Time to definitive fixation of femoral fractures: Association with morbidity and costs and the role of damage control orthopedics

By

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Abstract

**Literature Review**: A literature review was conducted to determine the recommended regarding the choice of early total care (ETC) or damage control orthopedics (DCO) in poly-trauma patients. PubMed, CINAHL, and Cochrane databases were queried for articles regarding damage control orthopedics resulting in 4 articles that met criteria for review. Hand searches of citations led to the identification of 3 additional articles. Articles were graded on 6 parameters resulting in three “good” articles, four “fair”, and one “poor”. The review of the literature did not result in consistent evidence that could be used to definitively guide clinical practice.

**Original Research Background**: The optimal time from injury to internal fixation of femoral fractures has been a point of contention in orthopedic literature. Some recent studies suggest that delaying definitive management of orthopedic injuries until the patient is suitably stabilized may lower morbidity and mortality. The purpose of this study was to reevaluate whether time to definitive fixation of femoral shaft fractures has an effect on patient morbidity or hospital costs.

**Methods**: We performed a retrospective cohort study using an existing trauma registry from one Level 1 trauma center. Of the patients contained in the registry over an 11 year period (2000-2010), 566 patients with a femoral shaft fracture were included in this analysis. Patients were dichotomized into cohorts by Injury Severity Score above and below 18. Time to fixation was defined as time from arrival at a hospital until definitive fixation was performed. Time was divided into periods in which fixation occurred: t₀ (<12 hours), t₁ (12-24 hours), t₂ (24-48 hours), t₃ (48-120 hours) and t₄ (>120 hours). t₀ served as the referent category. Morbidity was estimated using the following surrogate markers for morbidity: intensive care unit length-of-stay (ICU-LOS), days on ventilator (V DAYS), hospital length-of-stay (H-LOS), and discharge
disposition (DISPO). The effect of time to fixation on patient specific hospital costs (COST),
data for which was also present in the registry, was analyzed as well.

**Results:** In patients with ISS≤18 there was no demonstrated relationship between time to
management and ICU-LOS or VDAYS. Management after 48 hours was associated with
significantly longer H-LOS ($t_0$ 7.55 days versus $t_3$ 13.84 days, $p<0.001$; $t_4$ 15.60 days, $p=0.020$)
and higher hospital costs ($t_0$ $41,600 versus $t_2$ $66,500$, $p=0.006$; $t_3$ $72,100$, $p=0.005$). In
patients with ISS>18 management after 24 hours was associated with more VDAYS ($t_0$ 1.65 days
versus $t_2$ 4.57, $p=0.030$; $t_3$ 5.62, $p=0.012$; $t_4$ 10.84, $p<0.001$) and COST ($t_0$ $65,100$ versus $t_2$
$96,400$ $p=0.033$; $t_3$ 130,100, $p<0.001$; $t_4$ $210,200$, $p<0.001$). After 48 hours there was also a
significant increase in ICU-LOS ($t_0$ 3.77 days versus $t_3$ 7.91 days, $p=0.036$; $t_4$ 17.61 days,
$p=0.001$) and H-LOS ($t_0$ 11.90 days versus $t_3$ 22.44 days, $p=0.004$; $t_4$ 36.63 days, $p<0.001$).
There was no relationship found between time to fixation and DISPO.

**Conclusions:** Definitive management of femoral fractures more than 48 hours after injury is
associated with increased morbidity. Additionally, delayed management is more costly. These
data suggest that early appropriate care of femoral fractures can minimize patient morbidity and
financial burden in most patients.
Introduction

Following major trauma, patients are often afflicted by many different types of injuries to multiple organ systems.\(^1\) Common serious injuries include those to the head, thorax, abdomen and the musculoskeletal system. Femoral fractures are often associated with major trauma but no consensus has been reached regarding time to definitive management of these fractures.\(^2,3\)

During the 1960s, immediate surgical fixation, or early total care (ETC), of femur fractures was associated with mortality rates nearing 50%\(^4\). Mortality was thought to be most associated with fat embolism from manipulation of the fracture leading to pulmonary failure during a time when cardiopulmonary management was not as thoroughly established as it is currently. Management of femoral fractures generally consisted of traction alone or splints and slings until 10 to 14 days post-trauma when the patients were thought to be stable enough to deal with definitive surgical correction.\(^4\)

Delays in fixation of up to two weeks led to problems ranging from severe pain for the patient and logistical problems with moving the patient, which in turn led to increased lengths of intensive care unit (ICU) stays.\(^5\) The 1980s brought a different viewpoint on management of femoral fractures in the poly-trauma patient, emphasizing early definitive surgical management. Bone et al showed improved outcomes in patients operated on early in their hospitalization.\(^4,6\) However, the definitions of early versus late management were not clearly defined, and aggressive management of patients in the first 12 to 24 hours led to poor outcomes in some.\(^4\)
Through the 1990s focus shifted to the biochemical processes contributions to outcomes in poly-trauma patients and studies shifted once again suggesting that a new management scheme, termed damage control orthopedics (DCO), would improve patient outcomes. Damage control orthopedics uses external fixators to temporarily manage fractures allowing the patient to medically stabilize prior to definitive correction.2,3,7,8

Currently it is uncertain whether DCO is superior to ETC for poly-trauma patients.9-12 The purpose of this systematic review is to assess the literature to determine whether damage control orthopedics or early total care leads to better outcomes among poly-trauma patients with a femoral fracture. Outcomes of interest are mortality, incidence of acute respiratory distress syndrome (ARDS), multiple organ failure (MOF), and length of intensive care unit stay (ICU-LOS).

**Methods**

*Selection of Articles*

A search of the Medline database using Pubmed was conducted using the MeSH search terms “Femoral Fractures” inclusive of subheadings “complications”, “mortality”, pathology”, “surgery” cross-referencing articles that also contained the MeSH term “Multiple Trauma”. Additionally a keyword search was conducted using the terms “damage control orthopedics” and separately “damage control orthopaedics” limited to the last year. This additional search was conducted to capture recent articles not yet filed under MeSH headings. Searches of the CINAHL database and the Cochrane database were conducted using the terms “damage control orthopedics” and “damage control orthopaedics” as well. Articles focusing on surgical technique, biochemical markers, pediatrics, or elderly populations were excluded. Review
articles and case reports were also excluded. Citations within these articles were hand searched and appropriate citations were also included in this review. Limits were set to include English language studies only and patients 16-65 years of age.

Critical Appraisal of Articles

Studies that met inclusion criteria were graded by a single reviewer (DV) based on six criteria using a tool adapted from Pignone et al.\textsuperscript{13} and Sheridan et al.\textsuperscript{14} This tool (Figure 1) was used to assign a numerical score ranging from 0-2 for each criteria listed which were subsequently averaged. Articles with average scores >1.5 were considered good quality, 1.0-1.5 were fair, and <1.0 were considered poor.\textsuperscript{14}

Results

Search Results

The searches described led to 144 titles of which, 28 abstracts were examined. Twenty three of these were excluded leaving five articles for full text review. Three additional articles were added for review from hand searching citations. In total, seven articles met the set criteria and were sufficient for systematic review (Figure 2).

Study Characteristics

All studies included were retrospective cohort studies\textsuperscript{3,10,12,15-17} with the exception of one randomized controlled trial.\textsuperscript{8} Five of the seven studies (Table 1) were conducted at a single trauma center over a period of years.\textsuperscript{3,10,15-17} One study was conducted with data compiled from ten European trauma centers\textsuperscript{8} while another was sourced from a national trauma database that
included over 500 sites.\textsuperscript{12} The durations of the studies varied widely with most being conducted over a period of three to five years. One study was based on data collected over 19 years.\textsuperscript{3}

Early total care was defined in all\textsuperscript{3,8,10,15-17} but one\textsuperscript{12} of these studies as definitive treatment of femoral fractures within the first 24 hours of injury while DCO was defined as either external fixation within 24 hours with subsequent definitive correction, or definitive correction >24 hours post-injury. The study conducted by Morshed et al\textsuperscript{12} divided patients into subgroups with groups receiving treatment in the first 12 hours, 12-24 hours, 24-48 hours, and greater than 48 hours post-injury. The earliest of these time periods was used as the reference in this study. One of the articles provided subgroup analysis of patients enrolled individually examining those with Injury Severity Score (ISS) of >18 and <18.\textsuperscript{10}

The decision for treatment choice with ETC or DCO in two of the articles was based on changes in protocols on treatment of femoral fractures over time.\textsuperscript{3,17} In other words, all patients seen up to a certain date were treated with ETC. Patients seen after this date were treated early unless they were considered severely injured, at which time they received DCO treatment.\textsuperscript{3,17}

Outcomes varied between studies analyzed. Five of the seven studies measured mortality as a primary outcome\textsuperscript{10,12,16-18} with one of the studies having the sole outcome of mortality.\textsuperscript{12} All but one of the studies measured post-surgical outcomes like ALI, pneumonia, infection, and ARDS. Four studies\textsuperscript{3,8,11,16} measured parameters outside of surgical complications like length of stay in the ICU or hospital as well as time on ventilator.

\textit{Study Quality}

Three of the reviewed studies were considered “good” quality by our assessment.\textsuperscript{8,10,12} Three of the articles were of “fair” quality\textsuperscript{3,11,16,18} and one was graded as “poor” (Table 1).\textsuperscript{17}
Outcomes measured through analysis of the studies

Mortality

Five\textsuperscript{10,12,15-17} of the included articles stated in their methods that a primary outcome of interest would be in-hospital mortality but only four\textsuperscript{10,12,15,16} of them reported these values. The largest of these studies (n=3069) examined mortality as its sole outcome of interest.\textsuperscript{12} Numerical values for raw mortality data or corrected values were not provided but instead raw and statistically corrected relative risk ratio (RRR). Groups were similar in demographic measures between the time periods. Mortality was significantly lower in three of the four post injury time periods compared with definitive correction within 12 hours post-injury (Table 1). Fixation in the time period of 12-24 hours resulted in 0.45 RRR (95\% CI 0.15 to 0.98, p=0.03), 24-48 hours 0.83 (95\% CI 0.43-1.44, p=0.49), 48-120 hours 0.58 RRR (95\% CI 0.28 to 0.93, p=0.03), and >120 hours 0.43 (95\% CI 0.10 to 0.94, p=0.03).

Nahm et al (n=750) reported 8 total deaths in the portion of their population with ISS>18 (n=492) with a statistically significant difference between the groups with ETC 1.0\% and DCO 4.8\% (p=0.032). Each death was examined in detail and circumstances surrounding the death were reported.\textsuperscript{10} Damage control orthopedics patients in this portion of the Nahm study however did have a significantly higher ISS than the ETC group (36.4 vs 28.8, p<0.001) and failed to adjust for this difference statistically.

The two remaining studies both show higher mortality with DCO compared to ETC: ETC 2.0\% vs 17.9\% (p<0.05)\textsuperscript{18} and ETC <1\% vs DCO 9\% (p=0.001).\textsuperscript{16} These were both characterized by low total numbers of mortality and much smaller overall study sizes compared
to the first two but still had statistically significant differences in reported mortality. Statistically significant differences in ISS were again not adjusted for in these analyses.

Tuttle et al claimed in its methods to analyze data in reference to mortality but the study failed to report any data on this subject later in the article.\textsuperscript{17}

\textit{Acute respiratory distress syndrome}

Five studies reported values for ARDS\textsuperscript{3,8,10,17,18} but only one of the five demonstrated any statistically significant differences between ETC and DCO.\textsuperscript{3} Pape et al examined ETC and DCO in two time periods, 1981-1989 and 1993-2000.\textsuperscript{3} Rates of ARDS in the earlier time period were 32.7\% and 16.6\% (p<0.05) for ETC and DCO respectively while the late period had 15.1\% and 7.8\% (p<0.05).\textsuperscript{3} The inter-time period rates of ARDS for ETC and DCO for this study were also statistically significant 32.7\% versus 15.1\% for ETC between time periods (p=0.003) and 16.6\% versus 7.8\% for DCO between time periods (p=0.003 and p=0.002).

The remaining studies show varied outcomes in reference to ARDS (Table 2) with no major qualitative differences.\textsuperscript{8,10,15,17}

\textit{Intensive care unit length of stay}

Five of the eight studies reviewed reported on ICU-LOS\textsuperscript{8,10,17,18} with two of the studies showing statistical significant differences between ETC and DCO.\textsuperscript{10,18} Both statistically significant studies showed shorter ICU stays amongst patients who had ETC. Nahm et al calculated 5.2 days in the ICU for ETC and 12.9 days for DCO (p<0.001) with statistically significance maintained after correction for ISS scores and age.\textsuperscript{10} O’Toole et al reported 7.1 days
for ETC patients and 17.3 days for DCO (p<0.05) amongst patients with ISS>17. No statistical correction for age or ISS was performed in this study.

The three remaining articles that studied ICU-LOS showed no statistically significant difference. Two of the three showed decreased LOS with ETC compared to DCO while the third showed slight improvement in ICU-LOS with DCO.

*Multiple organ failure*

Multiple organ failure was reported on by four of the eight articles. Only one of the studies demonstrated statistically significant differences between ETC and DCO with ETC resulting in 1.2% of patients with MOF and DCO resulting in 6.0% (p=0.016). Two of the remaining articles that showed no statistical difference between ETC and DCO in reference to MOF had relatively even rates of MOF. Pape et al analyzed rates over different time periods and showed no statistical difference between the ETC and DCO rates of MOF within each era, but instead did demonstrate that rates of MOF between the ETC and DCO in the early time period was statistically different than the late time period.

*Discussion*

The decision on when to best treat femur fractures in poly-trauma patients has been in question for many years. The studies reviewed in this systematic review provide some insight on the topic, but do not provide consistent results between studies. Mortality data, as well as other post-surgical complications like MOF, ARDS and even parameters like ICU-LOS showed differing outcomes based on ETC or DCO care of patients.
Some studies showed statistically significant improvements in mortality in patients using ETC compared to those who received DCO. Two of the articles demonstrated an improvement in mortality amongst those who had ETC but had low overall number of mortalities precluding conclusions from being made based on these data. Each of these failed to correct for differences in ISS scores which may have reduced the effect of mortality amongst the studies. O’Toole et al found a significant improvement in mortality but again failed to correct for confounding factors like injury severity or age. Additionally, inclusion of children and the extreme elderly without details on mortality from the patients limits generalizability of these results. Conflicting results were provided by Morshed et al who demonstrated improvements in mortality with surgery between 12-24 hrs, and >48 hours post injury. Their large sample size along with appropriate statistical handling for confounding factors makes this the most generalizable of the studies reporting on mortality.

Only one study demonstrated a statistically significant difference in ARDS rates between ETC and DCO management of patients. This study examined patient care in two different time periods and within each period, there was an improvement in the rate of ARDS with DCO compared to ETC. This study had a large sample size and was conducted at one center over time which may have led to its ability to show statistical significance in ARDS while the other studies failed to.

Nahm and colleagues conducted the only study that demonstrated a statistically significant improvement in MOF rates when using ETC while two of the seven showed improvements in ICU-LOS. Nahm et al found significant differences in both of these areas and was graded a “good” quality study overall, but had some deficiencies. One potential confounder that could have affected results is the inclusion of femoral neck and trochanteric fractures which
could behave significantly different than femoral shaft fractures. The lack of control for patients transferred from another hospital could have affected time to definitive correction and may have shifted results away from the null. The study by O’Toole et al had a major deficiency in the comparability of subjects with DCO patients being significantly more severely injured with much higher ISS scores, rates of exploratory laparotomy, and shock. These deficiencies combined with the low number of DCO patients (n=28) limit the applicability of this study’s results.

The potential limitations of this review must be taken into account when considering these results. Though the searches conducted were thorough, there is a chance that some relevant articles were missed in this systematic review. Also limits on the searches including limiting articles to English language and only over the past 10 years could have caused us to miss important articles. Studies were only reviewed and graded by one individual which could have led to some reader biases. Also, though the metric used to grade studies was adapted from similar metrics cited in multiple articles, there may have been opportunity for assigned quality ratings to vary.

Reviewing the literature, we were unable to find sufficient consistent evidence to guide clinical practice. More studies reported statistically significant mortality data than any other parameter measured, but small sample sizes in many of these studies limits our ability to draw firm conclusions. Additionally, the highest quality study reviewed demonstrated improvements with DCO over ETC while the other studies had conflicting results. Similarly, ARDS, MOF, and ICU-LOS only demonstrated limited statistical significance in many of the studies. Additional statistical analysis correcting for age and injury severity scores in some of these studies may have led to an ability to demonstrate more difference between the groups analyzed. Only one of the studies reviewed was a randomized controlled trial, likely due to the ethical
concerns over randomizing severely injured trauma victims to different treatments. Future studies with larger sample sizes, preferably RCTs or well designed cohort studies are necessary to provide evidence to guide clinical decisions in poly-trauma patients with femoral fractures.
Time to definitive fixation of femoral fractures: Association with morbidity and costs

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Introduction

Trauma is one of the most common causes of morbidity and mortality in the United States. In patients under 45 years of age, trauma is the leading cause of death.\(^1\) Additionally, trauma is the fourth leading cause of death among all age groups. In trauma patients, the most likely causes of mortality are severe injuries to the head or abdomen.\(^2\) Trauma patients also commonly have musculoskeletal injuries, but these are generally considered lower priority and are addressed after initial stabilization of the patient.\(^2\)

Femoral fractures are a major musculoskeletal injury present in many severely injured trauma patients. Femoral shaft fractures are most commonly high energy injuries in the young, or low energy in the elderly or osteoporotic patient population.\(^{19,20}\) Many prior studies have examined predictors of post-fracture morbidity and mortality outcomes in patients with proximal femur fractures but few have studied such outcomes in femoral shaft fractures in patient populations other than the elderly.\(^{19,20}\) Previous studies have determined that in the elderly, the best predictors of post-surgical mortality are preexisting comorbidities including heart failure, chronic obstructive pulmonary disease (COPD), dementia, and metastasis.

The time from initial injury to internal fixation of femoral fractures has been a point of contention in orthopedic literature. Opinion regarding when to fix femoral fractures has been in flux since the 1970s. Prior to that period most femur fractures were managed with traction, and if surgery was undertaken it was delayed, often for weeks. In 1976, Riska et al published on the benefits of early fixation compared to delaying definitive care of femoral fractures.\(^{21}\) Articles in the 1980s strongly supported early fixation, which is now known as “early total care” (ETC), often urging fixation in the first 24 hours after injury. Bone et al reported decreased incidences of complications like fat embolism, pneumonia, and respiratory failure with ETC.\(^6\) Berhman et
al stratified their patient populations by Injury Severity Score (ISS) and found that those with early fixation had shorter hospital and intensive care unit (ICU) stays as well as decreased risk of pneumonia and pulmonary complications.22

Through the late 1990s and early 2000s focus shifted to the contributions of inflammatory processes to morbidity and mortality with resultant Systemic Inflammatory Response Syndrome (SIRS) in poly-trauma patients. Some began to recommend a new management scheme in the most severely injured patients termed “damage control orthopedics” (DCO) to limit this problem. Damage control orthopedics uses external fixators to temporarily stabilize fractures in severely injured patients, allowing them to at least partially resolve the acute inflammatory response to the “initial hit” of the poly-trauma prior to the “second hit” of surgery for definitive correction.3 Pape et al examined DCO and its relationship to patient outcomes but found only an increased risk of acute lung injury in ETC patients and no difference in ICU length-of-stay, pneumonia, sepsis or multiple organ failure.8 Morshed et al conducted a study examining time to definitive fixation of femoral fractures and its link to mortality.12 They demonstrated a decrease in risk of mortality in patients with ISS>15 with operations delayed more than 12 hours post-injury, with the largest reductions in mortality risk seen in fixation 12-24 hours post-injury and >120 hours post injury. Other studies, like that conducted by Tuttle et al, were unable to find any significant differences in mortality, acute respiratory distress syndrome, or multiple organ failure between early and delayed care of femoral fractures.17

Given that it is not clear whether delayed care is superior to early total care, the purpose of this study was to reevaluate in a large series of patients whether time to definitive fixation of femoral fractures has a clinically significant association with morbidity or hospital costs.
Methods

Study population

With approval from the University of North Carolina (UNC) Institutional Review Board, we searched the UNC Trauma Registry for patients with femoral fractures sustained between January 1, 2000 and December 31, 2010. Femur fracture could be open or closed as defined by the International Classification of Diseases, Clinical Modification (ICD-9-CM) diagnostic codes between 821.0 to 821.3. We restricted eligible patients to those between 16 and 55 years of age who had a definitive fixation of the femur within two weeks of initial admission. The age restriction was placed to avoid skeletally immature patients and minimize the possibility of diseases like osteoporosis affecting the results. This search yielded 690 potential patients. Patients were then excluded if they were: (1) transfer patients who did not have adequate documentation of the time from initial admission at a referring hospital until admission at our facility (n=68); (2) patients with missing or conflicting data regarding arrival time at our hospital (n=12); (3) individuals with missing or conflicting data on time of definitive fixation (n=35); (4) patients who died prior to fixation (n=6); or (5) patients with severe burn injuries (n=3). After application of exclusion criteria 566 patients remained for analysis.

Descriptive parameters and surrogates for morbidity

The trauma registry recorded patient data regarding age, sex, race, transfer status, Abbreviated Injury Scale (AIS) scores for each organ system, and ISS. Time from arrival in the emergency department until definitive correction of femoral fractures was also recorded and was used as an estimate of time from injury until fixation.
We reported on five surrogates markers for morbidity: intensive care unit length-of-stay (ICU-LOS), days on ventilator (V DAYS), hospital length-of-stay (H-LOS), hospital costs, and discharge disposition. Hospital costs were recorded in the trauma registry as total hospital charges assessed to patients or their guarantors. Discharge destination was classified as discharge home versus discharge to another care facility. Other care facilities were defined as rehabilitation facilities, skilled, nursing facilities, or transfers to other hospitals.

Study groups

Patients who met our inclusion criteria were dichotomized into two cohorts, those who had ISS ≤ 18 (n=379) and those with ISS > 18 (n=187) as was done in previous studies. Within these cohorts, patients were further divided into subgroups based on the time to definitive fixation after hospital arrival. Five periods were defined using cut-points described in previous literature: \( t_0 \) (less than twelve hours), \( t_1 \) (twelve to twenty-four hours), \( t_2 \) (twenty-four to forty-eight hours), \( t_3 \) (forty-eight to one hundred and twenty hours) and \( t_4 \) (greater than one hundred and twenty hours). The \( t_0 \) (less than twelve hours) period was used as the reference against which the other periods were compared in the analyses. In an effort to determine whether the most severely injured patients should have been considered for DCO, an additional subcohort was analyzed consisting of only those patients from the ISS > 18 cohort who had ISS ≥ 33 (n=50), representing the most severely injured population.

Statistical methods

Demographic data were compared between the cohorts using one-way analysis of variance. Multivariate linear regression analysis was used to compare the outcomes across
patients in time period groups adjusted for potential confounders, including age and gender. Chi square was used to analyze discharge disposition between the periods. P values less than 0.05 were considered statistically significant. All statistical analyses were conducted using STATA 11, Statistical Software: Release 11, College Station, TX: StataCorp LP.

Results

Characteristics of sample

Characteristics of the patients with ISS≤18 are shown in Table 1. Proportionately, more of this cohort’s patients had fixation in the earlier periods. Demographic characteristics of patients in the different time periods differed significantly only in age and AIS Head/Neck both of which rose as time to definitive fixation increased. The other demographic characteristics showed no significant differences between the periods (Table 1).

One-hundred and eighty-seven patients had ISS>18 and were examined separately from their counterparts who had lower ISS. Ages, percentage male, and race did not differ significantly amongst the time periods. Mean ISS trended upward overall $t_1=26.7$, $t_2=26.3$, $t_3=27.9$ and $t_4=34.2$ with a $p$ value of total differences between the periods that was significant ($p=0.010$). Abbreviated injury scores for chest and abdomen rose with increasing time to fixation as well but this was not statistically significant (Table 1).

Injury Severity Score Cohort ≤18

As compared to $t_0$, there were no significant differences in ICU-LOS in any of the other periods ($p>0.19$ in all periods) (Table 2, Figure 1). Similarly, compared to $t_0$ there were no significant differences in VDAYS in any period ($p>0.25$ in all periods) (Table 2, Figure 2).
Hospital length-of-stay increased (t₀ 7.55 days) in patients operated on 48 hours or more after arrival with patients in period t₃ staying 13.84 days (p<0.001), and t₄ 15.60 days (p=0.020) (Table 2, Figure 3).

_Injury Severity Score Cohort >18_

One-hundred and eighty-seven patients had ISS>18 and were examined separately from their counterparts who had lower ISS. Ages, percentage male, and race did not differ significantly amongst the time periods. Mean ISS trended upward overall t₁=26.7, t₂=26.3, t₃=27.9 and t₄=34.2 with a p value of total differences between the periods that was significant (p=0.010). Abbreviated injury scores for chest and abdomen rose with increasing time to fixation as well but this was not statistically significant (Table 1).

Compared to those operated on t₀ (3.77 days) ICU-LOS increased with definitive management after 48 hours (t₃ 7.91 days, p=0.036) and it sharply increased in patients operated on >120 hours after arrival (t₄ 17.61 days, p<0.001) (Table 2, Figure 1).

Compared to t₀ (1.65 days), patients had significantly longer VDAYS with management after 24 hours with those patients in period t₂ using the ventilator 4.57 days (p=0.030) and t₃ 5.62 days (p=0.012) with VDAYS markedly increasing with management >120 hours after arrival (t₄ 10.84 days, p<0.001) (Table 2, Figure 2).

Patients managed in t₀ had H-LOS of 11.90 days while those managed 48 hours or more after arrival had significantly longer H-LOS with those in periods t₃ staying 22.44 days (p=0.004) and t₄ 36.63 days (p<0.001) (Table 2, Figure 3).
**Injury Severity Score Subcohort ≥33**

An additional subgroup analysis of only those patients who were most severely injured was performed examining the same surrogate markers for morbidity. There was a significant increase in ICU-LOS compared to \( t_0 \) (4.44 days) in periods \( t_2 \) (13.39 days, \( p=0.043 \)) and \( t_4 \) (22.22 days, \( p<0.001 \)) (Table 3, Figure 1). Time on ventilator was longer in patients managed after 24 hours compared to reference \( t_0 \) (1.55 days) with those managed in \( t_2 \) using the ventilator 11.05 days (\( p=0.013 \)), \( t_3 \) 8.77 days (\( p=0.050 \)), and \( t_4 \) 15.01 days (\( p=0.001 \)) (Table 3, Figure 2).

The only statistically significant difference found in adjusted H-LOS compared to \( t_0 \) (12.10 days) was period \( t_4 \) (43.29 days, \( p=0.004 \)) (Table 3, Figure 3).

**Hospital cost**

In patients with ISS\(\leq18\) costs (\( t_0 \) $41,600) increased significantly with definitive fixation between 24-48 hours (\( t_2 \) $66,500, \( p=0.006 \)) and 48-120 hours (\( t_3 \) $72,100, \( p=0.005 \)). In patients managed 120 hours or more after arrival (\( t_4 \) $66,500, \( p=0.359 \)) there was not a statistical difference, but this period only consisted of 5 patients (Table 2, Figure 4).

Compared to \( t_0 \) ($65,100) hospital costs rose significantly in those with ISS\(>18\) with management after 24 hours with those in period \( t_2 \) costing $96,400 (\( p=0.033 \)) and \( t_3 \) $130,100 (\( p<0.001 \)). There was a sharp increase in COST with management >120 hours after arrival (\( t_4 \) $210,200, \( p<0.001 \)) (Table 2, Figure 4).

Hospital costs in the subcohort ISS\(\geq33\) increased as time to fixation increased beyond 24 hours compared to the reference period \( t_0 \) ($64,800). Time periods \( t_2 \) ($144,800, \( p=0.034 \)) and \( t_3 \) ($150,900, \( p=0.031 \)) showed relatively steady values before costs increased markedly in \( t_4 \) ($287,800, \( p<0.001 \)).
**Hospital Disposition**

Dichotomizing the patient cohort around an ISS score of 18, we did not detect a statistically significant relationship between time to fracture fixation and the probability of being discharged home (Table 4). There were suggestive trends for the percentage of patients who were discharged home to decrease as time to surgery increased but this did not reach statistical significance within either cohort of patients (ISS ≤ 18 p = 0.095 and ISS > 18 p = 0.074).

**Discussion**

Our data suggest that in patients with low ISS, early fixation lowers morbidity and cost. Additionally, in those with ISS > 18, these data do not support the contention that delayed fixation lowers morbidity in more severely injured patients. Upon subcohort examination of the ultra-severely injured (ISS ≥ 33), we still fail to see benefit of delayed management compared to management within the first 12 hours.

Upon careful examination of these ISS ≤ 18 data, there seemed to be a qualitative split between management in the first 24 hours after arrival and management after 24 hours in the cohort of patients with ISS ≤ 18. Periods t₂-t₄ had quantitatively longer ICU-LOS and VDAYS though the differences were not statistically significantly different from the reference t₀. Periods t₂-t₄ were all qualitatively more similar in value to each other than to the reference time of t₀ or even t₁. The periods representing fixation after 48 hours had slightly higher ages, which was adjusted for, and higher AIS for head and neck. Head and neck injuries are often cited as common reasons that surgical management of musculoskeletal injuries is delayed but data has thus far been inconsistent in determining whether early management of musculoskeletal injuries leads to worse central nervous system outcomes.²³
Of note, there was a suggestive, though not statistically significant, improvement in all four measured surrogate morbidity markers among patients who were managed in the second twelve hour period, $t_1$, as compared to the first twelve hour period, $t_0$. This is the only time period in which there was any suggested improvement of outcomes compared to management within the first 12 hours of arrival.

Other recently published literature also suggests that early management is appropriate in patients who have ISS≤18. Nahm et al examined the effect of early versus delayed management of femoral fractures in patients who had ISS<18 and ISS≥18. Amongst those with ISS<18, they did not find a significant increase in complication rates with early management (<24 hours). Nahm et al only dichotomized patients into definitive management in either less than or greater than 24 hours. With our more complex stratification of timing, our data suggested that management preferentially between 12 to 24 hours after arrival at the hospital might prove beneficial for patients compared to delayed care or immediate care, but further research and larger studies would be needed to determine whether the trends we have noted might be statistically significant with larger numbers of patients.

Among the cohort of patients with ISS>18, ISS in each time period increased as time to surgery was extended. Because it indicates that the patients who had longer times to definitive management of fractures were also more seriously injured, this could have contributed to some of the noted increases in LOS and hospital costs as time to definitive correction increased.

Our findings in patients with ISS>18 are corroborated in other studies suggesting that early appropriate care is safe in most patients. Nahm et al also found that in patients with ISS>18, management within 24 hours led to lower rates of complications compared to management after 24 hours (18.9% vs 42.9%, p<0.05). Additionally they stratified patients into
management in <24 hours, 24-48, 48-72, and >72 hours and found increasing rates of complications as time to definitive management was delayed.\textsuperscript{10}

Subgroup analysis of severely injured patients with ISS\textgeq 33 again found that definitive management of the femur fracture more than 24 hours after injury was associated with longer ICU-LOS, more VDAYS and higher hospital costs compared to management in the first 12 hours.

Of note is an apparent statistically significant dip in VDAYS with management performed 48-120 hours after injury (t\textsubscript{3} 8.77 days, p=0.050) versus 24-48 hours after injury (t\textsubscript{2} 11.05 days, p=0.013). This is suggestive of possible improvements in morbidity with avoidance of definitive management in the 2\textsuperscript{nd} 24 hrs in severely injured patients. This is the only data in this study which may support the precepts of DCO by suggesting a possible improvement in morbidity if surgery is delayed past the second 24 hours after injury, however it would still appear that operating in the first 24 hours is best.

There was a corresponding apparent dip in ICU-LOS in period t\textsubscript{3} compared to t\textsubscript{2}, although its value was non-significant (p=0.152). However, because of the small sample size in t\textsubscript{3} (n=9), these results could be due to sampling error. Larger studies with more patients who are severely injured are important to further explore this relationship.

Our study was unable to demonstrate any significant relationship between time to fracture fixation and probability of being discharged home. Though non-significant, there was a trend suggesting a higher likelihood of being discharged home with early management in both those with ISS\textless 18 and ISS>18. These data also suggest that higher ISS may lead to a lower likelihood of being discharged home in general.
Limitations

Several limitations of our study must be considered. Although we controlled for severity by stratification, the possibility of confounding by injury severity still exists.

We were unable to control for comorbid conditions in this study since our data set did not contain information on patient comorbidities. Patients could have had significant differences in comorbid conditions that went unaccounted for. We attempted to minimize the possible effects of this by limiting our study to those who were old enough to be skeletally mature, but still young enough to avoid osteoporosis and other comorbidities of age that could lead to increased incidences of femoral fractures or worse outcomes post surgically.

Other unmeasured confounders may have also influenced physicians’ decisions to choose when to operate. At this institution, operative fixation of femur fractures is performed by the orthopedic team generally within 24 hours of the patient receiving clearance for surgery by the general surgical trauma team. Thus our findings of increased morbidity and cost when surgery was delayed conceivably may have resulted from decision making by the trauma team surgeons who made an experience-based decision to delay orthopedic treatment in patients whom they recognized as more severely injured. Those more severely injured patients would therefore have been expected to do poorly. The increased ISS in the later time periods in the ISS>18 cohort suggests that this may have been true to some extent.

Another potential confounder is the lack of data regarding the application of external fixators to patients. Some authors argue strongly for the early application of external fixators with delayed definitive fixation in severely injured patients, so called Damage Control Orthopedics.8 Although there is no doubt that some of the patients treated at UNC were managed according to DCO precepts, the database did not accurately record external fixator use.
and only suggested that only 27 patients were managed in such a fashion. Without accurate records regarding the use of an external fixator and with so few patients in such a cohort, we are unable to evaluate the outcomes of such management.

Our study used time from arrival at the hospital until definitive fixation of the patient’s femoral fracture as a surrogate to estimate time from injury to fixation. If patients in earlier time periods preferentially arrived at the hospital more slowly or more rapidly than those who were in the later periods, our use of arrival time to time of fixation could skew data, but this seems unlikely. Other studies have used time of arrival at the hospital to fixation as an estimate of time from injury.17

Conclusions

In conclusion, this study demonstrates that delayed fixation of femoral fractures is associated with greater morbidity and increasing costs for patients. In those with ISS≤18, definitive management of femur fractures after 48 hours led to longer hospital stays and higher costs. Patients with ISS>18 had more days on ventilator and higher hospital costs with management after 24 hours and longer hospital and ICU stays when treated definitively after 48 hours. Early appropriate care of patients in this study was associated with lower morbidity and costs regardless of injury severity. An exception to this finding was the increased number of days on the ventilator in severely injured patients (ISS≥33) when managed between 24-48 hours as compared to 48-120 hours and was the only finding in support of DCO precepts (to delay surgery in the severely injured). However, operating in the first 24 hours in these severely injured patients was not associated with poor results.
With no statistically significant differences in most surrogate morbidity markers between treatment within 12 hours versus 24 hours, our data suggest that management of patients as soon as is feasible does not lead to worsening morbidity. Patient morbidity and costs to both the patient and healthcare systems are minimized when early definitive management of femoral fractures can be undertaken.
## Appendix A: Tables and Figures for Systematic Review

<table>
<thead>
<tr>
<th>Adequacy of study population</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Comparability of subjects</td>
<td></td>
</tr>
<tr>
<td>Validity and reliability of measurement</td>
<td></td>
</tr>
<tr>
<td>Appropriateness of outcome measure</td>
<td></td>
</tr>
<tr>
<td>Appropriateness of statistical analysis</td>
<td></td>
</tr>
<tr>
<td>Adequacy of control of confounding</td>
<td></td>
</tr>
<tr>
<td><strong>Total and mean</strong></td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Sample of tool used for grading of individual studies
Figure 2. Flowchart of study
<table>
<thead>
<tr>
<th>Source</th>
<th>Design</th>
<th>Quality Grade</th>
<th>Setting</th>
<th>Sample Size</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morshed et al, 2009</td>
<td>R-Cohort</td>
<td>1.83</td>
<td>567 Trauma centers in US</td>
<td>3069</td>
<td>2000-2004</td>
<td>In-hospital mortality</td>
</tr>
<tr>
<td>Nahm et al, 2011</td>
<td>R-Cohort</td>
<td>1.67</td>
<td>Single Level 1 Trauma Center</td>
<td>750</td>
<td>1999-2006</td>
<td>PE, ARDS, sepsis, DVT, ARF, MOF, mortality</td>
</tr>
<tr>
<td>O’Toole et al, 2009</td>
<td>R-Cohort</td>
<td>1.33</td>
<td>Single Level 1 Trauma Center</td>
<td>227</td>
<td>2002-2005</td>
<td>Mortality, ARDS</td>
</tr>
<tr>
<td>Pape et al, 2002</td>
<td>R-Cohort</td>
<td>1.33</td>
<td>Single Level 1 Trauma Center</td>
<td>514</td>
<td>1981-2000</td>
<td>ARDS, Infection, MOF, non-union, Hosp-LOS</td>
</tr>
<tr>
<td>Pape et al, 2007</td>
<td>RCT</td>
<td>1.5</td>
<td>10 European Trauma Centers</td>
<td>165</td>
<td>2000-2006</td>
<td>ICU-LOS, Vent time, PNA, ALI, ARDS, MOF, sepsis, SIRS</td>
</tr>
<tr>
<td>Tuttle et al, 2009</td>
<td>R-Cohort</td>
<td>0.67</td>
<td>Single Level 1 Trauma Center</td>
<td>462</td>
<td>1993-2006</td>
<td>ARDS, PNA, MOF, mortality, ICU-LOS, Hosp-LOS</td>
</tr>
</tbody>
</table>

Table 1. Summary of Included Articles
Abbreviations: R-Cohort, retrospective cohort; RCT, randomized controlled trial; PE, pulmonary embolism; ARDS, acute respiratory distress syndrome; DVT, deep vein thrombosis; ARF, acute renal failure; ALI, acute lung injury; MOF, multi organ failure; SIRS, systemic inflammatory response syndrome; ICU-LOS, intensive care unit length-of-stay; Hosp-LOS, hospital length-of-stay; PNA, pneumonia
<table>
<thead>
<tr>
<th>Source</th>
<th>Mortality</th>
</tr>
</thead>
</table>
| Morshed et al, 2009† | 12-24hrs: 0.45<sup>a</sup> RR  
|                    | 24-48hrs: 0.83<sup>a</sup> RR  
|                    | 48-120hrs: 0.58 RR  
|                    | >120hrs: 0.43<sup>a</sup> RR  |
| Nahm et al, 2011 ★ | ETC 1.0%  
|                    | DCO 4.8%<sup>a</sup>  |
|                    | ETC 1.7%  
|                    | DCO 4.8%  |
|                    | ETC 1.2%  
|                    | DCO 6.0%<sup>a</sup>  |
|                    | ETC 5.2 days  
|                    | DCO 12.9 days<sup>a</sup>  |
| O’Toole et al, 2009 | ETC 2.0%  
|                    | DCO 17.9%<sup>a</sup>  |
|                    | ETC 1.5%  
|                    | DCO 0.0%  |
|                    | ETC 7.1 days  
|                    | DCO 17.3 days<sup>a</sup>  |
| Pape et al, 2002*  | '81-'89 ETC 32.7%  
|                    | '81-'89 DCO 16.2%  
|                    | '93-'00 ETC 15.1%  
|                    | '93-'00 DCO 7.8%  |
|                    | '81-'89 ETC 21.7%  
|                    | '81-'89 DCO 16.6%  
|                    | '93-'00 ETC 16.2%  
|                    | '93-'00 DCO 11.5%  |
|                    | ETC 8.2 days  
|                    | DCO 12.4 days  |
| Pape et al, 2007#  | ETC 8.6%  
|                    | DCO 10.0%  |
|                    | ETC 5.0%  
|                    | DCO 5.0%  |
|                    | ETC 8.0 days  
|                    | DCO 11.0 days  |
| Scalea et al, 2000#| ETC <1.0%  
|                    | DCO 9.0%<sup>a</sup>  |
|                    | ETC 8.0 days  
|                    | DCO 11.0 days  |
| Tuttle et al, 2009 | ETC 1.81%  
|                    | DCO 1.79%  |
|                    | ETC 2.78%  
|                    | DCO 3.08%  |
|                    | ETC 13.2 days  
|                    | DCO 12.1 days  |

Table 2. Outcomes from studies appraised
†-Inverse probability treatment-weighted risk ratios shown in relation to management <12 hrs as baseline, values statistically significant
★-Data from patients with ISS>18. Patients with ISS<18 showed no statistically significant differences.
$-Compared stable versus borderline patients in
-Study defined over different time periods. '81-'89 refers to 1981-1989 while '93-'00 is 1993-2000. ARDS numbers were showed statistically significant differences when comparing ETC and DCO between time periods in addition to being statistically different comparing ETC to DCO within each time period. MOF was only statistically significantly different when comparing the early time period to the late.
#-Unadjusted numbers
a-p<0.05
### Appendix B: Figures and tables for original research

<table>
<thead>
<tr>
<th></th>
<th>ISS ≤18</th>
<th></th>
<th>ISS &gt;18</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(t_0) (0-12h) ((n=171))</td>
<td>(t_1) (12-24h) ((n=124))</td>
<td>(t_2) (24-48h) ((n=48))</td>
<td>(t_3) (&gt;120h) ((n=5))</td>
</tr>
<tr>
<td>Age</td>
<td>31.7 ± 11.5</td>
<td>32.7 ± 11.3</td>
<td>36.6 ± 11.9</td>
<td>39.1 ± 11.4</td>
</tr>
<tr>
<td>ISS</td>
<td>11.4 ± 3.0</td>
<td>10.9 ± 2.8</td>
<td>11.3 ± 2.8</td>
<td>11.8 ± 3.4</td>
</tr>
<tr>
<td>% White</td>
<td>49.1 ± 50</td>
<td>58.8 ± 49</td>
<td>50.0 ± 51</td>
<td>61.3 ± 50</td>
</tr>
<tr>
<td>% Male</td>
<td>78.7 ± 44</td>
<td>70.2 ± 46</td>
<td>70.1 ± 46</td>
<td>77.4 ± 43</td>
</tr>
<tr>
<td>% Transfer</td>
<td>31.0 ± 46</td>
<td>37.9 ± 49</td>
<td>47.9 ± 50</td>
<td>35.5 ± 49</td>
</tr>
<tr>
<td>AIS Head/Neck</td>
<td>0.17 ± 0.59</td>
<td>0.17 ± 0.59</td>
<td>0.23 ± 0.69</td>
<td>0.29 ± 0.69</td>
</tr>
<tr>
<td>AIS Face</td>
<td>0.17 ± 0.54</td>
<td>0.06 ± 0.32</td>
<td>0.06 ± 0.32</td>
<td>0.10 ± 0.40</td>
</tr>
<tr>
<td>AIS Chest</td>
<td>0.19 ± 0.65</td>
<td>0.25 ± 0.69</td>
<td>0.13 ± 0.49</td>
<td>0.26 ± 0.73</td>
</tr>
<tr>
<td>AIS Extremities</td>
<td>3.02 ± 0.15</td>
<td>2.99 ± 0.09</td>
<td>3.03 ± 0.20</td>
<td>3.03 ± 0.18</td>
</tr>
<tr>
<td>AIS Abdominal</td>
<td>0.19 ± 0.61</td>
<td>0.21 ± 0.62</td>
<td>0.38 ± 0.76</td>
<td>0.35 ± 0.84</td>
</tr>
<tr>
<td>AIS External</td>
<td>0.51 ± 0.70</td>
<td>0.40 ± 0.58</td>
<td>0.35 ± 0.60</td>
<td>0.42 ± 0.67</td>
</tr>
</tbody>
</table>

Table 1. Characteristics of trauma patients between 16 and 65 admitted with femur fractures by time of definitive fixation. Age and AIS Head/Neck had statistically significant differences \((p<0.05)\) amongst the means for those with ISS<18. ISS was statistically different among the means for those with ISS>18 \((p<0.05)\).
<table>
<thead>
<tr>
<th></th>
<th>$t_0$ (0-12h)</th>
<th>$t_1$ (12-24h)</th>
<th>$t_2$ (24-48h)</th>
<th>$t_3$ (48-120h)</th>
<th>$t_4$ (&gt;120h)</th>
<th>$t_0$ (0-12h)</th>
<th>$t_1$ (12-24h)</th>
<th>$t_2$ (24-48h)</th>
<th>$t_3$ (48-120h)</th>
<th>$t_4$ (&gt;120h)</th>
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<tbody>
<tr>
<td><strong>Hospital LOS</strong></td>
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<tr>
<td><strong>ICU-LOS</strong></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Raw</td>
<td>1.04 (0.43-1.65)</td>
<td>0.60 (0-1.32)</td>
<td>1.67 (0.51-2.82)</td>
<td>2.03 (0.60-3.47)</td>
<td>1.40 (0-4.98)</td>
<td>3.74 (1.64-5.83)</td>
<td>4.93 (2.89-6.96)</td>
<td>6.50 (4.03-8.97)</td>
<td>7.91 (4.74-11.09)</td>
<td>17.53 (13.84-21.22)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>1.02 (0.41-1.64)</td>
<td>0.59 (0-1.32)</td>
<td>1.68 (0.51-2.84)</td>
<td>2.09 (0.65-3.56)</td>
<td>1.60 (0-5.22)</td>
<td>3.77 (1.66-5.87)</td>
<td>4.86 (2.81-6.92)</td>
<td>6.52 (4.04-9.00)</td>
<td>7.91 (4.71-11.10)</td>
<td>17.61 (13.83-21.39)</td>
</tr>
<tr>
<td><strong>Ventilator Days</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw</td>
<td>0.47 (0.12-0.81)</td>
<td>0.22 (0-0.63)</td>
<td>0.81 (0.16-1.46)</td>
<td>0.90 (0.10-1.71)</td>
<td>0.190 (0.019-0.373)</td>
<td>1.65 (0-3.34)</td>
<td>2.76 (1.14-4.39)</td>
<td>4.54 (2.56-6.53)</td>
<td>5.57 (3.05-8.08)</td>
<td>10.59 (7.66-13.52)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>0.45 (0.10-0.79)</td>
<td>0.21 (0-0.63)</td>
<td>0.85 (0.20-1.50)</td>
<td>0.96 (0.15-1.78)</td>
<td>0.258 (0.032-0.484)</td>
<td>1.65 (0-3.35)</td>
<td>2.64 (1.00-4.29)</td>
<td>4.57 (2.58-6.56)</td>
<td>5.62 (3.08-8.14)</td>
<td>10.84 (7.85-13.83)</td>
</tr>
<tr>
<td><strong>Hospital Cost</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw</td>
<td>41.1 (32.9-49.4)</td>
<td>34.2 (24.5-43.9)</td>
<td>67.4 (52.1-82.8)</td>
<td>74.1 (54.8-93.4)</td>
<td>71.0 (19.0-123.1)</td>
<td>64.9 (46.9-8.9)</td>
<td>83.3 (65.8-100.9)</td>
<td>96.6 (74.9-118.4)</td>
<td>130.3 (102.2-158.4)</td>
<td>211.1 (176.7-245.6)</td>
</tr>
<tr>
<td>Adjusted</td>
<td>41.6 (33.3-49.9)</td>
<td>34.5 (24.8-44.2)</td>
<td>66.5 (51.1-81.9)</td>
<td>72.1 (52.6-91.6)</td>
<td>66.5 (14.1-119.0)</td>
<td>65.1 (46.9-8.8)</td>
<td>83.7 (65.9-101.4)</td>
<td>96.4 (74.5-118.4)</td>
<td>130.1 (101.7-158.4)</td>
<td>210.2 (175.1-245.4)</td>
</tr>
</tbody>
</table>

Table 2. Raw and adjusted (for age and gender) values for surrogate morbidity markers. 95% confidence intervals are within parenthesis. All outcomes are reported in days with the exception of hospital costs which is reported in thousands of dollars. There was no statistically significant difference among the models for ICU-LOS and ventilator days in the cohort of patients with ISS<18 (Prob>F >0.05).
<table>
<thead>
<tr>
<th></th>
<th>( t_0 ) (0-12h) n=11</th>
<th>( t_1 ) (12-24h) n=12</th>
<th>( t_2 ) (24-48h) n=8</th>
<th>( t_3 ) (48-120h) n=9</th>
<th>( t_4 ) (&gt;120h) n=10</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>p=0.294</td>
<td>p=0.284</td>
<td>p=0.284</td>
<td>p=0.071</td>
<td>p=0.001</td>
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<tr>
<td>Hospital LOS Adjusted</td>
<td>12.10 (0-25.48)</td>
<td>20.50 (8.13-32.87)</td>
<td>21.07 (5.58-36.28)</td>
<td>27.60 (13.25-41.96)</td>
<td>43.29 (29.14-57.44)</td>
</tr>
<tr>
<td></td>
<td>p=0.366</td>
<td>p=0.390</td>
<td>p=0.390</td>
<td>p=0.135</td>
<td>p=0.004</td>
</tr>
<tr>
<td>ICU-LOS Raw</td>
<td>4.00 (0-11.50)</td>
<td>8.00 (2.95-13.05)</td>
<td>13.625 (7.44-19.81)</td>
<td>10.89 (5.06-16.72)</td>
<td>22.4 (16.87-27.93)</td>
</tr>
<tr>
<td></td>
<td>p=0.269</td>
<td>p=0.025</td>
<td>p=0.025</td>
<td>p=0.093</td>
<td>p&lt;0.001</td>
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<tr>
<td></td>
<td>p=0.342</td>
<td>p=0.043</td>
<td>p=0.152</td>
<td>p=0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Ventilator Days Raw</td>
<td>1.2 (0-5.86)</td>
<td>5.27 (0.83-9.71)</td>
<td>11.38 (6.17-16.58)</td>
<td>9 (4.09-13.91)</td>
<td>14.9 (10.24-19.56)</td>
</tr>
<tr>
<td></td>
<td>p=0.222</td>
<td>p=0.007</td>
<td>p=0.029</td>
<td>p=0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Ventilator Days Adjusted</td>
<td>1.55 (0-6.37)</td>
<td>5.28 (0.78-9.78)</td>
<td>11.05 (5.77-16.33)</td>
<td>8.77 (3.80-13.75)</td>
<td>15.01 (10.11-19.91)</td>
</tr>
<tr>
<td></td>
<td>p=0.269</td>
<td>p=0.013</td>
<td>p=0.050</td>
<td>p=0.001</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Hospital Cost Raw</td>
<td>62.5 (17.9-107.0)</td>
<td>119.9 (72.3-162.6)</td>
<td>148.1 (95.8-200.3)</td>
<td>155.2 (99.3-211.0)</td>
<td>284.5 (232.2-336.7)</td>
</tr>
<tr>
<td></td>
<td>p=0.075</td>
<td>p=0.019</td>
<td>p=0.015</td>
<td>p=0.001</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Hospital Cost Adjusted</td>
<td>64.8 (18.3-111.4)</td>
<td>120.3 (77.0-163.6)</td>
<td>144.8 (91.4-198.1)</td>
<td>150.9 (93.5-208.4)</td>
<td>287.8 (232.7-343.0)</td>
</tr>
<tr>
<td></td>
<td>p=0.093</td>
<td>p=0.034</td>
<td>p=0.031</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3. Subgroup analysis of those with ISS≥33. Raw and adjusted (for age and gender) values for surrogate morbidity markers. 95% confidence intervals are within parenthesis. All outcomes are reported in days with the exception of hospital costs which is reported in thousands of dollars.
<table>
<thead>
<tr>
<th>Time interval</th>
<th>ISS≤18 % discharged home</th>
<th>ISS&gt;18 % discharged home</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t_0$</td>
<td>71.93</td>
<td>43.40</td>
</tr>
<tr>
<td>$t_1$</td>
<td>71.77</td>
<td>39.29</td>
</tr>
<tr>
<td>$t_2$</td>
<td>64.58</td>
<td>28.95</td>
</tr>
<tr>
<td>$t_3$</td>
<td>51.61</td>
<td>21.74</td>
</tr>
<tr>
<td>$t_4$</td>
<td>40.00</td>
<td>11.76</td>
</tr>
</tbody>
</table>

Table 4. Percent of patients discharged home versus care facility in each time interval. Chi square analysis demonstrated no statistical significant difference amongst the values for those with ISS<18 or ISS>18 ($p=0.095$ and 0.074).
Figure 1. ICU Length-of-stay. Statistical significance as compared to t₀ denoted by *.
Figure 2. Days on ventilator. Statistical significance as compared to t₀ denoted by *.
Figure 3. Hospital length-of-stay. Statistical significance as compared to $t_0$ denoted by *.

Hospital Length-of-stay

Days

<table>
<thead>
<tr>
<th>Time to definitive fixation</th>
<th>ISS≤18</th>
<th>ISS&gt;18</th>
<th>ISS≥33</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t_0$ (0-12 hours)</td>
<td>7.55</td>
<td>11.9</td>
<td>2.10</td>
</tr>
<tr>
<td>$t_1$ (12-24 hours)</td>
<td>6.91</td>
<td>14.3</td>
<td>1.0</td>
</tr>
<tr>
<td>$t_2$ (24-48 hours)</td>
<td>9.43</td>
<td>20.5</td>
<td>0.50</td>
</tr>
<tr>
<td>$t_3$ (48-120 hours)</td>
<td>16.87</td>
<td>21.07</td>
<td>1.07</td>
</tr>
<tr>
<td>$t_4$ (&gt;120 hours)</td>
<td>13.84</td>
<td>22.44</td>
<td>43.29</td>
</tr>
</tbody>
</table>
Figure 4. Hospital Costs in thousands of dollars. Statistical significance as compared to $t_0$ denoted by *.
References

1. Trauma TAAftSo. Trauma Facts 2011.


