International Journal of Surgery 61 (2019) 48–52

Contents lists available at ScienceDirect

International Journal of Surgery

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

Original Research

Systolic blood pressure lower than the heart rate indicates a poor outcome in patients with severe isolated traumatic brain injury: A cross-sectional study

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ARTICLE INFO

Keywords:
Systolic blood pressure (SBP)
Reversed shock index (RSI)
Traumatic brain injury (TBI)
Mortality

ABSTRACT

Background: A systolic blood pressure (SBP) lower than the heart rate (HR) could indicate a poor condition in trauma patients. In such scenarios, the reversed shock index (RSI) is < 1, as calculated by the SBP divided by the HR. This study aimed to clarify whether RSI could be used to identify high-risk adult patients with isolated traumatic brain injury (TBI).

Methods: This retrospective study reviewed 1216 hospitalized adult patients with isolated TBI at a Level I trauma center between January 1, 2009 and December 31, 2015. The patients were grouped and analyzed according to RSI (< 1 or ≥ 1). Subgroups of patients with severe TBI (Glasgow Coma Scale [GCS] ≤ 8) or non-severe TBI (GCS > 8) were also compared. The primary outcome was in-hospital mortality. The odds ratios (ORs) of categorical variables were calculated by chi-square tests with 95% confidence intervals (CIs). Mann–Whitney U-tests were used to analyze non-normally distributed continuous data.

Results: Among patients with isolated TBI, those with an RSI < 1 had higher mortality (44.7% vs. 7.1%, OR: 10.5, 95% CI: 5.36–20.75; P < 0.001) than those with an RSI ≥1. An RSI < 1 indicated a higher risk of mortality (OR: 5.1, 95% CI: 2.08–12.49; P < 0.001) in patients with severe isolated TBI but not in patients with non-severe isolated TBI (OR: 3.6, 95% CI: 0.45–28.71; P = 0.267).

Conclusion: Patients with isolated TBI may be at risk for shock. In trauma patients with severe isolated TBI, an SBP lower than the HR indicates a poor outcome.

1. Background

Traumatic brain injury (TBI) is commonly encountered in the emergency department [1–3]. Patients with TBI are evaluated according to their neurological symptoms and signs, using tools such as the Glasgow coma scale (GCS), measurements of pupil size, and other neurological examinations [4,5]. The GCS is broadly accepted as a standard metric to classify the severity of TBI [6]. However, despite its widespread use, the GCS has several significant limitations, including variations in interrater reliability and predictive validity [7]. Thus, the GCS may not be as reliable as previously believed [8]. To predict the outcome of patients with TBI, alternative parameters such as age, pupil size, and the presence of hypotension and anemia has been proposed to indicate a worse outcome [9,10].

Although most cases of isolated TBI are not associated with a change in blood pressure, some studies have demonstrated that TBI may influence blood pressure and mask the severity of the actual injury [11–13]. In contrast, shock may also result in change in mental status in trauma patients [14] and was identified as an important poor prognostic factor in patients with trauma injury [15–17]. To identify high-risk patients in shock in the emergency department, we previously introduced an easily-measured physiological marker, the reverse shock index (RSI) [18–20], which is the ratio of systolic blood pressure (SBP) to heart rate (HR). An SBP lower than the HR in trauma patients results in poor outcomes, including a higher mortality rate and a longer length of stay (LOS) in the hospital and intensive care unit (ICU) [15,16,18].

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https://doi.org/10.1016/j.ijsu.2018.11.030
Received 5 October 2018; Received in revised form 22 November 2018; Accepted 25 November 2018
Available online 10 December 2018
1743-9191/

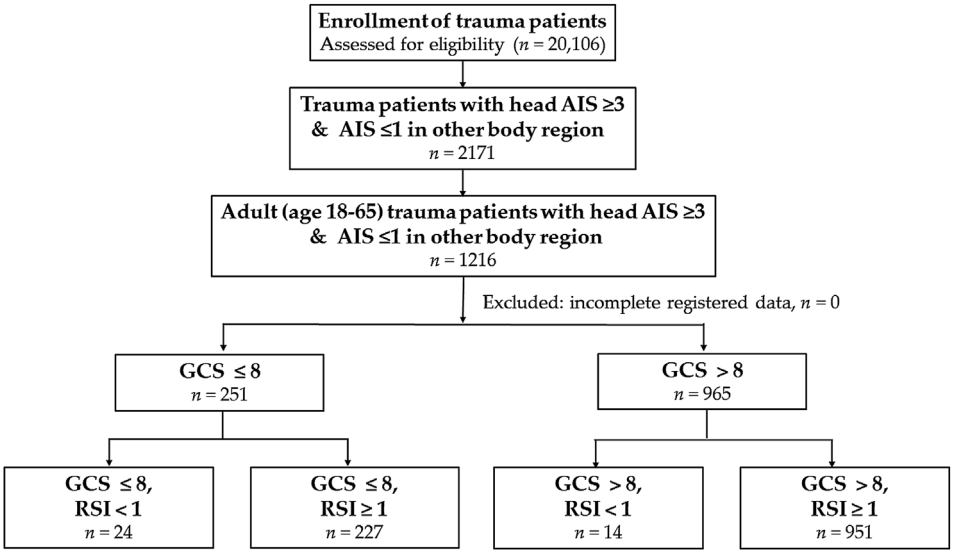

Fig. 1. Enrollment and grouping of adult patients with isolated traumatic brain injury.

Table 1
Comparisons of the injury characteristics and outcomes of patients with isolated traumatic brain injury according to RSI (< 1 or ≥ 1).

Variables	RSI < 1n = 38	RSI ≥1n = 1178	Odds Ratio(95% CI)	*P*
Gender, n (%)				
Male	26(68.4)	783(66.5)	1.1(0.55–2.19)	*0.863*
Female	12(31.6)	395(33.5)	0.9(0.46–1.83)	*0.863*
Age (years)	42.6 ± 14.9	44.2 ± 14.9	–	*0.521*
GCS [median, (Q_1-Q_3)]	6(3–15)	15(10–15)	–	*< 0.001*
≤8, n (%)	24(63.2)	227(19.3)	7.2(3.66–14.10)	*< 0.001*
9–12, n (%)	3(7.9)	121(10.3)	0.7(0.23–2.47)	*0.791*
≥13, n (%)	11(28.9)	830(70.5)	0.2(0.08–0.35)	*< 0.001*
ISS [median, (Q_1-Q_3)]	16(9.0–25.0)	16(10.0–16.3)	–	*0.013*
< 16, n (%)	12(31.6)	479(40.7)	0.7(0.34–1.35)	*0.315*
16–24, n (%)	12(31.6)	540(45.8)	0.5(0.27–1.09)	*0.098*
≥25, n (%)	1(36.8)	159(13.5)	3.8(1.89–7.38)	*< 0.001*
Head trauma, n (%)				
Cranial fracture	12(31.6)	302(25.6)	1.3(0.67–2.69)	*0.451*
EDH	6(15.8)	276(23.4)	0.6(0.25–1.48)	*0.332*
SDH	18(47.4)	589(50.0)	0.9(0.47–1.72)	*0.869*
SAH	18(47.4)	598(50.8)	0.9(0.46–1.67)	*0.743*
ICH	3(7.9)	116(9.8)	0.8(0.24–2.59)	*0.792*
Cerebral contusion	7(18.4)	283(24.0)	0.7(0.31–1.64)	*0.452*
Procedures in the ER, n (%)				
CPR	7(18.4)	1(0.1)	265.8(31.7–2226.2)	< 0.001
Intubation	7(18.4)	96(8.1)	2.5(1.09–5.93)	0.036
Chest tube insertion	1(2.6)	0(0.0)	–	0.031
Blood transfusion	7(18.4)	42(3.6)	6.1(2.54–14.67)	0.001
LOS in hospital (days)	6.5(2.0–12.3)	8.0(4.0–14.3)	–	*0.191*
ICU admission, n (%)	28(73.7)	788(66.9)	1.4(0.67–2.88)	*0.483*
LOS in ICU (days)	4.0(3.0–13.0)	4.0(3.0–7.0)	–	*0.222*
Operation, n (%)	14(36.8)	408(34.6)	1.1(0.56–2.15)	*0.863*
Mortality, n (%)	17(44.7)	84(7.1)	10.5(5.36–20.75)	*< 0.001*

Abbreviations: RSI, reversed shock index; CI, confidential interval; SBP, systolic blood pressure; ISS, Injury Severity Score; GCS, Glasgow coma scale; LOS, length of stay; ICU, intensive care unit; ER, emergency room; CPR, cardiopulmonary resuscitation; EDH, epidural hematoma; SDH, subdural hematoma; SAH, subarachnoid hematoma; ICH, intracerebral hematoma.

This study investigated whether RSI could be used to assist in the identification of the subjects with poor outcome among those patients with isolated TBI.

2. Methods

2.1. Study design

This was a retrospective study and the work has been reported with the STROCSS criteria [21]. All data from admitted trauma patients enrolled between January 1, 2009 and December 31, 2015 (see Fig. 1) were retrieved from the Trauma Registry System of a Level I regional trauma center [22,23]. Adult patients having isolated TBI with a head abbreviated injury scale (AIS) ≥ 3 and without severe injury to other regions (other AIS ≤ 1) were included. We excluded patients younger than 18 or older than 65 years of age. Patients with incomplete registered data were also excluded. The retrieved information included patient sex; age; comorbidities such as diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, cerebrovascular accident, and end-stage renal disease; vital signs that measured by the machine upon arrival at the emergency department; GCS; injury severity score (ISS) expressed as the median and interquartile range (IQR,

Table 2
Comparisons of the injury characteristic and outcomes of patients with severe isolated traumatic brain injury (GCS ≤ 8) according to RSI (< 1 or ≥ 1).

Variables	RSI < 1n = 14	RSI ≥1n = 951	Odds Ratio(95% CI)	*P*
Gender, n (%)				
Male	15(62.5)	165(72.7)	0.6(0.26–1.51)	*0.341*
Female	9(37.5)	62(27.3)	1.6(0.67–3.84)	*0.341*
Age (years)	44.3 ± 13.8	42.7 ± 15.6	–	*0.639*
LOS in hospital (days)	8.0(1.3–12.8)	14.0(5.0–27.0)	–	*< 0.001*
ICU admission, n (%)	21(87.5)	198(87.2)	1.0(0.29–3.65)	*1.000*
LOS in ICU (days)	6.0(3.0–14.0)	7.0(4.0–14.0)	–	*0.815*
Operation, n (%)	13(54.2)	139(61.2)	0.7(0.32–1.74)	*0.517*
Mortality, n (%)	16(66.7)	64(28.2)	5.1(2.08–12.49)	*< 0.001*

Abbreviation: RSI, reversed shock index; CI, confidential interval; LOS, length of stay; ICU, intensive care unit.

Q1–Q3); procedures performed in the emergency department, including cardiopulmonary resuscitation (CPR), intubation, chest tube insertion, and blood transfusion; hospital and ICU LOS; rates of ICU admission; and in-hospital mortality. Patients were grouped and analyzed according to RSI (< 1 or ≥ 1). The patients were also categorized as having severe TBI (GCS ≤ 8) or non-severe TBI (GCS > 8.)

The statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0. Categorical data were expressed as frequency (%) and compared using two-sided Fisher's exact or Pearson's chi-square tests. The odds ratios (ORs) with 95% confidence intervals (CIs) of the associated conditions of the patients were presented. For continuous variable associations, Mann–Whitney *U*-tests were used to analyze non-normally distributed continuous data, which was reported as means ± standard deviation. By plotting specific receiver operating characteristic (ROC) curves, the accuracy of SBP in predicting the mortality outcomes as an area under the curve (AUC) was calculated based on the maximal Youden index (sensitivity + specificity − 1). A nonparametric approach was performed to compare the accuracy of AUC ROC curves using the roc & roc.test function in the pROC package in R3.3.3 (R Foundation for Statistical Computing). P-values < 0.05 were considered statistically significant.

3. Results

3.1. Characteristics of patients with isolated TBI

A total of 1216 hospitalized adult patients with isolated TBI were enrolled in this study. As shown in Table 1, patients with isolated TBI grouped according to RSI < 1 (n = 38) or RSI ≥ 1 (n = 1178) showed no significant differences in age, gender, and co-morbidities. The GCS score of patients with RSI < 1 was significantly lower than that of patients with RSI ≥1 (median [Q_1-Q_3], 6 [3–15] vs. 15 [10–15], respectively; P < 0.001), with a higher incidence of GCS ≤ 8 and a lower incidence of GCS ≥ 13 in patients with RSI < 1. More patients had an ISS ≥25 (36.8% vs. 13.5%, respectively; p < 0.001), and patients with RSI < 1 had a higher ISS than that in patients with RSI ≥1 (median [Q_1-Q_3], 16 [9.0–25.0] vs. 16 [10.0–16.3], respectively; p = 0.013). Regarding TBI diagnosis, nearly half of the patients with isolated TBI had subarachnoid or subdural hemorrhages. However, there were no significant differences in the diagnoses of head trauma between patients with RSI < 1 and those with and RSI ≥1.

3.2. Outcome of patients with isolated TBI

Patients with RSI < 1 more often required emergent resuscitation than those with RSI ≥1. The rates of CPR, intubation, chest tube insertion, and blood transfusion were significantly higher in patients with RSI < 1 than in patients with RSI ≥1 (CPR, OR: 265.8, 95% CI: 31.7–2226.2; P < 0.001; intubation, OR: 2.5, 95% CI: 1.09–5.93; P = 0.036; blood transfusion, OR: 6.1, 95% CI: 2.54–14.67; P = 0.001). There were no significant differences in the hospital and ICU LOS, the rates of ICU admission, and the rates of operation between patients with RSI < 1 and with RSI ≥1. A lower SBP was associated with a higher odd of mortality. As shown in the Supplemental Fig. 1, those who had SBP < 90 mmHg had 11.4-fold of mortality than those patients with SBP ≥90 mmHg; in contrast, those who had SBP < 30 mmHg had 41.4-fold of mortality than those patients with a SBP ≥30 mmHg. However, a poor predictive accuracy (AUC 0.503) of SBP was found (Supplemental Fig. 2). The SBP can estimate the probability of dying of the patients with a sensitivity of 31.7% and specificity of 81.7% under the cutoff value of 83 mmHg. A significant ~10-fold higher mortality rate was observed in patients with RSI < 1 than in those with RSI ≥1 (OR: 10.5, 95% CI: 5.36–20.75; P < 0.001).

3.3. Outcome of patients with severe isolated TBI

Patients with severe isolated TBI were grouped according to RSI < 1 (n = 24) or RSI ≥ 1 (n = 227) (Table 2). There were no significant differences in patient gender, age, and comorbidities between these groups. The hospital LOS was significantly shorter in patients with RSI < 1 (median 8 days vs.14 days, respectively; P < 0.001). There were no significant differences in the ICU LOS, ICU admission rates, and the rates of operation between patients with RSI < 1 and those with RSI ≥1. A significantly higher mortality rate was observed in patients with RSI < 1 than in patients with RSI ≥1 (OR: 5.1, 95% CI: 2.08–12.49; P < 0.001).

3.4. Outcome of patients with non-severe isolated TBI

Patients with non-severe isolated TBI were grouped according to RSI < 1 (n = 14) or RSI ≥ 1 (n = 951) (Table 3). There were no significant differences in patient gender, age, and comorbidities between the groups. There were no significant differences in the hospital and ICU LOS, ICU admission rates, and the rates of operation between the patients with RSI < 1 and with RSI ≥1. No significant difference in mortality rate was observed between the groups (OR: 3.6, 95% CI: 0.45–28.71; P = 0.267).

4. Discussion

The results of this study demonstrated that an SBP lower than the HR (RSI < 1) indicated a worse outcome, including a longer hospital LOS and higher mortality, among patients with severe isolated TBI but not among patients with non-severe isolated TBI. In this study, we included only patients with isolated TBI. Patients with major bleeding from other body regions were excluded; therefore, significant blood loss could not explain the decreased SBP. Moreover, although increased intracranial pressure following head trauma can make vital signs unstable, this condition is generally accompanied by a high mean arterial blood pressure [24–27]. A decreased SBP with variant HR may occur in patients with a more serious head injury, such as brain stem failure, indicating the loss of sympathetic tone and ability to auto-regulate

Table 3
Comparisons of the injury characteristics and outcomes of patients with non-severe isolated traumatic brain injury (GCS > 8) according to RSI (< 1 or ≥ 1).

Variables	RSI < 1n = 14	RSI ≥1n = 951	Odds Ratio(95% CI)	*P*
Gender, n (%)				
Male	11(78.6)	618(65.0)	2.0(0.55–7.13)	*0.401*
Female	3(21.4)	333(35.0)	0.5(0.14–1.83)	*0.401*
Age (years)	39.7 ± 16.7	44.5 ± 14.7	–	*0.224*
LOS in hospital (days)	6.0(3.8–10.0)	8.0(4.0–13.0)	–	*0.672*
ICU admission, n (%)	7(50.0)	590(62.0)	0.6(0.21–1.76)	*0.410*
LOS in ICU (days)	4.0(2.0–4.0)	4.0(3.0–6.0)	–	*0.397*
Operation, n (%)	1(7.1)	269(28.3)	0.2(0.03–1.50)	*0.129*
Mortality, n (%)	1(7.1)	20(2.1)	3.6(0.45–28.71)	*0.267*

Abbreviation: RSI, reversed shock index; CI, confidential interval; LOS, length of stay; ICU,intensive care unit.

blood pressure [27–30]. Head injury may also attenuate changes in vital signs [11], and extremely high and low shock indexes are associated with higher mortality in patients with acute stroke [31]. Therefore, clinicians should never assume that isolated TBI is not accompanied by shock. In contrast, potential shock, demonstrated as RSI < 1, was associated with worse outcomes in these patients.

Patients in the emergency department were usually classified by the GCS score, as having severe (GCS score ≤ 8) or mild to moderate head injuries (GCS > 8) [4,14]. Patients with brain stem failure or impending brain stem failure would be expected to present with lower coma scale score and tended to sustain severe head injuries. Among patients with severe isolated TBI, a 5.1-fold increase in mortality rate was observed in those with RSI < 1 compared to the rate in patients with RSI ≥1. Moreover, patients with RSI < 1 had a shorter hospital LOS. This shorter LOS may be attributed to the higher mortality rate (66.7%) of these patients than the 28.2% mortality rate of patients with RSI ≥ 1. In contrast, among patients with mild to moderate isolated TBI (GCS > 8), there were no significant differences in mortality rate, rates of ICU admission, and hospital and ICU LOS between patients with RSI < 1 and with RSI ≥ 1. Shock was possible, although rare, in patients with higher GCS scores and without brain stem failure or impeding brain stem failure. An SBP lower than the HR may be attributed to unstable vital signs in patients with isolated mild and moderate head injuries. These trauma patients may also have different baseline characteristics (lower SBP or higher HR, orthotic hypotension) [32]. In contrast, among patients with non-severe (i.e., mild to moderate) isolated head injury, a higher blood pressure may be associated with severe conditions such as increased intracranial blood pressure or cerebral edema [24,26,33]. However, the extent of the detrimental effect of unstable vital signs may not be enough to cause a poor outcome in these patients. Among those non-severe TBI patients, shock could be attributed to other cause than neurogenic.

4.1. Limitations

This study had several limitations. First, this retrospective study had an inherent bias in the data analysis. In addition, all data were retrieved from a single center. Second, the RSI was calculated by the SBP and HR measured upon patient arrival at the emergency department; these values may not reflect hemodynamic status changes and may be affected if fluid or blood were administered during the transportation to the emergency department. Therefore, we cannot evaluate in this study whether there is dose-response of RSI, i.e. whether there is more unfavorable outcome in those patients with a longer duration of RSI. Third, the outcome of this study was evaluated by mortality rate, rate of ICU admission, and LOS in the hospital and ICU and no functional outcomes were considered. Fourth, this study was performed on one trauma center and the results may not be reproducible in other hospital. Fifth, different managements may exist among those who had different RSI, which may be related to different injured severity and outcome. In such scenario, a selection bias is expected; however, in this retrospective study, we can only assume there are uniform treatment for all these patients regardless of their RSI. Furthermore, the severity of brain damage could not be quantified by computed tomography examination. Finally, the number of patients was relatively small, which may have led to a false estimate of the relative odds of the risk of mortality and make an unreliable conclusion due to lack of statistical power. A study implemented on multiple trauma centers would be helpful to improve the statistical power and get a more confirmative conclusion.

5. Conclusion

SBP lower than the HR, i.e. RSI < 1, indicated a poor outcome in patients with severe isolated TBI but not in patients with non-severe isolated TBI.

Data statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Conflicts of interest

Not applicable.

Sources of funding

This study was supported by a grant from Chang Gung Memorial Hospital, Taiwan (CGRPG8F0011) to Ching-Hua Hsieh.

Ethical approval

This study was pre-approved by the Institutional Review Board (IRB) of Chang Gung Memorial Hospital (approved number: 201600245B0). The need for informed consent was waived according to IRB regulations.

Registration unique identifying number (UIN)

NCT03698214.

Guarantor

Ching-Hua Hsieh.

Author contributions

J.-F.H. wrote the manuscript, Y.-C.T. assisted with the study design, C.-S.R. was involved in the literature review, S.-Y.H. was responsible for the integrity of registered data, P.-C.C performed the statistical analyses and edited the tables, H.-Y.H. proofread the manuscript, and C.-H.H. designed the study and contributed to the data analysis and interpretation. All authors read and approved the final manuscript.

Acknowledgements

We thank the Biostatistics Center at the Kaohsiung Chang Gung Memorial Hospital for their help with the statistical analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijsu.2018.11.030.

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