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Effect of Damage Control Surgery on Heat Shock Protein in Patients with Severe Traumatic Liver Rupture

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Abstract

Introduction: To investigate the effect of Damage Control Surgery (DCS) on the clinical outcomes and Heat Shock Protein (HSP) expression of patients with severe traumatic liver rupture.

Materials and Methods: A randomized control study was conducted on 43 patients with severe traumatic liver rupture enrolled into our institute from January 2020 to June 2021. Twenty-five patients were assigned to Damage Control Surgery (DSC) group and 18 patients were assigned Early Comprehensive Treatment (ETC) group according to sample size calculation. The differences in clinical characteristics including intraoperative bleeding, operative duration, and length of hospitalization, postoperative complications, morbidity and mortality rates, and HSP expression were compared.

Results: Among 25 patients, there is 1 death (4%) and 24 successful resuscitation cases in the DSC group. The rate of resuscitation in DSC group was significantly higher than that of the ETC group (P<0.05). Intraoperative bleeding and operative time in the DCS group were (972.3 ± 87.6) mL and (105.4 ± 24.7) min, respectively, which were significantly lower than those in the ETC group (P<0.05 for both). The levels of Lactate (Lac), PT, APTT and TT were significantly decreased in both groups after surgery (P<0.05) compared to before, and the differences were statistically significant in the DCS group compared with the ETC group in these indexes (P<0.05). Compared with the preoperative period, HSP60, HSP70 and HSP90 were significantly lower in both groups, and the DCS group was significantly lower than the ETC group in these three postoperative indexes (P<0.05). In terms of postoperative biliary fistula, liver abscess and re-bleeding, the DCS group had significantly less incidences than the ETC group (P<0.05).

Conclusion: DCS is more effective in improving coagulation and Lac accumulation in patients with severe traumatic liver rupture, leading to a decrease in intraoperative bleeding and a reduction in perioperative complications, thus leading to a significant increase in the success rate of salvage. Meanwhile, HSP60, HSP70 and HSP90 expressions were significantly lower in DCS patients.

Keywords: Damage control surgery; Traumatic liver rupture; Heat shock protein

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Introduction

Severe trauma cases have been increasing over the past decade. Trauma is now the 5th cause of death in China, and the first cause of death among young adults [1]. Among all trauma cases, traumatic liver rupture is the most common. Heat Shock Proteins (HSP) are highly conserved proteins that are produced in response to environmental stimuli [2]. In 1962, Ritossa was the first to identify this protein when observing *Drosophila* larvae and found that it was associated with some key cellular physiological activities including translocation, assembly and folding of proteins [3]. Due to HSP is a class of non-specific cytoprotective proteins that enhances stress tolerance and cell survival, it is also strongly associated with many diseases' development [4]. Therefore, the changes in HSP expression in patients with severe traumatic liver rupture are of significant clinical value. With recent development in pathophysiology in severe trauma the Damage Control Surgery (DCS) has been getting more attention in the management of patients with severe multiple trauma [5]. Nowadays, DCS is one of the major breakthroughs in the whole development of trauma surgery and is considered as the main therapy in the management of patients with severe injuries [6]. This study compares the differences in serum HSP expression and clinical outcomes between DCS and Early

Comprehensive Treatment (ETC) in severe traumatic liver rupture patients.

Materials and Methods

Subjects

From January 2020 to June 2021, 43 patients with severe traumatic liver rupture were enrolled. Inclusion criteria: Patients with severe traumatic liver rupture, with definite abdominal injury experience; definite liver rupture on CT; all graded ≥ grade III; age ranges from 18 to 80; ISS score >25, all with severe abdominal organ damage such as severe liver rupture, high abdominal tension, large vessel damage, hemorrhage, coagulation abnormalities, fatal triad, etc. informed and consenting family members [7]. Exclusion criteria: lack of complete basic information or imaging information; loss to follow-up, psychiatric or neurological experience, tumor, severe organ (heart, liver, kidney) failure, etc., trauma to other organs or fracture of upper and lower extremities, etc., diseases that affect the assessment and recovery of upper and lower extremity function; failure to sign the informed consent form. The study was approved by the hospital ethics committee, and the patient's family gave informed consent (ethics number: [2020] 031-1). Based on the patient's wishes and intervention protocol, a case-control study was used to classify 25 of the observed subjects into the DCS group and the remaining 18 into the ETC group. Details of the patient data in both groups are shown in Outcome 2.1, and there was no statistical difference in the general data of the patients in both groups (all P>0.05).

Surgical method

The ETC group underwent ETC therapy, with routine intravenous fluid interventions upon patient admission, surgery during anticonvulsant period, full surgery in one stage, anatomically based repair of the trauma, and postoperative transfer to the Intensive Care Unit (ICU) for monitoring and resuscitation interventions.

In the DCS group, patients were treated with DCS therapy based on the following principles: Effective and timely hemostasis, adequate debridement, rapid hemostasis, comprehensive debridement, prevention of bile leakage, effective protection of healthy liver tissue, and reasonable and timely management of trauma. First, initial cleaning of the ruptured liver should be performed; hemostasis should be done by local decubitus suture ligation and tamponade. The hemorrhage is stopped by local mattress suture ligation, and dry gauze is stuffed and the number and location of the stuffed gauze are recorded. For patients with bile duct damage, three sets of triple-lumen drains should be placed in the low operating area; for patients with damage to the main vessels attached to the liver, repair treatment should be performed; then the patient should be transferred to the ICU for monitoring and resuscitation, involving effective correction of hypothermia and acidosis, effective improvement of coagulation dysfunction, effective restoration of the patient's circulation and respiratory function, and effective prevention of sepsis. The patient should be monitored and resuscitated. In addition, the patient's airway should be adequately ventilated, and if necessary, an advanced airway should be constructed, with oral (or nasal) tracheal intubation and tracheotomy interventions, and Mechanical Ventilation (MV) with the aid of a ventilator. After the operation, the patient is closely monitored for 3 days. The treatment effect is observed to avoid shock due to hypoglycemia, and active intervention is given as soon as possible for combined injuries. After 3 days, when the patient's basic physiological functions have recovered and no other emergencies were observed, definitive surgical interventions were performed.

Measurement on HSP expression level

Each specimen was collected immediately after admission and 7 days after surgery from patient on an empty stomach. Three ml of blood was collected for the HSP70, HSP60 and HSP90 measurement on a fully automated biochemical analyzer (model AU5800, purchased from Beckman, USA). The measurement procedures were in accordance with ISO 15189 laboratory quality management regulations.

Clinical and laboratory statistics

The Lactate (Lac) clearance time, hospital days, body temperature, blood transfusion volume, and prothrombin recovery time were observed and recorded in the 2 groups. Postoperative complications (including wound infection, pulmonary infection and abdominal abscess) and morbidity and mortality of the subjects in both groups were also counted.

Statistical analysis

For quantitative data, Kolmogorov-Smirnov (K-S) test was conducted for normality; and if normally distributed, it was presented by "mean ± standard deviation", Chi-square test was applied for baseline comparison, if the variance was not equal, and the rank sum test would be implemented if the variance was not equal. For frequency, the value would be presented number and proportion, Fisher's exact test would be used if the theoretical frequency was <1; if it was <5, the corrected χ^2 test was chosen; if it was ≥ 5, the χ^2 test was implemented. The condition for significant differences was P<0.05. SPSS 19.0 was used for statistical analysis in this study.

Results

Comparison of baseline

In the DCS group, there were 4 females and 21 males, with a mean age of 37.9 ± 5.4 (range: 15-71); ISS scores in the group have a mean value of 51.4 ± 6.5 (range: 25-75). For cause of trauma, there were 20 road traffic injuries, two falling injuries, one stabbing injury, one collapse crush injury and 1 machine crush injury; in terms of abdominal trauma types, there were 17 and 8 closed and open injuries, respectively; in the ETC group, there were 3 and 15 females and males; the patients have a mean age of 38.5 ± 5.9 (range: 15-72); ISS scores in the group have a mean value of 52.4 ± 7.3 (range: 25-75). For terms of injury-causing factors, there were 13 road traffic injuries, two collapse crush injuries, two machine crush injuries, and 1 falling injury; In terms of the types of abdominal trauma, there were 12 and 6 closed and open injuries. The baseline data of whether there are other organ injuries were combined, the time from trauma to surgery, whether oral anticoagulant drugs were taken outside the hospital, and the underlying diseases were compared in Table 1. Comparing the general data of patients in the two groups, there was no obvious difference, and the difference was not statistically significant (P>0.05).

Comparison of success rate of resuscitation and perioperative conditions

The incidence of deaths and successful resuscitation in the DCS group were 1 and 24, respectively, achieving a resuscitation success rate of 96.0% (24/25); the incidence of deaths and successful resuscitation in the ETC group were 6 and 12, respectively, showing a success rate of resuscitation of 66.7% (12/18); he DCS group had significantly higher success rate of resuscitation than the ETC group (P<0.05, Table 2). The intraoperative bleeding and operative duration were

Table 1: Comparison of general information between ETC group and DCS group.

	ETC group (n=18)	DCS group (n=25)	T/cardinality	P
Gender			0.003	0.953
Male	15	21		
Female	3	4		
Age (years)	38.5 ± 5.9	37.9 ± 5.4	0.346	0.731
ISS Score	52.4 ± 7.3	51.4 ± 6.5	0.473	0.639
Oral anticoagulants	4/14	4/21	0.267	0.605
Underlying disease (yes/no)	4/14	4/21	0.267	0.605
Complicated other organ damage (yes/no)	5/13	7/18	0	0.987

Table 2: Comparison of resuscitation success rate and perioperative conditions.

	ETC group (n=18)	DCS group (n=25)	T	P
Rescued successfully			-	0.015
Yes	12	24		
No	6	1		
Surgery time (min)	214.2 ± 36.5	105.4 ± 24.7	11.67	0.001
Intraoperative bleeding volume (mL)	1427.7 ± 135.7	972.3 ± 87.6	13.38	0.001
Length of hospitalization(d)	26.1 ±7.1	25.7 ± 7.8	0.172	0.864
Gauze stuffing (with/without)	0/18	7/18	-	0.03

Table 3: Comparison of coagulation and lactate indicators.

	PT		TT		APTT		Lactic acid (mmol/L)	
	Immediate admission	7d after surgery	Immediate admission	7d after surgery	Immediate admission	7d after surgery	Immediate admission	7d after surgery
ETC group (n=18)	36.54 ± 9.49	25.34 ± 6.76	29.88 ± 5.26	14.78 ± 4.13	53.57 ± 9.98	38.97 ± 7.82	3.56 ± 0.77	1.99 ± 0.37
DCS group (n=25)	34.33 ± 8.96	19.98 ± 7.43	27.23 ± 5.96	8.15 ± 2.64	53.28 ± 8.73	31.40 ± 8.51	3.67 ± 0.89	1.45 ± 0.54
t	0.778	2.422	1.509	6.423	0.101	2.975	0.423	3.663
P	0.441	0.02	0. 139	0.001	0.919	0.005	0.675	0.001

Table 4: Comparison of serum HSP.

	HSP60 (ng/ml)		HSP70 (ng/ml)		HSP90 (ng/ml)	
	Immediate admission	7d after surgery	Immediate admission	7d after surgery	Immediate admission	7d after surgery
ETC group (n=18)	0.464 ± 0.129	0.171 ± 0.068	0.697 ± 0.120	0.356 ± 0.132	0.616 ± 0.133	0.208 ± 0.054
DCS group (n=25)	0.453 ± 0.115	0.115 ± 0.047	0.652 ± 0.102	0.218 ± 0.079	0.653 ± 0.117	0.146 ± 0.055
t	0.294	3.197	1.326	4.28	0.966	3.674
P	0.77	0.003	0.192	0.001	0.34	0.001

Table 5: Comparison of complications.

Group Number of cases	Re-bleeding	Liver abscess	Biliary fistula	Mental disorders	Lung infection	Urinary tract infection	Ventilator pneumonia	Thrombotic complications	Liver insufficiency	Hyperbilirubinemia
DCS group (n=25)	0	1	0	1	3	2	1	2	1	2
ETC group (n=18)	4	6	6	5	4	6	6	3	1	2
P-value	0.025	0.015	0.003	0.067	0.427	0.052	0.015	0.999	0.999	0.999

972.3 ± 87.6 mL and 105.4 ± 24.7 min in the DCS group and 1427.7 ± 135.7 mL and 214.2 ± 36.5 min in the ETC group, respectively. Both were significantly lower in the DCS group when compared to the ETC group (P<0.05, Table 2). The length of postoperative hospitalization was 25.7 ± 7.8 days and 26.1 ± 7.1 days in the DCS and ETC groups, respectively, with no statistical difference. In the cases where gauze tamponade was used, it was significantly less in the DCS group when compared to the ETC group (P=0.03, Table 2).

Comparison of coagulation and lactate indexes

Before operation, there was no significant difference between the two groups in terms of LA, PT, TT and APTT (both P>0.05), After operation, these four indexes in the two groups were significantly lower than those before operation, and the DCS group was significantly lower than the ETC group. (P<0.05, Table 3).

Comparison of serum HSP

The difference between HSP60, HSP70 and HSP90 in the first serum of patients with different prognosis was found that there was no significant difference between the two groups in these three indicators before surgery (all P>0.05, Table 4). Both groups showed a significant decrease in these expression level of these three indicators after surgery. In the postoperative period, these three indicators were significantly lower in the DCS group than in the ETC group (P<0.05, Table 4).

Comparison of complications

The incidences of postoperative biliary fistulas, liver abscesses and re-bleeding was significantly lower in the DCS group than those in the ETC group (P<0.05, Table 5), and the incidences of urinary tract infections, pulmonary infections and mental disorders were lower in the DCS group than in the ETC group, but no significant difference was found (P>0.05, Table 5).

Discussion

Damage Control Surgery (DCS) is a new approach that has emerged in the last two decades and is of great practical value. The prototype of this theory, "damage control surgery", was the hemostasis of liver injury in the late 19^{th} century, first established by Rotondo [8]. It took only 20 years from the establishment of the theory to current clinical application of DCS, which had evolved rapidly to cover the treatment of non-trauma, trauma, and combat injuries [9].

The foundation of DCS is to control bleeding in a timely manner, prevent infection and take the survival of the patients as the goal and postoperative Quality of Life (QOL) as the prerequisite [10]. This indicator consists of 3 stages: (1) early surgery, with the simplest route to control infection and bleeding and rapid abdominal closure; (2) ICU resuscitation, including correction of acidosis, coagulopathy, hypothermia, and respiratory support; and (3) definitive surgery when the patient has certain conditions. Nowadays, the decision to perform DCS needs to be made within 15 min after the start of surgery. Asensio et al. [11] described the applicable conditions for DCS: Temperature below 34ºC, serum pH below 7.2, bicarbonate below 15 mM, transfusion volume above 4 L, fluid volume of 12 L, and proven intraoperative coagulation disorders. Compared to the previous condition, intraoperative transfusion volume, recovery time, presence of hypothermia, postoperative infections, and gastrointestinal complications are substantially reduced. Concomitant injury to other parts and organs should also be taken into account in those patients with severe trauma.

In abdominal surgery, traumatic liver rupture is the most widespread lethal factor. Traumatic liver injury, whether blunt or sharp, is usually critical due to the large amount of blood loss. Therefore, not only anti-shock intervention but also timely surgical hemostasis is required, which is heavily related to the success rate of resuscitation [12]. The clinical manifestations of traumatic liver rupture include: (1) There are 3 types of rupture: Central rupture, sub-peritoneal rupture, and true rupture. The first 2 types of rupture have less bleeding because the peritoneum is not damaged, and the signs of internal bleeding are not obvious in the clinic. There is a possibility that category 2 will be transformed into category 3, and there is a higher chance that central liver rupture will be transformed into secondary liver abscess. (2) After liver rupture, bile may be transferred to the abdominal cavity, so there are more obvious manifestations of abdominal pain and peritoneal irritation signs. (3) After liver rupture, blood may be transferred to the duodenum *via* the bile duct, resulting in vomiting of blood and black feces. Both hepatic firearm injuries and non-firearm injuries with cavity organ involvement require surgical intervention [13]. In patients with severe liver rupture, damage control surgery can effectively control the impact of the surgery on the internal environment, thereby improving the success rate and preventing a second strike to the patient. In traumatic liver rupture surgery, the patient's metabolic and physiological functions are restored through phase I surgery to strengthen the patient's resistance before proceeding to phase II surgery to restore liver tissue to health [14]. In this study, DCS was found to significantly improve coagulation and Lac in patients with severe traumatic liver rupture, resulting in decreased intraoperative bleeding, reduced operative time, and significantly reduced postoperative complications.

HSP has a regulatory role in intracellular protein synthesis, degradation and folding. It has been demonstrated that HSP overexpression may inhibit the production of protein aggregation in transgenic mouse models, thereby enhancing the antioxidant capacity of enzymes and reducing Oxidative Stress (OS) levels [15]. HSP70 overexpression was found to be neuroprotective in neurological diseases [16]. In clinical trials, HSP70 overexpression was found in the cerebrospinal fluid and serum of patients with severe TBI, and increased to a maximum at 3 days post-injury [17]. However, the prognostic value of HSP70 in patients with severe traumatic liver rupture is not yet clear. In this study, we found that HSP70 was over expressed in patients with severe traumatic liver rupture and decreased substantially after surgery. In addition, DCS had a significant down-regulation effect on HSP70 expression. HSP60 is a mitochondrial protein with a critical homeostatic function. It may be an indicator for mitochondrial stress as demonstrated by a model of cerebral ischemia [18]. HSP90, a member of the protein chaperone family, is highly sensitive [19]. Its overexpression has been shown to be effective in protecting against secondary damage and to reduce brain edema, oxygen radicals and inflammation in a model of cerebral ischemia [20]. In this study, both HSP60 and HSP90 were found to be highly expressed in patients with severe traumatic liver rupture, and both were significantly decreased after surgery. Thus, both HSP60 and HSP90 can be used to assess the condition of patients with severe traumatic liver rupture. In addition, the decrease of HSP60 and HSP90 expression was more significant in DCS patients, which may indicate that HSP60 and HSP90 have a unique predictive value for the surgical outcome of patients with severe traumatic liver rupture.

Conclusion

In this study, we found that DCS significantly improved coagulation and Lac accumulation in patients with severe traumatic liver rupture, reduced intraoperative bleeding, and reduced perioperative complications, which led to a significant increase in resuscitation success. In addition, patients treated with DCS showed lower expression of HSP60, HSP70 and HSP90, which could help to clarify the role of HSP in the management of patients with severe traumatic liver rupture.

References

1. Yu S G, Tian J, Wu T. Effect of damage control surgery on survival and related stress indicators in patients with traumatic liver rupture. J Pract Liver Dis. 2021;24(6):4.
2. Niu L, Xu RL. Effect of heat shock protein 70 on LPS-induced acute liver injury. J Shanxi Med University. 2011;42(3):199-201.
3. Liu S-T, Li S-Q, Ren J-T. Expression and significance of HSP70, IL-6 and TNF-α in CCl4-induced acute liver injury in mice. Shandong Med.

2011;51(35):17-9.

4. Peitu R, Xinxian R, Baochun L. Diagnosis and treatment of 41 cases of traumatic liver rupture. Chin J Hepatobiliary Surg. 2009(2):3.
5. Dai RW, Tian Fuzhou, Tang LJ. Damage control surgery for severe liver trauma (with retrospective analysis of 32 cases). Chin J Pract Surg. 2007;27(5):389-91.
6. Pei-Long S, Hong-Sheng W, Jing-Bo H. Damage control surgery. Chin J Modern Surg. 2009(1):4.
7. Wang YB. Damage control surgery as a strategy for the treatment of severe trauma. Chin J Trauma. 2005;21(1):4.
8. Dai RW, Fuzhou T, Tang LJ. Damage control surgery for severe liver trauma (with retrospective analysis of 32 cases). Chin J Pract Surg. 2007;027(005):389-91.
9. Peitu R, Xinxian R, Baochun L. Emergency treatment of severe traumatic liver rupture. Chin J Trauma. 2005;21(8):2.
10. Chen B, Hu YL, Jiang YF. Surgical treatment of severe traumatic liver rupture in 148 cases. Heilongjiang Medicine. 2010.
11. Li DK, Hua LC, Zhang QS. The treatment of severe traumatic liver rupture. Chin Emerg Med. 2009;29(3):2.
12. Li Jun, Zhang Hui, LI Jun. Surgical treatment of traumatic liver rupture. Chin J General Surg. 2010;19(7):3.
13. Fang KX, Liu QF. Management of traumatic liver rupture. Chongqing Medicine. 1981(5).
14. Fernández ED, Lange K, Lange R, Eigler FW. Relevance of two-stage total hepatectomy and liver transplantation in acute liver failure and severe liver-trauma. Transpl Int. 2001;14(3):184-90.
15. Donglin L, Jihong Z, Baohua L. Mechanism of action of glucocorticoids, glucocorticoid receptors and heat shock proteins on early liver injury after severe trauma in rats. Chin J Emerg Med. 2003;12(010):664-6.
16. Lai Y, Stange C, Wisniewski SR, Adelson PD, Janesko-Feldman KL, Brown DS, et al. Mitochondrial heat shock protein 60 is increased in cerebrospinal fluid following pediatric traumatic brain injury. Dev Neurosci. 2006;28(4-5):336-41.
17. Mukherjee S, Sivakumar G, Goodden JR, Tyagi AK, Chumas PD. Prognostic value of leukocytosis in pediatric traumatic brain injury. J Neurosurg Pediatr. 2020;27(3):335-45.
18. Truettner JS, Hu B, Alonso OF, Bramlett HM, Kokame K, Dietrich WD. Subcellular stress response after traumatic brain injury. J Neurotrauma. 2007;24(4):599-12.
19. Kharlamov EA, Lepsveridze E, Meparishvili M, Solomonia RO, Lu B, Miller ER, et al. Alterations of GABA(A) and glutamate receptor subunits and heat shock protein in rat hippocampus following traumatic brain injury and in posttraumatic epilepsy. Epilepsy Res. 2011;95(1-2):20-34.
20. Bavisotto CC, Gammazza AM, Cascio FLo, Mocciaro E, Vitale AM, Vergilio G, et al. Curcumin affects HSP60 folding activity and levels in neuroblastoma cells. Int J Mol Sci. 2020;21(2):661.