Prognostic Factors of Liver Injury in Polytraumatic Patients. Results from 895 Severe Abdominal Trauma Cases

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Abstract

Background and Aims. Prognosis of multiple injured patients is mainly limited by severe haemorrhage. Although mechanisms of altered immune response have been intensively investigated, little is known about the relevance of liver trauma as an independent predictive outcome factor in these patients. **Methods.** 10,469 patients from the DGU Trauma Registry (1993-2005) were retrospectively analyzed. Primary admitted patients with an injury severity score ≥16, without isolated head injury were included. Patients were analyzed according to the injury pattern as liver injury (Abbreviated Injury Scale - AIS abdomen <3 and AIS liver 2-5; n=321), non-liver abdominal trauma (AIS abdomen 2-5 or AIS liver <3; n=574) and control group without abdominal injuries (AIS abdomen or liver <3; n=9,574). **Results.** Severe liver injury was associated with excessive demands for volume resuscitation and induced a significantly increased risk for sepsis and multi-organ failure (MOF) compared to both other groups (sepsis 19.9% vs. 11.0%; MOF 32.7% vs. 16.6%). Furthermore, deleterious outcome was more frequently associated with severe liver trauma (mortality 34.9%) compared to severe abdominal trauma (12.0%). **Conclusion.** Severe liver trauma is an independent predictor for severe haemorrhage with a substantially increased risk of sepsis, MOF and trauma-related death. While conservative treatment of patients with liver trauma but no haemorrhage is effective, patients with hemodynamic instability seem to be from a subgroup where contemporary treatment modalities are not yet sufficient.

Key words

Liver injury – multiple injuries – immunology – sepsis – multi-organ failure – prognosis.

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Introduction

Isolated trauma of the liver is a rare event in blunt injuries of severely injured patients; yet liver injuries probably lead to a clear increase in post-trauma mortality due to the complex functioning of this organ. The immunological changes caused by blunt liver trauma are just as difficult to classify as the specific mortality. As the liver injury increases in severity, other organ systems become involved, so that total mortality results from the cumulation of all damaged organs. However, there are definitive indications leading to speculation that liver involvement superproportionally increases total mortality [1-4]. The mortality rate after liver trauma documented in the literature is widespread and ranges between 7 and 36% [5, 6] This is differentiated between early mortality, mainly due to blood loss, and late mortality. Late mortality is frequently based on secondary complications from intensive medical treatment in connection with immunological failure after a trauma which can cause sepsis/SIRS and multi-organ failure. The actual specific significance of liver injury for the emergency of such complications in this event is to date not yet fully understood.

The liver is crucial to the post-traumatic recovery of a severely injured patient. This is where proteins are formed, which constitute among other things components for coagulation and non-specific defense. It has a decisive effect on inflammatory processes and represents the center of the energy metabolism. Moreover, the Kupffer cells represent the largest macrophage pool in humans. The knowledge that liver damage alone negatively affects both early and late mortality may be an initial approach leading to organ-specific post-traumatic treatment.

In this context, it must be kept clearly in mind that the last two decades have seen a clear paradigm change concerning surgical treatment for liver injuries [7]. With the introduction of computer tomography and the availability of clotting factors, conservative treatment of the liver injury has become the method of choice for hemodynamically stable patients after blunt liver trauma [8]. Different studies have shown that 71-89% of all patients with blunt liver trauma can be successfully conservatively treated. As a result, the

survival rate is 85 to 94% [9]. There is also an agreement that despite all the opportunities for intensive fluid, blood and coagulation substitution, hemodynamically unstable patients must still be operated on [10].

Based on an analysis of the trauma registry data from the German Society of Trauma Surgery (DGU) [Deutsche Gesellschaft für Unfallchirurgie] from 1993 to 2005 (n=24,711), the present study examined whether the participating liver injury in a polytraumatized patient superproportionally increases the incidence of sepsis and multi-organ failure (MOF), and whether survival after polytrauma is definitively decreased when the liver is involved.

Methods

Between 1993 and 2005, a total of 24,771 patients from 113 hospitals were documented prospectively in the Trauma Registry of the German Society of Trauma Surgery (DGU). In this analysis the following eligibility criteria were used:

1. Injury Severity Score (ISS) ≥16;
2. Direct admission from scene to a trauma center;
3. No isolated head injury.

Injury severity score (ISS) and the severity of individual injuries were determined with the 1998 revision of the Abbreviated Injury Scale (AIS). The existence of sepsis was defined based on the criteria of Bone et al. [11]. The definition of organ failure followed the SOFA score (Sequential Organ Failure Assessment) [12]. An individual organ failure was defined by at least 3 SOFA score points; MOF was defined as simultaneous failure of at least two organs.

All those patients with a documented liver injury (AIS abdomen <3 and AIS liver 2-5) were assigned to the "liver trauma" group. Patients with abdominal injuries (AIS abdomen 2-5 or AIS liver <3) were placed in the "abdominal non-liver injury" group. All remaining patients who had an AIS abdomen or liver <3 were placed in the third "non-abdominal trauma" group (control group).

The restriction to cases with ISS ≥16 guaranteed a minimum injury severity of AIS 3 for the primary region in the respective study groups.

In order to assess the risk of death based on the initial severity of injury, a prognosis was made using the Revised Injury Severity Classification (RISC) [13]. In this context, the DGU trauma registry has used until 2003 the TRISS Score, an internationally-spread score system for the prognosis of trauma patients based on the American MTOS study. Some studies on prognostically relevant factors in trauma as well as criticism by other authors concerning TRISS have lead to the development of a new severity code classification system for the prognosis of estimate, using the data of the trauma registry. Using data of more than 2,000 patients and a multivariate statistical method, the RISC was developed and repeatedly validated within the register. The RISC takes into consideration: the age, the anatomical pattern of injuries (New ISS), the head injury, the severe pelvis trauma, clotting factors (PTT), the base excess, three indirect signs of bleeding (hypotension, low Hb-value, transfusion) as well as cardiac arrest. In order to be able to calculate a sensible prognosis in case some single values are missing, backup-variables have been named for all variables used (see annual report of the DGU trauma registry). Comparable analysis have shown that the RISC is significantly superior to the scores (e.g. TRISS) used so far. Since 2003, the RISC is being used as central instrument for the severity code classification as well as the variance analysis for the outcome parameter "survival" [14, 15]. The actual observed mortality is then compared with the estimated prognosis based on admission data. The relation of actual mortality and prognosis is expressed by the standardized mortality ratio (SMR).

Statistics

From 1993 until 2001, data were collected and entered on paper sheets. Since 2002, data collection was done with internet-based data entry software with integrated plausibility checks. The anonymized data were analyzed with the statistical program SPSS (Version 14, Chicago, USA). Incidences are presented with counts and percentages, continuous values with mean and standard deviation (SD). Analysis was mainly restricted to descriptive statistics. Statistical tests were avoided due to the multiple comparisons (several groups and outcome parameters), as well as the high sample size which could lead to irrelevant significances. In selected situations only, data from the group with liver trauma were compared statistically against the remaining groups (Chi^2 test for incidence rates and U-test for continuous values).

Results

The average age was 39.6±19.5 years, and 72.8% were male. The average ISS was 31.9±12.1 points (Table I). Patients with liver trauma were younger (liver 34.9±15.6; abdomen 37.7±18.2 years) and more frequently female (66.0% vs. 73.5%). The number of blunt traumas was only slightly less in the liver group (91.8%) than in the non-liver abdominal trauma group (93.5%). The incidence of a primary liver injury according to the criteria mentioned was rather small, with 3.1% in the total group studied (abdomen 5.5%).

Mortality

Mortality in the liver trauma group was significantly increased (34.9%) compared to patients in the abdominal trauma group (12.0%) and patients with no primary liver or abdominal injury (control group 12.0%) (Table II). Further analysis of these differences between abdominal trauma group and the control group showed that the higher mortality in the control group is explained by the high mortality of the accompanying head injuries. Thus, a subgroup analysis shows that of the 9,574 trauma patients in the control group, 2,160 patients had suffered a relevant head injury (AIS >3). In this subgroup, mortality even reached 32.8%. The investigation of early mortality showed that 27.3% of patients in the liver trauma group died within the first 24 hours, while this rate was only 6.6% in the non-liver

abdominal group.

Blood transfusion

Compared to patients with non-liver abdominal injuries, patients with severe liver trauma clearly had a greater need for blood transfusions (67.0% vs. 48.0%). The high blood loss in the liver group is correlated with the blood pressure pattern in both the preclinical and emergency room (ER) phases. Initial blood pressure was ≤ 90mmHg preclinically in 36.4% of the liver group and 30.0% of the abdomen group. Both groups are clearly above the rate in the control group (22.0%) (Table I). Blood pressure in the liver group could not be raised in any definitive way during initial clinical care (ER phase in contrast to the abdomen group (RR < 90mmHg, liver: 32.2% with delta RR 4.2 mmHG; abdomen: 18.2% with delta RR: 11.2mmHG). In the ER, an initial hemoglobin content of less than 8g/dl was much more frequent in the liver group with 38.1% than in the abdomen group with 16.9% and the control group with 13.9%. Analogous to this, the average amount of transfused erythrocyte concentrate (EC) until admission to the intensive care unit was much higher in the group of patients with liver injury (8.6 units) compared to the abdomen group (4.5 units) and the control group (2.1 units).

Patients who fulfilled the criteria of a massive transfusion (number of transfused EC >10, Table III) were filtered out of the liver and abdomen groups. Given that the average number of ECs and the average ISS in both groups of liver and abdominal trauma were almost the same (liver: 20.9 EC, ISS 39.2; abdomen 19.9 EC, ISS 38.5), the possible measured variable of an unequal EC quantity was leveled out. Thus, the high total mortality in the liver group (55.8%) compared to the abdomen group (36.5%) cannot be explained by the number of ECs. The same applies to the increased MOF (96.0% vs. 60.0%) and sepsis rate (72.0% vs. 36.0%) of the survivors.

Sepsis, Organ failure

Compared to the other groups, increased early mortality in the liver group did not lead to a simultaneous reduction in late mortality. Patients with a liver injury showed - apart from the patients with head injuries – an average late mortality of 7.8%. One cause for the increased late mortality in comparison with patients with no liver injury is possibly the high sepsis rate (19.9%), if the first 24 hours were survived (Table IV). The increased sepsis rate in the liver group is also reflected in the frequency of organ failure (OF 48.6%) and multi-organ failure (MOF 33.3%). Compared to patients

Table I. Demographic and clinical data after acceptance in a trauma centre and exclusion of an insulated head injury

		Liver trauma	Abdominal non-liver injury	Non-abdominal trauma	Total[aW]
Patients	n, %	321 (3.1)	574 (5.5)	9,574 (91.4)	10,469 (100)
Age	mean, SD	34.9±15.6	37.7±18.2	39.9±19.7	39.6±19.5
Male	%	66.0	73.5	73.0	72.8
ISS*	mean, SD	34.9±11.7	31.3±11.4	31.8±12.1	31.9±12.1
Blunt trauma	%	91.8	93.5	97.0	96.0
Blood transfusion	%	66.8	48.1	40.0	41.0
RR < 90mmHg, preclinical	%	36.4	30.0	22.0	23.1
RR < 90mmHg, ER	%	32.3	18.2	16.1	17.1
Hemoglobin < 8mg/dl		38.1	16.9	13.9	15.2
ECs until ICU entry	n	8.6	4.5	2.7	3.2

*ISS: injury severity score. The segmentation of the groups presented was done specifically according to the primary injury region: liver (AIS liver 3-5 and abdomen <3) and abdomen without liver (AIS abdomen 3-5, AIS liver <3).

a - The "non-abdominal trauma" group is marked without insulated head injuries patients (n=2,872).

Table II. Lethality, RISC and standardized mortality rate if RISC-prognosis is available (n=9,424)

		Liver trauma	Abdominal non-liver injury	Non-abdominal trauma	Total
Lethality, <24 hours	n, %	87 (27.3)	38 (6.6)	1,015 (10.6)	1,140 (10.9)
Lethality, >24 hours	n, %	25 (7.8)	31 (5.4)	857 (8.9)	913 (8.7)
Lethality, total	n, %	112 (34.9)	69 (12.0)	1,872 (19.5)b	1,997 (19.6)
RISC-prognosis	%	23.4	11.6	12.8	21.8
SMR*	%	1.41	1.03	0.98	1.0

* Standardized mortality ratio. The relation of predicted mortality to actual lethality is expressed by SM;.

b - Increased lethality caused by patients with head injuries. Total lethality without TBI (traumatic brain injury) patients 16.8%.

with abdominal injuries with no severe liver trauma, all three characteristics are significantly more fully developed (sepsis 11.0%, OF 33.2%, MOF 16.6%). Patients from the control group also showed a significantly decreased incidence for sepsis and multi-organ failure.

Table V shows the mortality of all patients with a relevant liver injury (AIS>2), before and after 2000. The frequency of a laparotomy is reduced from 71.6% (before 2001) to 60.4% (from 2001). Remarkably, mortality is reduced in the same period from 35.5 to 33.1%. The ISS is almost identical with 39.7 vs. 38.8.

Table III. Polytrauma with abdominal trauma w/o severe liver trauma after >10 erythrocyte concentrates (ECs)

		Liver trauma	Abdominal non-liver injury
Patients	n	104	85
ECs	n	20.9	19.9
ISS		39.2	38.5
Lethality	%	55.8	36.5
MOF	%, n	50.0/96c	43.2/60c
Sepsis	%, n	36.0/72c	24.0/36c

2 subgroups were formed from the patients with severe liver injury, and the patients with abdominal injury with no severe liver injury, who received more than 10 ECs.
c - Frequency of MOF and sepsis until patients' death or survival (2. item).

Table IV. Incidence of sepsis, organ failure and multi-organ failure (MOF) of patients who survived 24 hours (n=8,941)

		Liver trauma	abdominal non-liver injury	non-abdominal trauma	Total[d]
Sepsis	%	19.9	11.0	14.6	13.3
Organ failure	%	46.5	33.2	38.6d	40.7
MOF	%	32.7	16.6	21.1	22.3

d - Analyzed data from patients who survived at least 24 hours in hospital. Increased results of insulated organ failure are caused by patients with head injuries and central failures (TBI=34.7%).

Table V. Liver trauma patients who were treated before and after 2000

		1993-2000	2001-2005	Total
Patients (AIS liver >2)	n	338	523	861
Lethality	%	35.5	33.1	34.4
Laparotomy	%	71.6	60.4	64.8
ISS*		39.7	39.8	39.8

*Injury severity score

Severity adjustment

Adjusting for severity with the RISC Score shows that patients with liver trauma die significantly more frequently than expected. The 33.0% mortality observed (95.0% confidence interval 27.6 – 38.4) offsets a prognostic mortality rate of only 23.4%. In the other two groups of injuries, prognosticated mortality hardly deviates at all from the observed mortality. These results could imply that the resuscitation and/or operative management was suboptimal. However, this is not true. Liver trauma is rather underestimated regarding the expected prognostical impact and shows significantly worse mortality rates than in patients without liver injuries. Therefore, severe liver injury should be judged more critically with respect to mortality than the remaining abdominal injuries, with which the RISC prognosis illustrates actual mortality very well.

Discussion

The aim of this retrospective investigation was to evaluate possible differences in the characteristics early and late mortality, sepsis and multi-organ failure as a function of the area of organ injury. Consideration of purely isolated organ injuries would not do justice to the complexity of a polytrauma, and may possibly lead to conclusions of no clinical relevance. The selection criteria "great severity of injury" of a specific organ system, with no attention paid to the average frequency and severity of additional injuries, would inaccurately illustrate the value of the information regarding organ-specific characteristics. It is well-known that liver injuries almost always accompany injuries to other organ systems. To consider only isolated liver injuries would lead to the description of a group that does not occur in this form in reality. The present study illustrates a patient group with a most severely injured organ system and the approach chosen was meant to investigate the impact on an organ system, in view of additional injuries, on the development of early mortality, transfusion requirement, sepsis, organ failure and late mortality.

To date, the effects of an isolated or primary liver injury on immunological function parameters has not been examined in either humans or animals. Only a retrospective evaluation weighted according to the organ system can contribute to a more precise understanding of its significance for the outcome, sepsis and MOF.

The results presented here show a clear increase in the incidence of sepsis from MOF and early and late mortality with a severe liver injury. This increase seems to be liver-specific and stands out from the other organ systems investigated. Publications by Strong and Trunkey, which reported a mortality of over 11% in isolated liver injuries, show a significantly lower mortality after liver trauma. However, these were not assessed in a comparably severely injured collective [16, 17]. This stresses the significantly higher survival rates in patients with isolated liver injuries in comparison to poly-traumatized patients.

A review of the literature shows that the classification of more specific e.g. immunological consequences to different organ systems subsequent to polytrauma, has not yet been examined. This applies both to experimental and clinical investigations and therefore the results presented here seem debatable, since they are only limited, given the low amount of literature in this regard. Despite the small amount of data, it seems beyond question that the participation of the liver in a traumatic event leads to an increase in mortality. However,

there are some indirect references that characterize the liver as being a key organ after a trauma. At the beginning of the 1990s Tinkhoff et al had pointed out for the first time a connection between cirrhosis and outcome after trauma, this hypothesis was confirmed by numerous authors [1]. In a matched pairs study, Dangleben et al proved that cirrhosis of the liver is an independent prognosis marker of mortality, and with this they were able to demonstrate a correlation between mortality and the degree of the cirrhosis (defined according to Child-Pugh) [2]. These results were also verified by Christmas et al: in addition to an increase in mortality and length of hospital stay, they showed a significant increase in the sepsis rate after trauma [3]. Altogether, 55% of the patients with cirrhosis of the liver in their study population died from sepsis. 33% of the patients with cirrhosis died compared to only 1% in the non-cirrhosis control group. These studies on cirrhosis of the liver and polytrauma show a close association between liver function and outcome after trauma.

In animal experiments, depending upon the quantity of the liver tissue removed, a liver resection leads to a clear restriction of synthesis efficiency, particularly for coagulation products [18]. Furthermore, the clearance function for bacterial endotoxins is drastically reduced. The consequences can be expressed in a decompensated coagulation system, through to a Disseminated Intravascular Coagulation in a spontaneous MOF after sepsis or in refractory shock to the extent that the effects of a liver resection resemble those of traumatic liver destruction [19-21].

However, traumatic liver damage is not necessarily associated with a measurable reduction in liver function. This is why, for example, Perdrizet et al. were able to demonstrate a clear increase in early mortality after reperfusion using a pig model, in which a blunt liver trauma was combined with a hemorrhagic shock. The increase in mortality resulted from continuous post-ischemic shock [22].

The significance of the liver in early trauma events was also demonstrated by Perl et al after a thorax trauma in a mouse model. They showed for the first time a response to thorax trauma by Kupffer cells within 30 minutes. In so doing, the liver formed IL-6, TNF-alpha and IL-10 in high concentrations, without the liver itself being traumatized [23].

It has been proven that a tissue trauma leads to a significant reduction in immunological strength. The liver is a central organ of the reticuloendothelial system (RES) and its significance to the defense against infection has been described several times.

The results shown here from the trauma registry indicate that in the group with severe liver trauma, there was a clear increase in the number of ECs in the early and late phases after trauma. This observation after liver trauma is also supported by other research groups. Thus, for example, the number of transfused ECs constitutes an independent prognosis factor in the post-traumatic period after liver trauma. The authors argue that the blood products possibly lead to an increase in the incidence of sepsis due to their antigenicity [24]. Both Moore et al. and Malone et al. showed a clear connection between the number of transfused ECs and the occurrence of post-traumatic organ failure; Melone et al. even showed this correlation within the first 24 hours after trauma [25, 26]. Critical in this respect, however, is that the question should be raised whether and to what extent the administration of erythrocytes causes immunoparalysis, particularly since trauma patients can develop sepsis and MOF without erythrocytes being administered. Hence, it should be discussed whether the correlation between ECs and mortality must possibly be considered as only an epiphenomenon, e.g. an extended tissue ischemia period. So the number of transfused blood products is also always a marker for injury severity, incidence of shock and length of ischemia time. This cannot be obviously separated by a multivariance analysis. In order to examine this question more closely, two subgroups were formed in the present analysis (Table III). Here it shows up remarkably that despite a similar ISS and number of transfused ECs, the patients with severe liver participation continue to predominate, with regard to mortality, sepsis and MOF. In this context, immune modulating substances contribute to a considerable reduction in infectious complications. After polytrauma, proteins such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and interferon gamma can contribute to an improvement in post-traumatic immunoparalysis [27, 28]. Patients with immune insufficiency, e.g. also due to liver damage, could benefit from the early use of immune modulating substances.

The evaluation of the data from the trauma registry concerning liver trauma (AIS>2) and treatment before and after 2000 shows the paradigm shift starting in 2000 mentioned in the introduction. The reduction in the rate of laparotomies after 2000 to 11.2% in hospitals affiliated with the trauma registry proves a rethink in care after abdominal injury. This resulted in a reduction in mortality of 2.4% in similar patients (ISS: 39.7 vs. 39.8). In order to better support this advantage of conservative treatment, however, a more detailed study is necessary given that both preclinical and clinical care have made progress in the same time period. While in former times an exploratory laparotomy was nearly always performed, now conservative therapy under hemodynamically stable conditions is increasingly being recommended [29]. Therefore, the proportion in an American (multicenter) study was 47%. With 404 patients, a success rate of 98.5% was reported, where hemorrhaging appeared in only 3.5% of other complications [30].

In another series of 495 conservatively treated patients, the success rate was 94% and the average hospital treatment was 13 days, where only 1.9 EC/patient had to be given a transfusion. The complication rate was 6.2%, whereby there was only 2.8% with hemorrhages. Liver-related deaths or overlooked intestinal injuries were not observed [31].

Both groups predominantly involved not so serious liver traumas, whereas Moore type IV and V injuries (14%) were rather rare. In a study from Germany up to 2004, only 14% of all patients were treated conservatively. Moreover, the not so

serious Type I-III injuries were operated in 2/3 of the cases (31/44), where no liver-related mortality was observed. The authors came to the conclusion that in view of the convincing data from the multicenter studies mentioned and numerous other, at times large patient groups, laparotomy is probably an overtreatment in most patients with Type I-III injuries and seems to be of no real advantage regarding survival, morbidity and duration of treatment [32]. Data from our study corroborates this statement (Table V).

The matter of the urgent criteria for operating on abdominal and liver trauma is not clearly answered in the literature [33]. The criteria are not uniform and often refer to the term "unstable". It has been shown however by Clarke et al. that mortality increases by 1% every 3 minutes after a trauma involving hematogenic shock, so the time from arrival at the ER to the laparotomy has a crucial effect on the outcome [34].

In our opinion, unstable patients should be identified by the following parameters: 1) location of the source of bleeding, i.e., free fluid in the abdomen in the initial ultrasound, if need be with an increase in the course of action; 2) volume loss, i.e., substitution is required for hemodynamic stability when systolic blood pressure falls below 80 - 90 mmHG; 3) signs of systemic hypoperfusion with negative base excess and pH and where applicable with an initial hemoglobin under 8 g/dl with signs of consumptive coagulopathy.

The additional dangers from a liver injury may possibly be positively affected by e.g. a specific coagulation treatment and an early substitution of ECs. The immunological changes expected from a liver injury in the meantime may possibly even reinforce the frequently described post-trauma immunosuppression.

Conclusion

Severe liver trauma is an independent predictor for severe haemorrhage with a substantially increased risk of sepsis, MOF and trauma-related death. While conservative treatment of patients with liver trauma but no haemorrhage is effective, patients with hemodynamic instability seem to be from a subgroup where contemporary treatment modalities are not yet sufficient.

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Participating hospitals

Universitätsklinik der RWTH **Aachen**, Zentralklinikum **Augsburg**, Kreiskrankenhaus **Bad Hersfeld**, SANA Krankenhaus **Bergen / Rügen,** Charité - Campus Virchow-Klinikum **Berlin**, Martin-Luther-Krankenhaus **Berlin**, Vivantes Klinikum **Berlin Friedrichshain**, Klinikum **Berlin**-Buch, BG-Unfallklinik **Berlin**-Mahrzahn, Krankenanstalten Gilead **Bielefeld**, Südeifel-Kliniken Bitburg, BG-Klinik **Bochum** Bergmannsheil, Knappschaftskrankenhaus der Ruhr-Universität **Bochum**, Friedrich-Wilhelms-Universität **Bonn**, Städt. Klinikum **Braunschweig**, Zentralkrankenhaus Sankt-Jürgen-Straße **Bremen**, Zentralkrankenhaus **Bremen** Ost, Klinikum **Bremerhaven**-Reinkenheide, Landeskrankenhaus Bruck/Mur (Austria), Kreiskrankenhaus Burg, Allgemeines Krankenhaus **Celle**, Klinikum **Chemnitz**, Städt. Klinikum **Dessau**, Klinikum Lippe-Detmold, **Detmold**, Krankenhaus **Dresden**-Neustadt, Technische Universität **Dresden**, Krankenhaus **Dresden**-Friedrichstadt, Heinrich-Heine-Universität **Düsseldorf**, Krankenhaus der Barmherzigen Brüder **Eisenstadt** (Austria), Klinikum **Erfurt**, Kreiskrankenhaus **Eschwege**, Universitätsklinikum **Essen**, Evang. Krankenhaus Lutherhaus **Essen**, BG Unfallklinik **Frankfurt** / Main, Universitätsklinik **Frankfurt** / Main, Klinikum Frankfurt/Oder, Herz-Jesu-Krankenhaus **Fulda**, Klinikum **Fürth**, Johanniter-Krankenhaus **Geesthacht**, Städtisches Klinikum **Görlitz**, Klinik an Eichert **Göppingen**, Georg-August-Universität **Göttingen**, Universität **Graz** (Austria), Allg. Unfallvericherungsanstalt **Graz** (Austria), Kreiskrankenhaus **Grevenbroich**, Universitätsklinik **Groningen** (Netherland), Kreiskrankenhaus **Gummersbach**, BG Klinik Bergmannstrost **Halle/Saale**, BG-Unfallkrankenhaus **Hamburg**, Universitätsklinik **Hamburg-Eppendorf**, Kreiskrankenhaus **Hameln**, Medizinische Hochschule **Hannover**, Krankenhaus **Hannover**-Nordstadt, Friederikenstift **Hannover**, Ev. Krankenhaus **Hattingen**, Orthopäd. Universitätsklinik **Heidelberg**, St. Bernward Krankenhaus **Hildesheim**, Universität des Saarlandes **Homburg** / Saar, Waldviertel Klinikum **Horn** (Austria), LKH **Judenburg**-Knittelfeld (Austria), Städt. Klinikum **Karlsruhe**, Christian-Albrechts-Universität **Kiel**, Bundeswehrkrankenhaus **Koblenz**, Unfallchirurgische Klinik der Universität zu **Köln**, Städt. Klinikum **Köln**-Merheim, Allg. öff. Krankenhaus **Krems**/ Donau (Austria), Städt. Klinikum St. Georg **Leipzig**, Universität **Leipzig**, Ev. Krankenhaus **Lengerich**, Allg. öffentl. Krankenhaus **Linz** (Austria), Ev. Krankenhaus **Lippstadt**, Universitätsklinikum **Lübeck**, BG Unfallklinik **Ludwigshafen**, St.-Marien-Hospital **Lünen**, Krankenhaus Altstadt, Städt. Klinikum **Magdeburg**, Otto-von-Guericke-Universität **Magdeburg**, Johannes-Gutenberg-Universität **Mainz**, Universitätsklinikum **Mannheim**, Universität **Marburg**, Heilig Hart Ziekenhuis Roeselare, Menen (Belgium), Klinikum **Minden**, Krankenhaus Maria Hilf **Mönchengladbach**, Klinikum Großhadern der LMU **München**, Klinikum Innenstadt der LMU **München**, Städt. Krankenhaus München-Bogenhausen, Städt. Krankenhaus **München**-Harlaching, Westfälische Wilhelms-Universität **Münster**, BG-Unfallklinik **Murnau**, Lukaskrankenhaus der Städt. Kliniken **Neuss**, Marienhospital **Osnabrück**, Vogtland Klinikum **Plauen**, Klinikum **Remscheid**, Klinikum **Rosenheim**, St. Johanns-Spital Landeskrankenhaus **Salzburg** (Austria), Diakonissenkrankenhaus **Schwäbisch Hall**, Kreiskrankenhaus **Soltau**, Johanniter-Krankenhaus der Altmark **Stendal**, Klinikum St.

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Conflicts of interest

Nothing to declare.

References

1. Tinkoff G, Rhodes M, Diamond D, Lucke J. Cirrhosis in the trauma victim. Effect on mortality rates. Ann Surg 1990; 211: 172-177.
2. 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.
3. Christmas AB, Wilson AK, Franklin GA, Miller FB, Richardson JD, Rodriguez JL. Cirrhosis and trauma: a deadly duo. Am Surg 2005; 71: 996-1000.
4. Blair SL, Karpoff HM, Hodyl C, Fong Y. Pretreatment with IFN-gamma decreases infectious complications after partial hepatectomy in the rat. J Interferon Cytokine Res 1998; 18: 175-180.
5. Pachter HL, Feliciano DV. Complex hepatic injuries. Surg Clin North Am 1996; 76: 763-782.
6. Verney M, Becker H, Röher HD. Prognose und Therapie der Leberverletzungen beim polytraumatisierten Patienten. Chirurg 1990; 61: 711-716.
7. Malhotra AK, Fabian TC, Croce MA, et al. Blunt hepatic injury: a paradigm shift from operative to nonoperative management in the 1990s. Ann Surg 2000; 231: 804-813.
8. Pachter HL, Hofstetter SR. The current status of nonoperative management of adult blunt hepatic injuries. Am J Surg 1995; 169: 442-454.
9. Matthes G, Stengel D, Seifert J, Rademacher G, Mutze S, Ekkernkamp A. Blunt liver injuries in polytrauma: results from a cohort study with the regular use of whole-body helical computed tomography. World J Surg 2003; 27: 1124-1130.
10. Velmahos GC, Toutouzas K, Radin R, et al. High success with nonoperative management of blunt hepatic trauma: the liver is a sturdy organ. Arch Surg 2003; 138: 475-480.
11. Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. Chest 1992; 101: 1644-1655.
12. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/ failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med 1996; 22: 707-710.
13. Huber-Wagner S, Lefering R, Qvick LM, et al. Effect of whole-body CT during trauma resuscitation on survival: a retrospective, multicentre study. Lancet 2009; 373: 1455-1461.
14. Dutton RP, Lefering R, Lynn M. Database predictors of transfusion and mortality. J Trauma 2006; 60 (6 Suppl): S70-S77.
15. Ruchholtz S, Lefering R, Paffrath T, et al. Reduction in mortality of severely injured patients in Germany. Dtsch Arztebl Int 2008; 105: 225-231.
16. Strong RW, Lynch SV, Wall DR, Liu CL. Anatomic resection for severe liver trauma. Surgery 1998; 123: 251-257.
17. Trunkey DD. Hepatic trauma: contemporary management. Surg Clin North Am 2004; 84: 437-450.
18. Meijer C, Wiezer MJ, Hack CE, et al. Coagulopathy following major liver resection: the effect of rBPI21 and the role of decreased synthesis of regulating proteins by the liver. Shock 2001; 15: 261-271.
19. Schroder J, Gallati H, Kremer B. Increased serum levels of soluble tumor necrosis factor a-receptors in patients undergoing partial liver resection. Hepatogastroenterology 1998; 45: 1807-1812.
20. Vo NM, Chi DS. Effect of hepatectomy on the reticuloendothelial system of septic rats. J Trauma 1988; 28: 852-854.
21. Fukushima H, Ikeuchi J, Tohkin M, Matsubara T, Harada M. Lethal shock in partially hepatectomized rats administered tumor necrosis serum. Circ Shock 1998; 26: 1-14.
22. Perdrizet GA, Giles DL, Dring R, et al. Major hepatic trauma: warm ischemic tolerance of the liver after hemorrhagic shock. J Surg Res 2006; 136: 70-77.
23. Perl M, Gebhard F, Braumuller S, et al. The pulmonary and hepatic immune microenvironment and its contribution to the early systemic inflammation following blunt chest trauma. Crit Care Med 2006; 34: 1152-1159.
24. Robinson WP 3rd, Ahn J, Stiffler A, et al. Blood transfusion is an independent predictor of increased mortality in nonoperatively managed blunt hepatic and splenic injuries. J Trauma 2005; 58: 437-444.
25. Moore FA, Moore EE, Sauaia A. Blood transfusion. An independent risk factor for postinjury multiple organ failure. Arch Surg 1997; 132: 620-624.
26. Malone D, Napolitano LM, Genuit T, Bochicchio GV, Kole K, Scalea TM . Total cytokine immunoassay: a more accurate method of cytokine measurement? J Trauma 2001; 50: 821-825.
27. Lendemans S, Kreuzfelder E, Waydhas C, Schade FU, Flohé S. Differential immunostimulating effect of granulocyte-macrophage colony-stimulating factor (GM-CSF), granulocyte colony-stimulating factor (G-CSF) and interferon gamma (IFNgamma) after severe trauma. Inflamm Res 2007; 56: 38-44.
28. Flohé S, Lendemans S, Selbach C, et al. Effect of granulocyte-macrophage colony-stimulating factor on the immune response of circulating monocytes after severe trauma. Crit Care Med 2003; 31: 2462-2469.
29. Croce MA, Fabian TC, Menke PG, 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: 744–753.
30. Pachter HL, Knudson MM, Esrig B, et al. Status of nonoperative management of blunt hepatic injuries in 1995: a multicenter experience with 404 patients. J Trauma 1996; 40: 31–38.
31. Pachter HL, Feliciano DV. Complex hepatic injuries. Surg Clin North Am 1996; 76: 763–782.
32. Ott R, Schön MR, Seidel S, Schuster E, Josten C, Hauss J. Surgical management, prognostic factors, and outcome in hepatic trauma. Unfallchirurg 2005; 108: 127-134.
33. Kaiser GM, Kühne CA, Paul A, et al. Nonoperative management of gunshot liver trauma in a severely injured patient. Injury Extra 2006; 37: 228-229.
34. Clarke JR, Trooskin SZ, Doshi PJ, Greenwald L, Mode CJ. Time to laparotomy for intra-abdominal bleeding from trauma does affect survival for delays up to 90 minutes. J Trauma 2002; 52: 420-425.