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Increasing age is associated with worse outcomes in elderly patients with severe liver injury

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A B S T R A C T

While the incidence of geriatric trauma continues to increase, outcomes following severe blunt liver injury (BLI) are unknown. We sought to investigate independent predictors of mortality among elderly trauma patients with severe BLI. A retrospective study of the NTDB (2014–15) identified patients with isolated, high-grade BLI. Patients were stratified into two groups, non-elderly (<65 years) and elderly (≥65 years), and then two management groups: operative within 24 h of admission and non-operative. Demographics and outcomes were compared. Multivariable logistic regression was used to estimate association with mortality. A total of 1133 patients met our inclusion criteria. 107 patients required surgery and 1011 patients were managed non-operatively. Age was independently associated with mortality (AOR 1.04, $p < .001$). For patients <65 years, need for operative intervention was associated with a 55 times greater likelihood of death (AOR 55.1, $p < .001$). In patients ≥65 years, operative intervention was associated with a 122 times greater likelihood of death (AOR 122.09, $p = .005$). Age is independently associated with mortality in patients with high grade BLI.

Introduction

The elderly (≥65 years) population is the most rapidly expanding segment of the US population. There are expected to be 83.7 million elderly people by 2050.[1] Multiple studies have shown that elderly patients experience poorer outcomes after trauma compared to younger patients, despite having similar injury severity scores.[2–4] The reasons for this are multifactorial: elderly patients experience a diminished physiologic response to stress, are more likely to have medical comorbidities, and polypharmacy in the elderly may cause blunted response to injury or increase risk of bleeding, among others.

Elderly patients are more likely to experience blunt rather than penetrating trauma,[4] and the liver is one of the most frequently injured organs in blunt abdominal trauma.[5] There are several options for management after severe blunt liver injury (BLI). It is generally accepted that a patient with unstable vitals or peritonitis should undergo expedient operative exploration. In appropriately selected patients, an operation may allow for direct control of bleeding and the identification and management of associated life-threatening injuries. Hepatic operations for trauma, however, can be associated with a significant mortality, as high as 8.1% to 24%.[6,7] Studies have shown that mortality rate increases with injury grade. Asensio et al.[8] demonstrated a 14% mortality for patients with AAST grade 4 or 5 liver injuries, and Duane et al.[9] showed a 66% mortality for patients with high grade liver injuries, with 59% of these deaths resulting from uncontrolled bleeding.

In recent decades, there has been a shift from primarily operative management of liver injuries to non-operative management (NOM). Improved interventional techniques, along with the ability to perform ERCP and stenting, have made it possible to treat injuries that had previously only been managed in the operating room. Studies have shown that over 80% of BLIs can be managed nonoperatively.[3,6] In fact, Velmahos et al.[10] proposed an aggressive approach toward NOM, and suggested that NOM of liver injuries is

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safe and effective, regardless of the grade of liver injury.

Few studies have addressed the management of isolated severe BLI in the elderly population. Perhaps this is because complex hepatic injuries are rare even for Level 1 trauma centers, and major hepatic resection is infrequently performed.[6] Currently, there is controversy as to if and when to operate on elderly patients with severe liver trauma. EAST guidelines state that age over 55 years is no longer a contraindication to a trial of NOM in the hemodynamically stable patient.[11] However, NOM has been shown to be associated with increased red blood cell transfusion in the elderly[12] and is associated with a greater number of complications, such as pneumonia, subphrenic abscesses, and urosepsis.[13] Despite the potential risks of NOM, the high mortality associated with operative management of hepatic injuries in the frail, elderly population may be prohibitive. As elderly patients lack the physiologic reserve of younger patients, operative management frequently leads to a complicated hospital course with a high mortality rate. The objective of this study was to determine if age was independently associated with mortality in elderly patients undergoing operative management for BLIs.

Material and methods

The National Trauma Database (NTDB), maintained by the American College of Surgeons Committee on Trauma, is a repository of trauma related data, voluntarily reported by 746 participating trauma centers of which 237 were Level 1 centers, 259 were Level II centers, and 189 were Level III or IV centers.[14] The NTDB was used to identify patients with isolated blunt, severe hepatic injuries over a two-year period (2014–2015). Procedure codes were used to identify patients who underwent operation (including exploratory laparotomy and liver-specific operations), as well as those who underwent angio-embolization. Patients who underwent angio-embolization were identified by codes corresponding to “other endovascular procedure on other vessels” or “arteriography of other intra-abdominal arteries.” As procedure codes for angio-embolization were non-specific, patients with concomitant splenic, renal, or pelvic injuries were excluded from the analysis. In order to focus on patients whose predominant injury was BLI, patients with abbreviated injury score (AIS)[15] ≥ 3 in other body regions were excluded. The NTDB does not include information on American Association for Surgery of Trauma (AAST) liver grade classification, so abdominal AIS was used as a surrogate. “High grade” liver injuries were defined as patients with abdominal AIS $\geq$3 (roughly equivalent to AAST liver injury $\geq$ III). As only high grade hepatic injuries would generally be considered for operative intervention, patients with BLI and AIS $\leq$2 were excluded.

Patients were stratified into two age groups: non-elderly (<65 years, including patients under 18) and elderly ($\geq$65 years). Each age group was further stratified into two management groups: patients who received an operation in the first twenty-four hours of admission and patients who received NOM, including angio-embolization. Demographics, patient characteristics, and outcomes were compared using Chi Square test and Mann Whitney *U* Test. Multivariable logistic regression was used to determine independent predictors of mortality. In one model, risk for mortality was assessed using age as a continuous variable, and in a separate model, mortality risk was assessed as a function of age, selecting for patients over or under the cutoff of 65 years. Both regression models controlled for Charlson comorbidity index, Injury Severity Score (ISS), heart rate, systolic blood pressure, and trauma center type (Level 1 or 2 versus other hospitals). SPSS (IBM, version 23) was used to analyze data. *P* values < .05 were set for significance. This study received IRB waiver of exemption.

Results

Of the 1,779,200 patients in the NTDB data registry for 2014 and 2015, a total of 1133 patients with isolated, high-grade BLI were identified. Within the first 24 h of admission, 107 patients required surgery and 1011 patients were managed non-operatively (Table 1). Most patients were male (51.72%) and Caucasian (65.40%). Overall mortality was 2.55%. In the operative group, there were no significant demographic or physiologic differences between older and younger patients, except that elderly patients tended to present with lower heart rate (mean 73.42, SD 27.83 vs. 96.50, SD 31.92). Mortality was higher in the elderly group (42.85% vs. 20.43%). Hospital LOS and ICU LOS were not significantly different between the elderly and non-elderly.

In the non-operative subset, mortality was higher in the elderly group, although this did not reach significance (1.31% vs. 0.32%, $p = .18$). Elderly patients spent an average of one day longer in the hospital compared to non-elderly patients (median 5 days, IQR [3–7.75] vs. 4 days, IQR [2,5], $p < .001$), but there was no significant difference between the two groups for time spent in the ICU. In all age groups, overall complication rate was higher in those patients who received an operation within 24 h. Rate of complications was highest in elderly patients who received an early operation vs. younger patients who underwent early operation (71.4% vs. 38.7%, $p = .02$) (Table 1).

A multivariable logistic regression for factors contributing to mortality was performed. In the model using age as a continuous independent variable, age was found to be an independent risk factor for death (AOR 1.04, $p < .001$), and patients who required an operation were 53 times more likely to die (AOR 53.6, $p < .001$) (Hosmer and Lemeshow test: $p = .22$, AUC 0.93). Patients under 65 years of age were 55 times more likely to die if an operation was warranted (AOR 55.14, $p < .001$) (Hosmer and Lemeshow test: $p = .37$, AUC = 0.92). In patients $\geq$65 years, operative intervention was associated with a 122 times greater likelihood of death (AOR 122.09, $p = .005$) (Hosmer and Lemeshow test: $p = .95$, AUC 0.94) (Table 2).

Discussion

The geriatric population is a unique subset of trauma patients. Elderly patients have limited physiologic reserve that affects response to injury. In our study, there were no significant differences between elderly and non-elderly patients with respect to ISS or AIS in both the operative and non-operative groups. Despite having similarly severe injuries, elderly patients presented with lower heart rate (in both non-operative and operative groups) and higher systolic blood pressure (in non-operative group). This finding highlights that despite presenting with similar injury severity, elderly patients have fundamentally different physiologic responses to trauma. Medication use in the elderly may have also affected response to injury.

Management of severe injuries in this unique group can be challenging, and there is no consensus for appropriate management of BLI in the elderly. One study by Tsugawa et al.[13] examined elderly (defined as age >70 years) patients who underwent anatomic resection for severe BLI. The survival rate (65.5%) was relatively high, so the authors concluded that anatomic hepatic resection could be a safe and beneficial procedure for the elderly. Other studies, however, have shown that anatomic resection has traditionally been associated with prohibitively high mortality rates, and ideally should be performed by experienced hepatobiliary surgeons.[7,16] The trauma surgeon should proceed with non-anatomic resection when indicated.[17]

The results from our analysis demonstrate that mortality after

Table 1
Patient characteristics.

	All Patients (n = 1133)	OR within 24 h (n = 107)			Non-operative (n = 1011)		
		<65 (n=93)	>65 (n = 14)		<65 (n = 935)	>65 (n = 76)	
Demographics							
Gender				X^2 (1, n = 107) = 1.2,			X^2 (1, n = 1011) = 3.6,
Male	586 (51.72%)	61 (65.59%)	7 (50.00%)	$p = .25$	476 (50.90%)	30 (39.47%)	$p = .05$
Ethnicity				X^2 (3, n = 107) = 3.8,			X^2 (3, n = 1011) = 6.9,
White	741 (65.40%)	45 (48.38%)	10 (71.42%)	$p = .28$	616 (65.88%)	60 (78.94%)	$p = .07$
Black	192 (16.94%)	24 (25.80%)	2 (14.28%)		156 (16.68%)	7 (9.21%)	
Other	166 (14.65%)	21 (22.58%)	1 (7.14%)		133 (14.22%)	9 (11.84%)	
Asian	34 (3.00%)	3 (3.22%)	1 (7.14%)		30 (3.20%)	0	
ISS (median, IQR)	14 (10,18)	17 (11,25)	20 (16.75, 27)	$p = .14$	14 (10,17)	13 (10,17)	$p = .39$
Abdominal AIS (median, IQR)	3 (3,4)	4 (3,4)	4 (3,4)	$p = .39$	3 (3,4)	3 (3,4)	$p = .92$
Charlson Comorbidity Index (median, IQR)	0 (0,0)	0 (0,0)	0 (0,1)	$p = .07$	0 (0,0)	0 (0,1)	$p < .001$
Physiology							
SBP (mean, SD)	124.34, 25.44	115.14, 32.40	108.64, 61.30	$p = .70$	124.72, 22.57	138.04, 29.11	$p < .001$
% Hypotensive (SBP <110)	158 (13.94%)	27 (29.03%)	5 (35.71%)	$p = .87$	139 (14.86%)	11 (14.47%)	$p = .92$
HR (mean, SD)	93, 22.05	96.50, 31.92	73.42, 27.83	$p < .001$	93.48, 20.52	84.57, 16.53	$p < .001$
GCS (median, IQR)	15 (15,15)	15 (9,15)	15 (3,15)	$p = .63$	15 (15,15)	15 (15,15)	$p = .22$
Outcomes							
Mortality	29 (2.55%)	19 (20.43%)	6 (42.85%)	X^2 (1, n = 107) = 3.84 $p = .06$	3 (0.32%)	1 (1.31%)	X^2 (1, n = 1011) = 1.7, $p = .18$
Overall Complication Rate	209 (18.40%)	36 (38.7%)	10 (71.4%)	$p = .02$	144 (15.40%)	14 (18.4%)	$p = .48$
LOS, days (median, IQR)	4 (3,6)	8 (4.5, 16)	7 (1, 16.2)	$p = .36$	4 (2,5)	5 (3, 7.75)	$p < .001$
ICU days (median, IQR)	3 (2,4)	4.5 (2, 11.5)	7 (2.75, 17.75)	$p = .48$	2 (2,3)	3 (2,4)	$p = .09$
Vent days (median, IQR)	2 (1,6.25)	3 (2, 7.5)	3 (1,12)	$p = .66$	2 (1,3)	2 (1,6)	$p = .91$

Abbreviations: ISS: injury severity score, AIS: abbreviated injury scale, IQR: intraquartile range, LOS: length of stay, ICU: intensive care unit.

any operative intervention for BLI increases significantly with age, findings that other studies support. In their analysis of factors contributing to mortality after trauma laparotomy in geriatric patients, Joseph et al.[18] demonstrated a direct correlation with mortality for every decade of life after age 55 years. A meta-analysis examining predictors of mortality in geriatric trauma patients found that patients over age 84 years were 1.69 times more likely to die compared to patients 65–74 years of age ($p < .001$).[19] The complication rates are also higher for elderly patients with BLI following surgery. One study suggested a 40% complication rate for patients over 55 years who underwent emergent trauma exploratory laparotomy, with pneumonia and urinary tract infections representing the most common complications.[18] In our analysis, we demonstrated a higher overall rate of complications in patients who underwent an operation within the first 24 h of admission, with elderly patients experiencing significantly more complications compared to younger patients. As elderly patients with severe liver injury may be more likely to have experience higher morbidity and mortality compared to younger patients, the surgeon must weigh the risks and benefits of operative intervention. While surgery may indeed be indicated in this population, the trauma surgeon should recognize that these patients often have poor overall prognosis.

Thus, in these high-risk patients, an early goals of care discussion is warranted after initial resuscitation and intervention. In addition, early involvement of palliative care services may be beneficial. Current Eastern Association for the Surgery of Trauma (EAST) guidelines state that an aggressive initial approach should be pursued for management of the elderly patient, unless “it is in the judgment of an experienced trauma surgeon that the injury

Table 2
Logistic regression, factors that contribute to mortality.

	All Patients	Patients Under 65	Patients Over 65
Age	OR 1.04, $p < .001$ 95% CI [1.01–1.06]		
Need for Operative Intervention	OR 53.60, $p < .001$ 95% CI [16.72–171.95]	OR 55.14, $p < .001$ 95% CI [15.14–200.84]	OR 122.09, $p = .005$ 95% CI [4.34–3431.82]
Charlson Comorbidity Index	OR 1.22, $p = .48$ 95% CI [.69–2.17]	OR 1.32, $p = .42$ 95% CI [.66–2.6]	OR 1.86, $p = .23$ 95% CI [.66–5.20]
Trauma Center Type	OR 2.3, $p = .09$ 95% CI [.86–6.43]	OR 2.04, $p = .18$ 95% CI [.71–5.84]	OR 15.53, $p = .13$ 95% CI [.44–544.95]
AIS	OR 2.10, $p = .003$ 95% CI [1.29–3.59]	OR 1.90, $p = .022$ 95% CI [1.09–3.31]	OR 8.26, $p = .2$ 95% CI [.31–215.83]
SBP	OR .98, $p = .02$ 95% CI [.97-.99]	OR .98, $p = .09$ 95% CI [.97–1.002]	OR .98, $p = .32$ 95% CI [.94–1.01]
HR	OR 1.01, $p = .01$ 95% CI [1.00–1.03]	OR 1.01, $p = .08$ 95% CI [.99–1.02]	OR 1.02, $p = .42$ 95% CI [.96–1.08]

Abbreviations: AIS: abbreviated injury scale, SBP: systolic blood pressure, HR: heart rate, OR: odds ratio.

burden is severe."[20] If aggressive operative management is deemed non-beneficial and NOM is pursued, early palliative care involvement will help identify and coordinate both patient and family goals of care.[4] American College of Surgeons Trauma Quality Improvement Program (TQIP) palliative care guidelines recommend that a frailty screen using a five-item FRAIL scale should be performed on admission for all patients age 65 or older.[21] Additional scoring systems, such as the Trauma-Specific Frailty Index (TSFI), which incorporates patient comorbidities, ability to perform daily activities, and nutritional status, may accurately predict those elderly patients at risk for worse outcomes after trauma and can aid clinicians in patient disposition.[22]

While operative intervention for BLI in geriatric patients is associated with high mortality, NOM of liver injuries, even when 'successful', is traditionally associated with many complications, including biloma, liver abscess, and more rarely arteriovenous fistulas and hepatic necrosis.[23] Increased age is associated with increased likelihood of failure of NOM. One study that examined BLI using data from NTDB from 2002 through 2008 showed that for each year, increasing age and ISS resulted in a 2% increase in the odds of failed NOM.[24] In addition, elderly patients with BLI that undergo NOM may require a greater number of blood transfusions and a longer period of observation, which can translate into longer hospital stays. In our study, elderly patients managed non-operatively spent an average one day longer in the hospital, compared to younger patients.

Our study had several limitations. The NTDB represents a convenience sample that includes a disproportionate number of younger and more severely injured patients, and the database contains missing data on several patients. In addition, we used abdominal AIS as a surrogate for AAST hepatic injury grade as injury grade was not available; thus, AIS may not accurately correspond to injury grade in certain cases. In addition, though we excluded patients with concomitant splenic, renal and pelvic injuries, we did not exclude patients with concomitant bowel injuries. Additionally, the NTDB does not include data on blood transfusion. Future studies could incorporate this information to analyze potential delays to definitive operation in elderly patients who failed NOM. This could also be used to specifically examine failure rates of NOM in elderly patients.

The NTDB does not include information on patient medication such as anticoagulants or antiplatelet agents; this may be a confounding factor in our mortality analysis. In addition, we chose to stratify patients by those who had an operation within 24 h and after 24 h, yet we acknowledge that this time frame may have added confounders to our analysis, and twenty-four hours serves as an arbitrary time cutoff. Lastly, we defined elderly patients as $\geq$65 years, as this definition is commonly utilized in the literature, however we acknowledge that this describes a heterogeneous group of patients.[25,26] Frailty index combined with chronologic age may be a better indicator of physiologic difference between older and younger patients, and future studies may benefit from comparing patient outcomes incorporating frailty index scores.

Conclusions

Age is an independent predictor for mortality in patients with high grade BLI. This led us to conclude that given the exceedingly high risk of death among elderly trauma patients who sustain severe BLI, a goals of care discussion is warranted early in the hospital course, particularly when surgery is required, as operative intervention is associated with high morbidity and mortality. The practicing trauma surgeon should weigh the risks and benefits of operation for the elderly patient with severe BLI, taking into consideration that these patients often have poor outcomes.

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List of abbreviations

ISS: injury severity score
AIS: abbreviated injury scale
IQR: intraquartile range
LOS: length of stay
ICU: intensive care unit
SBP: systolic blood pressure
HR: heart rate
OR: odds ratio
BLI: blunt liver injury
NOM: non-operative management
NTDB: National Trauma Data Bank
EAST: Eastern Association for the Surgery of Trauma