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The Association of Reamed Intramedullary Nailing and Long-Term Cognitive Impairment

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Abstract

Objectives—To examine the association of reamed intramedullary nailing (IMN) and long-term cognitive impairment in trauma intensive care unit (TICU) survivors.

Design—Prospective observational cohort.

Setting—Academic Level-1 Trauma Center.

Patients—173 patients with multiple trauma (Injury Severity Score (ISS) >15) who presented to a Level I TICU from July 2006 to July 2007 without evidence of intrancranial hemorrhage (ICH)

Intervention—None

Main Outcome Measure—Twelve-month cognitive impairment defined *a priori* as 2 neuropsychological test scores 1.5 SD below the mean or 1 neuropsychological test score 2 SD below the mean.

Results—108/173 patients (62.4%) were evaluated 12-months after injury with a comprehensive battery of neuropsychological tests. There were 18 patients who received a reamed IMN and 14/18 (78%) of these patients had cognitive deficit at follow-up. Fracture treatment with a reamed IMN

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was associated with long-term impairment (27.4% vs. 8.2%, p= 0.03). Multivariable logistic regression found that a reamed IMN (OR: 3.2, 95% CI: 0.95-10.9; p=0.06) was a moderate risk factor for the development of cognitive impairment 12-months after injury, after controlling for ISS, level of education, intra-operative hypotension, and duration of mechanical ventilation.

Conclusions—Fracture fixation with a reamed IMN is moderately associated with cognitive impairment in this cohort of multiple trauma patients without ICH at 1-year post-injury. Orthopaedic trauma research should continue to investigate a potential association of acute fracture management and long-term cognitive outcome.

Keywords

Reamed Intramedullary Nail; Long-Bone Fracture; Polytrauma; Long-Term Cognitive Impairment

Introduction

The effect of long-bone fracture care strategies in multiply injured trauma patients is of substantial concern to the treating surgeon[1]. Established literature and recommendations support aggressive management of lower extremity long-bone fractures in a majority of patients[2, 3]. The challenge is identifying those patients at greatest risk for poor outcome after sustaining severe musculoskeletal injuries. Multiple reports describing the psychological effects following musculoskeletal trauma show a strong association with outcome, even greater than that associated with Injury Severity Score (ISS) [4-6]. It would appear intuitive that the neuropsychological consequences of musculoskeletal trauma are of great interest to the orthopaedic surgeon, although it has been mentioned in previous accounts that this is not routinely taken into consideration in the orthopaedic literature[6].

The presence of concomitant head injury has been studied extensively in patients with femur fractures; however, the results are not conclusive[7-10]. Guidelines directing appropriate treatment have been established, especially in an era of “Damage Control Orthopaedics” (DCO)[11, 12]. Most recently, “early total care” with a reamed femoral intramedullary nail (IMN) for patients with a normal cranial computed tomography (CT) scan was advocated in the absence of significant contraindicating pathophysiology (i.e. acidosis, coagulopathy, severe chest trauma)[13].

While the presence of radiographically identified head injuries has been the focus of much investigation within a subset of the multiply injured patient population, certain reports suggest that a significant majority of trauma patients admitted to the hospital may sustain un-identified head injuries[14]. The long-term neurologic consequences of these injuries are not as clearly defined but may portend a marked degree of cognitive impairment. It appears imperative that the orthopaedic surgeon consider patients at risk for adverse cognitive outcomes in order to potentially modify certain treatment methods and provide appropriate neuropsychological referral. Therefore, the purpose of this study was to examine the association of a reamed IMN and long-term cognitive impairment 1-year following injury in adult trauma intensive care unit (TICU) survivors. We hypothesized that a reamed IMN would be a significant risk factor for cognitive impairment 1-year following injury, after controlling for potential confounding variables of injury severity[15], level of education, intra-operative hypotension,[7, 16] and duration of mechanical ventilation.[17]

Methods

Subjects

This study was conducted as part of a prospective, observational investigation of long-term cognitive impairment in TICU survivors. One hundred and seventy-three consecutive patients admitted to the TICU of an academic Level-1 Trauma Center were enrolled between July 2006 and June 2007. Inclusion criteria were as follows: English speaking adults aged 18 or older, a head computed tomography (CT) scan showing no intracranial hemorrhage (ICH), and an ISS score >15 (indicative of at least moderately severe trauma). Patients with a spinal cord deficit were excluded from the study. The inclusion of patients without ICH was established to identify a large population often dismissed as suffering from “mild” injuries and not in need of follow-up.[14, 18] Institutional Review Board (IRB) approval was obtained prior to study initiation.

In-hospital Procedures

Patient demographic and injury characteristics were recorded prospectively. These included age in years, gender, race, level of education, ISS score, and duration of mechanical ventilation in days. A concussion was documented if there was a history of loss of consciousness. Physiologic data at the time of admission in the emergency department (ED) was collected, including hematocrit, systolic blood pressure, pulse, Revised Trauma Score (RTS), and Glasgow Coma Scale (GCS). Total blood transfusion within the initial 24-hours of admission was calculated. Patients with a long-bone fracture (Orthopaedic Trauma Association (OTA) Classification 12, 22, 32, or 42) were recorded. Time from hospital admission to operative intervention was obtained from the medical record, and was defined as ≤24 hours or >24 hours. The presence of intra-operative hypoxia (SpO_2 <90%) or hypotension (systolic blood pressure <90 mmHg) at the initial operative intervention were documented from the official anesthesiology operative record. Fracture treatment with a reamed IMN was gathered from the treating surgeon’s operative report.

Patients were asked by study personnel the highest level of education that they had completed. In addition, a validated surrogate questionnaire, the short form of the Informant Questionnaire of Cognitive Decline in the Elderly (IQCODE-SF)[19], was used to assess preexisting cognitive impairment. Pre-existing cognitive impairment was defined as a score of >3.3 on the IQCODE-SF, consistent with previously employed methods[18].

Follow-Up Assessment and Criteria for Cognitive Impairment

Patients were evaluated approximately 12 months after hospital discharge with a battery of neuropsychological instruments. Testing measures included assessments for neuropsychological domains including global cognition (Mini Mental State Exam)[20], verbal and visual memory (Rey Auditory Verbal Learning Test, Rey Osterreith Complex Figure Test – Delay)[21, 22], visuo-spatial construction (Rey Osterreith Complex Figure – Copy)[22], processing speed (Digit Symbol Coding)[23], visual attention/verbal attention (Trailmaking Test A, Digit Span)[23, 24], and 2 dimensions of executive functioning – verbal fluency (FAS)[25], and set shifting (Trailmaking Test B)[23]. Additionally, depressive and post-traumatic stress disorder (PTSD) symptoms were assessed using the Beck Depression Inventory-II (BDI-II)[26] and the Davidson Trauma Scale (DTS)[27], respectively. These testing instruments have been validated and described in similar studies involving the trauma population[18]. The cognitive impairment status of each patient was determined by comparing their neuropsychological test scores to normative population data. Criteria for determining cognitive impairment were established *a priori* and were significantly more restrictive than commonly used definitions of impairment from related medical and neuropsychological literature.

Cognitive impairment was defined as having 2 neuropsychological test scores 1.5 Standard Deviations (SD) below the mean or 1 neuropsychological test score 2 SD below the mean. For the purposes of this investigation, patients who had abnormal neuropsychological test results but who did not meet the above stringent criteria were considered not impaired.

Data Management and Statistical Analysis

Descriptive statistics were used to summarize all study variables (means, SD, and frequency) and to determine the distribution of cognitive impairment and the use of a reamed IMN in the study population. All neuropsychological test scores were converted to T-scores for consistency. On the Mini Mental State Exam, T-scores were derived from the age and education adjusted norms of Crum et al [28]. For Trails A and B and the Verbal Fluency Test (FAS), T- scores adjusted for age, education, and gender were obtained from the Heaton et al manual [27]. Age corrected scaled scores for the Digit Span and Digit Symbol Coding (DSC) were obtained from the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III), while age norms from Spreen and Strauss[26] were used for the Rey Osterreith Complex Figure (Copy and 30 Minute Delay) and the Rey Auditory Verbal Learning Test (RAVLT).

Patient demographic, injury and surgical characteristics were compared by presence or absence of cognitive impairment using Chi-square or Fishers exact tests and Mann-Whitney U tests. Selected variables (age, sex, education, ISS score, hospital length of stay, mechanical ventilation days and time from hospital admission to operative intervention) were compared between the two groups of reamed IMN and non-IMN using Chi-square and Mann-Whitney U tests. Multivariable logistic regression analyses was used to model 12-month cognitive impairment as a function of IMN, education, injury severity, mechanical ventilation days, and intra-operative hypotension. The level of significance was set at $p \leq 0.05$. All statistical analyses were performed using Stata Version 11.0 (Stata Corp, College Station, TX).

Results

A total of 108 patients (67% of all eligible patients) were available for neuropsychological evaluation at 1-year follow-up. Baseline demographics and injury characteristics of patients (including by cognitive impairment status) are presented in Table 1. Individuals assessed at follow-up had a mean age of 42 years (SD: 16.8), and 79 patients (73%) described having completed a high school education or less. Thirty-eight patients (35.2%) sustained a long-bone fracture. Over half of all patients (57.4 %) received mechanical ventilation, with a mean duration of 3.4 days (range: 1-38 SD: 6.4).

Long-term cognitive impairment was identified in 59 patients (54.6%) with only 3 (5.5%) of these patients demonstrating pre-existing impairment. Bivariate analysis found no statistical association between cognitive impairment and age, gender, race, injury severity, concussion, ED GCS, ED pulse, RTS, long-bone fracture, or early operative intervention (Tables 1 and 2). However, duration of mechanical ventilation was found to be significantly longer (4.1, SD: 6.6 days vs. 2.6, SD: 6.4 days; p=0.04) and fracture treatment with a reamed IMN significantly higher (27.4% vs. 8.2%, p=0.03) in patients with long-term cognitive deficits. ED hematocrit (35.4, SD: 6.3 vs. 38.1, SD: 6.6; p=0.03), systolic blood pressure (114.8, SD: 28.2 mmHg vs. 127.7, SD: 26.0 mmHg; p<0.05), and 24-hour blood transfusion (2.7, SD: 4.1 units vs. 1.3, SD: 3.5 units; p=0.04) were statistically different among impaired and non-impaired groups; however, these differences were not considered clinically significant. In addition, having completed a high school education or less and the presence of intra-operative hypotension trended towards significance with long-term cognitive impairment (p=0.09).

Reamed IMN

Eighteen patients (16.7%) sustained a long-bone fracture of the femoral or tibial shaft (OTA Classification 32 and 42, respectively) and were treated operatively with a reamed IMN. All other long-bone fractures were OTA classification 12 and 22, and were not treated with a reamed IMN. Patients treated with a reamed IMN were not significantly different from the remaining study population that did not undergo a reamed IM procedure (Table 3). No patient demonstrated clinical symptoms of fat embolism syndrome. Two fractures were managed with a reamer-irrigator-aspirator (RIA). Of the 2 patients who were treated with a RIA device both underwent early fracture care; 1 was noted to have demonstrated long-term cognitive deficits.

IMN and Cognitive Impairment

Cognitive impairment at 12-months following injury was seen in 14 patients who received a reamed IMN. Multivariable logistic regression found that a reamed IMN (OR: 3.2, 95% CI: 0.95-10.9; p=0.06) was a moderate risk factor for the development of cognitive impairment 12-months after injury, after controlling for ISS, level of education, intra-operative hypotension, and duration of mechanical ventilation (Table 4).

Discussion

Fracture care following polytrauma is a critical aspect in the initial evaluation and overall management of severely injured patients[1]. Established literature demonstrates that early total care of severe lower extremity fractures results in improved outcomes[2, 3, 28]. However, some authors have described that not all injuries are well served by early definitive care and that certain operative interventions may be associated with increased morbidity[7, 10, 29]. A recent retrospective study in patients with multiple trauma without evidence of intracranial bleeding identified a high incidence of long-term cognitive impairment[18]. The etiology of these cognitive deficits is unknown. We conducted this study to evaluate the association of reamed intramedullary nailing and neurocognitive outcome in patients with multiple trauma. Our data suggests that reamed nailing was associated with cognitive deficits in this population of multiple trauma patients and was a moderate risk factor (p-0.06) for long-term impairment, even after adjusting for potential confounding variables.

Reamed IM nailing is arguably the most successful treatment modality in orthopaedic trauma surgery and is one of the most common emergency procedures performed in a majority of trauma centers[30]. A reamed IMN is the “gold standard” treatment for fixation of femoral shaft fractures[31-33]. Recent evidence also provided that closed diaphyseal tibia fractures treated with a reamed IMN resulted in fewer complications and re-operations[34]. The biomechanical advantages of IM reaming afford insertion of a larger diameter nail, resulting in stable fixation and faster time to fracture union[30]. However, the adverse biological effects of reaming have also been well documented and contribute to obliteration of the endosteal vascular supply and increases in intramedullary pressure that is associated with bone marrow embolization. The release of marrow contents into the systemic circulation has been described to potentiate neurologic and pulmonary injury through a variety of mechanisms[13, 35].

While primary brain injury is the result of mechanical forces distributed to the cranial vault at the time of injury, secondary brain injury is a consequence of a trauma-initiated hyperinflammatory response[36]. This secondary injury has been described as resulting from hypoxia, hypotension, metabolic acidosis, or post-injury coagulopathy. The idea of preventing a “second hit” injury to the brain is commonly used to define a procedure or management strategy that reduces the detrimental effects of the post-traumatic hyperinflammatory state[37]. These concepts are relevant to the orthopaedic surgeon as methods of fracture fixation may influence the ultimate outcome of patients with traumatic brain injuries.

Hypotension, hypoxia, and decreased cerebral perfusion are associated with early noncranial, orthopaedic procedures.[7, 9, 16, 38] Inadequate attention to these resuscitation measures may result in secondary brain injury and subsequent adverse neurologic events. While multiple studies have investigated the neurologic outcome following early fracture fixation in severely head-injured patients, the results are not definitively conclusive (Table 5). It is important to recognize the methods of evaluating neurologic outcome in these studies have varied,[7, 9, 15] with some authors concluding that significant neurologic deficits are a function of initial injury severity.[39, 40]

Several investigations have focused on the detrimental effects of fracture fixation with intramedullary reaming following multiple trauma with closed head injury,[7, 9, 16, 39] however our study describes a unique population of patients without an ICH at admission. Patients with these injuries are routinely considered “less severe,” or to have no cranial injury at all, and most receive no further neurocognitive follow-up[14]. However, a recent evaluation of multiple trauma victims without an ICH documented that more than half of patients evaluated 1-year after injury demonstrated persistent cognitive impairment that was associated with functional deficits, poor quality of life, and an inability to return to work.[18]

This study evaluated a very successful and common orthopaedic procedure and the neurocognitive outcome in patients without an ICH at hospital admission. The interest of fracture care in victims of polytrauma with a normal head CT scan is highlighted by recent recommendations for early fracture fixation with a reamed IMN.[12, 13] Our rationale to include patients without evidence of an ICH on CT scan was chosen to include a large population of trauma patients who are often discharged without further neurocognitive evaluation. This method has been shown to be the most objective way to ensure that patients with gross brain injuries, notably those including moderate to severe TBI, would be excluded from the investigation[18].

The incidence of cognitive impairment in 54% of TICU survivors without ICH are in agreement with a previous study which document a similar incidence of long-term impairment following multiple trauma in patients without severe brain injury[18]. We utilized a well validated battery of neuocognitive assessments to establish the primary outcome of interest. It is important to consider that less than 5% of our study population was noted to have pre-existing impairment prior to the initial injury. These results suggest that despite negative findings from radiologic images of the brain the neuropsychological outcome may still be poor. We were unable to elucidate any association with neurologic morbidity and the timing of operative intervention or injury severity, as has been reported from previous studies[7, 15, 39, 41]. Furthermore, we did not find a significant association with a concussion and subsequent long-term impairment. The duration of mechanical ventilation, incidence of intra-operative hypotension, and patients’ level of education were shown to be associated with the primary outcome in bivariate analysis and are clinically significant differences, however, they failed to demonstrate significance in the final multi-variable regression model. While the overall rate of intraoperative hypotension appears high, a possible explanation for this finding is that more than half of the study population underwent early (≤24 hours) operative intervention, which has been shown to be associated with hypotension[16, 41].The moderate risk of an adverse cognitive outcome following a reamed IMN may be of interest to the orthopaedic surgeon as emerging studies document that the psychological impact of traumatic orthopaedic injuries influences patient satisfaction and outcome.[4, 5]

This investigation describes an interesting clinical finding; however, the results must be interpreted within the context of which they were performed. While patient enrollment and neurocognitive data was gathered prospectively, collection of operative data and treatment with a reamed IMN was gathered retrospectively. Therefore, any conclusions about a causative etiology directing the increased risk of cognitive impairment following a reamed IMN should not be abstracted from this study. Furthermore, the population of trauma patients without an ICH considered in this evaluation was large, yet the cohort of patients who received a reamed IMN was rather small, providing an opportunity for Type-I error. Last, we identified patients who sustained any diaphyseal long-bone fracture in order to evaluate potential associations with fracture injury and cognitive impairment, and found no statistically significant differences; however there was a significant difference in outcome in patients who received a reamed IMN. There was no group of study subjects with a lower extremity diaphyseal long-bone fracture who were not treated with a reamed IMN against which to compare those patients who received a reamed IM device. Comparison of patients who were treated with a reamed IMN to the remaining study population that were not treated with a reamed nail demonstrated that there were no differences with respect to age, injury severity, duration of mechanical ventilation, early operative intervention, or level of education. This should not, however, be interpreted in lieu of a standardized control group.

The results of this investigation offer insight into the long-term neurologic outcome in a population of orthopaedic trauma patients. We acknowledge that the reamed IMN is a well established and successful modality of stabilization for a majority of long-bone fractures. However, neuropsychological outcomes following orthopaedic trauma surgery have been described[4]. This study suggests that patients treated with IMN had a higher incidence of long-term cognitive impairment. While there are associated risk factors for long-term impairment, no causal effects can be ascertained without further investigation. Recent publications have commented that orthopaedic trauma research does not routinely take into account psychological distress, but that such impairment is common following severe musculoskeletal injury[6]. Of significant interest is that neuropsychological impairments are closely associated with patient satisfaction and outcome[4, 5]. Orthopaedic trauma research may benefit from continued investigation of the potential associations with acute fracture management and long-term cognitive outcome.

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TABLE 1

Demographic and Hospital Course Data

	All Patients (n=108)	Non-Impaired (n=41)	Impaired (n=67)
Age, mn (SD)	42.7 (16.8)	42.0 (16.6)	43.4 (17.1)
Education, n (%)[#]			
≤ High school	79 (73.2)	32 (65.3)	47 (79.7)
>High School	29 (26.9)	17 (34.7)	12 (20.3)
Sex: Female, n (%)	47 (43%)	23 (45%)	24 (41.4)
Male, n (%)	62 (57 %)	28 (55%)	34 (58.6)
Race: White, n (%)	94 (92.2)	43 (93.5)	51 (91.1)
Black, n (%)	8 (7.8)	3 (6.5)	5 (8.9)
Hospital LOS, mn (SD)	12.94(10.3)	11.9 (9.6)	13.8 (10.8)
Vent days, mn (SD)[*]	3.4 (6.5)	2.6 (6.4)	4.1 (6.6)
IQCODE-SF, mn (SD)	3.0 (0.3)	3.0 (0.1)	3.03(0.4)
Long-bone fracture, n (%)	38 (35.2)	13 (26.5)	25 (42.4)
IMN, n (%)[*]	18 (16.7)	4 (8.2)	14 (27.4)
Early OR, n (%)	66 (61.1)	27 (55.1)	39 (66.1)

[#] $p=0.09$;

[*] $p<0.05$

SD: standard deviation; mn: mean; ISS: Injury Severity Score; Ext AIS: Extremity Abbreviated Injury Severity; LOS: length of stay; Vent days: ventilator days; IQCODE-SF: Informant Questionnaire of Cognitive Decline in the Elderly-Short Form; IMN: Intramedullary Nail; Early OR: operative intervention <24h.

TABLE 2

Injury and Physiologic Data

	All Patients (n=108)	Non-Impaired (n=41)	Impaired (n=67)
ISS, mn (SD)	30.3 (9.2)	30.4 (9.1)	30.2 (9.5)
Ext AIS, mn (SD)	2.4 (1.1)	2.3 (1.0)	2.4 (1.2)
Concussion, n (%)	55 (50.1)	37.0 (56.9)	22 (51.2)
ED GCS, mn (SD)	12.6 (4.5)	12.7 (4.5)	12.5 (4.6)
ED pulse, mn (SD)	98.4 (25.3)	95.7 (22.4)	100.6 (27.4)
ED SBP, mn (SD)*	120.7 (27.9)	127.7 (26.0)	114.8 (28.2)
RTS, mn (SD)	10.6 (2.6)	10.8 (2.5)	10.5 (2.7)
ED hematocrit, mn (SD)*	36.6 (6.5)	38.1 (6.6)	35.4 (6.3)
24-hr blood trans, mn (SD)*	2.1 (3.9)	1.3 (3.5)	2.7 (4.1)
Intraop Hypoxia, n (%)	13 (12.0)	4 (8.2)	9 (15.3)
Intraop Hypotn, n (%)#	58 (53.7)	22 (49.9)	36 (61.0)

*p<0.05;

#p=0.09

Mn: mean; SD: Standard Deviation; ISS: Injury Severity Score; AIS: Abbreviated Injury Scale; ED: Emergency Department; GCS: Glasgow Coma Scale; SBP: Systolic Blood Pressure; RTS: Revised Trauma Score; 24-hour blood trans: 24-hour blood transfusions; Intraop Hypoxia: SpO2<90%; Intraop Hypotn: systolic blood pressure <90mmHg.

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TABLE 3

Results by IMN and Non-IMN population

	IMN (n=18)	Non-IMN (n=90)	p-value
Age, mn (SD)	40.7 (19.4)	42.3 (16.3)	0.71
Sex: Female, n (%)	9 (50)	36 (40)	0.43
Male, n (%)	9 (50)	54 (60)	
Education, n (%)			0.61
≤High School	14 (77.8)	65 (72.2)	
>High School	4 (22.2)	25 (27.8)	
ISS, mn (SD)	32.7 (8.8)	29.8 (8.3)	0.24
Hospital LOS, mn (SD)	15.1 (10.4)	11.8 (8.8)	0.16
Early OR, n (%)	16 (88.9)	50 (55.6)	0.14
Vent days, mn (SD)	5.6 (8.1)	3.7 (6.8)	0.29

IMN: Intramedullary Nail; SD: standard deviation; mn: mean; ISS: Injury Severity Score; LOS: length of stay; Early OR: operative intervention <24h; Vent days: ventilator days.

TABLE 4

Multivariable Logistic Regression

	Odds Ratio	95% CI	p-value
IMN	3.2	0.95-10.9	0.06
Education:			
≤High School	1.8	0.7 – 4.5	0.21
>High School	0.6	0.2-1.4	0.21
ISS	1.0	0.9 – 1.0	0.39
Vent days	1.0	0.9-1.1	0.25
Intraop Hypotn	1.6	0.7-3.6	0.28

IMN: Intramedullary Nail; Vent days: ventilator days; Intraop Hypotn: systolic blood pressure <90mmHg.

Table 5

Review of Fracture Care Literature with Neurologic Outcomes

Author	Year	Study Design	No. of Patients	Severity of Head Injury	Neurologic Outcomes	Primary Findings
Poole, et al.	1992	Retrospective Review	114	Fracture of vault or base of skull	Adverse neurologic events	Adverse neurologic events associated with lower admission GCS and higher Head/Neck AIS. Fracture fixation (≤24 hrs or > 24 hrs) not an independent predictor of adverse neurologic events.
Jaicks, et al.	1997	Retrospective Review	33	Head/Neck AIS >2	Neurologic complications, Discharge GCS	Similar neurologic complication rate and lower discharge GCS in early fracture fixation (≤24 hrs) compared to late fixation (>24 hrs).
McKee, et al.	1997	Retrospective case-control	145	Head/Neck AIS >3	Glasgow Outcome Score (GOS), Category Test, Trails A and B test at 1-year follow-up (n=10)	No difference in neuropsychological testing or GOS in early fracture treatment (≤24 hrs) group compared to control group.
Townsend, et al.	1998	Retrospective review	61	GCS<8 and CT demonstrating intracranial injury	Discharge GOS	Intra-operative hypotension more common in early fracture fixation (≤24 hrs). Discharge neurologic outcome reflected primary injury and not related to intra-operative events (i.e. hypotension).
Kalb, et al.	1998	Retrospective review	123	Head/Neck AIS ≥2, traumatic lesion on head CT	Discharge/Follow-up GCS	No difference in GCS at time of discharge in early (≤24 hrs) vs. late (>24 hrs) fracture fixation. Of 26 patients available for long-term follow-up, no difference in GCS.
Brundage, et al.	2002	Retrospective review	1362	Head/Neck AIS >2 (n=512)	Discharge GCS	In patients with significant head injury, no difference in discharge GCS compared with timing of fracture fixation (<24 hrs, 24-48 hrs, 48-120 hrs, >120 hrs).