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In-hospital mortality from femoral shaft fracture depends on the initial delay to fracture fixation and injury severity score- a retrospective cohort study from the NTDB 2002-2006

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Abstract

BACKGROUND—Optimal surgical timing for definitive treatment of femur fractures in severely injured patients remains controversial. This study was performed to examine in-hospital mortality for patients with femur fractures with regard to surgical timing, Injury Severity Score (ISS), and age.

METHODS—The National Trauma Data Bank version 7.0 was used to evaluate in-hospital mortality for patients presenting with unilateral femur fractures. Patients were stratified into four groups by surgical timing (ST) and four groups by ISS. χ^2 tests were used to evaluate baseline interrelationships. Binary regression was used to examine the association between time to surgery, ISS score, age, and mortality after adjusting for patient medical comorbidities, and personal demographics.

RESULTS—A total of 7,540 patients met inclusion criteria, with a 1.4% overall in-hospital mortality rate. For patients with an isolated femur fracture, surgical delay beyond 48 hours was associated with nearly five times greater mortality risk compared with surgery within 12 hours (adjusted relative risk, 4.8; 95% confidence interval, 1.6–14.1). Only severely injured patients (ISS, 26+) had higher associated mortality with no delay in surgical fixation (ST 1 < 12 hours) relative to ST2 of 13 hours to 24 hours with an adjusted relative risk of 4.2 (95% confidence interval, 1.0–16.7). The association between higher mortality rates and surgical delay beyond 48 hours was even stronger in the elderly patients.

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AUTHORSHIP

R.V.C. was involved in the literature search, study design, data analysis, data interpretation, writing, and critical revision. S.C.G. was involved in the literature search, study design, data analysis, data interpretation, writing, and critical revision. K.F.S. was involved in the literature search, study design, data collection, data analysis, data interpretation, writing, and critical revision.

DISCLOSURE

The authors declare no conflicts of interest.

This study was presented at the New England Orthopaedic Surgery Association Fall Meeting, November 2012; The Orthopaedic Trauma Association (OTA), October 2012, Minneapolis, Minnesota; The American Academy of Orthopaedic Surgery (AAOS), February 2012, San Francisco, California; and The American College of Surgeons New England Region Trauma Division Resident Competition, November 2011, Boston Massachusetts.

CONCLUSION—This study supports the work of previous authors who reported that early definitive fixation of femur fractures is not only beneficial, particularly in the elderly, but also consistent with more recent studies recommending at least 12-hour to 24-hour delay in fixation in severely injured patients to promote better resuscitation. (*J Trauma Acute Care Surg*. 2014;00: 00–00. Copyright * 2014 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE—Level II.

Keywords

Damage control; femoral shaft fracture; mortality; elderly; timing

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The optimal time for definitive fixation of femur fractures is an important topic in orthopedic surgery because it can impact the physiologic status and patient mortality. There has been an evolution over time in what is considered the ideal time for definitive fixation. Several studies in the 1980s supported early stabilization of long bone fractures in patients with multiple injuries.[1–10] In 1985, Johnson et al.[4] reported that early stabilization of femur fractures was associated with a fivefold reduction in the rate of adult respiratory distress syndrome (ARDS) compared with late fixation. In a 1989 prospective study, Bone et al.[11] showed that reamed intramedullary nailing of femur fractures within 24 hours of injury led to fewer complications and a shorter hospital stay compared with delayed treatment.

In recent years, the concept of “damage-control orthopedics” with delay of definitive fixation in patients with multiple injuries has taken hold.[12] Whether an external fixator,[13] traction, or an unreamed proximally unlocked retrograde nail[11] is used, proponents of damage-control orthopedics agree that definitive surgery should be delayed until the patient has more reserve and can tolerate a second inflammatory “hit.”[14]

Some have suggested that 2 days to 5 days after major injury is a potentially vulnerable time when further surgery can result in a significant release of inflammatory mediators that may increase the risk of ARDS, sepsis, and pneumonia.[15] Thus, those who advocate the avoidance of a “second hit,”during this 2-day to 5-day window, would support the delay of definitive fixation beyond 5 days.[1–10] As the technology and understanding of the physiology of major systemic injuries have progressed, whether delayed definitive fixation offers a significant advantage over primary intramedullary nail fixation remains a controversial question.

Although there have been many individual studies investigating this question, to date, few have used large databases. Morshed et al.[16] in 2009 used the National Trauma Data Bank (NTDB) version 5.0 for 2000 to 2004 to look at severely injured patients (Injury Severity Score [ISS] > 15) and found that delaying definitive fixation beyond 12 hours in these patients, particularly those with abdominal trauma, resulted in a lower relative risk of mortality. However, contrary to many surgeons’ personal experience and earlier findings that early fixation is better, they found no disadvantage to delaying fixation beyond 120 hours.

A 2012 systematic review by Nahm and Vallier[17] examined the literature from 1946 to 2011 and found that 38 studies met their inclusion criteria. Because of the heterogeneity of the studies, they were not able to obtain a pooled estimate but concluded that there was no difference in ARDS or mortality for early versus delayed fixation. They did find increased length of stay for those undergoing delayed fixation. The purpose of this study was to investigate the optimal time for definitive fixation of femur fractures for patients with varying levels of injury severity.

PATIENTS AND METHODS

Institutional Review Board Approval

Permission to perform this retrospective cohort study was obtained from the institutional review board.

Data Source

The study used the NTDB (version 7.0) (http://www.facs.org/trauma/ntdb/ntdbapp.html). This databank includes 1.48 million records at 712 hospitals from the years 2002 to 2006.

Patients

The target patient population was adults (>18 years of age) who sustained a unilateral open or closed femoral shaft fracture and underwent open or closed reduction and internal fixation.

Inclusion/Exclusion Criteria

Patients were included in the study if they (1) were 18 years or older, (2) had a unilateral closed or open fracture of the femoral shaft (DRG International Classification of Diseases—9th Rev. code 821.01 or 821.11), and (3) underwent closed or open reduction and internal fixation of the femur (Current Procedural Terminology code 79.15 or 79.35).

Patients were excluded from the cohort if they did not have a valid (1) mortality code based on hospital discharge status, (2) ISS, or (3) time to procedure date. Patients were also excluded if they (4) did not have a valid admission; (5) were transferred from another facility, which could make time to procedure data misleading; (6) were transferred out of the facility after surgery, which might bias in-hospital mortality; (7) were residing in a burn unit, which might affect surgical timing; and (8) were missing patient sex designation.

Definitions

Time to Surgery—Patients were stratified into four groups based on timing of intramedullary nailing from hospital presentation: (1) ST1 12 hours or less, (2) ST2 greater than 12 hours to 24 hours, (3) ST3 greater than 24 hours to 48 hours, and (4) ST4 greater than 48 hours to 30 days. These cohorts were selected to provide clinically relevant information, while allowing each group to contain enough patients to provide sufficient power to detect associations.

ISS Classification—To evaluate the effect of injury severity on survival, patients were stratified by ISS ranking into four groups as (*a*) mild (ISS, 9), (*b*) mild-to-moderate (ISS, 10–15), (*c*) moderate-to-severe (ISS, 16–25), and (*d*) severe (ISS > 26).

Patient age was dichotomized as 18 years to 64 years and older than 65 years.

Deyo-Charlson Comorbidity Index—The Deyo-Charlson comorbidity index was computed based on preexisting comorbidities provided for each patient within the NTDB by applying the protocol developed by Deyo et al.[18]

Limitations in the Data Source—Although it would be desirable to obtain information about concomitant procedures or types of provisional stabilization used, in the format of a large-database study, these details were not feasible to obtain. Further studies could certainly be designed to investigate the effects of these variables.

Funding Source

There were no external sources of funding for this study.

Statistical Methods

Sample descriptive statistics included means and SDs for continuous variables and frequencies for categorical variables and were evaluated individually and relative to in-hospital mortality.

Generalized linear modeling assuming a binary distribution using a Log link was used to estimate unadjusted and adjusted relative risks (RRs and ARRs, respectively) and in-hospital mortality rates associated with individual and multiple predictor models. The GLIMMIX procedure was used in SAS (SAS Institute, Cary, NC) version 9.3 running under the Windows Ultimate-64 operating system. The effects of surgical timing, injury severity, and patient age group and the three 2-way interactions among these predictors were of primary interest. Adjusting factors were sex, race (categorized as white, black, Hispanic, and other), the Deyo-Charlson comorbidity index (dichotomized as 0 and 1+), fracture type (open or closed), and surgical procedure (79.15 closed reduction internal fixation or 79.35 open reduction internal fixation).

RESULTS

Cohort

Within the NTDB, 14,046 patients (0.76%) had an open or closed femur fracture and underwent fixation. Of this cohort, 10,214 (72.9%) were older than 18 years. Of the 10,214 patients meeting the inclusion criteria, 34 (0.3%) were excluded because of a missing mortality code, 43 (0.4%) were excluded because of missing time to procedure codes, 73 (0.7%) were excluded because of missing or invalid ISS, 961 (9.6%) were excluded because they did not have a valid admission record, and 1,563 (17.2%) were excluded because they were transferred from another hospital. Thus, overall, 73.8% (7,540 of 10,214) of those meeting inclusion criteria were included in the analyses. Figure 1 summarizes the implementation of inclusion and exclusion criteria.

Sample

As summarized in Table 1, patients in our cohort were largely younger than 65 years (88%), were male (69%), were predominately white (64%), had a low incidence of life-threatening comorbidities (10%), and had predominately closed femur fractures (80%). The majority of patients (53%) were treated within 12 hours of admission, 23% between 12 hours and 24 hours of admission, 14% between 24 hours and 48 hours of admission, and 10% between 48 hours and 30 days of admission.

Relationship of Surgical Timing, ISS, and Age With In-hospital Mortality

Surgical time, ISS, and patient age groups each demonstrated significant main effects with patterns consistent with clinical experience. The adjusted mortality rates for the surgical timing, injury severity, interactions between surgical timing and age groups, as well as interactions between injury severity and age group are summarized in Table 2. Graphics of these interactions are shown in Figures 2 and 3. Selected adjusted relative risks are summarized in Table 3.

For patients with an isolated femur fracture (ISS, 9), there was no statistical difference in mortality if definitive surgery was performed within 12 hours, between 12 hours and 24 hours, or from 24 hours to 48 hours. Beyond 48 hours, the mortality rate increased substantially, with nearly five times greater mortality risk (ARR, 4.8; 95% confidence interval [CI], 1.6–14.1) after adjusting for age, sex, and medical comorbidities in the group where surgery was performed between 48 hours to 30 days versus the group where surgery was performed in 12 hours or less. Mildly-to-moderately injured patients (ISS, 10–15) had 4.2 times (95% CI, 1.28–13.74) greater risk of dying if surgery was delayed greater than 48 hours than if surgery occurred within the first 12 hours. For patients in the most severely injured ISS group (26+), surgical delay beyond 48 hours was also associated with significantly increased mortality risk (ARR, 4.7 vs. within 25–48 hours; 95% CI, 1.1–19.5). The only group in which there was reduced mortality risk with surgical delay was in the most severely injured patients (ISS, 26+) in whom surgical delay of greater than 24 hours but less than 48 hours was associated with the lowest mortality risk compared with surgery within 12 hours (ARR, 4.2; 95% CI, 1.0–16.7) (Tables 4 and 5)

Age was a significant factor in mortality at nearly all time points, with patients older than 65 years having significantly higher risks of dying. This effect was most pronounced in the later surgical timing groups with nearly nine times the risk in the 24-hour to 48-hour group and nearly seven times the risk in the 48-hour to 30-day group. Figure 3 depicts the effect of age on mortality by ISS.

DISCUSSION

Our findings show that most diaphyseal femur fractures in adults are treated with open or closed reduction and internal fixation within 24 hours of hospital admission. For patients with virtually all injury severity types, delaying definitive fixation beyond 48 hours was associated with increased mortality. For severely injured patients, there did seem to be an advantage in delaying definitive surgery by 12 hours to 24 hours. Presumably, this delay is a period of aggressive resuscitation that better prepares the patients for the stress of surgery. Even in the most severely injured group, there was increased mortality risk associated with delaying surgery beyond 48 hours.

The results of this investigation generally concur with other recent reports. In a similar retrospective database study using the NTDB version 5.0, Morshed et al.[16] found that surgery in severely injured patients within the first 12 hours after hospital presentation was associated with a higher mortality compared with the delayed groups. They attributed the improved survival in the delayed groups to improved "resuscitation." Delaying treatment had the greatest improvement in survival for patients with serious abdominal injury. They concluded that "damage-control" orthopedics and delayed definitive treatment of femur fractures in patients with multiple injuries may "reduce adverse outcomes."[19] Unlike our findings, however, the authors found that delaying surgery for more than 5 days resulted in the lowest adjusted mortality rates.

We found that for patients across virtually all injury severity types, surgical delay beyond 48 hours was associated with a significantly increased mortality risk. This finding held true after adjusting for age, sex, and medical comorbidities. These results are similar to those published by Nahm et al. who found that definitive stabilization of femur fractures within 24 hours of injury is safe for "most patients with multiple injuries."[17] The only difference is our finding that for severely injured patients, the 24-hour to 48-hour time frame may be safer than the 0-hour to 12-hour period.

There are some areas requiring further investigation. It has been suggested that severely injured patients may be particularly vulnerable to further surgical insult during the 2-day to 5-day period[2] as the inflammatory cascade peaks and a "second hit" could potentially lead to ARDS and multisystem organ dysfunction. A recent study by Lefaivre et al.[20] examined two Level 1 trauma registries and examined multiple factors for three distinct surgical timing groups. They found that femur fractures predicted mortality after controlling for other factors and was associated with ARDS. They found that fracture fixation within the 8-hour to 24-hour time window was associated with the lowest mortality compared with other time points and that fixation greater than 24 hours was associated with higher rates of ARDS. Our study supports these results and showed higher mortality rates when surgery was performed beyond 48 hours, but we did not specifically look at the 2-day to 5-day period because there were insufficient numbers in a group within this time frame.

One finding of the study that was puzzling to us was the predominance of the DRG International Classification of Diseases—9th Rev. code for open reduction internal fixation, rather than closed reduction internal fixation. In most cases, the dominant mode of fixation for intramedullary nailing could be accomplished without opening the fracture site. Current Procedural Terminology codes, which would likely be more specific for the procedure performed, were not reliably able to be searched for within the NTDB. This is an interesting result, which we presume represents differential coding for similar procedures (intramedullary nailing) rather than a predominance of opening the fracture site.

Moreover, patients with damage to specific organ systems might benefit from differential treatment. Patients with chest/thoracic trauma have been identified as a group that precise timing and decision to use an unreamed nail might be important to prevent ARDS.[10,19,21–24] Patients with chest and abdominal injuries have also been shown to have much higher rates of pulmonary complications, after controlling for other factors.[25] Optimum timing for femur fixation in patients with severe head injuries is also controversial, with some authors advocating for surgical delay for severely injured patients and others claiming that there is no significant effect.[19,26–29] Anglen et al.[30] have shown that close monitoring and aggressive resuscitation is especially important for patientswith severe brain injury to prevent intraoperative hypotension and worsening cerebral perfusion pressure; therefore, for these patients, damage-control principles might be warranted. Flierl et al.[31] in their 2010 review article outline the physiologic considerations for patients with head injuries and propose an algorithm for their treatment. Patients with severe damage in one of these or other organ systems have unique characteristics with regard to surgical timing and mortality that should also be considered.

There are some inherent limitations within the study design. It would be ideal to have further information on the patient cohort, such as which other organ systems were affected, methods of provisional stabilization, factors that led to a delay in the treatment, and additional information about medical comorbidities. However, unlike smaller prospective or retrospective studies, this type of information (such as external fixation or traction pin placement) is less readily and reliably obtained from large database studies. However, the large number of patients in the database improves the power of the study,[32] and even prospective studies on timing of fixation have led tovarying conclusions. Lozman et al.[33] in 1986 found improved cardiac index and lower shunting with immediate fixation in patients with femoral or tibial fractures randomized to immediate fixation versus traction or plaster casts and concluded that there was less pulmonary dysfunction with immediate fixation. In contrast, in a prospective evaluation using damage-control orthopedics for patients with multiple injuries, Taeger et al.[34] reported a 19.3% reduction in mortality compared with what would have been expected based on ISSs. Diversity among these smaller prospective studies suggests that although our study is retrospective, there may be some advantage to our larger database study, although there is certainly the potential for unmeasured confounders to affect the validity of the results.

Although the present study provides further evidence that early fixation of femur fractures is beneficial, it cannot answer the question definitively. With the database, it is not possible to control for factors before hospital presentation or for the potential diversity of initial treatment strategies in patients who did not have immediate intramedullary nailing. Although we stratified by injury severity, within each group, there is likely a spectrum of severity and patients with more severe injuries may have been selected to have undergone delayed fixation and had higher associated mortality. This is a source of potential confounding that cannot be completely eliminated within this retrospective study. There are potential interventions that might be proven to be beneficial such as the use of hypertonic saline, which Agudelo et al.[35] recently found in a small prospective trial to have an anti-inflammatory effect, which are not amenable to study using a large database. Similarly, the rate of various complications such as ARDS and multisystem organ failure in the database is not always complete, so the outcome of the study was mortality.

Despite some of these limitations, some conclusions emerged quite strongly. Elderly patients (>65 years) were more adversely affected by surgical delay than their younger counterparts. We know from the hip fracture literature that longer periods of immobility in this population are associated with higher rates of complications and increased mortality.[36–38] Unfortunately, all too often, this is the subset of patients in whom there is a delay for further diagnostic testing or medical optimization. In their population-based study, Enninghorst et al.[39] demonstrated that elderly femur fractures in Australia are a growing group and that this population often had delayed fixation beyond 24 hours. Our study lends further strength to the importance of femur fracture fixation being performed as expeditiously as possible in elderly patients.

Although the timing of femur fracture fixation will likely continue to be studied and additional insight obtained, there are several points that can be concluded from our study and are supported by a growing body of literature. First, definitive fixation within 12 hours in patients with an isolated femur fracture leads to a low rate of complications and a low mortality rate that persists up to 48 hours. Second, patients with multiple injuries will likely benefit from resuscitation before definitive stabilization of femur fractures. Third, although individual circumstances must be considered, for patients of all injury severity types, there was no apparent benefit to surgical delay beyond 48 hours. In fact, this seemed to have an adverse impact on mortality even after adjusting for other potential confounders. Finally, the adverse effect was even more pronounced in elderly patients; therefore, when possible, early fixation is even more important in this population.

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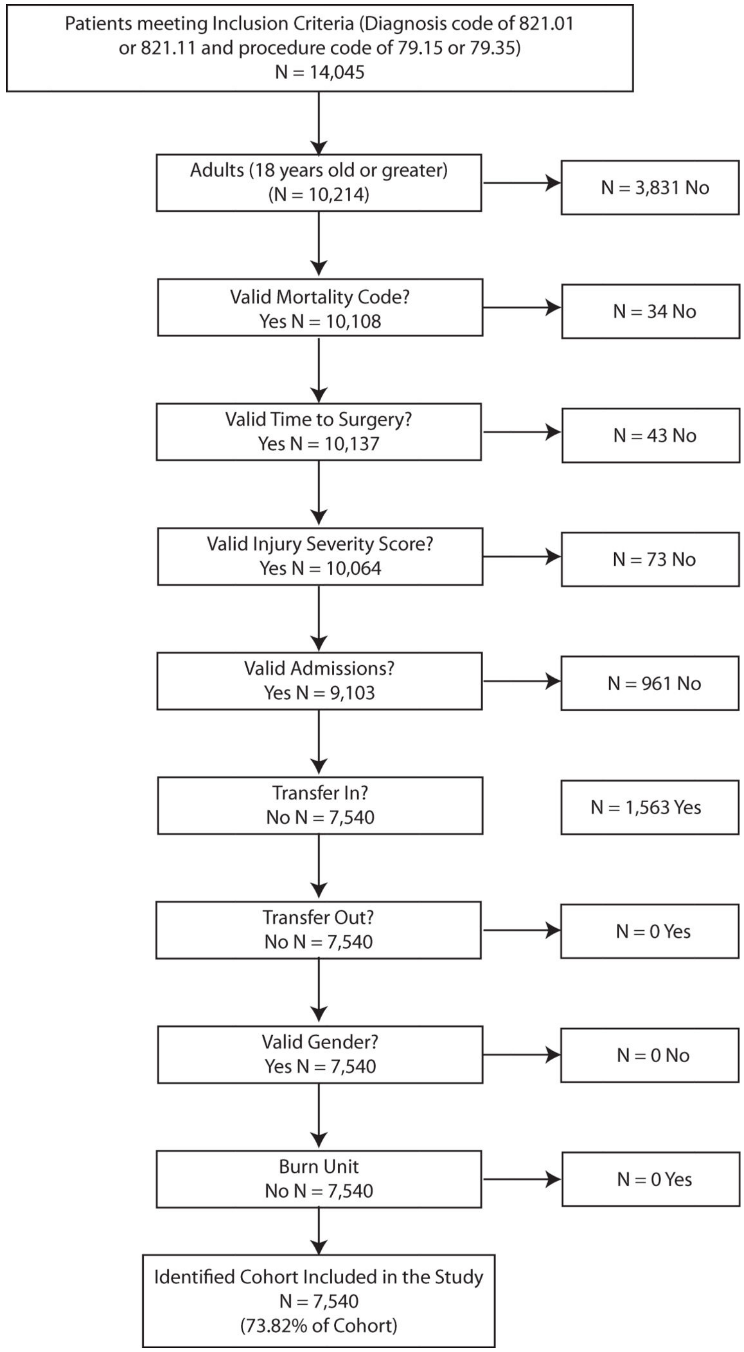
Patients meeting Inclusion Criteria (Diagnosis code of 821.01 or 821.11 and procedure code of 79.15 or 79.35)
N = 14,045
Adults (18 years old or greater)
(N = 10,214)
N = 3,831 No
Valid Mortality Code?
Yes N = 10,108
N = 34 No
Valid Time to Surgery?
Yes N = 10,137
N = 43 No
Valid Injury Severity Score?
Yes N = 10,064
N = 73 No
Valid Admissions?
Yes N = 9,103
N = 961 No
Transfer In?
No N = 7,540
N = 1,563 Yes
Transfer Out?
No N = 7,540
N = 0 Yes
Valid Gender?
Yes N = 7,540
N = 0 No
Burn Unit
No N = 7,540
N = 0 Yes
Identified Cohort Included in the Study
N = 7,540
(73.82% of Cohort)

Figure 1.

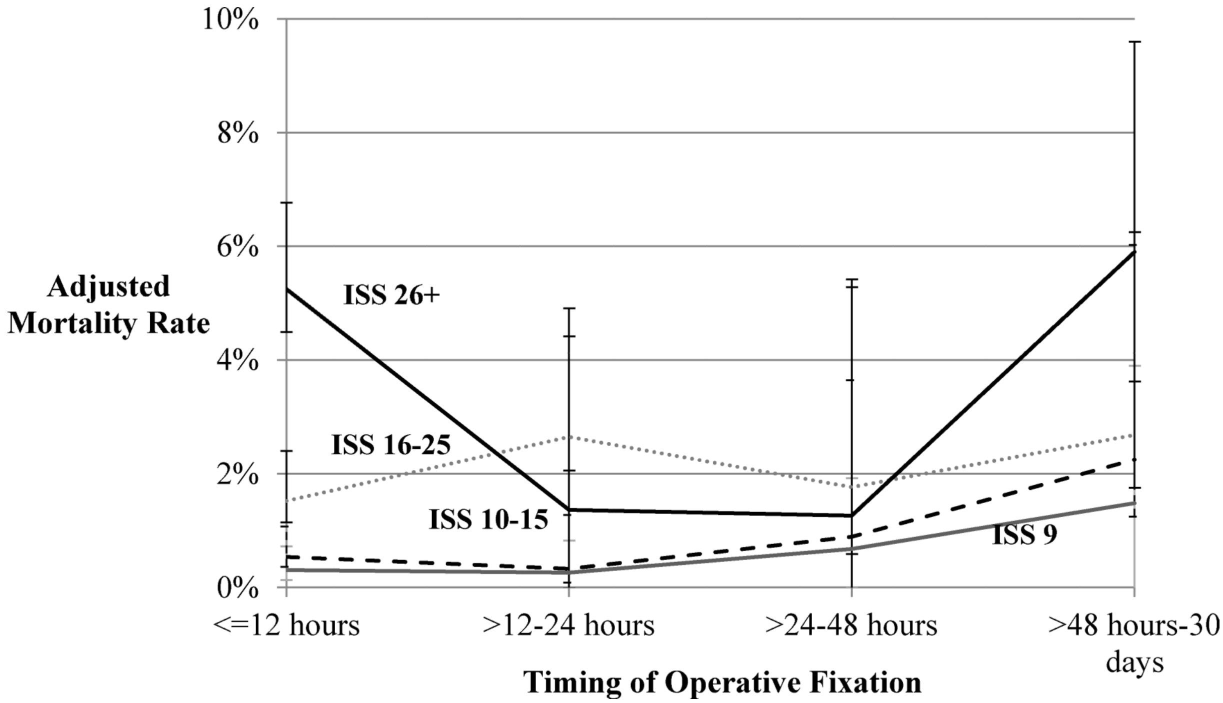

Figure 2.

Adjusted in-hospital mortality rates by timing of operative fixation for patients with isolated femur fractures (ISS=9), mild to moderate injuries to other systems (ISS 10-15), moderate to severe injuries to other systems(ISS 16-25) and severe multi-system injuries (ISS 26+).

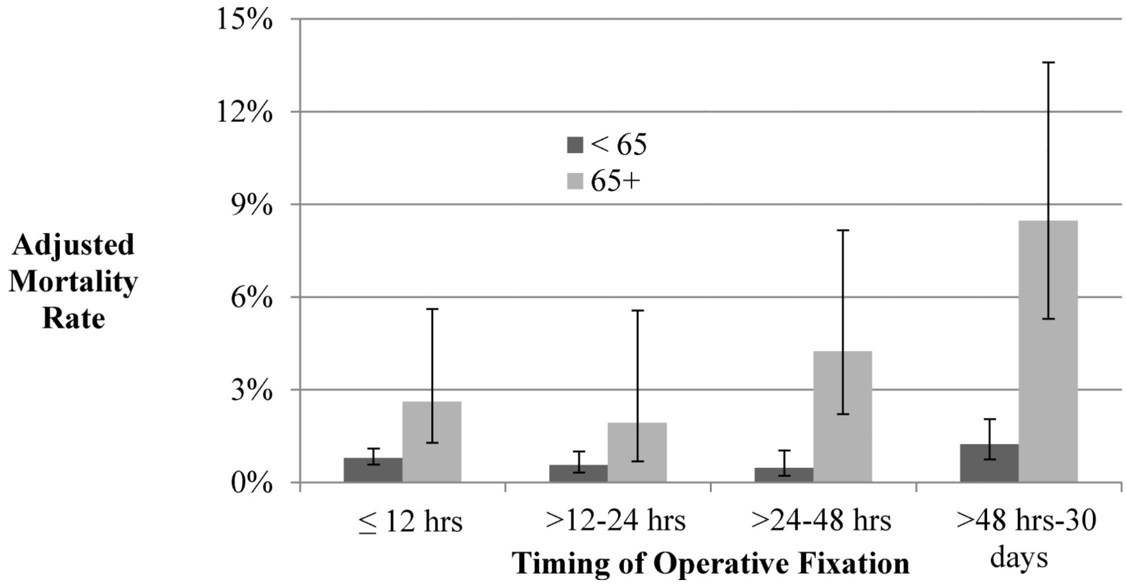

Figure 3.

Adjusted in-hospital mortality rates by timing of operative fixation for patients under and over 65 years of age.

TABLE 1

Patient Demographics and Adjusted* In-Hospital Mortality Rates With Selected Relative Risks

Variable	Category	Total (n = 7,540), n (%)	Unadjusted Mortality Rate (95% CI), %	Adjusted Mortality Rate (95% CI), %
Age, y	18 to 64	6,668 (88)	**1.11 (0.88–1.39)**	**0.64 (0.47–0.87)**
	65+	872 (12)	**3.56 (2.50–5.06)**	**2.92 (1.91–4.46)**
Sex	Female	2,314 (31)	1.64 (1.19–2.26)	0.70 (0.45–1.08)
	Male	5,226 (69)	1.28 (1.01–1.63)	0.74 (0.52–1.04)
Race	White	4,821 (64)	1.70 (1.37–2.11)	0.90 (0.65–1.25)
	Black	1,212 (16)	0.70 (0.39–1.43)	0.54 (0.27–1.06)
	Hispanic	720 (10)	0.40 (0.13–1.29)	0.25 (0.08–0.81)
	Other	787 (10)	1.40 (0.77–2.52)	0.80 (0.42–1.50)
Deyo-Charlson comorbidity index	DC = 0	6,819 (90)	1.33 (1.09–1.64)	0.73 (0.53–1.01)
	DC = 1+	721 (10)	1.94 (1.15–3.28)	0.64 (0.34–1.19)
ISS	9	2,796 (37)	0.82 (0.55–1.24)	0.47 (0.31–0.74)
	10 to 15	2,421 (32)	0.66 (0.41–1.08)	0.64 (0.41–1.02)
	16 to 25	1,264 (17)	**1.90 (1.28–2.82)**	**1.80 (1.23–2.62)**
	26+	1,059 (14)	**3.97 (2.95–5.33)**	**3.57 (2.63–4.85)**
Fracture type	Closed	6,340 (80)	1.37 (1.11–1.69)	—
	Open	1,200 (16)	1.50 (0.94–2.38)	—
Procedure	CRIF (79.15)	2,279 (30)	1.36 (0.96–1.93)	—
	ORIF (79.35)	5,261 (70)	1.41 (1.12–1.77)	—
Surgical timing	≤12 h	4,003 (53)	1.15 (0.86–1.53)	—
	>12 h to 24 h	1,751 (23)	0.80 (0.47–1.35)	—
	>24 h to 48 h	1,027 (14)	1.36 (0.81–2.30)	—
	>48 h to 30 d	759 (10)	**4.08 (2.87–5.81)**	—

*Adjusted for all variables in the model: surgical timing, ISS, patient age, sex, race, DC-CI, surgical procedure used to treat, and fracture type.

CRIF closed reduction internal fixation; DC-CI, Deyo-Charlson comorbidity index; ORIF, open reduction internal fixation.

TABLE 2

Adjusted* In-Hospital Mortality Rates (Shown as Percentages) With 95% CIs Associated With the Three Two-Way Interactions Involving Surgical Timing, ISS, and Patient Age

	ISS				Age, y	
Surgical Timing	**9**	**10–15**	**16–25**	**26+**	**>65**	**65+**
≤12 h	0.31% (0.13–0.72)	0.54% (0.26–1.10)	1.53% (0.84–2.77)	5.24% (3.59–7.66)	0.80% (0.58–1.10)	2.62% (1.28–5.62)
>12 h to 24 h	0.26% (0.08–0.80)	0.33% (0.09–1.28)	2.65% (1.30–5.41)	1.36% (0.36–5.14)	0.57% (0.32–1.00)	1.94% (0.68–5.56)
>24 h to 48 h	0.68% (0.30–1.55)	0.89% (0.30–2.66)	1.76% (0.59–5.28)	1.26% (0.33–4.83)	0.48% (0.22–1.04)	4.25% (2.21–8.16)
>48 h to 30 d	1.48% (0.73–3.00)	2.25% (0.87–5.79)	2.68% (1.05–6.84)	5.90% (3.63–9.60)	1.24% (0.75–2.05)	8.48% (5.29–13.60)

* In-hospital mortality rates adjusted for full model, surgical timing, injury severity, patient age, sex, race, and Deyo-Charlson comorbidities status.

TABLE 3

Adjusted Relative Risks for Mortality by Age and Surgical Timing

Interaction	Comparison		Adjusted Relative Risk (ARR)	95% CI, Lower Bound	95% CI, Upper Bound
Age, 18–64 y	>12 h to 24 h	Reference, ≤12 h	1.41	0.76	2.64
	>24 h to 48 h	Reference, ≤12 h	1.65	0.74	3.68
	>48 h to 30 d	Reference, ≤12 h	1.55	0.90	2.65
	>24 h to 48 h	Reference, >12 h to 24 h	1.17	0.46	2.96
	>48 h to 30 d	**Reference, >12 h to 24 h**	**2.19**	**1.07**	**4.49**
	>48 h to 30 d	**Reference, >24 h to 48 h**	**2.56**	**1.07**	**6.10**
Age, 65+ y	>12 h to 24 h	Reference, ≤12 h	1.38	0.38	4.98
	>24 h to 48 h	Reference, ≤12 h	1.59	0.60	4.22
	>48 h to 30 d	**Reference, ≤12 h**	**3.17**	**1.33**	**7.52**
	>24 h to 48 h	Reference, >12 h to 24 h	2.19	0.64	7.48
	>48 h to 30 d	**Reference, >12 h to 24 h**	**4.37**	**1.39**	**13.76**
	>48 h to 30 d	Reference, >24 h to 48 h	2.00	0.91	4.40
≤12 h	**65+**	Reference, 18 to 64	3.35	1.51	7.42
>12 h to 24 h	**65+**	**Reference, 18 to 64**	**3.44**	**1.03**	**11.43**
>24 h to 48 h	**65+**	**Reference, 18 to 64**	**8.79**	**3.22**	**24.01**
>48 h to 30 d	**65+**	**Reference, 18 to 64**	**6.85**	**3.55**	**13.23**

Note: Statistically significant ARRs are in bold.

TABLE 4

Adjusted Relative Mortality Risks Associated With Timing of Operative Fixation and ISS

ISS Group	Comparison	Adjusted Relative Risk (ARR)	95% CI Lower Bound	95% CI Upper Bound
9	>12 to 24; reference, ≤12 h	1.18	0.29	4.75
9	>24 to 48; reference, ≤12 h	2.21	0.69	7.07
9	**>48 h to 30 d; reference, ≤12 h**	**4.82**	**1.64**	**14.14**
9	>24 to 48; reference, >12 h to 24 h	2.61	0.68	9.98
9	**>48 h to 30 d; reference, >12 h to 24 h**	**5.69**	**1.61**	**20.14**
9	>48 h to 30 d; reference, >24 h to 48 h	2.18	0.81	5.85
10–15	>12 to 24; reference, ≤12 h	1.62	0.35	7.46
10–15	>24 to 48; reference, ≤12 h	1.66	0.45	6.13
10–15	**>48 h to 30 d; reference, ≤12 h**	**4.19**	**1.28**	**13.74**
10–15	>24 to 48; reference, >12 h to 24 h	2.69	0.48	15.17
10–15	**>48 h to 30 d; reference, >12 h to 24 h**	**6.79**	**1.32**	**34.97**
10–15	>48 h to 30 d; reference, >24 h to 48 h	2.53	0.60	10.56
16–25	>12 to 24; reference, ≤12 h	1.74	0.69	4.40
16–25	>24 to 48; reference, ≤12 h	1.16	0.33	4.02
16–25	>48 h to 30 day; reference, ≤12 h	1.76	0.58	5.33
16–25	>24 to 48; reference, >12 h to 24 h	1.50	0.41	5.55
16–25	>48 h to 30 d; reference, >12 h to 24 h	1.01	0.31	3.28
16–25	>48 h to 30 d; reference, >24 h to 48 h	1.52	0.36	6.39
26+	>12 to 24; reference, ≤12 h	3.85	0.97	15.28
26+	**≤12; reference, >24 h to 48 h**	**4.16**	**1.03**	**16.75**
26+	>48 h to 30 day; reference, ≤12 h	1.12	0.61	2.08
26+	>24 to 48; reference, >12 h to 24 h	1.08	0.16	7.13
26+	**>48 h to 30 d; reference, >12 h to 24 h**	**4.33**	**1.05**	**17.79**
26+	**>48 h to 30 d; reference, >24 h to 48 h**	**4.68**	**1.12**	**19.46**

Statistically significant ARRs are in bold.

TABLE 5

Adjusted Relative Mortality Risks Associated With ISS by Surgical Timing

Surgical Timing	ISS Comparison			Adjusted Relative Risk (ARR)	95% CI Lower Bound	95% CI Upper Bound
≤12 h	10–15	Reference	9	1.75	0.57	5.35
	16–25	**Reference**	**9**	**4.97**	**1.75**	**14.08**
	26+	**Reference**	**9**	**17.08**	**6.71**	**43.49**
	16–25	**Reference**	**10–15**	**2.84**	**1.12**	**7.23**
	26+	**Reference**	**10–15**	**9.76**	**4.33**	**22.00**
	26+	**Reference**	**16–25**	**3.44**	**1.70**	**6.97**
>12 h to 24 h	10–15	Reference	9	1.27	0.22	7.29
	16–25	**Reference**	**9**	**10.19**	**2.71**	**38.31**
	26+	Reference	9	5.24	0.92	29.86
	16–25	**Reference**	**10–15**	**8.00**	**1.74**	**36.70**
	26+	Reference	10–15	4.11	0.62	27.28
	26+	Reference	16–25	1.94	0.43	8.77
>24 h to 48 h	10–15	Reference	9	1.31	0.34	5.04
	16–25	Reference	9	2.60	0.67	10.05
	26+	Reference	9	1.86	0.39	8.92
	16–25	Reference	10–15	1.98	0.42	9.24
	26+	Reference	10–15	1.42	0.25	7.96
	26+	Reference	16–25	1.40	0.25	7.89
>48 h to 30 d	10–15	Reference	9	1.52	0.49	4.69
	16–25	Reference	9	1.81	0.57	5.71
	26+	**Reference**	**9**	**3.98**	**1.72**	**9.24**
	16–25	Reference	10–15	1.19	0.32	4.46
	26+	Reference	10–15	2.62	0.91	7.54
	26+	Reference	16–25	2.20	0.77	6.29

Statistically significant ARRs are in bold.