Severe traumatic brain injury and hypotension is a frequent and lethal combination in mountain trauma patients – an analysis of the International Alpine Trauma Registry

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Abstract

**Background:** Hypotension is associated with worse outcome in patients with traumatic brain injury (TBI) and maintaining a systolic blood pressure (SBP) $\geq 110$ mmHg is recommended. The aim of this study was to assess the incidence of TBI in patients suffering multi-trauma in remote and mountainous areas; to describe associated factors, treatment and outcome compared to non-hypotensive patients with TBI and patients without TBI; and to evaluate pre-hospital variables to predict admission hypotension.

**Methods:** Data from the International Alpine Trauma Registry including mountain multi-trauma patients (ISS $\geq 16$) collected between 2010 and 2019 were analysed. Patients were divided into three groups: 1) TBI with hypotension, 2) TBI without hypotension and 3) no TBI. TBI was defined as Abbreviated Injury Scale (AIS) of the head/neck $\geq 3$ and hypotension as SBP $< 110$ mmHg on hospital arrival.

**Results:** A total of 287 patients were included. Fifty (17%) had TBI and hypotension, 92 (32%) suffered TBI without hypotension and 145 (51%) patients did not have TBI. Patients in group 1 were more severely injured (mean ISS $43.1\pm 17.4$ vs $33.3\pm 15.3$ vs $26.2\pm 18.1$ for group 1 vs 2 vs 3, respectively, $p<0.001$). Mean SBP on hospital arrival was $83.1\pm 12.9$ vs $132.5\pm 19.4$ vs $119.4\pm 25.8$ mmHg ($p<0.001$) despite patients in group 1 received more fluids. Patients in group 1 had higher INR, lower haemoglobin and lower base excess ($p<0.001$). The rate of hypothermia on hospital arrival was different between the groups ($p=0.029$). Patients in group 1 had the highest mortality (24% vs 10% vs 1%, $p<0.001$).

**Conclusion:** Multi-trauma in the mountains goes along with severe TBI in almost 50%. One third of patients with TBI is hypotensive on hospital arrival and this is associated with a worse outcome. No single variable or set of variables easily obtainable at scene was able to predict admission hypotension in TBI patients.

**Background**

Traumatic Brain Injury (TBI) is the single most important cause of death from traumatic injury and represents a major cause of long-term disability among survivors. (1) Optimal pre-hospital management of patients with TBI can contribute to a favourable outcome and primarily focusses on the prevention of secondary injuries. (2) Within secondary injuries, hypotension plays a major role as its depth and duration have been associated with increased mortality and worse functional outcome. (3–5) Data on the prevalence of hypotension as a preventable cause of secondary injury is limited and available numbers are widely variable. A multicentre study from Switzerland found a rate of pre-hospital hypotension (defined as systolic blood pressure, SBP $\leq 90$ mmHg) of 4.1% in multi-trauma patients with TBI. (6) In a prospective study in the US, 24% of patients with TBI had hypotension (SBP $\leq 90$ mmHg) in the emergency department of a level-I urban trauma centre. (4) While in these studies hypotension was defined as SBP $\leq 90$ mmHg, current recommendations advise that patients with TBI should be considered hypotensive for SBP $< 110$ mmHg. (2, 7) When using a cut-off for SBP of 110 mmHg, the
frequency of hypotension occurring in the initial phase of resuscitation in TBI patients could be expected to be even higher than reported so far.

Avoiding hypotension can be challenging in the pre-hospital setting. Pre-hospital search and rescue (SAR) missions commonly feature prolonged times and patients often have critically impaired vital functions. (8–10) Hypotension in multi-trauma patients with TBI in remote and mountainous areas could therefore be even more common than in urban areas.

There is a lack of knowledge about the prevalence of hypotension in multi-trauma patients with TBI and the factors associated with it in remote and mountainous areas. The aim of the present study was to assess the incidence of TBI in patients suffering multi-trauma in in remote and mountainous areas; to describe associated factors, treatment and outcome of these patients compared to non-hypotensive patients with TBI and patients without TBI; and to evaluate pre-hospital variables able to predict admission hypotension in TBI patients.

**Methods**

Out-of-hospital and in-hospital data collected from trauma patients included in the International Alpine Trauma Register (IATR) (https://www.mountain-registries.org)(11) between December 2010 and October 2019 were analysed. The IATR is a transnational platform for the prospective collection and storage of data relating to severe trauma patients (Injury Severity Score, ISS ≥ 16) in mountainous or remote areas, that are not readily accessible by the regular emergency medical services. All trauma patients aged 16–80 years with an ISS ≥ 16 are included in the analysis and are called “multi-trauma patients” in this article. The registry is hosted in Bolzano (Italy)(11), and data are collected in North Tyrol (Austria), South Tyrol (Italy), Aosta region (Italy) and Chur area (Switzerland). Patients already in cardiac arrest upon arrival of the SAR team, burn patients (if the burn represented the predominant injury), and drowned patients are excluded from the IATR. In North Tyrol (Austria), patients who suffered accidents on prepared ski slopes are excluded. Only patients with vital signs at hospital admission were included in the current study. Data collection in the IATR is based on the Utstein-Style(12), which requires comprehensive data collection on multiple parameters. These parameters include accident (type of outdoor activity, mechanism of injury) and mission characteristics (technical difficulty of the terrain, terrestrial rescue, air rescue or combined rescue) and timing (time of accident, time of emergency call, time of arrival of the first rescue team, time of hospital admission). Medical data collected include: i) vital signs at the scene (i.e. SBP, respiratory rate, Glasgow Coma Scale (GCS) and body temperature); ii) out-of-hospital Advance Trauma Life Support (ATLS) interventions (i.e. endotracheal intubation, intravenous cannulation, fluid and drug administration); iii) ISS and Abbreviated Injury Scale (AIS) based on in-hospital diagnosis; iv) vital signs and laboratory data on admission (i.e. hemoglobin, INR, base excess, body temperature), plus out-of-hospital and in-hospital mortality rates.

**Statistical analysis**
Patients were classified into three groups based on clinical characteristics: group 1 included multi-trauma patients with TBI (defined as AIS ≥ 3 in the head/neck ISS body region) and hypotension defined as SBP ≤ 110 mmHg (2, 7) on hospital arrival; group 2 included multi-trauma patients with TBI but without hypotension on hospital arrival; group 3 included multi-trauma patients without TBI. Frequencies between the three groups were compared by means of Pearson’s chi-squared test, while for the two-group comparison Fisher’s exact test was used. Mean values between the three groups were compared by means of ANOVA or Kruskal-Wallis test as appropriate, while for the two-group comparison the independent samples t-test or Mann-Whitney U test was used as appropriate. Paired samples t-tests were performed to compare pre-hospital SBP and SBP on hospital arrival. The Holm-Bonferroni method was used to correct p-values for multiple comparisons.

Classification trees (13, 14) were performed to predict the three groups defined above, i.e. classification trees predicted whether patients will have TBI or not, and in case they had TBI, whether they will have admission hypotension or not. The following variables were assessed: gender, age, treatment free interval, mechanism of injury (avalanche, collision, fall, other), type of injury (blunt, penetrating), ISS, pre-hospital GCS, pre-hospital SBP, quantity of crystalloid, hypertonic and (hyper)oncotic fluids, use of vasopressors, tracheal intubation and AIS scores (of the following ISS body regions: face, chest, abdomen, extremity and external). The lengths of the branches of the classification trees is proportional to the discriminant ability of the variable (the longer the more discriminant). Cross-validation was used to evaluate the classification trees, i.e. a classification tree was created using 75% of cases (training set), randomly chosen, and its predicting ability was then evaluated on the remaining 25% of cases (testing set), calculating sensitivity and specificity. This procedure was repeated ten times and so ten classification trees were created, each generated by a different training set composed of 75% of cases selected randomly. SPSS version 25 statistical software (IBM Corp., Armonk, NY) was used. The classification trees were built by means of the library rpart of R version 3.4.1. (14, 15) Tests were two-sided and p < 0.05 was considered statistically significant. Values are reported as mean ± standard deviation unless stated otherwise.

Results

During the study period, a total of 308 cases were recorded in the IATR. Of them, 21 were excluded (17 patients had missing values for either pre- or in-hospital SBP and four patients suffered cardiac arrest during transport), and 287 patients were finally included in the analysis. A total of 142 patients had TBI, of them 50 patients (17%) had TBI and hypotension on hospital arrival (group 1), 92 (32%) suffered TBI but were not hypotensive on hospital arrival (group 2); 145 (51%) patients did not have TBI (group 3).

Demographics, type of activity leading to the accident and mechanism of injury are shown in Table 1. A difference between groups was found for gender (higher proportion of females in group 1 in comparison to group 3, p = 0.033) and for hiking (type of activity before the accident, performed more frequently in group 1 than in group 3, p = 0.002).
Table 1
Demographics, type of activity leading to the accident and mechanism of injury, subdivided by the three subgroups.

|                         | TBI with hypotension (group 1) n = 50 | TBI without hypotension (group 2) n = 92 | No TBI (group 3) n = 145 | p-value |
|-------------------------|--------------------------------------|------------------------------------------|--------------------------|---------|
| **Demographics**        |                                      |                                          |                          |         |
| Age, years, mean ± SD   | 46.4 ± 19.2                          | 42.4 ± 18.5                              | 44.5 ± 17.2              | 0.452   |
| Female sex, n (%)       | 16 (32%)                             | 20 (22%)                                 | 21 (14%)                 | 0.024   |
| **Type of activity**    |                                      |                                          |                          |         |
| Aviation, n (%)         | 1 (2%)                               | 4 (4%)                                   | 15 (10%)                 | 0.066   |
| Climbing, n (%)         | 6 (12%)                              | 15 (16%)                                 | 16 (11%)                 | 0.478   |
| Hiking, n (%)           | 22 (44%)                             | 24 (26%)                                 | 26 (18%)                 | 0.001   |
| Mountain biking, n (%)  | 0 (0%)                               | 2 (2%)                                   | 10 (7%)                  | 0.056   |
| Ski / snowboard, n (%)  | 11 (22%)                             | 33 (36%)                                 | 53 (37%)                 | 0.141   |
| Sledging, n (%)         | 2 (4%)                               | 2 (2%)                                   | 3 (2%)                   | 0.738   |
| Other, n (%)            | 8 (16%)                              | 11 (12%)                                 | 21 (15%)                 | 0.786   |
| **Mechanism of injury**|                                      |                                          |                          |         |
| Avalanche, n (%)        | 1 (2%)                               | 4 (4%)                                   | 8 (6%)                   | 0.579   |
| Collision with object / other person, n (%) | 11 (22%) | 29 (32%) | 27 (19%) | 0.087   |
| Fall, n (%)             | 37 (76%)                             | 59 (64%)                                 | 105 (74%)                | 0.203   |
| Other, n (%)            | 0 (0%)                               | 0 (0%)                                   | 2 (1%)                   | 0.368   |

Tests performed were Pearson's chi-squared tests, except for age ANOVA. TBI, traumatic brain injury.

Pre-hospital times, SBP, Glasgow Coma Scale (GCS) and selected pre-hospital therapeutic interventions, subdivided by the three groups, are shown in Table 2.
Table 2
Pre-hospital times, Glasgow Coma Scale (GCS), systolic blood pressure (SBP) and selected pre-hospital therapeutic interventions subdivided by the three groups.

|                                | TBI with hypotension (group 1) n = 50 | TBI without hypotension (group 2) n = 92 | No TBI (group 3) n = 145 | p-value |
|--------------------------------|---------------------------------------|------------------------------------------|-------------------------|---------|
| **Pre-hospital times**         |                                       |                                          |                         |         |
| Treatment free interval, min,  | 27.5 (3-130)                          | 16 (2-1001)                              | 20 (1-469)              | 0.239   |
| median (range)                 |                                       |                                          |                         |         |
| Total pre-hospital time, min,  | 82 (30-1560)                          | 88.5 (20-1047)                           | 80 (13-1274)            | 0.137   |
| median (range)                 |                                       |                                          |                         |         |
| **Level of pre-hospital care** |                                       |                                          |                         |         |
| No care, n (%)                 | 0 (0%)                                | 5 (5%)                                   | 9 (6%)                  | 0.195   |
| Basic life support, n (%)      | 5 (10%)                               | 12 (13%)                                 | 36 (26%)                | 0.014   |
| Advanced life support, n (%)   | 45 (90%)                              | 73 (80%)                                 | 93 (66%)                | 0.001   |
| **Pre-hospital SBP and GCS**   |                                       |                                          |                         |         |
| Pre-hospital SBP, mmHg, mean ± | 103.0 ± 26.2                          | 117.8 ± 26.0                             | 116.4 ± 23.3            | 0.012   |
| SD                             |                                       |                                          |                         |         |
| Pre-hospital GCS, mean ± SD    | 8.5 ± 4.3                             | 9.6 ± 4.3                                | 14.3 ± 1.7              | < 0.001 |
| Pre-hospital GCS ≤ 8, n (%)    | 27 (54%)                              | 39 (43%)                                 | 2 (1%)                  | < 0.001 |
| **Selected pre-hospital therapeutic interventions** | | | | |
| Crystalloid fluids, ml, mean ± | 758 ± 339                             | 587 ± 381                                | 580 ± 413               | 0.011   |
| SD                             |                                       |                                          |                         |         |
| Vasopressor therapy, n (%)     | 4 (12%)                               | 0 (0%)                                   | 2 (2%)                  | 0.005   |
| Intubation, n (%)              | 28 (56%)                              | 43 (47%)                                 | 19 (13%)                | < 0.001 |
| Intubation, n (%) in patients  | 24 (89%)                              | 35 (90%)                                 | 2 (100%)                | 0.883   |
| with GCS ≤ 8                   |                                       |                                          |                         |         |

Tests performed were Pearson's chi-squared tests, except for treatment free interval, total pre-hospital time and crystalloid fluids Kruskal-Wallis tests and for pre-hospital SBP ANOVA. TBI, traumatic brain injury.

Patients with TBI and hypotension (group 1) were more severely injured with a mean ISS of 43.1 ± 17.4 compared to 33.3 ± 15.3 (p = 0.001) and 26.2 ± 18.1 (p < 0.001) in patients of group 2 and 3, respectively.
The higher ISS in groups 1 and 2 compared to group 3 was mainly due to a higher AIS in the head/neck ISS body region (Table 3). Neither the total pre-hospital time nor the treatment free interval differed between the three groups.

Table 3
Glasgow Coma Scale (GCS), Abbreviated Injury Scale (AIS) divided by body region and laboratory parameters on hospital arrival.

|                      | TBI with hypotension (n = 50) | TBI without hypotension (n = 92) | No TBI (n = 145) | p-value |
|----------------------|-------------------------------|---------------------------------|------------------|---------|
| GCS on hospital arrival | 7.5 ± 5.1                     | 9.9 ± 5.1                       | 13.6 ± 3.4       | < 0.001 |
| ISS body region      |                               |                                 |                  |         |
| Head/neck, AIS       | 4.2 ± 1.0                     | 4.0 ± 0.9                       | 1.7 ± 0.5        | < 0.001 |
| Face, AIS            | 3.7 ± 1.2                     | 3.1 ± 0.7                       | 2.2 ± 1.0        | < 0.001 |
| Thorax, AIS          | 3.8 ± 0.8                     | 3.4 ± 1.0                       | 3.5 ± 1.0        | 0.169   |
| Abdomen, AIS         | 3.4 ± 1.0                     | 3.2 ± 0.7                       | 3.4 ± 1.0        | 0.743   |
| Extremities, AIS     | 3.6 ± 1.0                     | 3.1 ± 0.8                       | 3.4 ± 1.3        | 0.135   |
| External, AIS        | 3.0 *                         | 3.3 ± 0.9                       | 2.7 ± 1.0        | 0.384   |

Selected laboratory values on hospital admission

|                      | TBI with hypotension (n = 50) | TBI without hypotension (n = 92) | No TBI (n = 145) | p-value |
|----------------------|-------------------------------|---------------------------------|------------------|---------|
| Hemoglobin, g/dl     | 10.8 ± 2.8                    | 12.7 ± 1.9                      | 12.9 ± 2.2       | < 0.001 |
| INR                  | 1.6 ± 0.7                     | 1.2 ± 0.2                       | 1.2 ± 0.3        | < 0.001 |
| aPTT, sec            | 45.5 ± 39.6                   | 28.2 ± 5.6                      | 28.4 ± 9.3       | < 0.001 |
| Base excess          | -5.3 ± 6.7                    | -3.4 ± 4.2                      | -0.7 ± 7.7       | < 0.001 |

Values are reported as mean ± standard deviation. Tests performed were ANOVAs, except for GCS and AIS head and neck Kruskal-Wallis test. *only one case. aPTT, activated partial thromboplastin time; INR, international normalized ratio; TBI, traumatic brain injury.
Mean SBP on hospital arrival was 83.1 ± 12.9 in group 1 vs 132.5 ± 19.4 in group 2 vs 119.4 ± 25.8 mmHg in group 3 (p < 0.001). As depicted in Fig. 1, SBP decreased during the pre-hospital phase in group 1 (relative difference between SBP on scene and SBP on admission = -12%±23%; p < 0.001), while it increased in group 2 and remained stable in group 3 (+17%±30% with p < 0.001 and +2%±16% with p = 0.531, respectively).

Patients in group 1 received more crystalloid fluids during the pre-hospital treatment as compared to patients in group 2 and 3 (p = 0.018 and p = 0.012, respectively) (Table 2). On hospital arrival, patients in group 1 as compared to patients in group 2 and 3 had higher INR (p = 0.002 and p = 0.001, respectively), lower haemoglobin values (p < 0.001 and p < 0.001, respectively) and lower base excess (p = 0.070 and p = 0.001, respectively) (Table 3). We found a significant difference in the rate of hypothermia (defined as core body temperature < 35 °C) on hospital arrival between the three groups (41% vs 35% vs 21%, for group 1 vs 2 vs 3, p = 0.029). Patients in group 1 had a mortality rate of 24% compared to 10% and 1% in group 2 and 3, respectively (p < 0.001). Mortality stratified by categories of SBP values on hospital arrival for patients with TBI (i.e. only group 1 and 2) is shown in Table 4.

There was no difference in the rate of pre-hospital intubation between TBI patients with and without admission hypotension (i.e. group 1 vs 2, 56 vs 47%, p = 0.380). In Table 5, patients with TBI and admission hypotension (i.e. patients in group 1) are subdivided into patients who were intubated on scene and patients who were not, and different parameters are compared between the two groups. No difference between the two subgroups was found regarding SBP on scene and on admission, pre-hospital fluid and vasopressor therapy, ISS, AIS of the different body regions, hemoglobin, coagulation parameters or base excess. Only the GCS was lower both on scene and on hospital admission in TBI patients who were intubated on scene.

Table 4
Mortality rate per level of systolic blood pressure (SBP) on hospital arrival, only patients with traumatic brain injury, i.e. group 1 and 2

| SBP on hospital arrival | Died in hospital, n (%) |
|-------------------------|-------------------------|
| < 90 mmHg, n (%)        | 6 (25%)                 |
| 90–99 mmHg, n (%)       | 3 (30%)                 |
| 100–109 mmHg, n (%)     | 1 (13%)                 |
| 110–119 mmHg, n (%)     | 4 (25%)                 |
| ≥ 120 mmHg, n (%)       | 5 (7%)                  |

(p = 0.072, Pearson’s chi-squared test).
Table 5
Demographics, pre-hospital time, systolic blood pressure (SBP; pre-hospital and on admission), Glasgow Coma Scale (GCS; pre-hospital and on admission), selected pre-hospital therapeutic interventions, Injury Severity Score (ISS), Abbreviated Injury Scale (AIS) and selected laboratory values of patients with TBI and hypotension on hospital admission (group 1), subdivided between patients intubated and not intubated on scene.

| Parameter                              | TBI with hypotension (n = 50) | Pre-hospital intubation | p-value |
|----------------------------------------|-------------------------------|-------------------------|---------|
|                                        |                               | Yes                     | No      |         |
| Age, years, mean ± SD                  | 42.7 ± 19.6                   | 49.4 ± 18.6             | 0.243   |
| Female sex, n (%)                      | 7 (32%)                       | 9 (32%)                 | 1.000   |
| Pre-hospital SBP, mmHg, mean ± SD      | 102.0 ± 22.8                  | 103.8 ± 29.3            | 0.844   |
| SBP on hospital arrival, mmHg, mean ± SD | 81.1 ± 12.2                  | 84.8 ± 13.4             | 0.325   |
| Pre-hospital GCS, mean ± SD           | 5.8 ± 3.                      | 11.8 ± 3.2              | < 0.001 |
| GCS on hospital arrival, mean ± SD    | 3.3 ± 1.3                     | 12.0 ± 3.5              | < 0.001 |
| Crystalloid fluids, ml, mean ± SD     | 636 ± 303                     | 821 ± 346               | 0.194   |
| Vasopressor therapy, n (%)            | 1 (7%)                        | 3 (16%)                 | 0.613   |
| Total pre-hospital time, min, median (range) | 82 (33–221)                  | 82.5 (30-1560)          | 0.881   |
| ISS, mean ± SD                         | 41.1 ± 13.3                   | 44.6 ± 20.2             | 0.930   |
| AIS head and neck                      | 3.9 ± 0.9                     | 4.5 ± 1.1               | 0.054   |
| AIS face                               | 2.5 ± 0.7                     | 4.0 ± 1.2               | 0.133   |
| AIS thorax                             | 3.8 ± 0.8                     | 3.7 ± 0.9               | 0.846   |
| AIS abdomen                            | 3.2 ± 0.9                     | 3.6 ± 1.1               | 0.467   |
| AIS extremities                        | 3.7 ± 0.9                     | 3.6 ± 1.1               | 0.752   |
| AIS external                           | 3 *                           | -                       | -       |

* only one case. aPTT, activated partial thromboplastin time; INR, international normalized ratio. Tests performed were independent samples t-tests, except for pre-hospital GCS and GCS on hospital arrival, crystalloid fluids, total pre-hospital time, ISS and AIS head/neck, for which Mann-Whitney U test was used and for vasopressor therapy and female sex, for which Fisher's exact test was applied.

Tests performed were paired samples t-tests. Error bars represent standard deviation. TBI, traumatic brain injury.

AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; SBP, systolic blood pressure.
### Table

| Parameter           | TBI with hypotension (n = 50) |
|---------------------|-------------------------------|
|                     | Pre-hospital intubation       |
|                     | Yes                           | No               | p-value |
| Hemoglobin, g/dl    | 11.3 ± 2.7                    | 10.4 ± 2.8       | 0.221   |
| INR                 | 1.4 ± 0.6                     | 1.7 ± 0.7        | 0.254   |
| aPTT, sec           | 34.3 ± 21.6                   | 54.7 ± 48.6      | 0.135   |
| Base excess         | -6.3 ± 5.1                    | -4.6 ± 7.7       | 0.377   |

* only one case. aPTT, activated partial thromboplastin time; INR, international normalized ratio. Tests performed were independent samples t-tests, except for pre-hospital GCS and GCS on hospital arrival, crystalloid fluids, total pre-hospital time, ISS and AIS head/neck, for which Mann-Whitney U test was used and for vasopressor therapy and female sex, for which Fisher's exact test was applied.

Tests performed were paired samples t-tests. Error bars represent standard deviation. TBI, traumatic brain injury.

AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; SBP, systolic blood pressure.

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### Classification trees

One of the ten classification trees is shown as an example in Fig. 2. The mean sensitivity of the ten classification trees (applying them to the testing sets) was 38% [95% confidence interval (CI) 23%-54%] for TBI with admission hypotension and 54% (95% CI 41%-66%) for TBI without admission hypotension; specificity to detect patients without TBI was 85% (95% CI 82%-88%). The GCS was the only variable selected in all ten classification trees and a cut-off of 11 resulted to be the major discriminant between patients with and without TBI (first node of the tree; high discriminant ability reflected by the long branch). For further discrimination between TBI patients with or without admission hypotension, variable selection by the classification trees was inconsistent (supplemental table 1); following GCS, the most frequently selected variables were ISS, AIS abdomen and AIS extremities.

### Discussion

We found that half of the patients suffering multi-trauma in the mountains had concomitant TBI. One third of them was hypotensive with SBP ≤ 110 mmHg on hospital arrival, despite they received more fluids pre-hospitally than multi-trauma patients without admission hypotension. Hypotensive multi-trauma patients with TBI were more severely injured, had a more severe coagulopathy, lower hemoglobin levels and lower base excess values; body temperature was lower at hospital arrival. Hypotensive patients with TBI had the highest mortality rate compared to non-hypotensive multi-trauma patients with TBI and
multi-trauma patients without TBI. No single variable or set of variables could reliably predict admission hypotension in multi-trauma patients with TBI.

Outdoor activities in the mountains have gained popularity over recent years. In parallel, the number of SAR missions in mountainous environments has increased and the proportion of potentially life threatening injuries has notably risen. Data on TBI in severely injured trauma patients in mountainous areas is scarce. We found an incidence of TBI of about 50% among mountain multi-trauma patients, which is comparable to the rate of TBI among severely injured patients in urban or suburban areas. The major cause leading to TBI in mountain accidents was fall during hiking.

Hypotension is common in severely injured patients and is tolerated to a certain degree in order to avoid the adverse effects of early and high-dose fluid resuscitation. This concept of “permissive hypotension” is contraindicated in patients with TBI because the maintenance of an adequate perfusion is essential to ensure tissue oxygenation of the injured central nervous system and to avoid secondary brain injury. The current guidelines of the Brain Trauma Foundation recommend to maintain SBP at ≥ 100 mmHg for patients 50 to 69 years old and at ≥ 110 mmHg for patients 15 to 49 or over 70 years old. We found that one third of multi-trauma patients rescued in mountainous environment with TBI had SBP ≤ 110 mmHg on hospital arrival, in agreement with published data on urban trauma patients. These patients (group 1) had a marked drop of their SBP during the pre-hospital phase from a mean SBP of about 100 mmHg on scene to about 80 mmHg on hospital arrival, even though these patients received more aggressive fluid resuscitation as compared to the other groups of trauma patients. This might be due to several reasons. First, patients with TBI and admission hypotension were more severely injured and had a higher mean ISS compared to the other groups. We suspect that these patients had more severe traumatic bleeding, as they had lower hemoglobin levels, lower base excess values and more severe coagulopathy on hospital arrival, and hemorrhage is the most frequent cause of hypotension in trauma patients. Yet, the higher ISS was mainly due to a higher AIS of the head/neck body region, where severe traumatic bleeding is relatively uncommon. Second, the drop of SBP during the pre-hospital phase could indicate that the treatment performed on scene was either insufficient or that no other treatment was feasible. Stopping the bleeding whenever possible and the administration of fluids (and possibly vasopressors) are the main options to maintain or augment blood pressure. Patients in with TBI and admission hypotension received significantly more fluids, though the fluid administration in all three patient groups was conservative with volumes of far less than one liter. Vasopressors were seldomly administered. The administration of vasopressors to maintain a sufficient cerebral perfusion pressure could play an important role in the treatment of multi-trauma patients with TBI, in particular in mountain SAR operations with prolonged pre-hospital times. Vasopressors allow to maintain target blood pressure and at the same time to limit the amount of fluid and the negative consequences associated with an excessive volume therapy (such as dilution coagulopathy, interstitial edema or hypothermia). There is ongoing controversy regarding the role of vasopressor therapy in trauma patients. Current guidelines recommend the administration of vasopressors in addition to fluids to maintain target SBP in the presence of life-threatening hypotension and recent studies on the use of vasopressin in trauma patients with hemorrhagic shock are promising. A third factor
that could explain the drop in SBP during the pre-hospital phase in patients with TBI and admission hypotension is the induction of anesthesia and intubation on scene. Yet, the difference in the rate of pre-hospital intubation between TBI patients with and without admission hypotension was not different. Also, when comparing TBI patients with admission hypotension who were intubated on scene with TBI patients with admission hypotension who were not intubated on scene, no difference in SBP on admission was found.

We found that more than one third of patients in group 1 and 2 were hypothermic (body temperature < 35 °C) on hospital arrival while the rate of admission hypothermia was low in patients without TBI (group 3). This difference could be caused by the higher rate of anesthesia in group 1 and 2 compared to group 3. General anesthetics greatly impair thermoregulation, reducing the thresholds for vasoconstriction and shivering,(31) increasing the risk of hypothermia. Hypothermia is an independent predictor of mortality in trauma (32, 33) and hypothermia prevention is paramount, although often disregarded during the initial resuscitation and particularly difficult in the harsh environment encountered in mountain rescue.

We sought factors that could predict admission hypotension in order to identify at risk patients on scene and eventually adopt a more aggressive treatment. We used a relatively novel method in the field of medicine, i.e. classification trees.(13) Although a pre-hospital GCS of ≤ 11 could expectedly discriminate between patients with and without TBI, no single variable or any set of variables easily obtainable in the pre-hospital setting were able to predict admission hypotension with a reasonable sensitivity and specificity. Apart from GCS, the ISS and the AIS abdomen and AIS extremities were the variables most frequently selected in the classification trees. Both, the abdomen and the extremities can be a source of major bleeding, which affirms that hemorrhage is probably the main cause of hypotension multi-trauma patients with TBI and aggressive treatment of bleeding is paramount.

Limitations

First, the number of cases collected in the IATR is limited when compared to the large data sets of urban trauma cases. Second, some data were missing, which is a limitation inherent to almost all registries. Both limitations curb the possibility to draw specific treatment protocols for mountain trauma causalities from our analysis. This highlights the need to continue to prospectively collect high quality data on trauma patients in mountainous and remote areas to perform further in-depth analyses using a larger sample size. Third, in the IATR, head and neck injuries are grouped in a single category (head/neck) and therefore the rate of isolated or concomitant spinal cord injuries, which could contribute to hypotension and hypothermia, is unknown.

Conclusion

Multi-trauma in the mountains goes along with severe TBI in almost 50%. One third of patients with TBI is hypotensive on hospital arrival and this is associated with a worse outcome. No single variable or set of variables easily obtainable at scene was able to predict admission hypotension in TBI patients. Whether
more aggressive pre-hospital volume resuscitation or vasopressor administration can improve survival in these patients needs to be demonstrated in further studies.

**List Of Abbreviations**

AIS abbreviated injury scale

aPTT activated Partial Thromboplastin Time

ATLS Advance Trauma Life Support

BE base excess

GCS Glasgow Coma Scale

IATR International alpine trauma registry

INR International normalized ration

ISS injury severity score

SBP systolic blood pressure

TBI traumatic brain injury

**Declarations**

*Ethics approval and consent to participate*

The International Alpine Trauma Registry was approved by the ethics committee of the Bolzano Hospital, Italy (n. 27-2010).

*Consent for publication*

Not applicable.

*Availability of data and materials*

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

*Competing interests*

The authors declare that they have no competing interests.

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Authors’ contributions

SR, MM, PM, HB and GS conceived the study. TdC provided statistical advice on study design and analyzed the data. The IATR study group collected data. SR drafted the manuscript, and all authors contributed substantially to its revision. SR takes responsibility for the paper as a whole.

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Figures

Figure 1

Systolic blood pressure (SBP) change from pre-hospital to on hospital arrival, subdivided by the three groups. Tests performed were paired samples t-tests. Error bars represent standard deviation. TBI, traumatic brain injury.
Figure 2

Classification tree to predict traumatic brain injury (TBI) with and without hypotension and no TBI. AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; SBP, systolic blood pressure.

Supplementary Files

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- Supplementaltable1.docx