

Risk Factors for Hepatic Morbidity Following Nonoperative Management

Multicenter Study

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Hypothesis: Early risk factors for hepatic-related morbidity in patients undergoing initial nonoperative management of complex blunt hepatic injuries can be accurately identified.

Design: Multicenter historical cohort.

Setting: Seven urban level I trauma centers.

Patients: Patients from January 2000 through May 2003 with complex (grades 3-5) blunt hepatic injuries not requiring laparotomy in the first 24 hours.

Intervention: Nonoperative treatment of complex blunt hepatic injuries.

Main Outcome Measures: Complications and treatment strategies.

Results: Of 699 patients with complex blunt hepatic injuries, 453 (65%) were treated nonoperatively. Overall, 61 patients (13%) developed 87 hepatic complications including bleeding (38), biliary (bile peritonitis, 7; bile leak, 9; biloma, 11; biliary-venous fistula, 1; and bile duct injury, 1), abdominal compartment syndrome (5), and

infections (abscess, 7; necrosis, 2; and suspected abdominal sepsis, 6), which required 86 multimodality treatments (angioembolization, 32; endoscopic retrograde cholangiopancreatography and stenting, 9; interventional radiology drainage, 16; paracentesis, 1; laparotomy, 24; and laparoscopy, 4). Hepatic complications developed in 5% (13 of 264) of patients with grade 3 injuries, 22% (36 of 166) of patients with grade 4 injuries, and 52% (12 of 23) of patients with grade 5 injuries. Univariate analysis revealed 24-hour crystalloid, total and first 24-hour packed red blood cells, fresh frozen plasma, platelet, and cryoprecipitate requirements and liver injury grade to be significant but only liver injury grade (grade 4 odds ratio, 4.439; grade 5 odds ratio, 12.001) and 24-hour transfusion requirement (odds ratio, 6.446) predicted complications by multivariable analysis.

Conclusions: Nonoperative management of high-grade liver injuries is associated with significant morbidity and correlates with grade of liver injury. Screening patients with transfusion requirements and high-grade injuries may result in earlier diagnosis and treatment of hepatic-related complications.

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DURING THE PAST 2 DECADES, management of blunt hepatic injuries has changed dramatically. Nonoperative management of hemodynamically stable patients is now the standard of care. Successful nonoperative management of splenic injuries, the high rate of nontherapeutic laparotomies with associated complications in patients with liver injuries, the refinement of computed tomographic (CT) scanning, and more aggressive use of interventional radiology (IR) have all contributed to this dramatic change.¹ Numerous studies during the past 2 decades have confirmed this practice to be both fea-

sible and safe. Survival rates for those patients selected for nonoperative treatment generally approach 100%, with hepatic-related complication rates in most series ranging from 0% to 7%.²⁻⁶

Because these studies have included patients with all grades of liver injuries, the majority (>75%) of patients sustained low-grade injuries and only a small proportion of patients had high-grade injuries. Most studies examining complex injuries have focused on patients undergoing initial operative treatment and have included penetrating injuries. A large multicenter study in the late 1980s by Cogbill et al⁷ described 220 patients with complex liver injuries (only 44% had blunt

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mechanisms), all of whom underwent initial operative treatment. These patients had a high hepatic-related mortality rate (30%), as well as significant hepatic-related morbidity, including prolonged biliary leak (8%), intra-abdominal abscess (9%), and late hemorrhage (7%). Throughout the next decade, efforts focused on lessening mortality in these patients by earlier appropriate use of "damage control laparotomy" combined with nonoperative adjuncts such as IR embolization and drainage and endoscopic retrograde cholangiopancreatography (ERCP) to manage hepatic complications.^{8,9} Despite this multidisciplinary approach, overall the mortality rate for patients with grade 4 and 5 injuries who underwent early operation (predominately penetrating) was reported to be as high as 9%. Currently, nonoperative management is being used with increasing frequency in complex liver injuries, though some authorities claim we have gone too far.¹⁰ While nonoperative management clearly reduces hepatic-related mortality, current attention needs to be focused on reducing hepatic-related morbidity. We recently reported a series of 230 patients sustaining complex blunt hepatic injuries who underwent initial nonoperative treatment.¹¹ Although our overall complication rate was relatively low (11%), complications in patients with grade 4 and 5 injuries were surprisingly high with incidences of 21% and 63%, respectively. Additionally, once diagnosed, these complications were difficult to treat and frequently required multiple interventions with prolonged hospital stays. Therefore, the purposes of this multicenter study were to confirm our high complication rate and obtain a sufficient sample size to determine if early predictors of hepatic-related morbidity could be identified. Our basic premise was that if patients at high risk for developing complications could be identified early in their injury course, screening would allow for earlier intervention and thus reduce hepatic-related morbidity.

METHODS

During a 40-month period ending May 2003, 699 adult (≥ 14 years of age) patients with grade 3 through 5 blunt hepatic injuries were admitted to 7 level I trauma centers, including Denver Health Medical Center, Denver, Colo (117 patients), Memorial Hermann Hospital, Houston, Tex (115 patients), Harborview Medical Center, Seattle, Wash (79 patients), Parkland Health and Hospital System, Dallas, Tex (69 patients), Brooke Army Medical Center, Fort Sam Houston, Tex (30 patients), Stanford University Hospital, Stanford, Calif (23 patients), and Miami Valley Hospital, Dayton, Ohio (20 patients), as part of the American Association for the Surgery of Trauma Multicenter Trial Committee. Of these patients, 246 underwent immediate surgical intervention and were excluded from further analysis. The remaining 453 patients (65%) did not undergo immediate laparotomy (defined as within the first 24 hours of injury) and are the focus of the current study.

All medical records were retrospectively reviewed after institutional review board approval was obtained at each site. Demographic data collected included age, sex, mechanism of injury, intensive care unit (ICU) and total length of stay, Abbreviated Injury Score, and Injury Severity Score. Emergency department data collected included lowest systolic blood pressure, base deficit, and focused abdominal sonography for trauma (FAST) results. Additionally, crystalloid requirements in the

first 24 hours postinjury and systemic inflammatory response syndrome (SIRS) scores were recorded as were blood product requirements in the first 24 hours of admission and for total hospital stay. The grade of hepatic injury was determined and based on CT findings according to the American Association for the Surgery of Trauma Organ Injury Scale for hepatic injuries.^{12,13} For the current study, complex hepatic injuries were considered to be grades 3 to 5.⁷ The extent of hemoperitoneum was recorded when available.

Hepatic-related mortality was defined as deaths due to ongoing liver bleeding, liver failure, or deaths related to complications of massive fluid resuscitation. Hepatic-related morbidity was defined as a liver-related complication associated with an intervention: (1) bleeding if intervention, either angioembolization or laparotomy, was required (the need for blood transfusion or simply having undergone angiography of the liver for suspected bleeding was not considered a complication); (2) liver-related infection including a hepatic or perihepatic abscess or hepatic necrosis; (3) biliary, including the development of a biloma (whether sterile or infected), biliary-venous fistula, bile peritonitis, or bile duct injury, requiring treatment (hyperbilirubinemia itself was not considered a complication); (4) missed hollow viscus injury, actual or suspected, if a laparotomy was performed; and (5) development of abdominal compartment syndrome (ACS) requiring decompressive laparotomy.¹¹

Treatment of hepatic-related complications was multidisciplinary when appropriate and included early angiography and angiographic embolization, ERCP and stenting of biliary leaks, and CT-guided drainage of hepatic or perihepatic abscesses or biliary collections by IR. Surgical interventions included either laparotomy or laparoscopy.

Univariate associations between complications and predictor variables were estimated by the following methods. Continuous data were divided into quartiles for contingency table analyses, with the exception of blood products. All of the blood products had a median of zero, so they were dichotomized at zero. In addition to contingency table analyses, univariate logistic regression was performed on continuous variables. Only variables without significant missing values were analyzed (base deficit, extent of hemoperitoneum, results of FAST scans, and SIRS scores had significant missing data points and are therefore not reported). All variables with univariate *P* values $< .10$ were included as candidates in multivariable analysis, which was performed using multiple logistic regression with indicator variables for grade 4 and 5 injuries and continuous or dichotomous variables for continuously distributed variables. Model selection was performed by stepwise logistic regression followed by manual best subsets selection. A receiver operating characteristic curve was produced and area under the curve calculated to evaluate model prediction. All computations were performed using SAS 8.2 (SAS Institute, Inc, Cary, NC).

RESULTS

Of 60 842 blunt trauma admissions, 2851 patients (5%) sustained blunt hepatic injuries of which 699 (25%) were complex (grades 3-5). Nonoperative treatment was initially pursued in 453 patients (65%) with complex hepatic injuries (the study cohort), while the remaining 246 patients required immediate operative intervention. Mean age of the study patients was 33 years (range, 14-90 years); 249 patients were male (55%); and blunt mechanisms included 357 motor vehicle crashes (80%), 23 pedestrian accidents (5%), 24 falls (5%), and 49 other injuries (10%) (including motorcycle accidents). The median Abbreviated Injury Score was zero for spine (range, 0-5), head

Table 1. Variables Associated With Hepatic Complications*

Variable	Complications (n = 61)	No Complications (n = 392)	P Value
Age, y	35.8 ± 17.8	31.8 ± 15.8	.08
Male, %	53.4	63.9	.12
ISS	27.1 ± 10.9	25.2 ± 11.1	.25
Injury grade	3.97 ± 0.6	3.41 ± 0.5	<.001
Initial BP <90 mm Hg, %	10.4	14.8	.32
First 24-h crystalloid resuscitation volume, L	8.06 ± 4.7	5.36 ± 3.6	<.001
24-h PRBC requirement, U	5.21 ± 8.8	1.46 ± 3.5	.002
Total PRBC requirement, U	10.61 ± 20.1	2.48 ± 5.3	.003
24-h FFP requirement, U	2.75 ± 4.9	0.55 ± 1.9	.001
Total FFP requirement, U	5.57 ± 12.2	0.75 ± 2.5	.004
24-h PLT requirement, 6 pack	1.15 ± 2.6	0.17 ± 1.0	.006
Total PLT requirement, 6 pack	2.77 ± 6.5	0.34 ± 1.9	.006
ICU LOS, d	18.8 ± 18.9	2.9 ± 3.4	.008
Total LOS, d	26.2 ± 26.5	8.5 ± 7.5	.01
Mortality, %	8.2	4.8	.10

Abbreviations: BP, blood pressure; FFP, fresh frozen plasma; ICU, intensive care unit; ISS, Injury Severity Score; LOS, length of stay; PLT, platelet; PRBC, packed red blood cell.

*Values expressed as mean ± SD unless otherwise indicated.

(range, 0-5), face (range, 0-3), chest (range, 0-4), extremity (range, 0-3), and external (range, 0-2) but was 4 for abdomen (range, 3-5). There were 23 deaths (5%) but only 2 hepatic-related mortalities, both secondary to multiple organ failure (1 following hepatic resection for liver necrosis and the second after abdominal decompression for bleeding and ACS).

Overall, 61 patients (13%) developed 87 liver-related complications, including bleeding (38), biliary (29), infectious (15), and ACS (5). These patients required 86 interventions to treat these complications.

Table 1 presents demographic, injury severity, crystalloid and blood product requirements, and outcomes for patients who developed hepatic complications compared with those who did not. Significant differences include higher-grade injuries and more crystalloids and blood products administered in patients who developed complications. Additionally, their ICU and total length of stay were much higher. More than 10% of all patients had a systolic blood pressure of lower than 90 mm Hg on arrival in the emergency department and yet underwent initial nonoperative treatment, despite hemodynamic instability being traditional criteria for operative management of solid organ injuries.

The 35 study patients (8%) who developed 38 bleeding complications that required operative or IR management are shown in **Figure 1**. Twenty patients (57%) underwent early IR embolization (on the day of injury), of whom 3 (9%) experienced rebleeds that required delayed salvage operative interventions (1 grade 4 injury on postinjury day [PID] 1 and 2 grade 5 injuries on PIDs 2 and 3). In the remaining 15 patients, 12 had successful late IR embolization (9 on PID 1, 1 on PID 2, 1 on PID 8, and 1 on PID 22 [for hemobilia in a grade 5 injury]) and 3 were taken directly to the operating room (1 grade 3 injury on PID 4, 1 grade 4 injury on PID 3, and 1 grade 5 injury on PID 1), where bleeding was successfully controlled.

Seventeen patients developed 29 biliary complications that required 27 interventions (2 bilomas were ob-

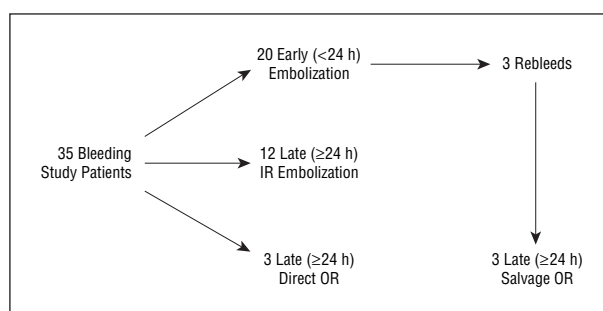


Figure 1. Management of 38 bleeding complications in 35 patients. IR indicates interventional radiology; OR, operating room.

served) (**Table 2**). Unlike bleeding complications, which tended to occur early, biliary complications developed at a mean 12 days postinjury (range, 2-38 days postinjury) and typically required multimodality interventions. Seven patients developed bile peritonitis, of whom 4 required multimodality interventions. Peritoneal wash-out was accomplished by laparoscopy in 4 and laparotomy in 3. One of these patients had an extrahepatic bile duct injury that was repaired at the time of laparotomy, 4 others subsequently required ERCP with stenting to control the bile duct leak, and 3 were later diagnosed to have bilomas (2 underwent IR drainage and 1 was observed). Another 6 patients presented with bilomas. One was observed and 5 had IR drainage, of whom 3 required ERCP with stenting. Another 3 patients were diagnosed with a primary bile duct leak at ERCP. The last patient underwent laparotomy for a biliary-venous fistula that failed to resolve by ERCP and stenting.

An additional 14 patients developed 15 infectious complications. Seven patients had liver abscesses diagnosed on average on PID 15 (range, PID 1-90) and 6 were treated successfully by IR drainage, with 1 patient requiring laparotomy for complete resolution. Two patients required liver resection for necrosis, which developed on PID 4 and 14. The first of these patients had ligation of the right

Table 2. Biliary Complications and Management Strategies

Complication	Treatment					PID (Range)
	E-lap	Laparoscopy	ERCP/Stent	IR Drainage	Observation	
Bile peritonitis	3	4	0	0	0	2-19
Bile leak	0	0	9	0	0	4-19
Biloma	0	0	0	9	2	5-38
BV fistula	1	0	0	0	0	7

Abbreviations: BV, biliary venous; E-lap, exploratory laparotomy; ERCP, endoscopic retrograde cholangiopancreatography; IR, interventional radiology; PID, postinjury day.

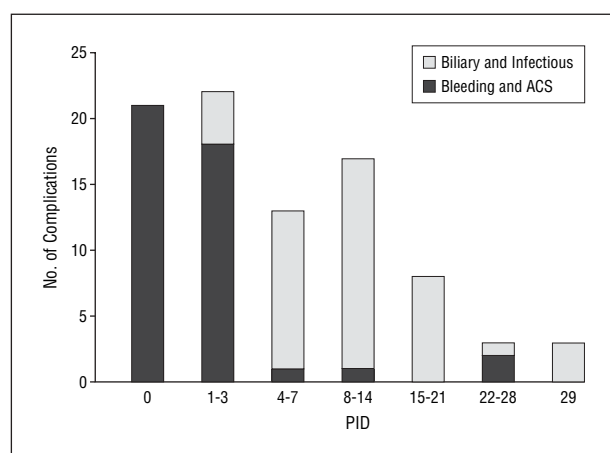


Figure 2. Temporal pattern for the development of complications. The presentation of bleeding complications and abdominal compartment syndrome (ACS) vs biliary and infectious complications over time are shown. Bleeding and ACS tended to develop within the first 3 days of injury while biliary and infectious complications developed in a delayed fashion. PID indicates postinjury day.

hepatic artery on PID 1 for ongoing bleeding and then required hepatic lobectomy for necrosis on PID 4, eventually dying of multiple organ failure. The second patient had a persistent SIRS response following initial angioembolization (PID 0) and was found to have liver necrosis at the time of laparotomy (PID 14), which was managed with a segmentectomy. Lastly, 6 patients underwent laparotomy for suspected abdominal sepsis, all of whom were without bowel injury. We therefore had a zero incidence of missed bowel injuries.

Finally, 5 patients developed ACS and all were decompressed. Four patients were treated by decompressive laparotomies (3 on PID 1 and 1 on PID 2), of whom 2 had previously undergone IR embolization. The fifth case of ACS developed on PID 22, with respiratory symptoms secondary to massive ascites, and was treated successfully by paracentesis alone. When complications were examined over time, a temporal pattern emerged (**Figure 2**). Typically, bleeding and ACS developed within the first 3 days of injury ($\leq$ PID 3), whereas biliary and infectious complications primarily developed in a delayed fashion ($>$ PID 3).

Liver-related complications developed in 5% (13/264) of patients with grade 3 injuries, 22% (36/166) of patients with grade 4 injuries, and 52% (12/23) of patients with grade 5 injuries. Complications by grade are pre-

Table 3. Hepatic Complications by Liver Grade

Complication	No. of Complications		
	Grade 3	Grade 4	Grade 5
Bleeding episodes	6	18	14
Early (<24 h) only	5	9	4
Late (≥ 24 h)	1	8	8
Rebleed (early and late)	0	1	2
Biliary complications	6	22	1
Bile peritonitis	3	4	0
Bile leak	2	6	1
Biloma	0	11	0
Biliary-venous fistula	0	1	0
Bile duct injury	1	0	0
Infections	3	11	1
Abdominal sepsis	0	6	0
Abscess	2	5	0
Necrosis	1	0	1
Abdominal compartment syndrome	2	1	2

sented in **Table 3**. Comparing grades, late bleeding (>24 hours postinjury) correlated with increasing liver grade: 17% (1/6) in grade 3 injuries, 45% (8/18) in grade 4 injuries, and 57% (8/14) in grade 5 injuries. Both biliary injuries and infectious complications tended to occur more often in grade 4 injuries (13% [22/166] and 7% [11/166], respectively) than in either grade 3 (2% [6/264] and 1% [3/264], respectively) or grade 5 (4% [1/23] and 4% [1/23], respectively) injuries. Surprisingly, ACS was seen in association with all liver grades.

Table 4 presents the following risk factors for hepatic complications identified by univariate analysis: liver injury grade; initial crystalloid resuscitation volume; and total and 24-hour packed red blood cell (PRBC), fresh frozen plasma, platelet, and cryoprecipitate administration. However, only liver injury grade and the need for transfusion (PRBCs) at 24 hours postinjury predicted complications by multivariable analysis with a receiver operating characteristic of 0.79 (**Table 5**). **Figure 3** depicts the probability of a hepatic-related complication vs the number of units of PRBCs received. Clearly, as the number of PRBCs increases, the risk of complication increases for all liver injury grades. Additionally, for a given probability of complication, the higher the liver injury grade, the lower the number of units required to be transfused prior to a complication developing.

Table 4. Risk Factors for Hepatic Complications Identified by Univariate Analysis

Variable	No. (%) of Patients	No. (%) of Complications	OR (95% CI)	P Value
Overall	453 (100)	61 (13.5)		
Age, y				
10-20	117 (25.8)	13 (11.1)	1.01 (0.99-1.03)	.38
21-27	111 (24.5)	10 (9.0)		
28-40	118 (26.1)	9 (7.6)		
41-90	107 (23.6)	14 (13.1)		
Male	249 (55.0)	26 (10.4)	0.99 (0.53-1.81)	.96
Female	204 (45.0)	20 (8.8)	1	
ISS				
4-17	104 (23.0)	11 (10.6)	1.00 (0.97-1.03)*	.81
18-26	100 (22.1)	7 (7.0)		
27-34	114 (25.2)	12 (10.5)		
35-75	61 (13.5)	8 (13.2)		
Data missing	74 (16.3)	8 (10.8)		
Injury grade				
Grade 5	25 (5.5)	10 (40.0)	20.83 (7.18-60.48)	<.001
Grade 4	170 (37.5)	28 (16.5)	6.16 (2.74-13.88)	<.001
Grade 3	258 (57.0)	8 (3.1)	1	
BP in ED				
SBP < 90 mm Hg	49 (10.8)	8 (16.3)	1.88 (0.82-4.30)	.13
SBP ≥ 90 mm Hg	404 (89.2)	38 (9.4)	1	
Total crystalloid requirement in first 24 h, L				
0.5-3.25	100 (22.1)	3 (3.0)	1.11 (1.03-1.18)*	.005
3.26-4.85	100 (22.1)	8 (8.0)		
4.86-6.88	100 (22.1)	12 (12.0)		
6.89-37.1	100 (22.1)	15 (15.0)		
Data missing	53 (11.6)	8 (15.1)		
Total				
PRBC requirement > 0 U	202 (44.6)	40 (19.8)	10.08 (4.18-24.33)	<.001
PRBC requirement = 0 U	251 (55.4)	6 (2.4)	1	
24-h				
PRBC requirement > 0 U	166 (36.6)	34 (20.5)	5.90 (2.96-11.77)	<.001
PRBC requirement = 0 U	287 (63.4)	12 (4.2)	1	
Total				
FFP requirement > 0 U	82 (18.1)	20 (24.4)	4.28 (2.25-8.14)	<.001
FFP requirement = 0 U	371 (81.9)	26 (7.0)	1	
24-h				
FFP requirement > 0 U	67 (14.8)	13 (19.4)	2.58 (1.28-5.20)	.007
FFP requirement = 0 U	386 (85.2)	33 (8.6)	1	
Total				
PLT requirement > 0, 6 pack	51 (11.3)	17 (33.3)	6.43 (3.21-12.87)	<.001
PLT requirement = 0, 6 pack	402 (88.7)	29 (7.2)	1	
24-h				
PLT requirement > 0, 6 pack	34 (7.5)	12 (35.3)	6.18 (2.81-13.55)	<.001
PLT requirement = 0, 6 pack	419 (92.5)	34 (8.1)	1	
Total				
Cryoprecipitate requirement > 0, 10 pack	18 (4.0)	7 (38.9)	6.46 (2.37-17.62)	<.001
Cryoprecipitate requirement = 0, 10 pack	435 (96.0)	39 (9.0)	1	
24-h				
Cryoprecipitate requirement > 0, 10 pack	14 (3.1)	6 (42.9)	7.48 (2.47-22.64)	<.001
Cryoprecipitate requirement = 0, 10 pack	439 (96.9)	40 (9.1)	1	

Abbreviations: BP, blood pressure; CI, confidence interval; ED, emergency department; FFP, fresh frozen plasma; ISS, Injury Severity Score; OR, odds ratio; PLT, platelet; PRBC, packed red blood cell; SBP, systolic blood pressure.

*For ISS and crystalloid requirement, measures of association computed by univariate logistic regression were performed only for complete data.

COMMENT

Nonoperative management of hemodynamically stable patients with blunt hepatic injuries has become the standard of care because the safety and feasibility have been well established. Recent series report that approximately 70% of all patients with liver injuries can be treated nonoperatively with no hepatic-related mortalities.² Since

death is no longer a significant threat, the focus now has shifted to lowering hepatic morbidity, particularly in patients with high-grade injuries. Treatment of these complex patients requires a high index of suspicion for the development of complications as well as access to multimodality intervention strategies.

We report complications and interventions required for the management of complex blunt hepatic injuries

Table 5. Multiple Logistic Regression Model

Variable	Parameter Estimate	Adjusted OR (95% CI)	P Value
Intercept	-4.3682		
Grade 4 injury	1.4904	4.439 (1.93-10.19)	<.001
Grade 5 injury	2.4850	12.001 (4.16-34.59)	<.001
24-h PRBC requirement	1.8634	6.446 (3.13-13.27)	<.001

Abbreviations: CI, confidence interval; OR, odds ratio; PRBC, packed red blood cell.

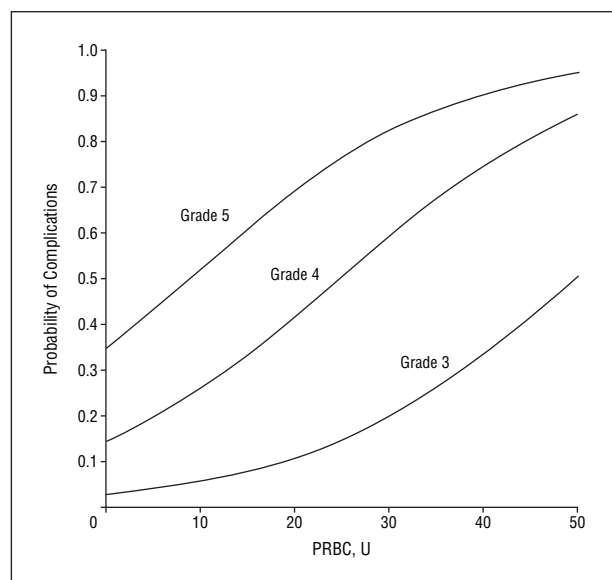


Figure 3. Probability of hepatic-related complication vs transfusion. PRBC indicates packed red blood cell.

at 7 level I trauma centers, representing, to our knowledge, the largest study to date of this patient population. Overall, 14% of patients developed hepatic complications, of which 5% were in patients with grade 3 injuries; 22%, in patients with grade 4 injuries; and 52%, in patients with grade 5 injuries. Complications (including bleeding, biliary, infectious, and ACS) developed, at times ranging from the day of injury through PID 90. Carillo et al¹⁴ reported a slightly higher incidence of complications in their series: 5% in grade 3 injuries, 51% in grade 4 injuries, and 70% in grade 5 injuries. Their series was smaller and single institution but, more importantly, they defined complications differently than in the current series, making a direct comparison difficult. They, as others, have stressed the importance of multimodality interventions in the nonoperative treatment of these patients.¹⁵

In fact, of the 86 treatment strategies we used to manage hepatic complications, only 34% (29) were operative. Endoscopic retrograde cholangiopancreatography with stenting and IR drainage procedures formed the mainstay of therapeutic options used. Interventional radiology angioembolization was the initial modality used for bleeding in 32 patients (91%). Only 3 patients went directly to the operating room for bleeding complications. An additional 3 patients required operative strat-

egies following rebleeds (PIDs 1, 2, and 3) after initial embolization (PID 0). Although this study was certainly not intended to make recommendations on length of hospitalization, our data suggest that bleeding is a rare complication after PID 3.

Biliary complications, in particular, mandated multiple treatment strategies. Of the 7 patients with bile peritonitis, all of whom underwent laparotomy or laparoscopy, 4 required subsequent ERCP with stenting and 2 of these patients then went on to need IR drainage of bilomas. Similarly, one third of the patients (2 of 6) diagnosed first with a biloma required ERCP and stenting in addition to IR drainage of the biloma. Finally, the patient with a biliary-venous fistula underwent laparotomy and ERCP with stenting to manage this complication and then later, IR drainage of a biloma.

Bile peritonitis was managed by both laparotomy as well as laparoscopy, ranging from PID 2 to 19. Delayed laparoscopy for management of biliary peritonitis (peritoneal and systemic signs suggestive of systemic inflammatory response) has been reported to be a safe and effective technique with rapid improvement in the systemic response.¹⁶ Routine ERCP and stenting postlaparoscopy has been proposed as an adjunct to management of bile peritonitis,¹⁷ and stenting rather than sphincterotomy is felt to expedite healing of biliary leaks.¹⁸ Although we had relatively few bile duct injuries (2%), the incidence of biliary complications is likely related to the degree to which they are sought. Sugimoto et al¹⁹ reported a 21.4% incidence of bile duct injuries when ERCP was performed in conjunction with CT scanning in patients with blunt liver injuries.

Hepatic-related infectious complications included liver abscesses, necrosis, and suspected abdominal sepsis. Importantly, all 6 patients with suspected abdominal sepsis underwent a negative laparotomy. It is likely that these patients underwent surgical exploration to rule out a missed hollow viscus injury vs bile peritonitis. Differentiating between the 2 entities remains a challenge because both conditions can present with localized abdominal symptoms as well as systemic signs of infection. Cogbill et al²⁰ noted that 64% of patients with complex liver injuries were hyperpyrexia for the first 3 postoperative days, presumably from devitalized hepatic parenchyma. We, therefore, had no missed hollow viscus injuries in this series. This is an important message for those surgeons who do not see a high volume of complex liver injuries. It is not unusual for these patients to have a distended abdomen with significant tenderness and SIRS. If in doubt, laparoscopy is a viable alternative to evacuate hemoperitoneum and bile.

Lastly, 5 patients developed ACS following resuscitation. Arguably, ACS is not a direct hepatic injury but in 4 of the 5 cases, hemoperitoneum can be implicated as the cause. The fifth patient was found to have only bowel edema and ascites as the etiology of their ACS.

After classifying complications, we next performed a univariate and then a multiple logistic regression analysis to identify risk factors for the development of hepatic complications. Liver injury grade and transfusion requirements were found to be predictive with a receiver operating characteristic of 0.79. Depending on the

surgeon's threshold, this model (Figure 2) may be used as a tool to justify routine surveillance for patients at high risk. For instance, if a surgeon chose to screen patients identified as having a 30% risk of complications, then all patients with grade 5 injuries would be included and patients with grade 4 injuries who received approximately 13 U of PRBCs and patients with grade 3 injuries who received approximately 38 U of PRBCs would be identified as at risk. If, on the other hand, a surgeon chose to screen only patients with a 60% risk of complications, then the transfusion threshold to justify screening would be about 14 U for grade 5 injuries, 30 U for grade 4 injuries, and more than 50 U for grade 3 injuries. Which threshold to choose remains an unanswered question.

A problem, however, with the current study is its retrospective nature. Because of this, potentially important predictive data, such as base deficit and SIRS scores, are missing in a substantial number of patients and therefore were unable to be entered into the prediction model. Additionally, the current study grouped early and late complications together, but as we have demonstrated, the types of complications that occur between the 2 points are different and predictable (Figure 3). Initial complications ($\leq$ PID 3) are primarily bleeding and ACS, with only a few cases of suspected abdominal sepsis. Delayed complications ($>$ PID 3), on the other hand, are primarily biliary and infectious in nature with few exceptions (delayed development of hemobilia and symptomatic ascites, for example). The current prediction model was intended to identify predictors of complications, which it has accomplished. However, it was not designed to take differences in time of onset of complications into account because this time pattern has not been previously identified. Future prospective studies should therefore focus on developing prediction models for early vs delayed complications. If an early complication could accurately be predicted based on initial postinjury data, then a number of presumptive interventions may be instituted. For example, bleeding risk could prompt a hepatic angiogram or decompressive laparotomy could be performed to avoid full-blown ACS. We have, in fact, previously developed a prediction model for the development of ACS based on criteria present at the time of ICU admission.²¹ Another possibility would be a semielective liver resection. Some surgeons argue that many of the hepatic complications we have described can be avoided if liver resection were more commonly used.^{10,22} On the other hand, if patients at risk for delayed complications could be identified, routine screening with CT scans may be warranted. Currently, no consensus as to whether routine CT scans are justified exists, with data suggesting that they are of limited value.^{23,24} However, if a select group of patients at known high risk could be identified, such screening may be beneficial. This would obviously only hold true if complications could be accurately identified and treated early and subsequent morbidity and delayed length of hospital stay, avoided.

An important next step, then, would be to perform a prospective study that used data collected at the time of injury (emergency department data as well as early ICU data) to predict early complications, as well as data obtained within the first several days of hospital admis-

sion to predict late complications. Cogbill et al²⁰ have identified several potentially important markers (hepatic enzymes, serum bilirubin level, and hyperpyrexia), which we did not analyze but could be of potential importance, particularly for late complications.

In conclusion, in this large multicenter experience, hepatic mortality is low but morbidity high following nonoperative management of complex blunt hepatic injuries. When present, complications frequently require multimodality treatment interventions and substantially prolong hospital stay. Though we have identified through a logistic regression model that liver injury grade (odds ratio, 4.439 for grade 4 and odds ratio, 12.001 for grade 5) and a 24-hour transfusion requirement (odds ratio, 6.446) are predictive of hepatic complications, we now propose that a prospective study is warranted to identify predictors of early vs delayed complications. The potential to limit hepatic morbidity even in patients with high-grade injuries exists; our goal now is to make this a reality. Good epidemiologic characterization is a vital first step.

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DISCUSSION

Gregory J. Jurkovich, MD, Seattle, Wash: I want to congratulate Dr Moore and his colleague Dr Kozar, who couldn't be here for the presentation, for the clear presentation and a comprehensive paper defining the largest experience to date on the management of severe blunt liver injuries.

This retrospective review from several level I trauma centers represents the current standard of care and expected outcomes from nonoperative management of the grade 3, 4, and 5 liver injuries. It is important to emphasize that there were no penetrating injury mechanisms in this cohort.

I believe this paper has the following key take-home messages:

First of all, even in this cohort of the most severe liver injuries, 65% were managed nonoperatively. However, 35% did undergo primary operative treatment. Operative skills in managing hepatic injury are required of the trauma surgeon.

Second, this paper represents a comprehensive and useful categorization of the 5 types of complications that occur following blunt hepatic injury. We should make use of this in further definitions and studies.

Third, catheter-based interventions are an essential part of hepatic trauma surgery management. This begs the question, should trauma surgeons be trained and competent in catheter interventions?

Fourth, there were only 2 deaths due to hepatic trauma out of almost 500 patients. I think you have to consider that hepatic injury-attributed mortality is preventable if nonoperative management is to be practiced.

Fifth, bleeding from hepatic injury occurs early, 24 to 48 hours, and rarely a 1.5% incidence in this paper.

Sixth, bile duct complications occur late, median of 12 days, but up to 1 month following injury, emphasizing the need for due diligence.

Finally, seventh, the complication rate of grade 4 and 5 injuries is very high, arguing, I would say, that all grade 4 and 5 should be managed at a level I trauma center.

With those key take-home points, I have the following questions for the authors:

First of all, what was the mortality rate attributed to liver injury in the operative cohort? I know that wasn't part of this paper but it would be nice to know.

Second, can you provide any insightful information or details on this small group of patients who presented with hypotension to the ER [emergency room], yet were managed nonoperatively? Do you mean to imply that any and all liver trauma patients should initially be managed nonoperatively?

Third, were all bile leak complications managed without hepatic resection? How long should one accept a bile duct leak prior to stenting or sphincterotomy? How long should one follow a leak before hepatic parenchymal resection should be used to manage that bile duct leak?

And my final question is, was there any clustering of the complications at 1 of the 7 institutions?

This well-written paper ends with a call for a prospective validation of these findings. I would argue that this is unnecessary. I would rather that the authors give consideration to a randomized investigation of earlier operative intervention compared to the prolonged nonoperative management of bile leaks. We should be questioning how we can improve these morbidity statistics and give consideration to earlier operative intervention.

Dr Moore: Thank you, Dr Jurkovich, for that thoughtful discussion. I am certain that you have struggled with these patients as much as we have.

Unfortunately, we didn't review the charts of the patients who underwent early operative intervention and that would be very interesting data, especially in regards to decision making about nonoperative treatment. The traditionally coded mortality for operations on grade 4 injuries is about 40% to 50% and grade 5, as high as 80%. Dr Asensio is going to present later this morning that if you exclude the ER thoracotomies and aggressively use multimodality interventions that grade 4 injury mortality can be decreased to 20% and grade 5, down to 65%.

You next questioned whether patients who are hypotensive in the emergency department should be considered for nonoperative treatment. Now, 14% of our cohort have an emergency department systolic blood pressure less than 90 mm Hg and by traditional consideration would be defined unstable. Unfortunately, as you know, defining instability is very difficult.

Meredith et al in a 1994 publication about nonoperative treatment had an interesting scoring system and it had 5 grades. Grade 3 instability was a patient who presented hypotensive but responded to initial volume resuscitation. And I believe that that would be a patient who would qualify for nonoperative therapy, and we would take that patient to the CT scanner.

What we would be looking for is a blush, because if the patient didn't have a blush and stabilized, they could be treated nonoperatively. If they had a blush, depending where it was, they would either go to the operating room or to interventional radiology.

We have found that patients with blushes deep in the posterior right lobe benefit by early IR embolization. Now, all of our bile duct leaks were managed without resection, but in retrospect, I believe that some patients would have benefited by earlier intervention.

What basically happens is that we wait until the patient declares himself to be very sick, and then we pursue the diagnosis. And we find that the patients have a bile duct leak but by that time the patient really is septic and too debilitated or their abdomen is much too hostile to allow us an operative resection.

You asked how long can we wait before intervening with a bile duct leak. As you know, most peripheral bile duct leaks will seal by themselves. However, I am more concerned about

missing the proximal duct injuries. And as we just discussed, if you don't intervene early on those patients and you wait until 12, 15 days, your only alternative is delayed endoscopic bile duct stenting with interventional radiologic drainage.

You next asked was there any clustering of injuries at 1 institution, and the numbers of complications from these 7 institutions were really too low to get any statistical comparisons. There was 1 institution that had a notably low rate of complications, and I think this can be explained by their low rate of nonoperative treatment, which is about 50%. Most of the other centers were above 70%, and they had no grade 5 injuries, which they had treated nonoperatively. Therefore, if you aggressively pursue nonoperative treatment, you probably will have more liver-related morbidity but hopefully you will have lower mortality.

Lastly, you brought up the point about earlier resection. And I believe that now technology does exist and that we could intervene on patients on postinjury day 2 or 3, once their bleeding has subsided, and successfully remove a lobe with a very low morbidity. I am interested in thinking about a prospective trial; I just don't know how we would get enough patients.

James G. Tyburski, MD, Detroit, Mich: I have a question about nosocomial infections. Whenever you give a lot of blood products, the nosocomial infection rate always goes up, no matter what the injury. Do you have any data on ventilator-associated pneumonias in this cohort? Second, in a patient who has a bad liver injury, has a bit of a pulmonary contusion on that side, and develops a ventilator-associated pneumonia, was that considered a liver-related death? How was that put in the results?

Dr Moore: One, we didn't look at other complications. Obviously this patient cohort would have an extremely high rate of associated complications. The patient who develops a pneumonia from pulmonary contusion would not be considered a liver-related mortality.

Edward T. Peter, MD, Red Bluff, Calif: In 1981, Dr Charles Van Dang and I reported packing liver injuries, the major liver injuries 4 and 5. And this was a major step in improving our mortality and reducing the morbidity. We did treat some liver injuries nonoperatively, but most of those were lesser injuries. How do you decide when the patient comes into the emergency department whether you are going to treat them operatively or nonoperatively early on? Is it strictly a hemodynamic situation or are there other factors?

Dr Moore: When a patient arrives in the emergency department, the decision is driven by hemodynamic stability and the results of a FAST exam. The ultrasound that is used in trauma (FAST exam), unfortunately, is not 100% sensitive, so we have developed a protocol for the patient who comes into the emer-

gency department, is hypotensive, and remains tachycardic despite volume loading. We do a standard diagnostic peritoneal lavage and look at the peritoneal aspirate. So when we aspirate the DPL [diagnostic peritoneal lavage] catheter and get frank blood and this patient remains hypotensive, the patient is taken to the operating room.

If the patient stabilizes, I would cautiously opt to go to the CT scanner. Our CT scanner is located about 20 ft from the trauma room. It is a 40-head detector CT scan, which means we can complete the imaging study in about 20 minutes. This approach would not be applicable in institutions that don't have a CT scanner immediately available. As a caveat, if you don't have interventional radiologic angiography immediately available, then perhaps you better head to the operating room and call your angiographers while you pack the liver. That would be another alternative.

Daniel Cullinane, MD, Rochester, Minn: My question involves specifically those patients that did get angiographic embolization. Were you able to see what the overlap was in your group that had hepatic abscess, hepatic infarction, and also angiographic embolization? Are they the same groups? There were a small number of infectious complications in the study. Were all of those patients embolized?

Dr Moore: I would have to go back to the data. The 2 necroses were in patients who had undergone embolization. I don't know about the infectious complications. Something I did learn from preparing for this is that when somebody does a right hepatic embolization, even though it is distal, you can have necrosis of the gallbladder. And that has been reported by several people. I guess it is because they just get proximal deployment of whatever they are putting into the catheter and it can cause the gallbladder to rupture in a delayed fashion.

Randall W. Smith, MD, Temple, Tex: Any data on activated factor VII administration to enhance hemostasis? If you were going to design a prospective study, how would that fit into the algorithm?

Dr Moore: Well, as you know, there is a lot of enthusiasm by factor VIIA. There actually was a study that just was published in *The Journal of Trauma*. Now, I am very much interested in this product and I kept on hearing the results of this study and I was very much enthused. Then I actually read the paper. The paper shows that on intention to treat there is no difference. Perhaps in blunt trauma there is a reduction in 3 U of blood. Factor VIIA is a very expensive product. We use it, but it is done under very strict protocol. I think that in a patient who is really coagulopathic and you have given them a lot of fresh frozen plasma that it probably plays a role, but I don't think there is data to support its early use in trauma.