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■ Original Article ■

Traumatic Liver Injury: Factors Associated with Mortality

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Background: We postulate that a delay in the implementation of hepatic arterial embolization for traumatic liver injury patients will negatively affect patient prognosis. Our work also seeks to identify factors related to the mortality rate among traumatic liver injury patients.
Methods: From January 2008 to April 2014, patients who had been admitted to the emergency room, were subsequently diagnosed with traumatic liver injury, and later underwent hepatic arterial embolization were included in this retrospective study.
Results: Of the 149 patients that underwent hepatic arterial embolization, 86 had the procedure due to traumatic liver injury. Excluding the 3 patients that were admitted to the hospital before procedure, the remaining 83 patients were used as subjects for the study. The average time between emergency room arrival and incidence of procedure was 164 min for the survival group and 132 min for the non-survival group; this was not statistically significant ($p = 0.170$). The average time to intervention was 182 min for the hemodynamically stable group, and 149 min for the hemodynamically unstable group, the latter having a significantly shorter wait time ($p = 0.047$). Of the factors related to the mortality rate, the odds ratio of the Glasgow Coma Score (GCS) was 18.48 ($p < 0.001$), and that of albumin level was 0.368 ($p = 0.006$).
Conclusions: In analyzing the correlation between mortality rate and the time from patient admission to arrival for hepatic arterial embolization, there was no statistical significance observed. Of the factors related to the mortality rate, GCS and albumin level may be used as prognostic factors in traumatic liver injury.

Key Words: embolization, therapeutic; intervention; liver injury; time factors.

Introduction

Hemorrhage following traumatic injury is one of the main causes of mortality worldwide. One of the most important factors in treatment is to determine the site of hemorrhage and control the bleeding.[1] Traditionally, if the hemodynamic status of a patient suffering from abdominal injury is unstable, an investigative laparotomy is first considered. According to Clarke et al.,[2] for patients with severe internal abdominal organ damage, the mortality rate increases by 1% for each 3-min period without surgical treatment. This demonstrates the need for an aggressive treatment system for traumatic injury and hemorrhage.

There has been an increase in the number of patients with abdominal injury as a result of trauma such as traffic accidents; in such cases, the incidence of injury to the liver and spleen is high.[3] Therefore, hepatic arterial embolization as a non-surgical treatment method is a subject of active study.[4-9]

According to Olthof et al.,[10] Time to intervention did not differ significantly between hemodynmically unstable patients treated with transcatheter arterial embolization and patients treated with splenic surgery. Thus, carrying out an intervention in hemodynamically unstable patients does not necessarily equate to a loss in time. According to Beardsley and Gananadha,[4] 80%

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of traumatic liver injury patients undergo non-surgical treatment with no increase in the mortality rate. With regard to non-surgical hepatic arterial embolization, there have not been any clear reports on whether it must be performed within a certain time limit or whether timeliness of the procedure improves prognosis. Moreover, no guidelines have been presented on whether this treatment method should take priority over others for hemodynamically unstable patients or whether such patients need to be hemodynamically stable to ensure successful treatment. As such, we postulate that a delay in the implementation of hepatic arterial embolization for traumatic liver injury patients will negatively affect patient prognosis. Our work also seeks to identify factors related to the mortality rate among traumatic liver injury patients.

Materials and Methods

1) Patients and data collection

The subjects of this study were patients who were admitted to the emergency room between January 2008 and April 2014, who had been diagnosed with liver injury based on abdominal computed tomography results and who had undergone hepatic arterial embolization. Based on the electronic charts of the patient group, a retrospective study was conducted. Patients who underwent angiographic embolization for other organ injuries were excluded. Moreover, patients who were diagnosed with liver injury but were observed for prognosis and those admitted specifically for hepatic arterial embolization were also excluded. Nursing records were referenced to obtain information, including vital signs upon hospital arrival, time of arrival, time until procedure, and volume of blood transfusion. Emergency room initial consultation records and admission and discharge records were also referenced to assess patient status and diagnosis at the time of the procedure. Depending on the hemodynamic status at the time of visit, patients were divided into hemodynamically stable and unstable groups; this was due to the high likelihood that treatment would have differed depending on patient hemodynamics. The time (in min) from hospital arrival to hepatic arterial embolization was investigated, from the point of reception to the moment where the patient was moved to the angiography room, according to records. This time was defined as the time to embolization.

2) Definition

Liver injury grades were assessed in accordance with the American Association for the Surgery of Trauma liver injury grading scale; grades I and II were included in the low grade group and grades III and above were defined as the high group. A hemodynamically unstable patient was defined as having a systolic blood pressure (SBP) of ≤ 100 mmHg or a heart rate of ≥ 120 bpm upon arrival at the hospital. Those who did not meet these criteria were assigned to the hemodynamically stable group. Moreover, when the trauma patient visited the emergency room, they were assessed for the Glasgow Coma Scale (GCS) score, with ≤ 8 points being considered low and ≥ 9 points being considered high. Patients who underwent hepatic arterial embolization in the emergency room and were then moved to the operating room for a secondary abdominal surgery were evaluated; these patients were defined as having embolization complications. Patients were also categorized by the manner in which they arrived at the hospital, with those who arrived via a call to 119 or 129 grouped accordingly. For blood work, the test results obtained after initial sampling at the emergency room were used for assessment. For blood transfusion, the amount of packed red blood cells used while waiting in the emergency room or waiting for treatment was taken into account. The central venous pressure (CVP) after inserting the central line in the emergency room was also investigated.

3) Outcomes

For the primary outcome, the mortality rates of the hemodynamically stable and unstable groups were assessed across various arrival-to-embolization times. For secondary outcomes, factors associated with mortality were analyzed, such as each group's test values, GCS, injury severity score (ISS), liver grade, transfusion amount, intervention complications, length of hospital stay, and length of artificial respirator use.

4) Statistical analysis

Statistical analysis was conducted, and the mean, standard deviation, and median values of each result were analyzed. The interquartile range (IQR) was defined as 25-75. For continuous variables, those that followed a normal distribution were analyzed using a Student's *t*-test, while those with an abnormal distribution were analyzed using a Mann-Whitney Test. For categorical variables, Chi-squared and Fisher's exact tests were conducted. In addition, a regression analysis was carried out to confirm the odds ratio of each factor and set a confidence interval (CI) of 95%. In the logistic analysis, the mortality odds ratio for continuous variables was analyzed according to the unit increase or decrease, while the odds ratio for non-continuous variables was analyzed after dividing them into two groups. For statistical analysis, SPSS version 18 (SPSS Inc., Chicago, IL, USA) was used, and statistical significance was set as a p value < 0.05.

Results

1) Inclusion criteria

Of 149 patients that underwent hepatic arterial embolization at our hospital, 86 had the procedure due to traumatic liver injury. Excluding the 3 patients that were admitted to the hospital before procedure, the remaining 83 patients were used as subjects for the study.

2) Total patient group analysis

Of the total patients, 63% were male and 37% were female (53 and 30 patients, respectively), with the average age being 40.8 years. The mortality rate was 14.5% (12 patients), and of the patients who died, 58.3% died within 1 day of arriving at the hospital. As for the trauma mechanism, passenger's traffic accidents accounted for 49% of total patients, whereas traumas that were pedestrian traffic accidents and caused by other mechanisms (motor vehicle accident, fall down, slip down) accounted for 20.5% and 30.1%, respectively. Those who arrived at the hospital through a call to 119 accounted for 41.0% of total patients. Those with a liver laceration grade of III or IV accounted for 81.9% of all patients. The average ISS was 22.1, average stay at the hospital of survival patient was 39.2 days, average number of transfusion units used was 3.3, and average CVP was 6.7 (Table 1).

3) Total group time to embolization

The average time to intervention for the entire group was 159.8 min (IQR = 118-192).

4) Mortality (Table 2)

The time to embolization was 164 min (range: 44-436 min) for the survivor group and 132 min (range: 46-210 min) for the non-survivor group, with no statistical significance observed between the groups ($p = 0.170$). The odds ratio between the mor-

Table 1. Baseline characteristics

		Total (n, %)	Mean ± SD	IQR (25-75)
Sex	Male	53 (63.9)		
	Female	30 (36.1)		
Age, yr			40.8 ± 18.6	25.0-53.0
Mortality	Survival	71 (85.5)		
	Non-survival	12 (14.5)		
Time to death	≤ 1 day	7 (58.3)		
	> 1 day	5 (41.7)		
Trauma mechanism	Passengers	41 (49.4)		
	Pedestrian	17 (20.5)		
	Others	25 (30.1)		
Referral	119	34 (41.0)		
	129	49 (59.0)		
GCS score			13.0 ± 4.0	14.0-15.0
Hb			11.6 ± 2.4	10.0-13.0
Another injury	Yes	73 (88.0)		
	No	10 (12.1)		
Grade of liver injury	Low	13 (15.7)		
	High	70 (84.3)		
ISS			22.1 ± 7.6	17.0-27.0
Hospital stay length			34.8 ± 34.9	13.0-48.0
CPR	Yes	9 (10.8)		
	No	74 (89.2)		
ICU days			12.6 ± 25.2	2.0-13.0
Ventilator days			7.5 ± 25.4	0.0-4.0
Operation (complication)	Yes	8 (9.6)		
	No	75 (90.4)		
Time to intervention			159.8 ± 72.4	118.0-192.0
Transfusion			3.3 ± 4.0	1.0-5.0
CVP			6.7 ± 5.0	4.0-8.0

SD: standard deviation; IQR: interquartile range; GCS: glasgow coma scale; Hb: hemoglobin; ISS: injury severity score; CPR: cardiopulmonary resuscitation; ICU: intensive care unit; CVP: central venous pressure.

Table 2. Mortality

		Survival		Non-survival		p value
		Total (n, %)	Mean	Total (n, %)	Mean	
Trauma mechanism	Passengers	35 (85.4)		6 (14.6)		0.372
	Pedestrian	13 (76.5)		4 (23.5)		
	Others	23 (92.0)		2 (8.0)		
Referral	119	29 (85.3)		5 (14.7)		0.957
	129	42 (85.7)		7 (14.3)		
GCS score			13.9		7.8	< 0.001
Hb			11.8		10.3	0.070
Albumin			3.6		2.7	0.008
Another injury	Yes	63 (86.3)		10 (13.7)		0.633
	No	8 (80.0)		2 (20.0)		
Brain injury	Yes	7 (58.3)		5 (41.7)		0.012
	No	64 (90.1)		7 (9.9)		
Grade of liver injury	Low	11 (84.6)		2 (15.4)		0.664
	High	60 (85.7)		10 (14.3)		
ISS			21.4		25.8	0.237
Hospital stay length			39.2		9.0	< 0.001
Operation (complication)	Yes	8 (100.0)		0 (0.00)		< 0.001
	No	63 (84.0)		12 (16.0)		
Time to intervention			164.5		132.0	0.170
Initial SBP			101.9		51.9	0.007
Initial HR			96.7		81.6	0.766
SBP after embolization			118.1		95.3	0.006
Transfusion			2.5		7.9	< 0.001
CVP			6.7		6.3	0.979

GCS: glasgow coma scale; Hb: hemoglobin; ISS: injury severity score; SBP: systolic blood pressure; HR: heart rate; CVP: central venous pressure.

Table 3. Logistic regression

	p value	Odds ratio	95% Confidence interval	
GCS (compared to the high group)	< 0.001	18.48	4.27	79.90
Albumin	0.006	0.368	0.18	0.75
Transfusion	0.002	1.432	1.14	1.79
Brain injury (compared to the no injury group)	0.008	6.531	1.63	26.16
ISS	0.076	1.073	0.99	1.16
Liver grade (compared to the low group)	0.918	1.091	0.21	5.67
Hospital stay length	0.004	0.901	0.84	0.97
Initial SBP	0.001	0.950	0.92	0.98
SBP after embolization	0.002	0.948	0.92	0.98
Time to angiography	0.15	0.992	0.98	1.00

GCS: glasgow coma scale; ISS: injury severity score; SBP: systolic blood pressure.

tality rate and time to embolization was 0.992 but was not statistically significant ($p = 0.150$). The GCS score was 13.9 for the survivor group and 7.8 for the non-survivor group, and was significantly different between groups ($p < 0.001$). The mortality rate odds ratio for the low (GCS ≤ 8) and high group (GCS ≥ 9) was 18.5, which was statistically significant ($p < 0.001$; Table 3). Brain injury was significantly different between groups ($p < 0.012$), and the mortality rate odds ratio was significant, at 6.531 ($p = 0.008$; Table 3). The albumin value was significantly lower in the non-survivor group (2.7) than for survivors (3.6) ($p = 0.008$). The mortality rate odds ratio was 0.368, which was statistically significant ($p = 0.006$; Table 3). Trauma mechanism, referral via a 119 call or from another hospital, ISS, liver grade, and embolization complications were not statistically significant factors. All 8 cases of embolization complications were observed in the survivor group (Table 4). The SBP at the time of hospital arrival was significantly different for the survivor group (101 mmHg) and the non-survivor group (51 mmHg) ($p < 0.007$); post-procedure SBP was also significantly different for survivors (118 mmHg) and for those in the non-survivor group (95 mmHg) ($p < 0.006$). Moreover, there was a significant difference in the number of transfusion units used between the survivors ($n = 2.5$) and those in the non-survivor group (n = 7.9) ($p < 0.001$); the odds ratio was also significant (odds ratio = 1.432; p = 0.002; Table 3).

5) Hemodynamic stability (Table 5)

Of the total patients, the hemodynamically stable group accounted for 32.5%, with the remaining 67.5% categorized as being hemodynamically unstable (27 and 56 patients, respectively). In terms of mortality, there were 26 survivors and 1 patient who died in the hemodynamically stable group, yielding a mortality rate of 3.7%; there were 45 survivors and 11 patients who died in the hemodynamically unstable group, resulting in a mortality rate of 19.6%. There was no significant difference between the 2 groups (p = 0.92). However, there was a significant difference in the average times to embolization between the hemodynamically stable and unstable groups, at 182 min (range: 46-397 min) and 149 min (range: 44-436 min), respectively (p = 0.047). In cases where the patient was transferred from another hospital, there was a high incidence of unstable hemodynamics (p = 0.475) and the distribution of traffic accident was higher in this group (p = 0.039). Moreover, the GCS score was 12.6 for this group, which was significantly lower than that in the hemodynamically stable group (GCS = 14; p = 0.016). The hemoglobin value was also significantly lower in the unstable group (11.0 g/dl) than in the stable group (12.7 g/dl) (p = 0.001). Both the aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels revealed higher values for hemodynamically unstable patients than for stable ones, although ALT levels were not significant. In addition, there was no significant difference between the 2 groups regarding the existence of accompanying injuries or liver injury grade. However, the ISS was significantly higher in the hemodynamically unstable group (23.7) than the

Table 4. Operations in cases of embolization complications

M/16	Hepatic arterial ligation
M/19	Splenectomy and bleeding control
F/15	Nephrectomy
F/12	Exploratory laparotomy and bleeding control
49/F	Exploratory laparotomy and primary repair of duodenum
48/M	Exploratory laparotomy and primary repair of T-colon
38/F	Exploratory laparotomy and splenectomy
50/M	Exploratory laparotomy and bleeding control

Table 5. Hemodynamic stability

		HD stable		HD unstable		p value
		Total (n, %)	Mean	Total (n, %)	Mean	
Mortality	Survival	26 (36.6)		45 (63.4)		0.920
	Non-survival	1 (8.3)		11 (91.7)		
Trauma mechanism	Passengers	9 (22)		32 (78)		0.039
	Pedestrian	5 (29.4)		12 (70.6)		
	Others	13 (52)		12 (48)		
Referral	119	13 (38.2)		21 (61.8)		0.475
	129	14 (28.6)		35 (71.4)		
GCS score			14.0		12.3	0.016
Hb			12.7		11.0	0.001
AST			490.0		663.9	0.033
ALT			319.9		434.0	0.092
Albumin			3.8		3.3	0.011
Another injury	Yes	22 (30.1)		51 (69.9)		0.282
	No	5 (50)		5 (50)		
Grade of liver injury	Low	5 (38.5)		8 (61.5)		0.749
	High	22 (31.4)		48 (68.6)		
ISS			18.6		23.7	0.004
Hospital stay length			22.8		40.6	0.037
CPR	Yes	1 (11.1)		8 (88.9)		0.259
	No	26 (35.1)		48 (64.9)		
ICU days			5.7		15.9	0.012
Ventilator days			1.6		10.3	0.001
Operation (complication)	Yes	0 (0)		8 (100)		0.049
	No	27 (6)		48 (64)		
Time to intervention			182.4		148.8	0.047
SBP after embolization			121.3		111.7	0.021
Transfusion			1.8		4.0	0.002

GCS: glasgow coma scale; Hb: hemoglobin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ISS: injury severity score; CPR: cardiopulmonary resuscitation; ICU: intensive care unit; SBP: systolic blood pressure.

stable group (18.6) ($p = 0.004$). Hemodynamically unstable patients displayed significantly longer time in the hospital, in the intensive care unit (ICU), and on ventilators than those with stable status. Abdominal surgeries, which we define as embolization complications, were not found among the hemodynamically stable patients, while a total of 8 unstable patients were moved to the operating room after embolization ($p = 0.049$). The average number of transfusion units used was significantly different between the hemodynamically stable (1.8) and unstable groups (4.0) ($p = 0.002$).

Discussion

Recently, due to increases in traffic accidents and associated injuries, the number of trauma patients visiting the emergency room has increased. Among these patients, liver injury caused by abdominal trauma is the most frequently occurring injury after spleen injuries. Traditionally, in the case of traumatic liver injury, surgical treatment takes priority, but a number of reports are addressing the practical benefits of non-surgical treatments.[11-13] Kim et al.[7] argued that embolization can be considered a primary treatment method in the case of patients with stable hemodynamics or the ability to attain this state via intravenous fluids. This treatment can also be highly effective in cases where there is no accompanying internal abdominal injury requiring emergency surgery or in cases of patients with a grade III liver injury (or higher). Therefore, this research was conducted on patients with both stable and unstable hemodynamic statuses.

The time to embolization among emergency room traumatic liver injury patients was 164 min for the survivor group and 132 min for the non-survivor group, with no significant difference observed between the groups ($p = 0.170$). According to Yun et al.,[8] the initial SBP, hemoglobin, and liver injury scale of traumatic liver injury patients were risk factors for mortality. This study identified the GCS score, albumin, initial SBP, post-procedure SBP, and transfusion volume as factors associated with mortality. In the logistic regression analysis, the GCS score, albumin, and transfusion amount were found to be significant factors. The GCS is commonly used to assess the consciousness of the patient and to make neurological assessments at the time of arrival of the trauma patient, with a score of ≤ 8 indicative of a serious head injury.[14,15] In the study by Fearnside et al.,[16] a correlation between the GCS score and mortality rate was identified, evaluating 315 patients with a score of ≤ 8. The GCS score in this study proved to be significantly correlated with both mortality rate and hemodynamic status. In the logistic regression analysis, when patients were categorized into high and low groups according to the GCS score, the low group had a significantly higher mortality rate than the high group (approximately 18-fold) ($p < 0.001$; odds ratio = 18.48; 95% CI = 4.274-79.90). This result is postulated to help with assessing the prognosis of the liver injury patient, in addition to contributing to the neurological assessment at an early stage of trauma. On the other hand, when logistic analysis was used to assess the relationship between the GCS score or brain injury and mortality, the odds ratio for GCS was significant (17.8), while the odds ratio for brain injury was not (1.1). This may be related to the fact that the GCS - which evaluates neurological prognosis - showed low scores for brain injury and also that the GCS score was closely related to other factors such as hemodynamic status or accompanying injury.

According to literature that addresses the relationship between existing laboratory findings and traumatic liver injury, the odds ratios for white blood cells and AST are 1.347 and 1.007, respectively; in regions where prompt imaging tests such as computed tomography are not available, such blood tests can be used as an early warning system.[17] In this study, a low level of albumin was observed in the non-survivor group ($p = 0.008$). Moreover, an overall lower level of albumin was associated with a significant 2.72-fold higher mortality rate than a higher level ($p = 0.006$; odds ratio = 0.368; 95% CI = 0.182-0.746). This indicates that albumin levels can be an important factor in forecasting the prognosis of liver injury patients after trauma.

In an analysis based on categorization of hemodynamics, the time to embolization was shorter for hemodynamically unstable patients (148 min) than for stable ones (182 min). This seems to be due to a difference in how much more aggressively treatment and testing is carried out when the patient exhibits unstable hemodynamics. However, no correlation between hemodynamic status and mortality was observed ($p = 0.92$). Those with unstable hemodynamics presented with a significantly lower GCS score and hemoglobin, longer hospital and ICU stays, and longer reliance on the ventilator as well as more transfusions. Howell et al. [18] conducted a study by categorizing patients with unstable hemodynamics into groups where therapeutic interventional radiology was conducted either quickly or slowly, and reported that the risk of mortality was about 2 times higher in the slow group. In this study, the odds ratio for the time to embolization and mortality rate was not statistically significant (odds ratio = 0.992; 95% CI = 0.982-1.003). The difference in results may be due to the difference in the total number of patients studied and the fact that this study was limited to evaluation of a single organ (liver). Therefore, further large-scale, multiple-organ studies may be required in the future.

Our work has several limitations. First, the sample size is not sufficiently large. In our study, it was a single-institution experience and so its sample size was relatively small. Second, the time for hepatic arterial embolization was measured in minutes from the time of hospital reception to the moment the patient was moved to the angioplasty room. However, there was a difference between patients who were transported quickly to the hospital via a 119 ambulance from a nearby area and patients who were transferred from another hospital. There was also a difference in the timeliness of treatment and test administration, depending on the condition of the patient. These variables may have affected the results. However, in the present study, there was no statistically significant difference in mortality between patients who visited the hospital via a 119 or 129 call. This is likely because it was difficult to determine the exact time of the accident in a retrospective study. As such, future prospective studies will be needed to address this limitation. Third, because the study had a retrospective design, there is uncertainty in the patient data. The study was based on electronic medical records, review records, and patient database information; thus, there is the possibility of error, omission, or insufficient verification. Finally, the total mortality rate determined in this study was 16%, which is slightly higher than the 10-12% reported in other literature.[4,9,19] However, this may be due to the fact that patients who were diagnosed with traumatic liver injury and underwent preservative treatment were excluded from the study, while patients who underwent hepatic arterial embolization were included. The characteristics of the sample group may have affected the analysis, and as such, a follow-up assessment using a variety of study subjects is recommended.

No statistical significance was observed in the relationship between time of arrival to embolization and mortality rate, once the traumatic liver injury patient arrived at the emergency room. Some factors did, however, affect the mortality rate of liver injury patients; the low GCS score group had an 18.48-fold higher mortality rate than the high group, while a lower albumin level was associated with a 2.72-fold higher mortality rate than higher levels of albumin. These factors could be used as prognostic indicators in traumatic liver injury patients, and therefore, additional research is needed. Among patients with more severe symptoms and unstable hemodynamics, a more aggressive treatment and intervention system was found to be adopted and a shorter time to embolization was observed. It should be noted, however, that there was no significant difference between these patients and those with stable hemodynamics. The data suggest that the use of aggressive treatment by medical professionals can help lower the mortality rate for traumatic liver injury patients with unstable hemodynamics.

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