Mortality in Polytrauma Patients with Moderate to Severe TBI on Par with Isolated TBI Patients: TBI as Last Frontier in Polytrauma Patients.

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PII: S0020-1383(22)00004-3
DOI: https://doi.org/10.1016/j.injury.2022.01.009
Reference: JINJ 9949

To appear in: Injury

Accepted date: 2 January 2022

Please cite this article as: MJS Niemeyer MD, D Jochems MD, RM Houwert MD, PhD, MA van Es MD, PhD, LPH Leenen MD, PhD, Professor, KJP van Wessem MD, PhD, Mortality in Polytrauma Patients with Moderate to Severe TBI on Par with Isolated TBI Patients: TBI as Last Frontier in Polytrauma Patients., Injury (2022), doi: https://doi.org/10.1016/j.injury.2022.01.009

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Highlights

- ICU mortality rates are shifting towards TBI as ARDS, Exsanguination and MOF as mortality causes are in decline.
- This research compares Isolated TBI with polytrauma TBI, showing comparable mortality.
- These results confirm that TBI is a rising concern, thus stressing TBI as the last frontier in acute care.

Mortality in Polytrauma Patients with Moderate to Severe TBI on Par with Isolated TBI Patients: TBI as Last Frontier in Polytrauma Patients.

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Abstract

Background: Mortality caused by Traumatic Brain Injury (TBI) remains high, despite improvements in trauma and critical care. Polytrauma is naturally associated with high mortality. This study compared mortality rates between isolated TBI (iTBI) patients and polytrauma patients with TBI (pTBI) admitted to ICU to investigate if concomitant injuries lead to higher mortality amongst TBI patients.

Methods: A 3-year cohort study compared polytrauma patients with TBI (pTBI) with AIS head ≥3 (and AIS of other body regions ≥3) from a prospective collected database to isolated TBI (iTBI) patients from a retrospective collected database with AIS head ≥3 (AIS of other body regions ≤2), both admitted to a single level-I trauma center ICU. Patients <16 years of
age, injury caused by asphyxiation, drowning, burns and ICU transfers from and to other hospitals were excluded. Patient demographics, shock and resuscitation parameters, multiple organ dysfunction syndrome (MODS), acute respiratory distress syndrome (ARDS), and mortality data were collected and analyzed for group differences.

**Results:** 259 patients were included; 111 pTBI and 148 iTBI patients. The median age was 54 [33-67] years, 177 (68%) patients were male, median ISS was 26 [20-33]. Seventy-nine (31%) patients died. Patients with pTBI developed more ARDS (7% vs. 1%, p=0.041) but had similar MODS rates (18% vs. 10%, p=0.066). They also stayed longer on the ventilator (7 vs. 3 days, p=<0.001), longer in ICU (9 vs. 4 days, p=<0.001) and longer in hospital (24 vs. 11 days, p=<0.001). TBI was the most prevalent cause of death in polytrauma patients. Patients with pTBI showed no higher in-hospital mortality rate. Moreover, mortality rates were skewed towards iTBI patients (24% vs. 35%, p=0.06).

**Discussion:** There was no difference in mortality rates between pTBI and iTBI patients, suggesting TBI-severity as the predominant factor for ICU mortality in an era of ever improving acute trauma care.

**Keywords**
TBI, polytrauma, mortality, ICU, acute care, multitrauma

**Introduction**
Traumatic brain injury (TBI) poses a major global health challenge with the highest morbidity and mortality rates among trauma patients, estimated at 69 million patients suffering from severe TBI per annum[1]. In Europe, TBI is the primary cause for disability under the age of 40. These patients endure time-, resource- and dedication-consuming treatments, with annual costs exceeding €33 billion euros ($37 billion dollars) in Europe[2]. TBI has a tremendous and long-lasting effect on these patients and their families[3].
Treatment of severely injured patients demands specialized and well-developed trauma and intensive care unit (ICU) systems. These were successfully developed over the previous decades to improve morbidity and mortality in polytrauma patients[4]. Such advancements may have contributed to the decline in mortality from exsanguination, acute respiratory distress syndrome (ARDS) and multi-organ dysfunction syndrome (MODS), leaving central nervous system-related mortality as most prevalent cause of death in trauma[5,6].

Prevention of secondary brain injury- caused by coagulopathy, hypotension, fever and hypoxia, which initiate a sequence of ischemic and damaging biochemical processes- is key in acute TBI-management[7]. All of these insults are commonly found in polytrauma patients, therefore polytrauma could worsen brain injury.

Critical trauma care is ever-improving and TBI-related mortality rates are rising compared to other causes of death in ICU[4,8,9]. Therefore, the question arose whether mortality in our TBI population is mainly associated with the severity of polytrauma injuries or with the severity of the brain injury. The principal aim of this research was to compare outcomes in polytrauma patients with TBI (pTBI) and patients with isolated TBI (TBI), both with moderate-to-severe TBI. The second aim was to assess TBI patient characteristics by comparing resuscitation parameters, MODS and ARDS incidences, and neurological outcomes.

Methods

Population and study setting
All patients with moderate or severe TBI, primarily admitted to the Emergency Department (ED) of the University Medical Center Utrecht between January 2015 and December 2017, were identified. Patients <16 years of age, injury caused by asphyxiation, drowning, burns and ICU transfers from and to other hospitals were excluded.

Patient identification and data on polytrauma patients with TBI (pTBI) were derived from a prospective ICU registration in our hospital and were compared to patients with isolated TBI (iTBI) who were identified retrospectively by the Trauma Care Network of the central Netherlands and were complemented by ED and patients records. The pTBI cohort included patients admitted to ICU with an Injury Severity Score (ISS) of >15 and an Abbreviated Injury Score (AIS) head ≥ 3. The iTBI cohort included patients with an AIS head ≥ 3 and the AIS in other body regions ≤ 2.

Clinical data and resuscitation variables

The primary outcome measure was in-hospital mortality rate. Secondary outcome measures were data on MODS, ARDS, inflammatory complications, days on the ventilator, ICU length of stay (ICU-LOS), hospital length of stay (H-LOS), and functional outcome, measured through the Glasgow Outcome Scale (GOS) scores at discharge. The GOS is measured on a scale ranging from: death (1), unresponsive wakefulness syndrome (2), severe disability (3), moderate disability (4), and minor to no disability (5)[10].

MODS was defined as a Denver Multiple Organ Failure score of >3, at least 48 hours after injury.[11] Denver MOF scores were preferred over the Sequential Organ Failure Assessment (SOFA), as the Glasgow Coma Score (GCS) forms a big part of the latter, and the GCS is unreliable in sedated patients[12]. ARDS was calculated and registered according to the Berlin definition[13]. Both daily MODS scores and ARDS were assessed in ICU up to day 28 of admission.
Data on trauma patients included: patient demographics (age and sex), mechanism of injury, injury severity score (ISS), abbreviated injury score (AIS) for different body regions, pelvic fractures, and shock parameters. Arterial blood gas, temperature and coagulation status were routinely collected as per ED protocol and were repeated in ICU. Urinary output was measured during the first hour after ICU admission. Registered interventions included emergency laparotomies and neurosurgical interventions by intracranial pressure (ICP) monitoring or decompressive craniotomy. Resuscitation products were registered during the first 24 hours of admission. Mortality rates were corrected for severity of head injury and age in two separate subanalyses.

Statistical analysis
Data were presented following STROBE guidelines. Statistical analyses were performed using IBM SPSS Statistics, version 25.0.0 (Armonk, NY, USA). Group differences were calculated using the Mann-Whitney U test for continuous data. Differences in distribution of dichotomous variables were calculated with Pearson’s Chi square test of homogeneity. Fisher’s exact test was used if expected cell count was less than five. Statistical significance was defined as P < 0.05. Results are displayed in N(%) or median [Q1,Q3].

Results
Over the three-year study period, 259 eligible patients were admitted to ICU with 111 pTBI patients and 148 iTBI patients. Most patients were male (68%), suffered from blunt force trauma (98%), with a median age of 54 [33-67] years, a median ISS of 26 [20-33], and a median AIS head of 4 [4-5]. Further demographics and AIS scores are displayed in Table 1. Fifty-three patients (21%) developed MODS and 11 (4%) developed ARDS during ICU stay. Seventy-eight (30%) of the patients suffered from infectious complications, of which the largest group of 34 (44%) patients suffered from a hospital-acquired-pneumonia. In total, 256
(98%) patients were intubated: Most (134 patients, 52%) were intubated in the prehospital setting and 83 patients (32%) in ED. Patients remained ventilated for a median of 4 [2-7] days. Median stay in ICU was 5 [4-11] days and subsequently 17 [11-29] days in hospital. Ultimately, 79 patients (31%) died in hospital.

Patients with iTBI vs. patients with pTBI

Patients with iTBI patients were significantly older (49 [32-62] vs. 57 years [38-70], p=0.009). Patients with pTBI, understandably, had higher ISS scores (33 [25-38] vs. 21 [17-26], p<0.001). Moreover, these patients seemed to have higher AIS head scores than iTBI (4 [4-5] vs. 4 [3-5], p=0.004) (Table 1, Figure 3). Thirty-one pelvic fractures were in pTBI patients. One pelvic fracture was scored as 2 (moderate) on the AIS extremities scale, thus classified as iTBI. On ED arrival pTBI patients had lower systolic and diastolic blood pressures, higher leucocyte counts, and higher PaCO\textsubscript{2} and PaO\textsubscript{2} levels. Patients with pTBI had longer prothrombin times; lower base deficits. Repeated ICU measurements were comparable regarding systolic and diastolic blood pressures, temperatures, hemoglobin and base deficits levels, and arterial PaO\textsubscript{2} levels between cohorts. Both cohorts were mildly acidotic on presentation but only iTBI patients were normalized on ICU admission. Arterial PaCO\textsubscript{2} levels were higher in patients with pTBI in ED but normalized clinically in most patients in ICU. Patients with iTBI had significant higher urine output after the first hour in the ICU (295 [120-413]ml vs. 150 [78-380]ml, p=0.005).

Patients with iTBI received significantly more neurosurgical interventions (43% vs. 22%, p<0.001). Patients with pTBI received significantly more units of crystalloids, packed red blood cells (PRBC), fresh frozen plasma (FFP), platelets and tranexamic acid in both the first 8 hours and 24 hours (Table 2).
Patients with pTBI suffered more from ARDS (7% vs 2%, p=0.041) and inflammatory complications (43% vs. 20%, p<0.001) but showed comparable MODS rates (18% vs 10% p=0.066). Patients with pTBI were intubated more often in the prehospital setting compared to iTBI patients, who were mostly intubated in the ED, OR or ICU (62% vs. 44%, p= 0.004). Patients with pTBI had to be ventilated longer (7 [3-12] vs. 3 [2-9] days, p<0.001); with longer ICU (9 [4-16] vs. 4 days [3-10], p<0.001), and hospital stays (24 [9-35] vs. 11 days [4-23], p<0.001). There was no significant difference in distribution of GOS between pTBI and iTBI cohorts (3 [2-3] vs. 3 [1-4], p=0.606). However, more patients with pTBI were discharged with severe disability (GOS 3; 57% vs. 33%, p<0.001). GOS distribution is shown in figure 1.

There was no difference in mortality rates between the pTBI and iTBI patient cohorts (24% vs. 35%, p=0.061) (table 3). Fatal intracranial pressure rises accounted for 19 (37%) deaths in the iTBI cohort, whereas the remaining 32 (63%) mortalities were withdrawn from life-sustaining treatment after a very poor neurologic prognosis was acknowledged. In the pTBI cohort, most patients (n=12, 44%) died due to fatal intracranial pressures. One patient died due to severe sepsis after gastric perforation and one died of brain ischemia following an aortic dissection. Twelve pTBI patients (44%) were withdrawn from life-sustaining treatment; 10 with poor neurological prognosis, two patients suffered cervical spinal cord injury-related respiratory insufficiency and one patient was withdrawn after a C1-C2 complete spinal cord injury.

The median number of days before death was 7 [2-9] in pTBI and 4 [2-8] days in iTBI patients. When mortality was stratified in age (<65 and ≥65 years), comparable rates were
observed in PTBI and ITBI cohorts for both age groups (<65: n=16, 19% vs. n=24, 24%, p=0.435 and ≥65: n=11, 42% vs. n=28, 61%, p=0.129). Correction for mortality and injury severity (AIS head) showed similar mortality rates when compared between PTBI and ITBI cohorts respectively in AIS 3 (10% vs. 9% p>0.999), AIS 4 (24% vs. 36% p=0.198) and AIS 5 (43% vs. 49% p=0.576).

Discussion

In this population of ICU admitted TBI patients, the in-hospital mortality following moderate-to-severe TBI was 31%. In-hospital mortality was similar for both groups, although PTBI patients suffered from concomitant injuries, stayed longer on the ventilator, in ICU and in hospital.

Polytrauma-associated mortality in the western world used to be predominantly caused by exsanguination, ARDS, multi-organ failure, and sepsis[14]. Yet nearly all deaths in this study were attributed to brain injury or related unfavorable prognosis. This trend has been previously observed in studies performed in our hospital with reported TBI-related mortality up to 59.9% as shown by Lansink et al. in the first decade of the 21st century, which increased to 76% in the period from 2013 to 2016 as shown by Jochems et al.[5,8]. We suppose that the successful decline in exsanguination may be attributed to successful implementations in damage control surgery, resuscitation protocols, and polytrauma management over the last two decades[9]. Furthermore, our trauma center employs dedicated polytrauma teams, who stay involved during the entire hospital stay in addition to a 24-hour attending trauma specialist regime; both presumably to good effect when observing critical processes in acute care in our trauma center[8,9,15]. However, this successful shift in outcomes poses new challenges, as patients - who would initially have succumbed to their polytrauma injuries - must now face TBI-related morbidities with meagre treatment options.
Our results showed comparable overall distributions in GOS scores between groups but showed more pTBI patients with GOS 3 (severe disability) on discharge. It is likely that many of these patients suffered invalidating injuries to extremities before discharge, resulting in a dependency in activities of daily living. Earlier research on polytrauma patients by Jochems et al. showed significant rises in GOS scores over a one-year period after rehabilitation. However, there was a small but comparable number of patients with GOS 2 (unresponsive wakefulness syndrome) in both groups[5]. (Figure 1) These limited numbers are in line with Dutch ethical and moral believes, who commonly share the idea that interminable unresponsiveness is not worth surviving for, resulting in patients (or their next of kin) preferring withdrawal of life sustaining treatment over extensive treatment when very poor neurological prognosis is imminent.

Treatment options for TBI are frustratingly limited. Therefore, treatment is focused on supporting cerebral oxygenation and perfusion[3,14]. Hypoxemia in pTBI patients (with or without chest injury) might have gone underrecognized in the prehospital setting and may show room for improvement, as 62% of the pTBI patients were intubated prehospitaly and measured worse PaO$_2$ and PaCO$_2$ levels upon ED presentation. In addition, the higher pTBI prehospital intubation rate may be explained by the higher number of thorax injuries. yet, neither could have caused the mortality rate to exceed the iTBI mortality rate. Furthermore, patients with pTBI in our population presumably lost more blood prior to hospital admission and in ED, as they recorded lower blood pressures on admission and received considerably more resuscitation products in both the first 8 and following 24 hours after admission. Prolonged periods of cerebral hypoperfusion potentially aggravates secondary insults[3,16]. Inversely, severe brain injury is also known to have effect on hemostatic and inflammatory
pathways as well[17]. Blood pressures remained stable on presentation and after resuscitation in both groups, which may indicate successful resuscitation among P TBI patients.

It may be disputed that P TBI patients were as injured as was previously claimed, based on the adequate hemoglobin levels and systolic blood pressures on ED presentation. (Table 2)

However, previous research in our hospital by Van Wessem et al. showed comparable patient and injury characteristics, and laboratory measurements. The index hospital is an urban situated level-1 trauma center with a relatively small service perimeter with short prehospital times; preventing physiologic measurements to worsen before presentation.[6] Our polytrauma patients were undeniably severely injured with an ISS of 33 (28% of them sustained pelvic fractures, 19% underwent urgent laparotomies, 22% emergency neurosurgical interventions), were mildly acidotic and coagulopathic, and were all admitted to the ICU.

Patients with ITBI showed significantly higher injury severity to the head and received nearly twice the number of neurosurgical interventions (43% vs. 22%). Yet we observed comparable overall mortality rates and when corrected for head injury severity (AIS head), despite concomitant injuries in P TBI patients. The AIS scoring method is a useful and validated instrument in trauma care for distinguishing injury type and severity but may not be applicable in relating AIS scores to TBI severity and outcomes. It is likely that ITBI and P TBI patients suffered from dissimilar injury types while scored within the same AIS category. For example, diffuse axonal injury and an epidural hematoma could be scored within the same severity category, but treatment and outcomes differ greatly.
The ITBI population was significantly older and while mortality rates were comparable in both groups, this could have account for the skewed mortality rate towards the ITBI patients. Age is an independent predictor of TBI-mortality; associated with frailty, anticoagulant use, and higher risks of low energetic falls with blunt force brain injury[18], while younger patients typically sustain sports, work, and traffic related injuries and are more prone to polytrauma injuries [19,20]. These different types of patient characteristics, trauma mechanisms and kinetics to the brain illustrate the heterogeneity of TBI and stress the difficulties in TBI approaches[20].

This study had certain limitations. Firstly, the retrospective nature of this study resulted in missing variables mostly in ITBI patients in the ED phase, rendering many included variables in the TBI database invalid. Secondly, mortality was not adjusted for pre-injury comorbidities and as patients in our study were relatively old, they possibly had important comorbidities, obscuring the relation between injury type and mortality. Although comparable mortality rates were observed when stratified in age, the age-adjusted and injury adjusted mortality samples may have yielded insufficient power for an adequate comparison. Thirdly, this single center observational study was performed in a level-1 trauma center servicing the central region of the Netherlands: An urban and densely populated area with short prehospital times in general. This data should therefore be handled with care, as the relation between patient characteristics (i.e. Trauma mechanism, age, and prehospital times) and outcomes may be inapplicable to trauma centers in other countries.

In conclusion, this study compared isolated TBI patients with polytraumatized TBI patients, both with moderate-to-severe brain injury, to investigate the extent to which extracranial injuries influence mortality rates in an era of rising TBI-related mortality. No significant
distinction was observed in mortality between polytrauma patients and patients with isolated TBI, suggesting that mortality is predominantly related to TBI severity regardless of extracranial injuries. This research shows potential signs for improvements in prehospital intubation and oxygenation therapy among polytraumatised TBI patients.

Presented at

Annual Dutch association for Traumasurgery | oral presentation | Januari 24, 2020 (Postponed indefinitely) 21st European Congress of Trauma & Emergency Surgery (ECTES 2020) | April 26–28, 2020 • Oslo/Norway | oral presentation (accepted)

Level of evidence

level III, retrospective cohort study

Article type

Original Article, prognostic/epidemiologic research

Ethical approval

Waivers of consent for rTBI and iTBI cohorts were approved by our institutional review board. (reference number: WAG/mb/16/026664 & WAG/mb/16/025499).

Declaration of Competing Interest

The authors declare no conflict of interest, financially or otherwise.

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| Table 1. Baseline variables | Total (n=259) | Polytrauma TBI (n=111) | Isolated TBI (n=148) | P value |
|----------------------------|--------------|------------------------|----------------------|---------|
| **Median [Q1-Q3]**         |              |                        |                      |         |
| Age                        | 54 [33-67]   | 49 [32-62]             | 57 [38-70]           | 0.009*  |
| ISS                        | 26 [20-33]   | 33 [25-38]             | 21 [17-26]           | <0.001* |
| AIS head                   | 4 [4-5]      | 4 [3-5]                | 4 [4-5]              | 0.004*  |
| Median                     | 116.09       | 140.44                 |                      |         |
| Mean rank                  |              |                        |                      |         |
| AIS face                   | 0 [0-2]      | 0 [0-2]                | 0 [0-2]              | 0.128   |
| AIS chest                  | 0 [0-3]      | 3 [2-3]                | 0 [0-0]              |         |
| AIS abdomen                | 0 [0-0]      | 0 [0-2]                | 0 [0-0]              |         |
| AIS extremities/pelvis     | 0 [0-2]      | 2 [0-3]                | 1 [0-1]              |         |
| AIS external               | 1 [0-1]      | 0 [0-1]                | 1 [0-1]              |         |
| Number (%)                 |              |                        |                      |         |
| Sex (%male)                | 177 (68)     | 83 (75)                | 94 (64)              | 0.054   |
| MOI (%blunt)               | 253 (98)     | 107 (96)               | 146 (99)             | 0.233   |
| Prehospital intubation     | 134 (52)     | 69 (62)                | 65 (44)              | 0.004*  |
| Pelvic fracturea           | 32 (12)      | 31 (28)                | 1 (1)                | <0.001* |
| Emergency department       |              |                        |                      |         |
| SBP (mmHg) | 130 [108-150] | 120 [100-136] | 140 [120-160] | <0.001* |
|----------------|----------------|----------------|----------------|----------|
| DBP (mmHg) | 79 [60-90] | 73 [54-85] | 80 [70-90] | 0.003* |
| Hb (mmol/l) | 8.2 [7.4-9.1] | 7.9 [7.2-8.9] | 8.2 [7.8-9.1] | <0.001* |
| Leucocytes (x10^9/L) | 12.3 [8.3-17.4] | 14.5 [9.8-20.4] | 10.7 [7.6-15.2] | <0.001* |
| Platelets (x10^9/L) | 220 [185-275] | 223 [185-278] | 219 [187-268] | 0.801 |
| PT | 14.7 [13.8-16.2] | 15.4 [14.5-17.6] | 14.1 [13.6-15.3] | <0.001* |
| pH | 7.34 [7.29-7.39] | 7.33 [7.28-7.38] | 7.35 [7.29-7.40] | 0.084 |
| PaCO2 (mmHg) | 46 [41-52] | 48 [43-54] | 45 [40-50] | 0.007* |
| PaO2 (mmHg) | 208 [122-307] | 180 [101-286] | 225 [136-316] | 0.023* |
| BD (mmol/L) | 2.0 [1-5] | 3.0 [0-7] | 1.0 [2-4] | <0.001* |
| Bicarbonate (mmol/L) | 24 [21-26] | 23 [20-25] | 25 [22-27] | <0.001* |
| INR | 1.07 [1.00-1.20] | 1.10 [1.04-1.23] | 1.01 [0.99-1.13] | <0.001* |

Intensive care unit

Median [Q1-Q3]

| SBP (mmHg) | 122 [105-139] | 119 [104-137] | 125 [107-142] | 0.256 |
|----------------|----------------|----------------|----------------|----------|
| DBP (mmHg) | 64 [56-73] | 65 [56-72] | 64 [57-75] | 0.647 |
| Temperature (°C) | 35.1 [34.2-35.8] | 35.0 [34.2-35.7] | 35.1 [34.2-35.9] | 0.550 |
| Hb (mmol/l) | 7.7 [7.0-8.4] | 7.6 [6.8-8.2] | 7.8 [7.0-8.4] | 0.111 |
| pH | 7.35 [7.29-7.40] | 7.33 [7.28-7.38] | 7.36 [7.31-7.41] | 0.007* |
| PaCO2 (mmHg) | 42 [38-46] | 43 [39-48] | 41 [37-46] | 0.026* |
| PaO2(mmmHg) | 142 [109-189] | 140 [105-182] | 147 [110-195] | 0.164 |
| BD (mmol/L) | 3.4 [1-5.4] | 3.5 [1.8-5.5] | 3.1 [0.7-5.2] | 0.065 |
| Bicarbonate (mmol/L) | 22 [21-24] | 22.4 [21-24] | 22.5 [21-25] | 0.335 |
| Urinary production (mL) | 220 [100-400] | 150 [78-380] | 295 [120-413] | 0.005* |

Abbreviations: MOI: Mechanism of injury. ISS: Injury Severity Score. AIS: Abbreviated Injury Scale. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, PT: Prothrombin time, PaCO2: Partial pressure of arterial Carbon Dioxide, PaO2: Partial pressure of arterial Oxygen, BD: Base deficit, INR: International Normalised Ratio.

* Statistically significant (P <0.05)
a: One pelvic fracture in the iTBI was classified as a mild injury according to the AIS.
b: Total UP production registered in first hour after ICU admission.

Table 2. Interventions and resuscitation

| Number (%) | Total n= 259 | Polytrauma TBI n= 111 | iTBI n= 148 | P value |
|------------|--------------|-----------------------|------------|---------|
| Urgent laparotomy | 21 (8) | 21 (19) | 0 (0) | <0.001* |
| Neurosurgical intervention | 87 (34) | 24 (22) | 63 (43) | <0.001* |
| PRBC (n)a | | | | |
| < 8 hours | 62 (24) | 48 (43) | 14 (10) | <0.001* |
| < 24 hours | 110 (43) | 51 (46) | 23 (16) | <0.001* |
| FFP (n)a | | | | |
| < 8 hours | 50 (19) | 42 (38) | 8 (5) | <0.001* |
|                | < 24 hours | < 8 hours | < 24 hours | <0.001* |
|----------------|------------|-----------|------------|---------|
| **Platelets (n)\(^a,b\)** |            |           |            |         |
| < 8 hours      | 12 (5)     | 11 (10)   | 1 (1)      | <0.001* |
| < 24 hours     | 38 (15)    | 24 (22)   | 14 (10)    | 0.008*  |
| **Tranexamic acid (n)\(^a\)** |            |           |            |         |
| < 8 hours      | 123 (48)   | 69 (62)   | 54 (37)    | <0.001* |
| < 24 hours\(^c\) | 119 (46)   | 66 (60)   | 53 (36)    | <0.001* |

**Median [Q1-Q3]**

|                | < 8 hours | < 24 hours | <0.001* |
|----------------|-----------|------------|---------|
| **Crystalloids (L)\(^d\)** |          |            |         |
| < 8 hours      | 2.6 [1.0-5.0] | 4.4 [2.5-6.6] | 1.5 [0.5-3.2] | <0.001* |
| < 24 hours     | 4 [1.8-7.3]  | 7.2 [4.7-10.3] | 2.5 [1.0-4.3]  | <0.001* |

Abbreviations: **PRBC**: Packed red blood cells, **FFP**: Fresh frozen plasma,
* Statistically significant (P <0.05)

a: Displayed as number of patients receiving transfusion with respective of total percentage of administered units within cohort (%).
b: One unit contains material from 5 donors.
c: Lower frequencies <24h compared to <8h were caused by deceased patients between 8 and 24h after admission.
d: Prehospital fluids were excluded.

**Table 3. ICU outcomes**

|                | Total n= 259 | Polytrauma TBI n= 111 | iTBI n= 148 | P value |
|----------------|-------------|-----------------------|-------------|---------|
| **Median [Q1-Q3]** |            |                       |             |         |
| Days on ventilator | 4 [2-7]     | 7 [3-12]              | 3 [2-9]     | <0.001* |
| Days in ICU       | 5 [4-11]    | 9 [4-16]              | 4 [3-10]    | <0.001* |
| Days in hospital  | 17 [11-29]  | 24 [9-35]             | 11 [4-23]   | <0.001* |
| **Number (%)**    |            |                       |             |         |
| MODS              | 53 (21)     | 20 (18)               | 15 (10)     | 0.066   |
| ARDS              | 11 (4)      | 8 (7)                 | 3 (2)       | 0.041*  |
| Infectious complications | 78 (30) | 48 (43)               | 30 (20)     | <0.001* |
| In-hospital mortality | 79 (31)   | 27 (24)               | 52 (35)     | 0.061   |

Qualitative variables are displayed as N(%) and quantitative variables are displayed as median [q1,q3] according to the distribution.
Abbreviations: **ICU**: Intensive Care Unit, **MODS**: Multi Organ Dysfunction syndrome, **ARDS**: Acute respiratory distress syndrome.
* Statistically significant (P<0.05)
Figure 1. GOS at discharge

GOS at Discharge

pTBI (n)  | iTBI (n)  |
---------|----------|
27/4/63  | 52/7/49  |
6/10     | 28/11    |

Figure 2. AIS head distribution between cohorts

Figure 3. Mortality stratified in AIShead
Mortality / AIShead

- % iTBI
- % polytrauma

III  IV  V