RAPID COMMUNICATION

Pre-existing cirrhosis is associated with increased mortality of traumatic patients: Analysis of cases from a trauma center in East China

Zuo-Bing Chen, Lin-Mei Ni, Yuan Gao, Chen-Yan Ding, Yun Zhang, Xue-Hong Zhao, Yun-Qing Qiu

Zuo-Bing Chen, Lin-Mei Ni, Yuan Gao, Chen-Yan Ding, Yun Zhang, Xue-Hong Zhao, Yun-Qing Qiu, Department of Emergency Surgery, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou 310003, Zhejiang Province, China

Correspondence to: Yun-Qing Qiu, MD, Department of Emergency Surgery, First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qing-chun Road, Hangzhou 310003, Zhejiang Province, China. bigzyun1@sina.com

Telephone: +86-571-87236303 Fax: +86-571-87236626

Received: June 29, 2007 Revised: August 6, 2007

Abstract

AIM: To determine the impact of cirrhosis on trauma patients and define the factors predicting death.

METHODS: The data on patients admitted to the trauma center from January 2000-2005 were studied retrospectively. The clinical variables were recorded and compared to identify the factors differentiating cirrhotic trauma survivors from non survivors. Child's classification criteria were derived from the reviewed charts of cirrhotic trauma patients to evaluate their predictive value in cirrhotic trauma. Trauma registry was also used to generate a trauma control group by matching for age, sex, abbreviated injury score (AIS) over the same period of time. The outcome variables compared were mortality rate, time of ICU and hospital stay. Results were expressed as mean $\pm$ SD. These data were analyzed by SPSS.11.0 statistical software. Univariate analysis was performed to identify significant medical factors for survivor and non survivors subjected to chi-square test. Fisher's exact test and Student's *t* test were performed to determine the statistical difference between cirrhotic and control groups. $P < 0.05$ was considered statistically significant.

RESULTS: Poor prognosis of traum patients was associated with one or more of the following findings: ascitcs, hyperbilirubinemia (more than 2 mg/dL), hypoalbuminemia (less than 3.5 mg/dL), and prolonged prothrombin time (more than 12.5 seconds). Although Child's classification was used to predict the outcome in cirrhotic patients undergoing portacaval shunt procedures, no significant difference was found in mortality rate as a function of Child's classification.

CONCLUSION: Cirrhosis is associated with a higher

mortality, a longer time of ICU and hospital stay of trauma patients. It seems that treatment of trauma patients with pre-existing severe liver disease is a challenge to surgeons.

© 2007 WJG. All rights reserved.

Key words: Pre-existing cirrhosis; Trauma; Mortality rate

Chen ZB, Ni LM, Gao Y, Ding CY, Zhang Y, Zhao XH, Qiu YQ. Pre-existing cirrhosis is associated with increased mortality of traumatic patients: Analysis of cases from a trauma center in East China. *World J Gastroenterol* 2007; 13(42): 5654-5658

<http://www.wjgnet.com/1007-9327/13/5654.asp>

INTRODUCTION

Liver cirrhosis is the tenth leading cause of death^[1]. Although cirrhosis-related deaths have decreased over the years, the impact of cirrhosis remains with approximately 30 000 deaths annually, mostly in Asian countries^[2]. Cirrhotic patients often suffer from complications^[3]. Cirrhosis impairs nutrition, alters response to stress, and affects the functions of other organ systems.

Trauma continues to be a major public health problem in the world. Due to the rapid economic development in China, the number of motor vehicles has increased tremendously in the past decade^[4], leading to more deaths and injuries resulting from trauma. WHO predicts that trauma injuries will result in about 2.3 million deaths globally by 2020, becoming the third contributor to the global death^[5]. Trauma not only causes a significant loss of life, but also results in loss of economic, medical, educational, and legal resources.

Trauma, in combination with cirrhosis in patients, brings about a unique challenge. Surgeons in trauma centers treat a variety of patients every day, but treatment of traumatized cirrhotic patients remains a challenge^[6]. It has been shown that the mortality and morbidity rates increase in patients with cirrhosis undergoing elective or emergency surgery^[7]. Also the degree of hepatic insufficiency is a prime factor for determining the outcome in these patients^[8]. Despite the interest in the surgical outcome of cirrhotic patients, few reports are available on the outcome of cirrhotic patients after traumatic

injury. This study reviews and analyzes the data on trauma patients with pre-existing cirrhosis who were admitted to a trauma center in East China from 2000 to 2005.

MATERIALS AND METHODS

Data on more than 11 000 trauma patients (64 trauma patients with pre-existing liver cirrhosis) admitted to the Trauma Center of the First Affiliated Hospital, College of Medicine, Zhejiang University, China, from January 2000 to January 2005 were contained in their respective trauma registries. The data on patients under the ICDM-3 index for cirrhosis patients with chronic liver disease were analyzed. The trauma registry abstracts and medical records of all patients diagnosed as hepatic cirrhosis were reviewed. Diagnosis of hepatic cirrhosis was confirmed by the past medical history, clinical examination, operation findings, biopsy, and/or imaging.

The clinical variables were recorded and compared to identify the factors affecting prognosis of the patients and prolonging survival of the patients. In addition, evidence of hepatic insufficiency was evaluated by ascites, hyperbilirubinemia (more than 2 mg/dL), hypoalbuminemia (less than 3.5 mg/dL), elevated alkaline phosphatase (more than 125 st/L), serum glutamic oxaloacetic transaminase (SGOT more than 40 st/L), and/or prothrombin time (more than 12.5 s) detected at admission.

The trauma registry was also used to generate a trauma control group consisting of 86 patients by matching for age, sex, abbreviated injury score (AIS) over the same period of time. The AIS-85 scores were used because they permitted us to match patients with similar injuries. No cirrhosis or chronic liver failure was found in patients within the control group. The outcome variables compared were mortality rate, time of ICU and hospital stay.

Results were expressed as mean $\pm$ SD. The data were analyzed by SPSS.11.0 statistical software. As our sample size was too small to perform multivariate analysis, a univariate analysis was performed to identify the significant predictive factors. The data were subjected to chi-square test. To determine the statistical difference between the cirrhotic and control groups, we compared the mortality rates by Fisher's exact test. Parametric values of AIS, and time of hospital and ICU stay were compared by Student's *t* test. *P* < 0.05 was considered statistically significant.

RESULTS

Sixty-four cirrhotic trauma patients (5.9 per 1000 trauma patients) admitted to the Trauma Center of the First Affiliated Hospital, College of Medicine, Zhejiang University were included in this study. These patients were diagnosed as cirrhosis before admission and during laparotomy for traumatic injury, respectively. The etiology of cirrhosis was related to HBV infection and alcohol in 62 and 1 patients, respectively and unidentified in 1 patient. The demographic and outcome data are listed in Table 1. Although the major causes for injury were motor vehicle accidents (MVA) (Table 2), 30.77% (4 of 13) of deaths were due to accidental fall. Other causes for injury included superficial abdominal

Table 1 Demographic and survival data on patients studied (48 males, 16 females)

(<i>n</i> = 40)	Range
Mean age = 52	31-84
Mean TS = 12	6-16
Mean ISS = 12	5-34
Surv = 87.5%	

Table 2 Mechanism of injury

Mechanism of injury	Total	Non survivors <i>n</i> (%)
Fall	13	4 (30.77)
MVA	48	3 (6.25)
Other	3	1 (33.33)

Table 3 Injury characteristics

Site	Total	Non survivors <i>n</i> (%)
Head	22	2 (9.09)
Thorax	7	2 (28.57)
Abdomen	9	3 (33.3)
Pelvis/Ext	26	1 (3.85)
Multiple	27	6 (22.22)
Single	37	2 (5.41)

stab wound, criminal assault. Seven patients had sustained blunt thoracic traumas including rib fracture, pulmonary contusion. Blunt abdominal trauma as evidenced by hemoperitoneum, splenic rupture, and/or liver laceration was the predominant injury in 9 patients. Pelvic fracture or limbic long-bone fracture occurred in 36 patients. Twenty-seven patients had injuries involving multiple sites. The remaining 37 patients had injuries involving a single site and two of them died (Table 3).

The clinical or laboratory findings associated with hepatic insufficiency in this group of patients are outlined in Table 4. Ascites was confirmed during operation or radiological examination in 16 patients (6 of them died). An elevated prothrombin time of over 12.5 s was found in 15 patients (including 7 non survivors). Serum bilirubin exceeding 2 mg/dL was found in 15 patients at admission (6 of them died). The presence of any of these parameters was associated with a significant increase in mortality rate (*P* < 0.05). SGOT, alkaline phosphatase and hypoalbuminemia were elevated in many patients, but did not significantly affect their outcome.

Child's classification could predict the outcome of cirrhotic patients undergoing portacaval shunt procedures. In order to identify the predictive value of Child's classification, we retrospectively derived Child's classification criteria from the reviewed charts of cirrhotic trauma patients. The mortality of cirrhotic trauma patients according to the (retrospective) Child's classification is listed in Table 5, showing that 92.2% of our cirrhotic trauma patients corresponded to Child's class A or B. No

Table 4 Presence of HEPATIC insufficiency

Parameters of hepatic insufficiency	Total	Non survivors <i>n</i> (%)
Ascites	16	6 (37.50) ^a
SGOT > 40 μ/L	36	3 (8.33)
Alk phos. > 125 μ/L	32	3 (9.37)
Ser bili. > 2.0 md/dL	15	6 (40) ^a
Ser alb. 6 ≤ 3.0 md/dL	16	6 (37.5) ^a
PT > Control	15	7 (46.67) ^a

^a*P* < 0.05 vs survivors.Table 5 Effect of Child's classification on mortality in cirrhotic trauma patients *n* (%)

Child's classification	No. of patients (% total)	Mortality
Class A	44 (68.75)	5 (11.38)
Class B	15 (23.44)	2 (13.33)
Class C	5 (7.81)	1 (20)
Total	64 (100)	8

significant difference in mortality as a function of Child's classification was found (*P* > 0.05).

The second part of our study focused on comparing the trauma registry data between the cirrhotic trauma and control groups (Table 6). The cirrhotic trauma patients had a statistical ISS score similar to the control trauma patients. The time of ICU and hospital stay, and the mortality rate in the cirrhotic trauma group were greater than those in the control group (*P* < 0.05).

DISCUSSION

Hepatitis B is one of the most common infectious diseases in Asian countries^[9], and about 10% of Chinese people have been infected with hepatitis B virus (HBV)^[10]. It is estimated that about 350 million people worldwide are chronically infected with HBV, approximately 15%-40% of them are expected to develop cirrhosis and end-stage liver disease^[11], which is frequently followed by hepatocellular necrosis. Cirrhosis, regardless of its etiology, inhibits the liver's response to injury. The predominant histological features are wide-spread fibrosis and nodule formation with loss of normal hepatic architecture. These changes are manifested clinically as hepatic failure and portal hypertension, the magnitude of which determines the course and prognosis of individual patients^[12].

Although great progress in traumatology has been made, the number of traumatic casualties still increases^[13]. In China, trauma and intoxication were the 9th, 7th and 4th leading cause of deaths in 1975, 1985 and 2000, respectively. More than 100 000 people die of traumatic injury and millions of people are injured each year in China. Furthermore, experts predict that the number of traumatic casualties will double in the 22nd century^[14]. All these suggest that trauma in combination with cirrhosis is a challenge to Chinese doctors.

Adequate hepatic function is necessary in physiological response to surgery or traumatic injury^[15]. The liver plays a vital role in protein synthesis, detoxification, and immune

Table 6 Comparison of outcomes of trauma patients and cirrhotic trauma patients

	Cirrhosis	Control
Age (yr)	51.80 ± 13.01	48.70 ± 15.4
Percentage male	75%	76.11%
AIS	14.25 ± 8.31	13.67 ± 6.56
hospital stay	21.26 ± 5.61	8.21 ± 4.25 ^a
length of ICU stay	11.24 ± 4.21	4.23 ± 1.36 ^a
Mortality rate	12.53%	1.26% ^a

^a*P* < 0.05 vs cirrhotic patients.

responses. In a patient subjected to surgical intervention for traumatic injury, any degree of hepatic insufficiency would diminish the liver's ability to carry out these vital metabolic functions^[16]. Because of impaired cirrhotic reserves, a surgical or trauma cirrhotic patient would be at a great risk of developing complications and death may occur during the recovery period^[17].

The increased risk of cirrhotic patients undergoing surgery has been well documented^[18]. The Child's classification system has been used to define the surgical mortality in cirrhosis patients^[19] and is moderately accurate in predicting mortality and complications of portacaval shunt surgery, but less predictive when it is applied to other types of surgery^[20]. The Child's classification is mainly to classify the risk of cirrhotic patients undergoing portosystemic shunt surgery^[21], showing that the degree of hepatic decompensation correlates with the rate of operative mortality in these patients. Furthermore, if therapeutic measures are taken to improve the clinical status and Child's class of cirrhotic patients before operation, the outcome of portosystemic shunting can be improved.

Child's classification criteria could not be used to classify these patients because nutritional status and response to therapy are unavailable^[22]. Furthermore, changes in mental status at admission cannot be solely attributed to the etiology of cirrhosis^[23]. However, hepatic insufficiency, as determined by the presence of ascites and/or elevated prothrombin time, is correlated with the outcome of these patients undergoing surgical intervention. Multivariate analysis revealed that cirrhotic trauma victims presenting with ascites, hyperbilirubinemia, or elevated prothrombin time exhibit a uniformly lower rate of survival independent of injury characteristics^[24].

The impact of cirrhosis on trauma patients has recently been addressed^[25]. Thirty percent of trauma patients with pre-existing liver disease have an increased risk of death and an increased time of hospital stay^[26]. Tinkoff *et al*^[27] have also tried to define the variables predicting the outcome of survivors and non survivors. The results of these studies suggest that trauma cirrhotic patients behave as cirrhotic patients requiring emergency surgery with similar stress and compensatory responses and that the mortality is directly related to the extent of injury.

In addition, hepatic insufficiency further diminishes survival, regardless of the injury sustained^[28]. In the present study, cirrhosis was associated with a higher mortality, a longer time of ICU and hospital stay of trauma patients.

Factors predicting death are APACHE II, ISS, RTS2,

the number of packed red blood cells transfused and organs injured, which are associated with the severity of injury^[29]. Our study showed that liver insufficiency was positively associated with a poorer outcome. The lower survival and increased complication rates of cirrhotic trauma patients suggest that there is no "margin for error" in managing these patients. Thus, several management suggestions can be proposed for the improvement in cirrhotic patients with abdominal trauma^[30]. It is critical to promptly diagnose and treat injuries in cirrhotic trauma patients. Since bleeding complications are frequent in cirrhotic patients, early and aggressive correction of coagulation parameters and hypothermia is crucial^[31]. Poor nutrition is common in these patients and low albumin is different in survivors and non survivors. Therefore, early appropriate nutritional support should be provided. Solutions rich in branched-chain amino acids and low in aromatic amino acids can reduce hepatic encephalopathy and improve the outcome^[32,33].

In conclusion, cirrhotic patients constitute a small subset of trauma patients admitted to our institution. Cirrhosis has a significantly independent adverse impact on survival of these patients. Treatment of trauma patients with severe pre-existing liver diseases remains a challenge to the surgeon.

COMMENTS

Background

Liver cirrhosis is the tenth leading cause of death. Although cirrhosis-related deaths have decreased, it leads to approximately 30 000 deaths annually, mostly in Asian countries. Trauma is a major public health problem in the world. Trauma in combination with cirrhosis brings about unique challenges and problems in patients. Surgeons in a trauma center treat a variety of patients every day, but treatment of trauma cirrhotic patients remains a challenge.

Research frontiers

Many reports have shown that mortality and morbidity rates are increased in patients with cirrhosis undergoing elective or emergency surgery. Also the degree of hepatic insufficiency is a prime factor for determining the outcome of these patients. Despite the interest in the outcome of surgical cirrhotic patients, few reports are available on their outcome.

Innovations and breakthroughs

The authors reviewed and analyzed the data on trauma patients with pre-existing cirrhosis admitted to a trauma center in East China from 2000 to 2005. This study showed that liver insufficiency was positively associated with a poorer outcome, suggesting that cirrhosis has a significantly independent adverse impact on survival of these patients.

Applications

Several management suggestions are proposed for the improvement in cirrhotic patients with abdominal trauma. It is critical to promptly diagnose and treat injuries for cirrhotic trauma patient. Since bleeding complications are frequent in cirrhotic patients, early and aggressive correction of coagulation parameters and hypothermia is crucial. Early appropriate nutritional support should be provided.

Terminology

Hepatic cirrhosis: a kind of pathological changes in liver. Hepatic cirrhosis is frequently followed by hepatocellular necrosis. Cirrhosis, regardless of its etiology, inhibits the liver's response to injury. The predominant histological features are wide-spread fibrosis and nodule formation with loss of normal hepatic architecture. These changes are manifested clinically as hepatic failure and portal hypertension, the magnitude of which determines the course and prognosis of individual patients.

Peer review

This is an interesting manuscript, showing that cirrhosis is associated with a higher mortality, a longer time of ICU and hospital stay in trauma patients. Treatment of trauma patients with severe pre-existing liver disease remains a challenge to the surgeon.

REFERENCES

- 1 Yao XX, Jiang SL, Yao DM. Current research of hepatic cirrhosis in China. *World J Gastroenterol* 2005; **11**: 617-622
- 2 Xiao Z, Yan H, Wang Z, Zou Z, Xu Y, Chen J, Zhang H, Ross CA, Keyes BB. Trauma and dissociation in China. *Am J Psychiatry* 2006; **163**: 1388-1391
- 3 Di Bisceglie AM, Loyet M, Peters M. Long term follow up of bone mineral density in patients with primary biliary cirrhosis. *Minerva Med* 2004; **95**: 529-534
- 4 Tam MM. Occult pneumothorax in trauma patients: should this be sought in the focused assessment with sonography for trauma examination? *Emerg Med Australas* 2005; **17**: 488-493
- 5 Lu W, Wai CT. Surgery in patients with advanced liver cirrhosis: a Pandora's box. *Singapore Med J* 2006; **47**: 152-155
- 6 Cohen SM, Te HS, Levitsky J. Operative risk of total hip and knee arthroplasty in cirrhotic patients. *J Arthroplasty* 2005; **20**: 460-466
- 7 Sandor L, Kiss L. Isolated injury of the gallbladder. A rare cause of hemorrhagic shock after blunt abdominal trauma in a patient with liver cirrhosis. *Chirurg* 2006; **77**: 730-736
- 8 Demetriades D, Constantinou C, Salim A, Velmahos G, Rhee P, Chan L. Liver cirrhosis in patients undergoing laparotomy for trauma: effect on outcomes. *J Am Coll Surg* 2004; **199**: 538-542
- 9 Zhang FK, Zhang JY, Jia JD. Treatment of patients with alcoholic liver disease. *Hepatobiliary Pancreat Dis Int* 2005; **4**: 12-17
- 10 Wang ZX, Fu ZR, Ding GS, Zhang JJ, Fu H, Zhang M, Zhang CY. Prevention of hepatitis B virus reinfection after orthotopic liver transplantation. *Transplant Proc* 2004; **36**: 2315-2317
- 11 Zheng SS. Promoting improvement of liver transplantation in China. *Zhonghua Ganzhangbing Zazhi* 2004; **12**: 321-322
- 12 Fan WM, Zhu WF, Zhang SY, Wang QX, Yin LM, Wan H, Gao Y, Tian XL, Yu M, Jin J, Xu XY, Wei L, Zhuang H. Nine-year follow-up of hepatitis C virus infection in a rural area of Hebei province, China. *Zhonghua Yixue Zazhi* 2004; **84**: 392-396
- 13 Xiao Z, Yan H, Wang Z, Zhou Z, Xu Y, Cheng J, Zhang H, Ross CA, Keyes BB. Dissociative experiences in China. *J Trauma Dissociation* 2006; **7**: 23-38
- 14 Zhou JH, Zhao XC, Jiang ZQ, Zhu SY, Zhou JC. Investigation on road traffic safety of the mountain areas in southwest China based on Wulong County, Chongqing Municipality. *Traffic Inj Prev* 2005; **6**: 193-196
- 15 Lin VY, Chee GH, David EA, Chen JM. Medial canal fibrosis: surgical technique, results, and a proposed grading system. *Otol Neurotol* 2005; **26**: 825-829
- 16 Lai CC, Ding LW, Hsueh PR. Wound infection and septic shock due to *Aeromonas* trota in a patient with liver cirrhosis. *Clin Infect Dis* 2007; **44**: 1523-1524
- 17 Ferri-de-Barros JE, Winter DH, César KG, Gavinier LC, Alencar MJ, Faria MC. Alcohol drinking-related disorders in 1901 patients treated at Taubaté's Municipal Emergency room in 2000: a contribution to sociocentric education in neurology. *Arq Neuropsiquiatr* 2004; **62**: 307-312
- 18 Krishna PD, Malone JP. Isolated adult supraglottic stenosis: surgical treatment and possible etiologies. *Am J Otolaryngol* 2006; **27**: 355-357
- 19 Ludwig D, Borsa JJ, Maier RV. Transjugular intrahepatic portosystemic shunt for trauma? *J Trauma* 2000; **48**: 954-956
- 20 Tanaka S, Tanaka H, Kubo S, Shuto T, Takemura S, Yamamoto T, Uenishi T, Hai S, Osugi H, Hirohashi K. Bowel injury associated with liver surgery for hepatocellular carcinoma. *Hepatogastroenterology* 2006; **53**: 571-575
- 21 K C S, Matsutani S, Maruyama H, Fukamachi T, Nomoto H, Akiike T, Ebara M, Saisho H. Portal-systemic encephalopathy

- in two patients without liver cirrhosis and portal hypertension. *Hepatol Res* 2002; **23**: 122-129
- 22 **Mattox TW**, Teasley-Strausburg KM. Overview of biochemical markers used for nutrition support. *DICP* 1991; **25**: 265-271
- 23 **Sharp GB**, Mizuno T, Fukuhara T, Tokuoka S. Lack of association between acute exposure to ionizing radiation and liver cirrhosis. *Int J Radiat Biol* 2006; **82**: 231-240
- 24 **Mayberry JC**, Welker KJ, Goldman RK, Mullins RJ. Mechanism of acute ascites formation after trauma resuscitation. *Arch Surg* 2003; **138**: 773-776
- 25 **Dangleben DA**, Jazaeri O, Wasser T, Cipolle M, Pasquale M. Impact of cirrhosis on outcomes in trauma. *J Am Coll Surg* 2006; **203**: 908-913
- 26 **Velanovich V**. Blunt splenic injury in adults: a decision analysis comparing options for treatment. *Eur J Surg* 1995; **161**: 463-470
- 27 **Tinkoff G**, Rhodes M, Diamond D, Lucke J. Cirrhosis in the trauma victim. Effect on mortality rates. *Ann Surg* 1990; **211**: 172-177
- 28 **Cheadle WG**, Mercer-Jones M, Heinzelmann M, Polk HC. Sepsis and septic complications in the surgical patient: who is at risk? *Shock* 1996; **6** Suppl 1: S6-S9
- 29 **Gerke P**, Hapke U, Rumpf HJ, John U. Alcohol-related diseases in general hospital patients. *Alcohol Alcohol* 1997; **32**: 179-184
- 30 **Kosaka A**, Hayakawa H, Kusagawa M, Takahashi H, Okamura K, Mizumoto R, Katsuta K. Successful surgical treatment for implanted intraperitoneal metastases of ruptured small hepatocellular carcinoma: report of a case. *Surg Today* 1999; **29**: 453-457
- 31 **Nishiwaki M**, Ashida H, Nishimura T, Kimura M, Yagyu R, Nishioka A, Utsunomiya J, Yamamura T. Posttraumatic intra-gallbladder hemorrhage in a patient with liver cirrhosis. *J Gastroenterol* 1999; **34**: 282-285
- 32 **Morris JA**, MacKenzie EJ, Edelstein SL. The effect of preexisting conditions on mortality in trauma patients. *JAMA* 1990; **263**: 1942-1946
- 33 **Chiarla C**, Giovannini I, Boldrini G, Castagneto M. The branched-chain amino acids. *Minerva Gastroenterol Dietol* 1997; **43**: 189-196

S- Editor Liu Y L- Editor Wang XL E- Editor Liu Y