



Gunshot liver injuries grade I–III and related liver enzyme values

Vrednosti hepatičnih enzima kod povreda jetre vatrenim oružjem, I–III stepena

Miodrag Radunović*, Marko Vuković*, Nemanja Radojević*, Ranko Lazović*,
Miroslav Radunović†

*Clinical Centre of Montenegro, Podgorica, Montenegro; University of Montenegro,

†Faculty of Medicine, Podgorica, Montenegro

Abstract

Background/Aim. The liver is one of the most commonly injured solid organ in patients with abdominal gunshot wounds. The aim of this study was to investigate correlation between aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels as well as correlation between liver enzymes and Injury Severity Score (ISS) among patients sustained a gunshot liver injury. **Methods.** The study included 30 patients with a gunshot liver injury. Patients were divided into three groups, according to the American Association for the Surgery of Trauma injury grade. We included only patients with first (I), second (II) and third degree (III) injury. AST and ALT levels were also initially measured, and then consecutively each day, up to the fifth post-traumatic day, in order to determine which of them is better and more stable predictor of severity of gunshot liver injury. **Results.** ALT had significant positive correlation with a low-degree gunshot liver injury, on the day zero, post-traumatic day one and day two. Nevertheless, AST/ALT relation throughout post-traumatic five day period regarding an injury grade correlates best in II grade injury. At the end, strong positive correlation between ALT and ISS was observed ($p < 0.05$). **Conclusion.** Presented data clearly shows that ALT is better gunshot liver injury predictor than AST, with strong predictive value regarding injury severity, in first days after liver trauma. Therefore, it could be easily available, cheap and reliable prognostic tool for complexity of liver trauma. ALT prediction value is more significant for I and II injury, grade. Correlation between AST and ALT exists only for specific injury grade (II), but not in general.

Key words:

wounds, gunshot; liver; injury severity score; transaminases.

Apstrakt

Uvod/Cilj. Jetra je jedan od najčešće povređivanih organa kod pacijenata sa povredama zadobijenim projektilima male početne brzine. Cilj rada bio je da se utvrdi korelacija između vrednosti jetrenih enzima, aspartat aminotransferaze (AST) i alanin aminotransferaze (ALT), kao i korelacija između i skora na Internacionalnoj skali za merenje ozbiljnosti povreda (ISS) među pacijentima sa strelnim povredama jetre. **Metode.** Ispitivanjem je bilo obuhvaćeno 30 bolesnika sa strelnim povredama jetre. Oni su bili podeljeni u tri grupe u skladu sa sistemom vrednovanja Američke asocijacije za traumatsku hirurgiju. Studijom su obuhvaćeni ispitanici sa prvim (I), drugim (II) i trećim stepenom strelnih povreda jetre. Nivoi AST i ALT mereni su inicijalno, kao i svakog narednog dana, do petog dana posle traume, u cilju određivanja enzima koji bi bio bolji prediktor stepena ozbiljnosti strelnih povreda jetre. **Rezultati.** Pozitivna korelacija sa niskogradusnim strelnim povredama jetre utvrđena je za ALT nultog dana, kao i prvog i drugog posttraumatskog dana. Pored toga, AST/ALT odnos najbolje je korelisao sa II stepenom oštećenja jetre tokom svih pet dana posle traume. Nađena je pozitivna korelacija između vrednosti ALT i ISS ($p < 0.05$). **Zaključak.** Našom studijom je dokazano da je ALT bolji indikator strelnih povreda jetre u odnosu na AST, sa jakom prediktivnom vrednošću u odnosu na stepen povrede, prvih dana posle traume. Taj enzim bi mogao biti pouzdan, lako dostupan i jeftin indikator kompleksnosti strelnih povreda jetre. Pored toga, prediktivna vrednost ALT je značajnija za I i II stepen povrede. Korelacija između enzima AST i ALT postoji samo za II stepen strelnih povreda jetre, ali ne i uopšteno.

Ključne reči:

rana vatrenim oružjem; jetra; povrede, indeksi težine; aminotransferaze.

Introduction

Liver is one of the most commonly injured solid organ in patients with abdominal gunshot wounds¹ and its injury is

reported in approximately 5% of all trauma². Leading cause of death in severe liver injuries is uncontrollable bleeding, while multiple organ failure and residual sepsis are the primary causes of late death and morbidity³.

The Injury Severity Score (ISS) correlate well with survival and provides a numerical description of the overall severity of injury for patients with multiple trauma⁴. It could be also related to the severity of liver injuries which is universally classified according to the American Association for the Surgery of Trauma (AAST). The majority of patients admitted for liver injuries have grade I, II or III⁵. Liver injury releases transaminases, mitochondrial and cytoplasmic enzymes that are found in hepatocytes, neurons, pancreatic and muscle cells and the two most common transaminases are aspartate aminotransferase (AST) and alanine aminotransferase (ALT)⁶. AST and ALT elevation are known to correlate to liver injury and occur immediately after the trauma⁷⁻⁹. Nevertheless, it appears that high-grade (AAST grades III–VI) liver injury results in higher AST and ALT levels than low-grade liver injury (AAST grades I–II)¹⁰.

The aim of this study was to investigate the correlation between AST and ALT levels as well as correlation between liver enzymes and ISS score among patients sustained a gunshot liver injury.

Methods

We evaluated 30 patients with gunshot liver injuries and accompanying injuries of other organs if sustained in some cases, but any of them was not life-threatening. The patients were divided into three groups, according to AAST injury grade. We included only patients with first (I), second (II) and third degree (III) gunshot liver injury. There were 10 patients in each group. Every patient underwent abdominal computed tomography (CT) during initial evaluation with ISS scoring; AST and ALT levels were also measured, initially and then consecutively each day, up to the fifth post-traumatic day in order to determine which of them was better and more stable predictor of severity of gunshot liver injury. The ELISA tests on Cobas c 311/501 analyzer (COBAS, Roche Diagnostics GmbH, D-68305 Mannheim, Germany) for measurement of AST and ALT levels in human serum was used. The threshold of blood AST and ALT upper margin normal reference range level was set at 50 IU/L⁶. The patients with severe, life-threatening injuries were excluded as well as those with severe bleeding, previous liver diseases or any other chronic disease and those who had initially increased levels of AST and ALT upon admission. Parameters

observed were: age, gender, ISS, blood AST and ALT levels and CT diagnosed liver injury grade, according to the AAST scale⁶.

Statistical analysis

Statistical analysis was performed by the Statistical Package for the Social Sciences (SPSS) version 11 for Windows software package (SPSS Inc., Chicago, USA). Since data do not follow normal distribution we used the nonparametric Spearman's correlation. Methods of statistical description included the Student *t*-test in order to determine statistical significance. The difference of the obtained values was considered to be significant at $p < 0.05$.

Ethics

Each subject signed the acceptance of the study protocol, in which the Ethical Principles for Medical Research Involving Human Subjects (The Helsinki Declaration) were clearly stated. They all signed the informed consent form.

Results

The patients were divided into three groups, according to the gunshot liver injury grade. Each grade comprises 10 patients, with levels of AST and ALT measured from day zero up to the fifth post-traumatic day. Average age of patients was 41.3 ± 15.2 (ranging from 19 to 72) years and 21 out of 30 patients were males. There were 11 patients who sustained concomitant right colon injury, 7 patients had right kidney injury, while 3 patients had accompanied duodenal penetration. In Table 1 a correlation between serum enzymes values injury grades is given and it is evident that ALT had significant, positive correlation with low-degree gunshot liver injury, on the day zero, post-traumatic day one and day two.

Table 2 represents AST/ALT ratio throughout post-traumatic five day period in regard to injury grade. It correlated best with II grade injury. Table 3 provides information about correlation between AST and ALT levels among patients as well as correlation between serum liver enzymes values and ISS where strong positive correlation between ALT and ISS was observed ($p < 0.05$).

Table 1
Correlation between liver injury grade and liver enzyme values during five days after injury

Days after injury	AST		Days after injury	ALT	
	Injury grade I–II	Injury grade II–III		Injury grade I–II	Injury grade II–III
0	-0.341	0.093	0	0.692*	0.157
1	0.389*	0.509*	1	0.574*	-0.407
2	0.480*	0.438*	2	0.492*	-0.421
3	-0.157	0.531*	3	0.063	-0.392
4	-0.137	0.470*	4	0.261	-0.530
5	0.577	0.265	5	0.218	-0.530

* Statistically significant correlation among groups.

AST – aspartate aminotransferase; ALT – alanine aminotransferase.

Table 2

AST/ALT correlation throughout post-traumatic five day period regarding injury grade

AST/ALT ratio throughout five days after injury	Grade injury		
	I	II	III
AST 0 / ALT 0	-0.081	-0.040	-0.001
AST 1 / ALT 1	0.362	-0.125	0.291
AST 2 / ALT 2	-0.304	0.550*	-0.051
AST 3 / ALT 3	-0.404	0.385*	0.038
AST 4 / ALT 4	-0.248	0.510*	0.063
AST 5 / ALT 5	-0.412	0.578*	0.409*

*Statistically significant correlation between groups.

AST – aspartat aminotransferase; ALT – alanine aminotransferase.

Table 3

Spearman's rank correlation coefficient between AST and ALT and ISS during five days after injury for 30 patients, regardless of injury grade

Spearman's rank correlation (ρ)		ALT 0	ALT 1	ALT 2	ALT 3	ALT 4	ALT 5	ISS
AST 0	p	-0.073	-0.218	0.090	0.181	0.133	-0.006	0.119
	t-test	0.703	0.246	0.637	0.339	0.483	0.973	0.532
AST 1	p	0.146	0.275	0.187	0.135	0.112	-0.059	0.252
	t-test	0.442	0.141	0.322	0.477	0.557	0.758	0.179
AST 2	p	0.194	0.377*	0.272	0.301	0.397*	0.253	0.021
	t-test	0.303	0.040	0.147	0.105	0.030	0.178	0.914
AST 3	p	0.193	0.389*	0.283	0.318	0.447*	0.329	-0.076
	t-test	0.306	0.034	0.130	0.087	0.013	0.076	0.691
AST 4	p	0.192	0.366*	0.120	0.188	0.315	0.191	0.121
	t-test	0.308	0.047	0.528	0.321	0.090	0.312	0.525
AST 5	p	0.117	0.393*	0.146	0.231	0.357	0.313	-0.025
	t-test	0.537	0.032	0.441	0.220	0.053	0.092	0.896
ISS	p	0.084	0.335	0.401*	0.383*	0.400*	0.397*	
	t-test	0.658	0.071	0.028	0.037	0.029	0.030	

* Statistically significant correlation with corresponding group.

AST – aspartat aminotransferase; ALT – alanine aminotransferase; ISS – Injury Severity Score.

Discussion

This study evaluated patients with I, II and III degree gunshot liver injury and according to recent data, a majority of patients admitted for liver trauma worldwide refer to these grades⁵. Correlation between AST and ALT levels in patients with liver trauma and grade of gunshot liver injury could be related to ISS which predicts survival rate. Bruhn et al.⁶ found equally reliable significance of AST and ALT in detecting gunshot liver injury. However, in general, our study showed that there was no significant positive correlation between AST and ALT, and that significant correlation existed only between ALT and ISS which could signify strong prediction value of ALT in trauma severity. According to a study conducted by Narci et al.¹¹, ISS was more valuable than other trauma scoring systems for prognostic evaluation of trauma patients; thus, based on our study, ALT could be easily available, cheap and reliable prognostic tool for complexity of gunshot liver trauma. Nevertheless, when we observed separate enzyme values regarding a gunshot liver injury grade, we noticed a significant positive correlation of AST/ALT ratio with II grade gunshot liver injury ($p < 0.05$). A study made by Zagory et al.¹² showed the same positive trend of correlation between liver enzymes and gunshot liver injury grade, although it referred to pediatric patients. It is also evident that in each injury grade there exists

negative correlation between them on the day zero of injury ($\rho = -0.08$, $\rho = -0.04$, $\rho = -0.001$). Some authors^{13,14} tried to determine whether AST and ALT could predict severity of gunshot liver injury. Only Koyama et al.⁹ established optimal cut-off values for AST (> 100 U/L) and ALT (> 80 U/L) as a useful screening tool for CT scan in otherwise stable patients. However, blood samples were taken only immediately upon arrival, unlike in our study where we checked enzyme levels every day, up to the fifth post-traumatic day, and revealed that ALT developed strong positive correlation between I and II injury grade on the day zero, as well as the first and second postinjury day ($\rho = 0.69$; $\rho = 0.57$; $\rho = 0.49$, respectively). This means that ALT could be better predictor for I and II grade gunshot liver injury than AST. On the other hand, AST showed strong positive correlation on the first, second and third post-injury day among patients with II–III grade injury, which means that AST could be better predictor of severity of gunshot injury grade after the first day of the injury. We did not determine cut-off values for liver enzymes. Instead, we tried to predict injury grade in regard with AST or ALT blood level. Besides that, study presented here included patients with gunshot injury, instead of blunt liver trauma observed in forementioned studies. We believe that this makes presented research different and important. Bruhn et al.⁶ claimed that initial evaluation of AST and ALT could be a useful diagnostic tool to predict the need for CT.

Unlike that study, we proved that ALT could be important in estimation of severity of gunshot liver injury, in first days upon trauma which could predict patients outcome, especially in I and II grade injuries. On the other hand, AST correlates with II and III grade injuries, but only after 24 h of trauma initiation, which could be too late for a decision on further diagnosis (CT) or treatment options.

Data gained from the study performed are consistent with the existing literature in the context that the presence of significant gunshot liver injury can indeed be expected to result in raised liver enzyme levels⁶. Unlike the other recently published studies, we tried to estimate the prediction values of liver enzymes concerning the severity of gunshot liver injury and to determine whether any of these enzymes significantly correlated with specific injury grade in first hours of injury. However, limitation of our study is the absence of IV, V and VI liver injury grade, inability to confirm positive predictive trend of ALT even in those with severe injury grades as well as lack of liver enzyme correlation with CT findings which could be of significant importance for further treatment modalities. The reason is high mortality rate of patients with those grades in prehospital period. Nevertheless, there are no contemporary studies concerning gunshot liver injury and relation between liver enzymes and ISS nor predictive value of AST and ALT regarding a gunshot liver injury grade. Thus, we think that our study deserves attention

and could be of significant importance for future research of this subject.

Conclusion

Presented data clearly shows that ALT is better predictor of gunshot liver injury than AST, with strong predictive value regarding injury severity (ISS) in first days after liver trauma. Therefore, it could be easily available, cheap and reliable prognostic tool for complexity of liver trauma. ALT prediction value is more significant for I and II injury grade. Correlation between AST and ALT exists only for specific injury grade (II), but not in general.

Acknowledgement

During the research, Dr Radojevic was a fellow of Fogarty International Center of the National Institutes of Health's "Research Ethics Education in the Balkans and Black Sea Countries" (Award Number R25TW008171), provided by Icahn School of Medicine at Mount Sinai New York USA and School of Medicine University of Belgrade, Serbia. As so, ethical principles conducted during the research were influenced by the education acquired. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

R E F E R E N C E S

1. Feliciano DV, Burch JM, Spjut-Patriney V, Mattox KL, Jordan GL. Abdominal gunshot wounds. An urban trauma center's experience with 300 consecutive patients. *Ann Surg* 1988; 208(3): 362–70.
2. Croce MA, Fabian TC, Menke PG, Waddle-Smith L, Minard G, Kudsk KA, et al. Nonoperative management of blunt hepatic trauma is the treatment of choice for hemodynamically stable patients. Results of a prospective trial. *Ann Surg* 1995; 221(6): 744–53; discussion 753–5.
3. Beal SL. Fatal hepatic hemorrhage: An unresolved problem in the management of complex liver injuries. *J Trauma* 1990; 30(2): 163–9.
4. Baker SP, O'Neill B, Haddon W, Long WB. The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *J Trauma* 1974; 14(3): 187–96.
5. Coccolini F, Catena F, Moore EE, Ivatury R, Biffl W, Peitzman A, et al. WSES classification and guidelines for liver trauma. *World J Emerg Surg* 2016; 11: 50.
6. Bruhn PJ, Østerballe L, Hillingsø J, Svendsen LB, Helgstrand F. Posttraumatic levels of liver enzymes can reduce the need for CT in children: A retrospective cohort study. *Scand J Trauma Resusc Emerg Med* 2016; 24(1): 104.
7. Nishida T, Fujita N, Nakao K. A multivariate analysis of the prognostic factors in severe liver trauma. *Surg Today* 1996; 26(6): 389–94.
8. Cogbill TH, Moore EE, Feliciano DV, Jurkovich GJ, Morris JA, Mucha P. Hepatic enzyme response and hyperpyrexia after severe liver injury. *Ann Surg* 1992; 58(7): 395–9.
9. Koyama T, Skattum J, Engelsen P, Eken T, Gaarder C, Naess PA. Surgical intervention for paediatric liver injuries is almost history: A 12-year cohort from a major Scandinavian trauma centre. *Scand J Trauma Resusc Emerg Med* 2016; 24(1): 139.
10. Tinkoff G, Esposito TJ, Reed J, Kilgo P, Fildes J, Pasquale M, et al. American Association for the Surgery of Trauma Organ Injury Scale I: Spleen, liver, and kidney, validation based on the National Trauma Data Bank. *J Am Coll Surg* 2008; 207(5): 646–55.
11. Nari A, Solak O, Turhan-Haktanir N, Ayçiçek A, Demir Y, Ela Y, et al. The prognostic importance of trauma scoring systems in pediatric patients. *Pediatr Surg Int* 2009; 25(1): 25–30.
12. Zagory JA, Dossa A, Golden J, Jensen AR, Goodhue CJ, Upperman JS. Re-evaluation of liver transaminase cutoff for CT after pediatric blunt abdominal trauma. *Pediatr Surg Int* 2017; 33(3): 311–6.
13. Tan K, Bang S, Vijayan A, Chiu M. Hepatic enzymes have a role in the diagnosis of hepatic injury after blunt abdominal trauma. *Injury* 2009; 40(9): 978–83.
14. Lee W, Kuo L, Cheng Y, Chen C, Lin Y, Lin T, et al. Combination of white blood cell count with liver enzymes in the diagnosis of blunt liver laceration. *Am J Emerg Med* 2010; 28(9): 1024–9.

Received on December 15, 2016.

Revised on March 02, 2017.

Accepted on March 03, 2017.

Online First March, 2017.