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Intraoperative Secondary Insults during Orthopedic Surgery in Traumatic Brain Injury

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Abstract

Background—Secondary insults worsen outcomes after traumatic brain injury (TBI). However, data on intraoperative secondary insults are sparse. The primary aim of this study was to examine the prevalence of intraoperative secondary insults during orthopedic surgery after moderate-severe TBI. We also examined the impact of intraoperative secondary insults on postoperative head computed tomography (CT) scan, intracranial pressure (ICP) and escalation of care within 24 hours of surgery.

Methods—We reviewed medical records of TBI patients 18 years old with Glasgow Coma Scale (GCS) score <13 who underwent single orthopedic surgery within 2 weeks of TBI. Secondary insults examined were: systemic hypotension (systolic blood pressure < 90mmHg), intracranial hypertension (ICP > 20mmHg), cerebral hypotension (Cerebral Perfusion Pressure < 50mmHg), hypercarbia (End-tidal CO₂ > 40mmHg), hypocarbia (End-tidal CO₂ < 30mmHg in absence of intracranial hypertension), hyperglycemia (glucose >200 mg/dL), hypoglycemia (glucose <60mg/dL) and hyperthermia (temperature > 38°C).

Results—78 patients [41(18–81) years, 68% male] met inclusion criteria. The most common intraoperative secondary insults were systemic hypotension (60%), intracranial hypertension and cerebral hypotension (50% and 45% respectively in patients with ICP monitoring), hypercarbia (32%) and hypocarbia (29%). Intraoperative secondary insults were associated with worsening of head CT, postoperative decrease of GCS score by 2 and escalation of care. After Bonferroni correction, association between cerebral hypotension and postoperative escalation of care remained significant (p<0.001).

Conclusions—Intraoperative secondary insults were common during orthopedic surgery in patients with TBI and were associated with postoperative escalation of care. Strategies to minimize intraoperative secondary insults are needed.

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Introduction

Traumatic brain injury (TBI) contributes to 30% of all injury related deaths in the United States and each year approximately 1.7 million people suffer a TBI leading to 275,000 hospitalizations and 52,000 deaths.¹ The estimated direct and indirect medical cost of TBI management amounts to greater than \$76.5 billion annually in the United States.² Secondary physiological insults such as hypotension, hypoxia, intracranial hypertension, hypercarbia and hypocarbia are known to adversely impact outcomes after TBI.^{3–8} Although previous studies have examined secondary insults in the pre-hospital period, during transportation to a tertiary care center, in the emergency department and in the intensive care setting,^{3–8} data on intraoperative secondary insults are limited.^{9,10} Moreover, patients with TBI frequently have associated orthopedic injuries requiring surgical intervention and data on secondary insults during orthopedic surgery in TBI and their impact on neurological outcomes are sparse and old.^{11–14}

The importance of intraoperative and anesthetic period in TBI management is increasingly being recognized¹⁵ and intraoperative data elements have recently been incorporated in the Common Data Elements (CDEs)¹⁶ for TBI recommended by the National Institute of Health (NIH) (<http://www.commondataelements.ninds.nih.gov/>). Given the advances in anesthetic and intraoperative management in general, and the modification of clinical care guidelines for TBI management (such as change in the recommended cerebral perfusion pressure {CPP} goal to 50–70 mmHg),¹⁷ it is important to quantify the current burden of intraoperative secondary insults and examine their impact. We have previously reported on intraoperative secondary insults during craniotomy for TBI^{9,10} but secondary insults in other surgical settings were not examined. The primary aim of this retrospective study was to examine the prevalence of intraoperative secondary insults during orthopedic surgery within 2 weeks of moderate-severe TBI. We also examined the effect of timing of orthopedic surgery on the secondary insults and the impact of intraoperative secondary insults on postoperative head computed tomography (CT) scan, intracranial pressure (ICP) and escalation of care within 24 hours.

Material and methods

Inclusion / Exclusion criteria

After Institutional Review Board approval, we retrospectively reviewed the electronic medical and anesthesia records of TBI patients 18 years with admission Glasgow Coma Scale (GCS) score <13 who underwent single orthopedic surgery for long bone or pelvic injuries within 2 weeks of TBI at Harborview Medical Center (level-1 trauma center) between 2007 and 2011. Patients < 18 years of age, those with admission GCS score 13, those who had associated chest / lung / spinal injuries those who underwent more than one extracranial surgery or surgery beyond 2 weeks of TBI were excluded. The requirement for written informed consent was waived by the IRB.

Data sources

The list of eligible patients was generated using the institutional trauma registry matched against the electronic anesthesiology database. The trauma registry was queried to generate a list of patients admitted during the study period with all of the following criteria: 1) ICD-9 (*International Classification of Diseases, ninth revision*) codes reflecting diagnoses of TBI related cerebral concussion, contusion, subarachnoid / subdural / extradural hemorrhage, and unspecified injury, 2) Age ≥ 18 years, 3) admission GCS score ≤ 13 and, 4) associated orthopedic injuries. This list was matched against the institutional anesthesiology database to identify the patients who underwent orthopedic surgery during that same hospital admission. Finally, patients who underwent multiple extracranial surgeries or surgery beyond 2 weeks of TBI were excluded to compile the final list of eligible patients.

Trauma registry records were used to abstract demographics and select clinical characteristics, including injury severity scores, and outcomes including discharge disposition, discharge GCS and mortality. Anesthetic and intraoperative physiological data was obtained from the electronic anesthesia records and immediate postoperative physiological data and intervention information from the intensive care unit records. The intraoperative physiological data was electronically captured every minute. However, the output of this data could be abstracted only for every 5-minute period. Official reports of head CT scans signed by attending radiologists, which were documented in the medical records were used to abstract radiographic diagnoses pertaining to TBI.

Institutional Anesthetic Management of TBI

During the study period, there was no standardized protocol for timing of orthopedic surgery in patients with TBI. All patients were cleared for surgery by a neurosurgeon based on stable neurological condition, CT scans and ICP while considering the urgency of orthopedic procedure. There was also no formal protocol for anesthetic care. However, consistent with best evidence, patients typically received general anesthesia with <1.0 minimum alveolar concentration isoflurane/ sevoflurane without nitrous oxide, or intravenous anesthesia with propofol infusion and intermittent boluses of rocuronium / vecuronium and opioid at the discretion of the attending anesthesiologist. Arterial catheters were used for continuous blood pressure monitoring in all patients and blood was sampled for PaCO₂, and glucose at the discretion of the anesthesia team. ICP monitoring was continued intraoperatively in patients who had ICP monitors in situ. Mannitol (0.5–1 g/kg) and / or hyperventilation were used to treat intracranial hypertension, if required. Isotonic non-glucose-containing intravenous fluids were used intraoperatively, and colloid use was infrequent. Transfusion of blood products and treatment of hypotension including the choice of vasopressor agents was at the discretion of the attending anesthesiologist. Normothermia was targeted by adjusting the temperature of forced air blankets and intravenous fluids. All patients received head CT scans immediately postoperatively.

Definitions

Secondary insults were defined as: *Systemic hypotension*: Systolic blood pressure <90 mmHg,¹⁸ *Cerebral hypotension (Low CPP)*: CPP < 50 mmHg,¹⁷ *Intracranial hypertension*: ICP > 20 mmHg,¹⁹ *Hypercarbia*: End-tidal CO₂ > 40 mmHg, *Hypocarbia*: End-

tidal CO₂ < 30mmHg in the absence of intracranial hypertension, *Hyperglycemia*: Blood glucose > 200mg/dL, *Hypoglycemia*: Blood glucose < 60mg/dL, *Hyperthermia*: Core temperature > 38°C

We used End-tidal CO₂ rather than PaCO₂ values to define hypercarbia and hypocarbia due to lack of sampling of arterial gases in majority of patients. Although the definition of hyperglycemia is frequently debated, we used a threshold of blood glucose > 200mg/dL because in clinical practice, values above this usually trigger treatment.

Patient Level Outcomes were defined as

- *Worse Postoperative CT scan*: new / increased cerebral edema, hemorrhage, mass effect, midline shift or hypodensity within 24 hours of surgery
- *Postoperative Intracranial hypertension*: ICP > 20mmHg within 24 hours of surgery requiring treatment
- *Postoperative decrease in GCS score*: best GCS score within 24 hours of surgery lower than preoperative GCS score by 2 points
- *Immediate postoperative escalation of care*: new onset institution of ICP monitoring or new treatment of intracranial hypertension / cerebral hypotension (low CPP) or unexpected mechanical ventilation or use of vasopressors.

Statistical Analysis

The analysis was performed using SPSS version 19 (SPSS Chicago, Illinois, USA). Descriptive statistics were used to describe preoperative clinical characteristics, CT scan lesions, timing of craniotomy or orthopedic surgery after TBI, intraoperative characteristic and secondary insults. Data are reported as number (percent), median (range), and mean (SD) as appropriate. Categorical data (use of inhalation anesthesia, presence or absence of intraoperative secondary insults – systemic hypotension, intracranial hypertension, cerebral hypotension, hypercarbia, hypocarbia, hyperthermia, hyperglycemia) for patients undergoing surgery within 2 days after TBI versus 3–14 days after TBI were compared using either Pearson Chi-Square or Fisher Exact Test. Independent-Samples Median Test was used for continuous variables (age, anesthesia and surgical time, total crystalloid, estimate blood loss, blood pressure, ICP, CPP, End tidal CO₂, temperature and blood glucose). Univariate analysis was used to test the association of intraoperative secondary insults and timing of orthopedic surgery with immediate postoperative neurological outcomes (worse head CT scan, intracranial hypertension and escalation of care). Bonferroni correction was used to account for multiple comparisons. Statistical significance was considered for values of P<0.05.

Results

During the study period 3,990 patients were admitted to Harborview Medical Center with TBI and polytrauma, and 480 (12%) of these patients underwent extracranial surgery. In total, 78 patients met all inclusion criteria for this study and were included in the final analysis.

Preoperative Characteristics (Table 1)

The preoperative characteristics are detailed in Table 1. Briefly, the median age of eligible patients was 41 (18–81) years and 53 (68%) of them were males. The median admission GCS was 3 (3–11) and the median pre-operative GCS was 10 (3–15). Forty-one (52%) patients had surgery within 2 days of TBI. There was no difference in the age or gender of patients who had surgery within 2 days or between 3–14 days after TBI (median age 34 [18–86] versus 47 [18–83] years; $p=0.11$ and 75% versus 59% males; $p=0.13$). Patients who underwent surgery 3–14 days after TBI had higher ISS score (47 [27–59] vs 34 [9–66], $p<0.001$), higher AIS score (5 [2–5] vs 4 [2–5], $p<0.001$) and lower preoperative hematocrit (27 [18–45] % vs 33 [22–41]%, $p=0.007$) compared to the patients who surgery within 2 days.

Intraoperative Characteristics (Table 2)

Seventy-four (94.8%) patients received inhalational anesthesia. There was no difference in the duration of anesthesia and surgery, choice of inhalational anesthesia, and total doses of narcotics between the patients who underwent early versus delayed surgery (Table 2). Patients in both groups were comparable in terms of intraoperative fluid volume administered, estimated blood loss, number of episodes of hypotension and intraoperative blood transfusion (Table 2).

Intraoperative Secondary Insults (Table 3)

Eighty-seven percent of the patients had at least one intraoperative secondary insult and 50% had two or more secondary insults. The most common intraoperative secondary insult was systemic hypotension, followed by intracranial hypertension and cerebral hypotension. Preoperative pneumonia was associated with intraoperative hypercarbia (0.04). There was no difference in intraoperative secondary insults based on the timing of orthopedic surgery except that hyperthermia was more common in patients who had surgery 3–14 days after injury compared to those who had surgery within 2 days. However, none of these patients had new onset intraoperative hyperthermia and 19% and 21% patients in the two groups respectively had preoperative hyperthermia ($p=0.55$). Serum sodium levels were documented for preoperative, intraoperative as well as postoperative for 48 patients. The median preoperative, intraoperative and postoperative sodium values for these patients were 140(132–157) mmol/L, 139(135–154) mmol/L and 140(131–150) mmol/L, respectively ($p=0.96$).

Association between Intraoperative Secondary Insults and Timing of Surgery on Immediate Postoperative Neurological Outcomes (Tables 4)

Of the 78 patients, worsening of postoperative head CT scan occurred in 6 (7%) patients and postoperative intracranial hypertension in 7 (8%) patients while 9 patients (11.5%) required escalation of care and 9 (11.5%) patients had a postoperative decrease of GCS score by 2 (Table 4). Intraoperative secondary insults that were associated with worsening of postoperative head CT scan were cerebral hypotension ($p=0.03$) and hypocarbia ($p=0.04$). Also, intraoperative cerebral hypotension was associated with postoperative decrease of GCS score by 2 ($p=0.01$). Postoperative escalation of care was associated with

intraoperative intracranial hypertension ($p=0.03$) and cerebral hypotension ($p<0.001$). The most common indication of postoperative escalation of care was intracranial hypertension which itself, was not associated with any specific intraoperative secondary insult. After Bonferroni correction for multiple comparisons, only the association between cerebral hypotension and postoperative escalation of care remained significant ($p<0.001$). There was no association between timing of surgery and postoperative worsening of head CT scan ($p=0.73$), intracranial hypertension ($p=0.18$) or escalation of care ($p=0.22$).

Postoperative GCS for the entire cohort was 9.5 (3–15) and was not significantly different from the preoperative GCS ($p=0.93$). Overall in-hospital mortality in this cohort was 2.5% and 17 (22%) patients had discharge GCS < 13. There was no association between intraoperative secondary insults and discharge GCS < 13 or in-hospital mortality. The low mortality in this cohort likely represents a selection bias because these patients probably underwent surgery since they were expected to survive. The patients with TBI and polytrauma who were unlikely to survive and had higher mortality rate, probably died before undergoing orthopedic surgery and were therefore not included in this cohort.

Fifteen (19%) patients in this cohort had pneumonia 2 (2.5%) had pleural effusion. None of the patients had Adult Respiratory Distress Syndrome (ARDS) but 2 patients suffered postoperative pulmonary embolism. One patient had sepsis.

Discussion

Our results indicate that in adult patients undergoing orthopedic surgery within 2 weeks of moderate-severe TBI (1) intraoperative secondary insults were common (2) the most common intraoperative secondary insult was systemic hypotension followed by intracranial hypertension, cerebral hypotension, hypercarbia and hypocarbia and, (3) intraoperative cerebral hypotension was associated with postoperative escalation of care. These findings provide an estimate of the burden of intraoperative secondary insults for TBI patients requiring orthopedic surgery and their association with immediate postoperative outcomes. Secondary insults can occur during any phase of TBI from pre-hospital to the intensive care but the intraoperative period is physiologically distinct. While TBI itself can lead to myocardial and pulmonary dysfunction,^{20,21} the anesthetic agents also affect cerebral^{22–24} and cardiovascular physiology.^{25,26} In addition, surgical intervention leads to fluid shifts and blood loss. Secondary insults during craniotomy for TBI have been reported,^{9,10,27–32} and as evidenced by our data here, secondary insults are also common during orthopedic surgery in patients with TBI and may contribute to worse outcomes. Therefore, anesthesiologists can potentially contribute to improving TBI outcomes by reducing the burden of secondary insults during craniotomy as well as extracranial surgery.

Systemic Hypotension and Intracranial Hypertension during Orthopedic Surgery in TBI

The higher prevalence of intraoperative systemic hypotension we observed in this series (60%) compared to the 7–43% reported by previous studies^{11–14} is likely due to more accurate capturing of physiological data with the electronic medical record system. All patients in our series had continuous arterial blood pressure recording but it is unclear if the previous studies used invasive or non-invasive blood pressure measurements. Nevertheless, it

is concerning that majority of patients were hypotensive under anesthesia irrespective of the timing of surgery. Unlike Townsend et al¹¹ who recommended delaying surgery to prevent secondary insults including hypotension, similar to our results, Velhams et al.¹² and Kalb et al.¹⁴ reported no difference in intraoperative hypotension based on timing of orthopedic surgery. Interestingly, the prevalence of intraoperative hypotension in this series is similar to the 65% prevalence we recently reported during craniotomy for TBI⁹ indicating that hypotension is a common problem, irrespective of the type of surgery in TBI patients. Avoidance of hypotension may be crucial even in patients undergoing surgery days after TBI because cerebral autoregulation may be impaired up to 2 weeks after moderate-severe TBI,³³ predisposing them to the risk of cerebral ischemia. Although we did not observe an association of intraoperative hypotension with postoperative head CT changes, intracranial hypertension or escalation of care, we cannot rule out cerebral ischemia due to hypotension because cerebral oxygenation and cerebral blood flow were not monitored during surgery nor can we rule out subtle brain damage or impact on long term neurological outcomes. Strategies for avoiding / rapidly treating systemic hypotension during extracranial surgery include adequate fluid / blood product replacement, avoiding anesthetic / narcotic overdose and rational use of inotropes / vasopressors.

Approximately half of the 20 patients in our series who had ICP monitoring, had intracranial hypertension and cerebral hypotension during general anesthesia. However, these estimates may be conservative since the majority of our patients did not have ICP monitoring. Increased ICP intraoperatively may be due to cerebral vasodilatory property of inhaled anesthetic agents,³⁴ inadvertent hypercarbia³⁵ and improper positioning.³⁶ Although majority of the patients in our series received volatile anesthetics, the anesthetic concentration was below 1.0 Minimum Alveolar Concentration (MAC) and hence, unlikely to contribute to ICP elevations.^{37,38} Using CPP < 70 mmHg to define low CPP based on the existing guidelines at that stage, Townsend et al¹¹ and Kalb et al¹⁴ reported 74% and 26% patients as having intraoperative cerebral hypotension. Using the current Brain Trauma Foundation guidelines definition, we observed that 45% patients had intraoperative CPP < 50 mmHg with no difference based on the timing of surgery. Avoidance of intracranial hypertension and maintenance of cerebral perfusion, two major goals of TBI management, seem to be relatively unmet intraoperatively.

Hypercarbia, Hypocarbica and Hyperglycemia during Orthopedic Surgery in TBI

Our observation of the high prevalence of inadvertent hypercarbia as well as hypocarbica calls for closer attention to intraoperative ventilatory management. While hypercarbia can lead to intracranial hypertension,³⁹ hypocarbica can cause cerebral vasoconstriction contributing to cerebral ischemia.⁴⁰ In the absence of intracranial hypertension, normocapnea is recommended in TBI patients, especially in the absence of monitoring of cerebral blood flow or cerebral oxygenation.¹⁵ While hypercarbia and hypocarbica may be more accurately defined by PaCO₂ values, we used end-tidal CO₂ values because PaCO₂ was documented in only 27 patients. Interestingly, none of the previous studies examined inadvertently high or low CO₂ values and our study provides the first estimates of these secondary insults during extracranial surgery in TBI. Intraoperative hyperglycemia was

uncommon in this series although glucose was monitored in less than half the patients during surgery.

Hyperthermia during Orthopedic Surgery in TBI

Hyperthermia is detrimental to the injured brain because it is associated with increased ICP and higher mortality.⁴¹ Perioperative hyperthermia may be due to infection, non-infectious inflammation, allergic reactions and blood in the fourth ventricle but intraoperative hyperthermia is rare, possibly due to the redistribution of body heat from the core to periphery and the impairment of thermoregulation by anesthetic agents.⁴² In fact, there may be a dose-dependent inhibition of fever with volatile anesthetics and opioids.⁴² In this cohort, hyperthermia was present preoperatively in 19% and 21% patients who underwent surgery 3–14 days and < 2 days after TBI. Under anesthesia, hyperthermia was still present in 16% and 7.5%, respectively but no patient had new onset hyperthermia. The significant difference in intraoperative hyperthermia between the patients undergoing surgery at different time periods may represent closer attention to temperature management under anesthesia in one group. Irrespective, our data suggest a need for closer monitoring of temperature under anesthesia.

Impact of Intraoperative Secondary Insults on Neurological Outcomes in TBI

Intraoperative secondary insults during craniotomy for TBI has been shown to be associated with increased risk of poor outcome.^{27,29,30,43} Townsend et al¹² observed that patients with intraoperative ICP > 20 mmHg or CPP < 70 mmHg during femur fixation had a low chance of good neurologic outcome after TBI. In univariate analysis, we found an association of ICP > 20 mmHg, CPP < 50 mmHg and hypocarbia with immediate postoperative radiological worsening of TBI and escalation of the level of care, irrespective of the timing of surgery. Intraoperative CPP < 50 mmHg was also associated with postoperative decrease of GCS score by 2 points. However, intraoperative secondary insults were not associated with mortality, discharge GCS < 13 or discharge disposition probably due to rapid correction of secondary insults under anesthesia and due to postoperative escalation of care incorporating appropriate interventions although this could also be due to relatively low mortality overall and small sample size. Moreover, after Bonferroni correction for multiple comparisons, only association between cerebral hypotension and postoperative escalation of care remained significant ($p < 0.001$).

Limitations

The limitations of this study include the retrospective study design and the reliance on medical records not designed for data collection specific to this study. The possibility of artifacts making into the electronic anesthesia records cannot be completely excluded. Also, there is no reliable method to eliminate these artifacts. Moreover, we did not analyze the impact of duration of each secondary insult on outcomes. It is possible that brief periods of secondary insults may cause less injury to the brain. Very few patients received intravenous anesthesia limiting our ability to compare anesthetic agents and few patients had ICP monitoring which may affect our estimates of intraoperative intracranial hypertension and cerebral hypotension. We cannot rule out more subtle neurological damage resulting from secondary insults and we do not have long-term outcome data. While there appears no

association between radiologic worsening and relatively coarse indices of outcome at this stage, there's the possibility that a more detailed functional assessment may reveal an association, which would require a prospective trial. We did not have the Therapeutic Intensity Level (TIL) scores. Instead, we used "escalation of care" as a measure of increase in the postoperative treatment intensity. However, it is difficult to ascertain whether the escalation of care was due to neurological worsening or altered physiological need as a result of exposure to anesthetic agents, narcotics or neuromuscular blocking agents. While the exact etiology of escalation in care may not be clear, in general, it would reflect a worse physiological status after exposure to anesthesia / surgery. Another limitation is the rather small number of patients to examine the impact of timing of surgery on outcomes. We performed Bonferroni correction to account for the multiple univariate associations. However, the Bonferroni correction is highly conservative and may fail to detect the differences. Larger studies would be needed to further confirm the association of intraoperative secondary insults with postoperative outcomes. Our results also need to be interpreted in light of the fact that the patients had recovered to variable degrees by the time of extracranial surgery and we cannot ascertain whether the secondary insults were better (or worse) tolerated by patients who have recovered to be extubated after TBI (compared to those who continued to remain intubated and required ICP monitoring). Despite the above limitations, this study highlights an important and under studied aspect of anesthetic care, which is typically not represented in studies of TBI.

In summary, despite the advancements in anesthetic care, intraoperative secondary insults were common during orthopedic surgery in patients with TBI and were associated with postoperative escalation of care. Strategies to minimize intraoperative secondary insults may potentially improve TBI outcomes.

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Table 1

Preoperative characteristics of patients with Traumatic Brain Injury (TBI) who underwent single orthopedic surgery within 14 days of moderate-severe TBI (n=78). Data are presented as number (%) or median (range).

Preoperative characteristics	
Age (years)	41 (18–81)
Male gender	53 (68%)
Admission Head Abbreviated Injury Scale (AIS)	4 (2–5)
Admission Injury Severity Score	35 (14–59)
Admission Glasgow Coma Scale (GCS) Score	3 (3–11)
Traumatic Brain Injury type	
Subarachnoid Hemorrhage	53 (68%)
Subdural Hemorrhage	14 (18%)
Contusion/concussion	8 (10%)
Other TBI	3 (3.8%)
Preoperative Glasgow Coma Scale (GCS) score	10 (3–15)
Preoperative Systolic Blood Pressure (mmHg)	120 (88–192)
Preoperative Intracranial Pressure (mmHg) (n=20)	11 (1–22)
Preoperative Cerebral Perfusion Pressure (mmHg) (n=20)	77 (49–118)
Preoperative Hematocrit (%)	30 (21–39)
Intubated and mechanically ventilated prior to surgery	53 (68%)
Craniotomy within the same 14 days	3 (4.2%)
Timing of surgery orthopedic surgery after TBI	
0–2 days	41 (52%)
3–14 days	37 (48%)

Table 2

Intraoperative characteristics based on timing of orthopedic surgery after moderate-severe Traumatic Brain Injury (TBI). Data are presented as number (%) or median (range).

	Total (n=78)	Orthopedic Surgery within 2 days of TBI (n=41)	Orthopedic Surgery 3–14 days after TBI (n=37)	P (95% CI)
Anesthesia Time (min)	196 (44–456)	199 (63–420)	192 (40–456)	0.36 (–28.26, 55.67)
Surgical Time (min)	136 (0–378)	142 (27–378)	126 (0–338)	0.07 (–22.25, 60.09)
Total Crystalloid (mL)	1553 (100–4500)	1850 (350–4500)	1500 (100–3800)	0.9 (–48.39, 884.23)
Estimated blood loss (mL)	100 (0–1000)	100 (0–1000)	75 (0–850)	0.3 (–83.71, 111.24)
Patients requiring Blood transfusion	9 (15.3%)	3 (3.8%)	6 (7.6%)	0.21 (–146.34, 49.46)
Inhalation Anesthesia	74 (94.8%)	38 (92%)	36 (97%)	0.6 (0.54, 14.92)
Fentanyl (mcg)	250 (0–750)	250 (0–600)	250 (0–750)	0.1 (–103.90, 36.40)
Hydromorphone (mg)	2 (0–7)	2 (0–7)	1.2 (0–6)	0.2 (–0.30, 1.62)
Phenylephrine (mcg)	300 (0–1824)	200 (0–1337)	400 (0–1824)	0.4 (–6.23, 2.05)
Episodes of hypotension	1 (0–26)	3 (0–26)	2 (0–17)	0.7 (–2.50, 3.52)

Table 3

Intraoperative Secondary Insult data for Orthopedic Surgery in Patients with moderate-severe Traumatic Brain Injury (n=78). Data are presented as number (%) or median (range).

	Overall N=78	Orthopedic Surgery within 2 days of TBI (n=41)	Orthopedic Surgery 3–14 days after TBI (n=37)	<i>P</i> (95% CI)
Systemic Hypotension (SBP <90 mmHg)	47 (60%)	25(61%)	22 (59%)	0.89 (0.38, 2.33)
Lowest SBP (mmHg)	50 (0–88)	87 (65–88)	78 (0–88)	0.66 (–6.77, 7.13)
Intracranial Hypertension (ICP >20mmHg)	10/20 (50%)	5/8 (62%)	5/12 (42%)	0.60 (0.24, 3.35)
Highest ICP (mmHg)	19 (10–44)	21 (14–44)	19 (10–38)	0.65 (–6.37, 10.62)
Cerebral Hypotension (CPP <50 mmHg)	9/20 (45%)	4/8 (50%)	5/12 (42%)	0.55 (0.17, 2.80)
Lowest CPP (mmHg)	56 (29–101)	51 (29–83)	58 (40–101)	0.65 (–22.79, 12.62)
Hypercarbia (ETCO ₂ > 40 mmHg)	25 (32%)	13 (32%)	12 (32%)	0.98 (0.50, 2.95)
Highest ETCO ₂ (mmHg)	51 (30–68)	42 (30–68)	42 (30–60)	0.50 (–4.38, 4.45)
Hypocarbica (ETCO ₂ < 30 (mmHg)	33 (29%)	11 (27%)	12 (32%)	0.23 (0.50, 3.47)
Lowest ETCO ₂ (mmHg)	31 (20–51)	31 (20–41)	31 (23–51)	0.72 (–3.54, 0.87)
Hyperthermia (core temperature >38°C)	9 (12%)	3 (7.5%)	6 (16%)	0.02 (0.09, 1.17)
Highest temperature (°C)	37.3 (35.6–39.1)	37.3 (36.5–38.3)	37.4 (35.6–39.1)	0.09 (–0.64, 0.11)
Hyperglycemia (Blood glucose >200 mg/dL)	2/30 (6.7%)	1/13(7.7%)	1/17(5.9%)	0.47 (0.05, 14.92)
Highest blood glucose (mg/dL)	129 (83–293)	148 (87–293)	122 (83–240)	0.14 (–23.00, 46.56)

SBP= Systolic Blood Pressure. ICP= Intracranial Pressure. CPP=Cerebral Perfusion Pressure. ETCO₂= End tidal CO₂

Table 4

Univariate analysis for association of intraoperative secondary insults and timing of orthopedic surgery with immediate postoperative neurological outcomes in patients with moderate-severe Traumatic Brain Injury (n=78). Data presented as p values for the relationship. (SBP = Systolic Blood Pressure, ICP = Intracranial Pressure, CPP = Cerebral Perfusion Pressure). After Bonferroni correction for multiple comparisons, only association between cerebral hypotension and postoperative escalation of care remained significant (p<0.001).

Intraoperative Secondary Insult	Worse Postoperative Head CT scan* (n=6)	Postoperative Intracranial Hypertension** (n=7)	Postoperative Escalation of Care*** (n=9)	Postoperative GCS decrease 2 (n=9)	Discharge GCS < 13 (n=15)
Systemic Hypotension (SBP < 90 mmHg) (n=47)	0.16	0.53	0.76	0.25	0.08
Intracranial Hypertension (ICP > 20mmHg) (n=10)	0.26	0.24	0.03	0.67	0.26
Cerebral Hypotension (CPP < 50mmHg) (n=9)	0.03	0.05	<0.001	0.01	0.79
Hypocarbica (End-tidal CO ₂ > 40mmHg) (n=25)	0.40	0.15	0.87	0.57	0.82
Hypocarbica (End-tidal CO ₂ < 30mmHg) (n=33)	0.04	0.18	0.30	0.79	0.72
Hyperglycemia (Blood Glucose>200mg/dL) (n=2)	0.90	0.89	0.12	0.17	0.29
Hyperthermia (Core Temperature > 38°C) (n=9)	0.40	0.38	0.70	0.33	0.81

* Worse Postoperative Head Computed Tomographic Scan: New / increased cerebral edema, hemorrhage, mass effect, midline shift or hypodensity within 24 hours of surgery

** Postoperative Intracranial Hypertension: Intracranial Pressure > 20 mmHg within 24 hours of surgery requiring treatment

*** Postoperative Escalation of care: New institution of ICP monitoring / treatment of intracranial hypertension / cerebral hypoperfusion or unexpected mechanical ventilation / use of vasopressors within 24 hours of surgery.