.011
Gastrointestinal injury	73 (7.5)	37 (4.3)	0.136	35 (6.2)	30 (5.3)	0.038
ISS, median (IQR)	26 (17–38)	26 (17–34)	0.043	25 (17–35)	27 (17–35.5)	0.041
Frequency of abdominal angiography for liver injury per hospitals, median (IQR)	0.38 (0.26–0.50)	0.55 (0.40–0.67)	0.900	0.44 (0.36–0.59)	0.45 (0.38–0.59)	0.082
Abdominal surgery, n (%)	41 (4.2)	57 (6.7)	–	23 (4.1)	39 (6.9)	–

Table 2. Outcomes of patients with liver injuries who did and did not undergo abdominal angiography

	Total	Abdominal angiography (+)	Abdominal angiography (–)	Odds ratio (95% CI)	P value
All patients	N = 1,821	N = 854	N = 967		
Abdominal TAE, n (%)		511 (59.8)			
In-hospital mortality, n (%)		126 (14.8)	249 (25.7)	0.499 (0.392–0.631)	<0.001
Propensity score-matched patients	N = 1,124	N = 562	N = 562		
Abdominal TAE, n (%)		321 (57.1)			
In-hospital mortality, n (%)		87 (15.1)	143 (25.4)	0.544 (0.398–0.739)	<0.001

Odds ratios were calculated for liver injury patients with versus without abdominal angiography. CI, confidence interval; TAE, transarterial embolization.

**Fig. 2.** Odds ratios for in-hospital mortality related to abdominal angiography.

angiography differed between the different participating centers in that those that performed angiography frequently tended to do so also for liver injuries. However, these differences between the facilities were well-adjusted for by PS matching. AA may better identify active bleeding, cessation of which improves outcomes.

The EAST and WSES guidelines recommend AA for patients with stable hemodynamics.^{5,6} However, we found that AA for blunt liver injury was associated with lower in-hospital mortality both in patients who were in shock and in those who were not. A significant interaction means that the outcome effects depend on the state of hemodynamics. Previous reports suggested that rapid trauma management improved survival.^{26–28} Appropriate interventional radiology requires a trauma management system and careful staff training. Not all institutions are prepared for such emergency

situations. We suggest that our results reflect the need for appropriate trauma management in Japan. Our findings suggested that if emergency AA can be performed safely and promptly, it should be possible to improve the outcomes of liver injury patients even if they are in shock.

In addition, we found that the use of AA for liver injury was associated with lower in-hospital mortality in patients of all ages, in those with AAST-OIS grade III, IV, or V injuries, in those with an ISS ≥ 25 , as well as those who underwent abdominal surgery. A significant interaction was observed between the AAST-OIS grade and ISS. We found a relationship between the performance of AA and less in-hospital mortality in both elderly and younger adults. We previously reported a similar relationship in children with liver and spleen injuries.⁷ The findings also in adults reported here suggest that AA may be generally effective in

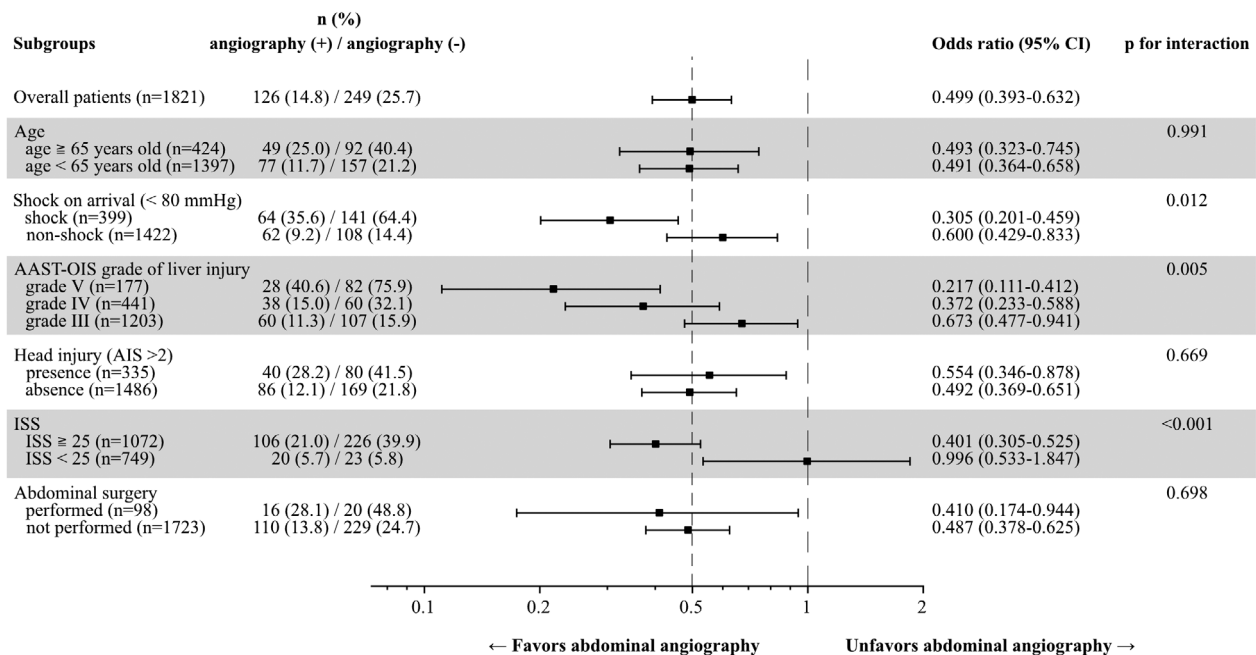


Fig. 3. Subgroup analysis of the association between in-hospital mortality and abdominal angiography; patient characteristics were not adjusted. AAST-OIS, American Association for the Surgery of Trauma-Organ Injury Scale; ISS, injury severity score.

patients with liver injuries regardless of age. The WSES guidelines suggest that it is essential to consider anatomical information (AAST-OIS grade) when classifying liver injury and physiological data (systolic BP) when making a treatment decision.^{6,29} We also found an interaction between the shock status on arrival and AAST-OIS grade. Thus, AA may be generally effective, especially for patients with severe liver injuries. We also found that AA was associated with less in-hospital mortality in patients with an ISS >25 but not in those with an ISS <25. Very few patients with a low ISS died, and the prognoses of this particular subgroup were not improved by AA. Finally, we note that AA was also related to lower in-hospital mortality whether or not abdominal surgery was performed. Thus, angiographic evaluation may help determine an appropriate management strategy, such as a combination of surgery and TAE.

Limitations

This study has several limitations. First, data on contrast extravasation evident on enhanced CT are lacking in the JTDB database. Second, vital signs on hospital admission served as covariates of the propensity score; we lacked data on dynamic changes in physiological parameters. Third, we could not evaluate whether abdominal surgery or TAE more

effectively reduced in-hospital mortality because few JTDB-registered patients had undergone such surgery. The secondary outcome has not been thoroughly analyzed because detailed information about TAE was not available in the JTDB. Because there are few complications such as liver necrosis in TAE for liver injury, if any abnormality is observed by angiography, it may be overtreated at that time. It may reflect Japan's trauma treatment system, where angiography is performed more often than in other countries. In addition, details regarding the purpose of surgery (hemostasis or repair for gastrointestinal damage) and time were not explicit in the JTDB. Fourth, we could not discern whether death was caused by hemorrhage, traumatic brain injury, or liver-related complications. However, our subgroup analysis revealed that patients receiving AA for liver injury with/without head injury had a significantly reduced in-hospital mortality rate (Fig. 3). Moreover, the two groups of PS-matched patients showed a very similar distribution of covariates, including being matched for head injuries. These findings suggest that the performance of AA is beneficial for reducing hemorrhage-related trauma death. Fifth, because the intra-abdominal organ other than kidney and spleen cannot be distinguished for AA within the variables of the JTDB, AA may have been performed not only for the liver but also for other intra-abdominal organs such as the

pancreas and mesentery. Lastly, because this was a retrospective observational study, it cannot be excluded that some potentially confounding factors may not have been accounted for.

CONCLUSIONS

IN THIS STUDY population, the performance of AA for adult patients with blunt liver injury was associated with significantly lower in-hospital mortality than seen in patients without this assessment.

ACKNOWLEDGEMENTS

WE THANK OUR colleagues at the Osaka University Center of Medical Data Science and those working on the Advanced Clinical Epidemiology Investigator's Research Project for sharing their insight and expertise.

DISCLOSURE

Approval of the Research Protocol with Approval No. and Committee Name: The Medical Institutional Ethics Committee of the National Hospital Organization of Osaka National Hospital approved the study (approval no. 19–9).

Informed Consent: The requirement for informed consent of patients was waived.

Registry and the Registration No. of the Study/Trial: N/A.

Animal Studies: N/A.

Conflict of Interest: None declared. Neither the Japanese Association for the Surgery of Trauma nor the Japanese Association for Acute Medicine can take any responsibility for any conclusions of investigators reflected in the original data, text, tables, or figures of the present paper.

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- AAST-OIS, American Association for the Surgery of Trauma-Organ Injury Scale; AIS, Abbreviated Injury Scale; BP, blood pressure; CT, computed tomography; FAST, Focused Assessment with Sonography for Trauma; IQR, interquartile range; ISS, injury severity score; SMD, standardized mean difference.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Subgroup analysis of frequency of TAE and abdominal surgery among unadjusted patients with abdominal angiography. TAE, transarterial embolization.