Injury xxx (xxxx) xxx

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Increased S-100 B levels are associated with fractures and soft tissue injury in multiple trauma patients

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ARTICLE INFO

Article history:
Accepted 3 March 2020
Available online xxx

Keywords:
S100 B
Biomarker
Multiple trauma
Fractures
Diagnosis

ABSTRACT

Background: S-100 B protein was identified as a biomarker for traumatic brain injury, but studies suggest that extracranial injuries may also lead to increased S-100 B serum levels. In this study, we aim to quantify the impact of injury patterns on S-100 B levels in patients with suspected multiple trauma.
Methods: Patients with suspected multiple trauma treated at a Level 1 Trauma centre in Switzerland were included in this retrospective patient chart review. Extent of injuries and severity was assessed and S-100 B levels on admission measured. Potential predictors of increased S-100 B levels (>0.2 µg/L) were identified through uni- and multivariable analyses.
Results: In total, 1,338 patients with suspected multiple trauma were included. Multivariable logistic regression showed a significant association with increased S-100 B levels in long bone fracture (OR 2.3, 95% CI: 1.3–4.1, $p=0.004$), non-long bone fracture (OR 3.0, 95% CI: 2.2–4.3, $p<0.001$), thoracic injury (OR 2.6, 95% CI: 1.6–4.2, $p<0.001$), and deep tissue injury/wounds (OR 1.9, 95% CI: 1.4–2.6, $p<0.001$). Head trauma with intracerebral bleeding was only weakly associated (OR 2.0, 95% CI 1.2–3.5, $p=0.01$) and head trauma without intracranial bleeding was not associated with an increased S-100 B protein level ($p=0.71$). Trauma severity was also related to increased S-100 B levels (OR per ISS: 1.1, 95% CI 1.0-1.1, $p<0.001$). S-100 B levels <0.57 µg/L had a high diagnostic value to rule out in-hospital mortality (negative predictive value: 1.0, 95% CI: 0.98–1.00).
Conclusion: Fractures and thoracic injuries appeared as main factors associated with increased S-100 B levels. Head injury may only play a minor role in S-100 B protein elevation in multiple trauma patients. A normal S-100 B has a good negative predictive value for in-hospital mortality. S100-B levels were associated with trauma severity and might thus be of use as a prognostic marker in trauma patients.

Introduction

Trauma is the most common cause of death in adults between 24 and 44 years in the United States of America (USA) with almost every third death in this age group resulting from an accident [1,2]. As a consequence, research over the last decades focused on preclinical and clinical care of severely injured patients. To improve the medical care and outcome of patients with multiple trauma in the emergency department (ED), scoring systems and biomarkers [3], including serum levels of protein S-100 B [4], were investigated.

S-100 B protein was first described in 1965 by Moore in an attempt to identify a protein that would reflect brain tissue damage [5]. In subsequent studies, several authors related pathologically increased serum levels of the isomer S-100 B with minor or major head trauma [4,6] and S-100 B was consecutively studied as a prognostic biomarker in patients with traumatic brain injury [7–10]. Several studies further investigated whether S-100 B would support decision-making with regard to whether a cerebral computer tomography would be needed in patients with head injury [11]. Further, it was shown that increased levels of S-100 B protein predict unfavourable clinical outcomes in patients with head

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https://doi.org/10.1016/j.injury.2020.03.012

trauma [10]. As a consequence, measurement of S-100 B protein is recommended in current traumatic brain injury guidelines and is thus used in the clinical emergency routine for head trauma patients [12,13].

However, more recent studies showed that increased serum levels of S-100 B are also observed in patients with large extracranial trauma [14–17], especially in patients with fractures [18,19]. Hence, the exact role and diagnostic value of S-100 B protein values in trauma patients and the association of injury pattern with increased S-100 B level remain unknown.

In this study, we therefore aimed to quantify the impact of injury pattern on S-100 B level in trauma patients and investigated the role of S-100 B level in the light of injury severity and clinical outcome.

Methods

Study site

The ED of Bern University Hospital, Bern, Switzerland (Inselspital) is a level 1 trauma centre and one of the largest EDs in Switzerland. More than 45'0000 patients are treated every year at our ED.

Study design & eligibility criteria

This is a retrospective patient data chart review. Adult patients (>16 years) admitted to the ED with suspected multiple trauma in the more than three-year study period (01-2008 to 02-2011) were eligible for inclusion.

Exclusion criteria were as follows: patients with neurological diseases that lead to increased S-100 B levels, patients with documented neoplasia and patients without retrievable imaging studies. Further, we excluded patients transferred from other hospitals (ED not initial treatment) as well as patients with insufficient data available. This could be caused by i) an insufficient documentation of injuries (defined as missing/incomplete diagnosis list) or ii) missing S-100 B levels. See Fig. 1 for a study flow chart.

S-100 B quantification

S-100 B levels were routinely measured from EDTA samples over the study period. All measurements were performed in a central, certified laboratory (Centre for Laboratory Medicine, Inselspital, Bern, Switzerland)

EDTA samples underwent centrifugation at 1000 g for ten minutes, after which the plasma was collected for further analysis. All samples stored at minus seventy degrees Celsius. A Roche Modular E179 electrochemiluminescence immunoassay (S-100 A1B and S-100 BB) was used for quantitative analysis.

Data collection & extraction

This is a secondary analysis of an already published cohort [7]. The first publication evaluated the impact of S-100 B protein on in-hospital mortality [7].

Patients were identified through key-word search of patient charts in order to identify patients with suspected multiple trauma in our patient database (Qualicare Office, Medical Database Software, Qualidoc AG, Bern, Switzerland). Medical reports were extracted in full-text, and the following variables were coded: age, sex, aetiology of trauma, type of injury (signs of internal abdominal, thoracic, intracranial and traumatic brain injury, as well as luxation, deep tissue injury/ flesh wound and contusion), type of fracture (see below) and in-hospital mortality. All injuries were coded manually based on the AIS handbook 2008 [20]. ICD-10 codes were not used. Trauma severity was assessed through the abbreviated injury scale (AIS) including the eight different regions (head/neck, face, spine, thorax, abdomen/pelvic contents, upper extremity, lower extremity, external) on a scale from 1 (minor) to 6 (maximal) [21]. The three highest AIS scores are squared and summed to produce an overall trauma severity score, the injury severity score (ISS) [22].

Definitions

Increased S-100 B level

A S-100 B level of above 0.2 µg/L was defined as increased, as in line with previous publications [23]. In other studies, cut-off values between 0.1-0.2 µg/L were used [24].

Multiple trauma

The diagnosis "multiple trauma" was assigned if the ISS was ≥16 points [25]. A suspected multiple trauma was assigned if the patient was initially treated in the resuscitation bay.

Aggregation of fractures

Fractures were aggregated into two groups with the following fractures aggregated in the variable "long bone fracture": humerus, radius, ulna, femur, fibula, tibia. All other bone fractures were summarized in the variable "non-long bone fracture" [26]. In addition, a variable "any open fracture" was coded as such.

Predictor variables

In the multivariable models, the following parameters were used as potential predictor variables:

i) Fracture variables: long bone, non-long bone, and any open fracture
ii) Concomitant injury variables: brain injury with/ without cerebral bleeding, thoracic injury, abdominal injury, joint luxation, deep tissue/flesh wound, and soft tissue contusion.
iii) Trauma severity variable: ISS.

In addition, age and sex was adjusted for in the final model.

Statistical analysis

The statistical analysis was performed using Stata® 13.1 (StataCorp, The College Station, Texas, USA). For descriptive analysis, the distribution of continuous variables is described with median (and interquartile range) and of categorical variables with its frequency (and proportion).

Associations of an increased S-100 B level with the potential predictor variables were evaluated using Chi-square tests. Multivariable logistic regression with the above presented potential predictor variables (final model) was used to identify predictor variables that predicted an increased S-100 B level and to quantify the strength of association. The measure of strength of association was the odds ratio (OR) accompanied by the 95% Confidence Interval (CI). Different models were calculated for sensitivity analysis: i) inclusion of all fractures instead of aggregated fracture variables, ii) stepwise backward selection model of co-variables including AIS as marker for injury severity, iii) a subgroup analysis with restriction of the final model to consultations without traumatic brain injury, and iv) a linear multivariable regression model with the log-transformed S-100 B levels – to account for a skewed distribution – and the predictor variables of the final model. The exponentiated coefficients of this model illustrate the geometric mean ratio

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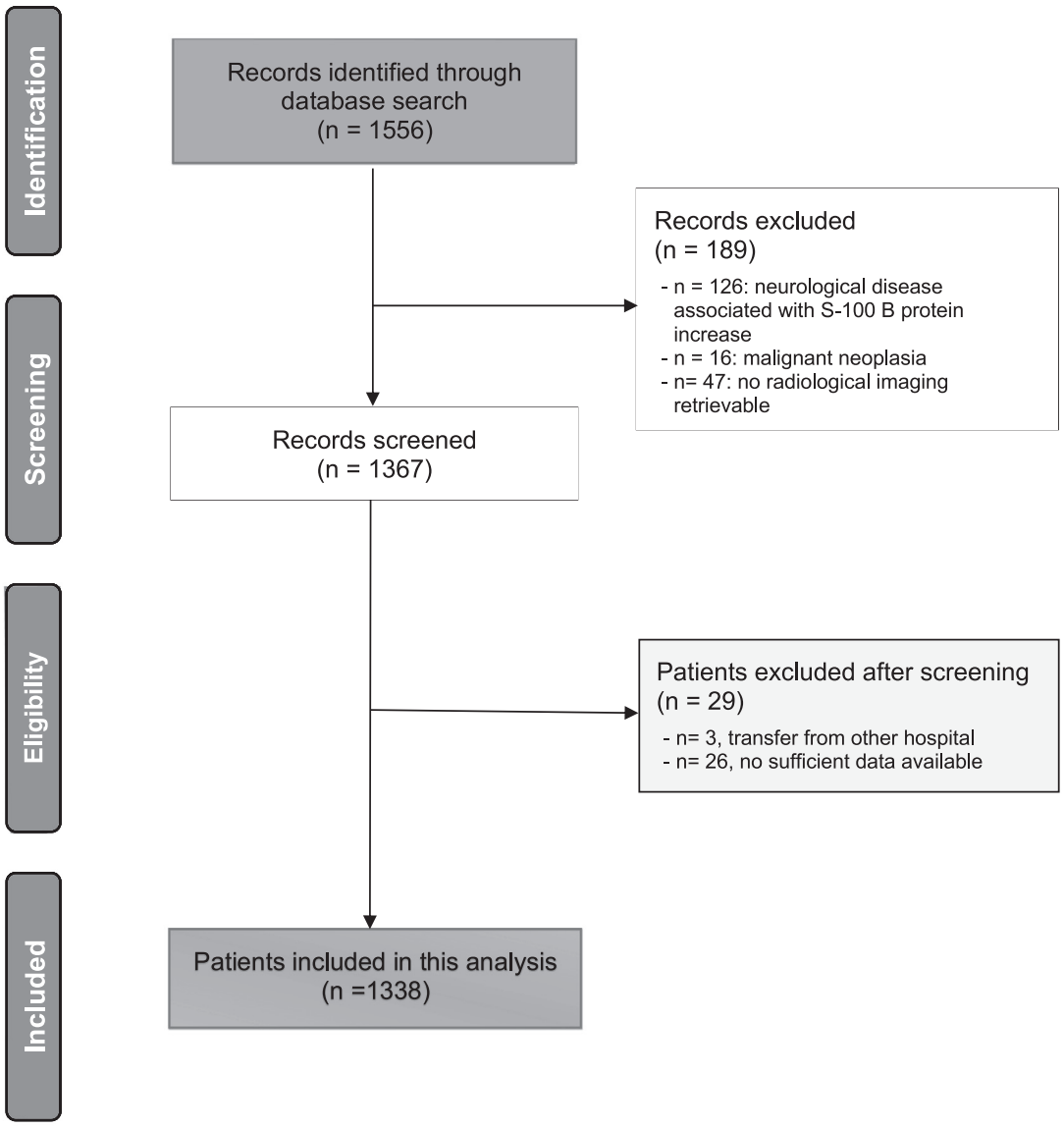

Fig. 1. Study flow chart.

between the geometric mean of the S-100 B level in the presence vs. the absence of a specific predictor variable.

To further examine the diagnostic value of an increased S-100 B level to predict in-hospital mortality, the sensitivity, specificity, negative as well as positive predictive values were presented in groups defined by the S-100 B level quartiles.

To account for multiple comparisons, a *p*-value of <0.005 was considered significant throughout this study.

Results

Twenty-nine (0.2%) of the total population of 1,367 patients with suspected multiple trauma were excluded: three patients were transferred from another hospital and 26 patients could not be included due to missing data. Thus, 1,338 patients (referred to as total cohort) were included in this study. A study flow chart is given in Fig. 1.

Patient characteristics

The median age of the total population was 43 (Inter Quartile Range (IQR): 27-59) years and 72.9% of the patients were male. Leading causes of injury were traffic accidents (39.8%), followed by sport injuries (18.2%). Multiple trauma defined by ISS≥16points was observed in 28.4% of patients. 5.7% of all patients died in-hospital. In total, 1,023 patients (76.5%) had an increased S-100 B level (>0.2 µg/L). Table 1 shows the association of an increased S-100 B level with baseline/patient characteristics: a significant association ($p<0.001$) was observed with age, multiple trauma, Glasgow Coma Scale (GCS), and in-hospital death.

The impact of concomitant injuries on S-100 B level

Univariable associations

The median S-100 B level was 0.57 (IQR 0.21–1.52) µg/L. Table 2 shows the association of concomitant injuries with increased S-100 B levels.

Multiple injuries were positively associated with increased S-100 B levels including long bone fractures (OR 3.4, 95% CI: 2.1-5.4), any open fracture (OR 7.8, 95% CI: 2.4–24.8), and non-long bone fracture (OR 5.4,95% CI: 4.0-7.3) (all $p\leq0.001$). Brain injury with intracerebral bleeding was also associated with an increased S-100 B level ($p<0.001$), but brain injury without intracerebral bleeding did not show a significant association ($p=0.934$).

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Table 1
Baseline characteristics and its association with an increased (n = 1,023) vs. a normal S-100 B level (n = 315) at admission.

	Total (n = 1,338)	Odds ratio (95% CI)	p-value[#]
Age, [med (IQR)]	43.0 (27-59)	1.01 (1.01 – 1.02)	<0.001
Sex, [n (%)]			
Female	362 (27.1)	1.00 base	
Male	976 (72.9)	1.35 (1.03 - 1.78)	0.032
Injury situation, [n (%)]			
Work	207 (15.5)	1.00 base	
House	225 (16.8)	1.03 (0.66 – 1.61)	
Traffic	533 (39.8)	1.21 (0.83 – 1.77)	
Sport	244 (18.2)	1.12 (0.72 – 1.74)	
Other	110 (8.2)	0.60 (0.36 – 1.00)	
Not specified	19 (1.5)	0.41 (0.15 – 1.16)	0.011
GCS, [n (%)]*			
13-15	654 (72.1)	1.00 (base)	
9-12	88 (9.7)	3.62 (1.78 – 7.36)	
<9	165 (18.2)	3.84 (2.23 – 6.61)	<0.001
Multiple trauma, [n (%)]	380 (28.4)	5.88 (3.86 – 8.96)	<0.001
Death in hospital, [n (%)]	76 (5.7)	24.84 (3.44 – 179.4)	<0.001

Abbreviations: CI, Confidence Interval; GCS, Glascow Coma Scale; IQR, Interquartile Range; med, median.
* Documented in 907 (67.8%) consultations.
# Chi-squared or Wilcoxon rank sum test as appropriate.

Table 2
Univariable associations of concomitant injuries with an increased S-100 B level.

	Odds ratio (95% CI)		p-value
Joint luxation	0.88	(0.60 – 1.30)	0.514
Deep tissue injury/ Flesh wound	2.18	(1.68 – 2.82)	<0.001
Soft tissue contusion	0.63	(0.48 – 0.82)	0.001
Brain injury without intracerebral bleeding	1.01	(0.76 – 1.36)	0.934
Brain injury with intracerebral bleeding	3.40	(2.26 – 5.10)	<0.001
Abdominal injuries	3.79	(1.96 – 7.32)	<0.001
Thoracic injuries			
None	1.00	(base)	
With rib fracture	8.58	(4.73 – 15.6)	<0.001
Without rib fracture	2.24	(1.27 – 3.95)	0.005
Any open fracture	7.76	(2.43 – 24.8)	0.001
Long bone fracture	3.40	(2.13 – 5.44)	<0.001
Humerus	2.85	(1.12 – 7.25)	0.028
Lower arm	2.56	(1.21 – 5.40)	0.014
Ulna	2.75	(0.97 – 7.81)	0.057
Radius	3.32	(1.31 – 8.38)	0.011
Femur	7.64	(2.39 – 24.4)	0.001
Lower leg	4.91	(2.13 – 11.3)	<0.001
Tibia	4.91	(1.97 – 12.2)	0.001
Fibula	3.49	(1.50 – 8.14)	0.004
Non-long bone fracture	5.41	(4.00 – 7.31)	<0.001
Spine	6.22	(3.79 – 10.2)	<0.001
Cervical	2.68	(1.45 – 4.94)	0.002
Thoracic	8.44	(3.69 – 19.3)	<0.001
Lumbar	10.63	(3.89 – 29.0)	<0.001
Pelvis	5.14	(2.37 – 11.2)	<0.001
Skull	7.78	(3.15 – 19.2)	<0.001
Skull, open*	-	-	-
Viscerocranium	2.01	(1.34 – 3.01)	0.001
Clavicula	5.19	(1.87 – 14.4)	0.002
Sternum	15.8	(2.17 – 114.9)	0.006
Scapula	7.52	(2.35 – 24.1)	0.001
Rib fracture	8.52	(4.32 – 16.8)	<0.001
Rib series	10.72	(3.93 – 29.3)	<0.001
Hand bone	1.56	(0.76 – 3.24)	0.228
Foot bone	13.44	(1.84 – 98.1)	0.010

Abbreviations: CI, Confidence Interval.
* Skull open fracture predicts an increased S-100 B level perfectly

All AIS regions showed a positive association with increased S-100 B levels (see Table 3). Apart from AIS in the region of spine (p = 0.009), face (p = 0.036) end external (p = 0.075), all associations were significant on a level of p<0.001. Per one-point increase of the ISS to the next, the odds for an increased S-100 B level increased about 20% (OR 1.2, 95% CI: 1.1–1.2).

The distribution characteristics of A) baseline variables, B) concomitant injuries, C) fractures, and D) trauma severity in accordance to the S-100 B level are shown in Supplement 1.

Multivariable association

In multivariable logistic regression (Table 4), the following variables showed a significant association with increased S-100 B lev-

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Table 3
Univariable logistic regression analysis of trauma severity reflected by the AIS and ISS scores with an increased S-100 B levels.

	Odds ratio (95% CI)		*p*-value
AIS, per point more			
Head/ Neck	1.37	(1.23 – 1.52)	<0.001
Face	1.20	(1.01 – 1.43)	0.036
Spine	1.19	(1.04 – 1.35)	0.009
Thorax	2.21	(1.83 – 2.66)	<0.001
Abdomen/ Pelvic	1.58	(1.25 – 1.99)	<0.001
Upper extremity	1.63	(1.37 – 1.95)	<0.001
Lower extremity	1.60	(1.37 – 1.87)	<0.001
External	1.74	(0.95 – 3.22)	0.075
ISS, per point more	1.15	(1.12 – 1.18)	<0.001

Abbreviations: AIS, Abbreviated Injury Scale; CI, Confidence Interval; ISS, Injury Severity Score.

Table 4
Multivariable logistic regression to model an increased S-100 B level (n=1,338).

	Odds Ratio (95% CI)		p-value
Sociodemographic characteristics			
Sex, male	0.90	(0.65–1.23)	0.494
Age, per year more	1.00	(1.00–1.01)	0.378
Concomitant injuries			
Long bone fracture	2.31	(1.32–4.07)	0.004
Non-long bone fracture	3.04	(2.16–4.29)	<0.001
Any open fracture	2.01	(0.55–7.42)	0.292
Traumatic brain injury without bleeding	1.07	(0.75–1.52)	0.706
Traumatic brain injury with bleeding	2.02	(1.19–3.45)	0.010
Thoracic injury	2.60	(1.62–4.18)	<0.001
Abdominal injury	1.29	(0.60–2.77)	0.509
Joint luxation	0.91	(0.57–1.45)	0.702
Deep tissue injury/ Flesh wound	1.90	(1.39–2.60)	<0.001
Soft tissue contusion	0.81	(0.59–1.09)	0.167
Trauma severity			
ISS, per point more	1.06	(1.03 - 1.09)	<0.001

Abbreviations: CI, Confidence Interval; ISS, Injury Severity Score.

els: long bone fracture (OR 2.3, 95% CI: 1.3–4.1, p = 0.004), non-long bone fracture (OR 3.0, 95% CI: 2.2–4.3, p<0.001), thoracic injury (OR 2.6, 95% CI 1.6–4.2, p<0.001), deep tissue injury/flesh wounds (OR 1.9, 1.4–2.6, p<0.001), and trauma severity (OR per ISS: 1.1, 95% CI 1.0–1.1, p<0.001).

In multivariable analysis without aggregating the fractures, lumbar (p = 0.001) and thoracic spine (p = 0.002), thoracic injuries (p = 0.001), flesh wounds (p<0.001), as well as trauma severity (p<0.001) showed a positive association with an increased S-100 B level (Supplement 2).

Sensitivity analysis

In sensitivity analysis the associations found were similar if i) a stepwise backward logistic regression (p<0.005) model was used to define the final model (Supplement 3), ii) a linear regression analysis to model the S-100 B level was used (Supplement 4 and 5), or if iii) the analysis was restricted to suspected multiple trauma patients without any traumatic brain injury (n = 675) (Supplement 6).

Predicting mortality out of S-100 B levels

The in-hospital mortality rate was 5.7% (95% CI: 5.0–7.0%) in the total population.

The lower (0.21 µg/L) and upper quartile (1.52 µg/L) as well as the median (0.57 µg/L) of the S-100 B levels were used to divide the cohort in quartiles. Using the cut-offs defined by the quartiles, the area under the curve (AUC) to determine in-hospital mortality out of the S-100 B level group was 0.814 (95% CI: 0.775–0.852). S-100 B levels below 0.574 µg/L had a high diagnostic value to rule out in-hospital mortality (negative predictive value: 1.00, 95% CI: 0.98–1.00), see Table 5.

Discussion

The aim of this study was to investigate the potential impact of different injury patterns on S-100 B levels in patients with suspected multiple trauma. Fractures, particularly of long bones, and chest trauma were observed to be associated with increased S-100 B levels.

Although S-100 B was historically discovered and described to be specific for neural tissue and therefore used as a marker for traumatic brain injury, it was soon recognized that S-100 B can also be increased without traumatic brain injury, which indicates expression in additional tissues and can explain false-positive results without brain injury [5,7,27–31]. Further, it was suggested that extracranial tissue must somehow contribute to S-100 B release since its levels are also raised in healthy marathon runners [28] and multiple trauma patients without traumatic brain injury [7,27,29,30,32,33]. As potential source, soft tissue injury and fractures were discussed [7,27,29,30,32,33]. However, the impact of extracranial S-100 B protein release on its systemic level in multiple trauma patients was not investigated or quantified yet. In this study, we showed a detailed analysis of factors that contribute to S-100 B elevation in patients with multiple trauma. In our cohort, soft tissue damage, fractures, and thorax trauma were leading causes of S-100 B level.

Evidence from animal and laboratory studies shows that despite previous assumptions, the beta isomer of the S-100 protein is not solely expressed in glial cells (astrocytes, oligodendrocytes,

Table 5
Diagnostic value of different S-100 B levels (p25, p50, p75) to predict of all-cause in-hospital mortality (incidence: 5.7%, 95% CI: 5-7%, n = 1,338).

S-100 B level*	>0.210 µg/L (p25)	>0.574 µg/L (p50)	>1.520 µg/L (p75)
Sensitivity	0.99 (95% CI: 0.93–1.00)	0.92 (95% CI: 0.84–0.97)	0.78 (95% CI: 0.67–0.86)
Specificity	0.26 (95% CI: 0.24–0.29)	0.53 (95% CI: 0.50–0.55)	0.78 (95% CI: 0.76–0.80)
PPV	0.07 (95% CI: 0.06–0.09)	0.1 (95% CI: 0.08–0.13)	0.18 (95% CI: 0.14–0.22)
NPV	1.00 (95% CI: 0.98–1.00)	0.99 (95% CI: 0.98–1.00)	0.98 (95% CI: 0.97–0.99)
LR (+)	1.34 (95% CI: 1.29–1.40)	1.94 (95% CI: 1.77–2.11)	3.55 (95% CI: 3.03–4.16)
LR (-)	0.05 (95% CI: 0.01–0.35)	0.15 (95% CI: 0.07–0.33)	0.29 (95% CI: 0.19–0.44)
OR	26.9 (95% CI: 4.69-#)	12.9 (95% CI: 5.68–29.2)	12.4 (95% CI: 7.15–21.5)

Abbreviations: CI: Confidence Interval; LR, Likelihood-Ratio; NPV, Negative Predictive Value; OR, Odds Ratio; P, Percentile; PPV, Positive Predictive Value.
* Test defined as positive if S-100 B level greater than p25, p50 or p75 respectively.
# Value could not be determined

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Schwann cells), but also in similar concentrations in other cells such as melanocytes, chondrocytes and adipocytes [31,34]. This might explain why S-100 B protein is increased in patients with major damage caused by blunt or sharp injury to the subcutis, as this tissue mostly consists of adipocytes. Further, both yellow and red bone marrow contain large numbers of adipocytes, which might explain high S-100 B protein levels in patients with long bone fractures and thoracic injury. In the latter, the costal cartilage injury through shearing forces might even potentiate S-100 B release due to chondrocyte damage. In addition, every fracture is inevitably associated with soft tissue damage. Thus, in patients with fractures as well as multiple trauma patients, the source of S-100 B protein elevations is probably multifactorial and, as our study suggests, is associated with overall trauma severity.

Even though, S-100 B protein is a classical "traumatic brain injury" marker and was used and recommended for triage in patients with head trauma for years [7–10,12,13], our study shows that its use in head trauma patients should be questioned. Based on current understanding S-100 B protein is expressed in several glial cells, i.e. astrocytes, oligodendrocytes, and Schwann cells and should be released upon cell contusion or destruction [5,31,34]. Therefore, if S-100 B protein levels remain below the threshold, it was proposed that significant head injury can be ruled out and the patient discharged [12,35]. In contrast, this study shows that only head trauma with intracerebral bleeding is associated with increased S-100 B protein levels, head trauma without head injury is not. However, head trauma without bleeding can still significantly impact patient outcome and mortality (e.g. if contusions are present), especially in multiple trauma patients [36,37]. Hence, relying on S-100 B protein levels to rule out significant head injury in suspected multiple trauma should be applied with caution.

Further, despite the fact that brain trauma with intracerebral bleeding remained associated with increased S-100 B protein levels in the multivariable analysis, the association was markedly weaker when compared to the odds for long bone fractures and thoracic trauma. This might imply that the extent of S-100 B protein expressing tissue damage is proportionally larger in extra-cranial vs. intracranial regions in patients with multiple trauma, which should be considered when S-100 B protein is used in this clinical setting.

Limitations

Our study has several limitations. First, external validity is limited through the monocentric design of this study. Further, as this is a retrospective study, it is possible that potential patients were missed due to documentation errors. Third, since S-100 B levels were measured once only upon admission, we could not capture the dynamics of S-100 B in the course of hospitalisation. Fourth, confounding factors influencing in-hospital mortality such as secondary complications were not evaluated and cause of death data is missing. Fifth, we used the definition of multiple trauma based on the ISS. While a high ISS reflects severe trauma and does not necessarily imply multiple trauma, however our used definition (ISS$\geq$16 points), is commonly used and widely accepted.

Conclusion

S-100 B protein may be useful in critically ill Intensive Care Unit (ICU) patients. As this study shows, S-100 B protein levels are associated with injury severity and increased mortality in multiple trauma patients. This might imply a potential use as a triage tool for multiple trauma patients for non-maximal care hospitals without dedicated intensive care units, in which unnecessary transport to larger facilities could theoretically be avoided.

Further, today almost all patients with suspected multiple trauma undergo head-to-toe "polytrauma" computed tomography (CT) as per current guidelines [38]. Whole body CT scan, however, is not only associated with radiation exposure, but also increased health care costs [39,40]. Hence, whole-body CTs should be ordered with care [40,41]. Recent evidence from a prospective European multi-centre study showed that performing of whole-body CT scans in patients with suspected major trauma does not reduce mortality when compared to selective conventional radiological assessment [38], suggesting that routine whole-body CT scans in patients with suspected multiple trauma should be reassessed. S-100 B protein might help as a risk stratification tool in trauma patients where the pre-test probability for multiple trauma is low (e.g. patients with GCS 15 and hemodynamically and respiratorically stable), despite triage standards putting the patient in the category "potential multiple trauma" because of a high-speed accident or airbag activation. In respective patients, evaluation of S-100 B protein might in the future support to avoid radiation exposure and allow for more individualized symptom-oriented imaging studies. Importantly, however, the use of S-100 B protein in this clinical setting needs to be further explored. In conclusion, fractures and thoracic injuries appear as the main predictors for increased S-100 B levels in patients with multiple trauma. Despite common perception, head injuries play a minor role as predictor of S-100 B protein elevation. S-100 B has a good negative predictive value for in-hospital mortality and is clearly associated with trauma severity and can be used as a prognostic marker in trauma patients and may help to avoid unnecessary transfers and computed tomography in the future.

Ethics approval and consent to participate

The study was approved by the competent ethics committee of the Canton of Bern, Switzerland (EC no.: 10-01-13) and individual informed consent was waived by the ethics committee.

Authors' contributions

MM and CAP conceived the study and designed the trial. CAP supervised the conduct of the trial and data collection. MM provided statistical advice on study design and analyzed the data; MM, JMM, JLG, and CAP drafted the manuscript, AKE, WEH and JCS revised the manuscript for important intellectual content, all authors read and approved the final draft.

Source of funding

MM was funded by a CTU-Grant from the Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland .

Declaration of Competing Interest

WEH received speaker honoraria from the AO Foundation Zürich and research funding from Mundipharma Medical Basel. CAP and JCS report grants from Orion Pharma, Abbott Nutrition International, B. Braun Medical AG, CSEM AG, Edwards Lifesciences Services GmbH, Kenta Biotech Ltd, Maquet Critical Care AB, Omnicare Clinical Research AG, Nestle, Pierre Fabre Pharma AG, Pfizer, Bard Medica S.A., Abbott AG, Anandic Medical Systems, Pan Gas AG Healthcare, Bracco, Hamilton Medical AG, Fresenius Kabi, Getinge Group Maquet AG, Dräger AG, Teleflex Medical GmbH, Glaxo Smith Kline, Merck Sharp and Dohme AG, Eli Lilly and Company, Baxter, Astellas, Astra Zeneca, CSL Behring, Novartis, Covidien, and Nycomed outside the submitted work. The money was paid into departmental funds; no personal financial gain applied. All other authors report no conflict of interest and have nothing to disclose.

Please cite this article as: M. Müller, J.M. Münster and W.E. Hautz et al., Increased S-100 B levels are associated with fractures and soft tissue injury in multiple trauma patients, Injury, https://doi.org/10.1016/j.injury.2020.03.012

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.injury.2020.03.012.

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Please cite this article as: M. Müller, J.M. Münster and W.E. Hautz et al., Increased S-100 B levels are associated with fractures and soft tissue injury in multiple trauma patients, Injury, https://doi.org/10.1016/j.injury.2020.03.012