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Inferior clinical outcomes after femur fracture in the obese are potentially preventable

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ABSTRACT

Introduction: Obese patients with operative orthopedic trauma have increased risk of adverse outcomes, although the mechanisms accounting for the relationship remain unknown. This study examines the effect of body mass index (BMI) on outcomes after femur fracture fixation, and explores the mediating effects of pathophysiologic factors and clinical management.
Methods: A retrospective chart review was performed of adult patients with femur fractures undergoing surgical fixation at a Level 1 trauma center from 2010 to 2016. Demographics, Injury Severity Score (ISS), Glasgow Coma Scale (GCS) and mechanism of injury (MOI) were collected along with operative data and complications. Primary outcomes were hospital length of stay (HLOS), ICU length of stay (ICU-LOS), mortality, complications, and time to mobility (time first out of bed, TFOB). Bivariate correlations and multiple regression models were used to examine the relationship between BMI and outcomes. Path analysis tested whether the relationship between BMI and clinical outcomes was mediated by differences in 1) clinical management, or 2) physiologic variables.
Results: Of 333 patients included, the majority were male (57.4%) with a mean age of 43.4 (22.7) years and ISS of 12.5 (6.8). Predominant MOIs were motor vehicle crashes (42.8%) and falls (34.5%). There was no association between BMI category and age, ISS, or GCS. In univariate analysis, higher BMI was linked to longer HLOS ($r = .12$), longer ICU-LOS ($r = .15$), longer TFOB, ($r = .18$), and higher number of complications ($r = .12$), $p < 0.05$. Controlling for age and ISS, obese patients had 6.66 times the odds of respiratory failure (p = 0.021, 95% CI 1.3,33.3) and a 3.88 odds of any complication (p = 0.020, 95% CI 1.24,12.1) compared to their normal weight counterparts. For every one point increase in BMI, time first out of bed was delayed 2.3 h ($p < 0.001$; 95% CI 1.08, 3.62). The effect BMI on poor outcomes was accounted for by delayed mobility (longer TFOB) in a mediation model.
Conclusions: Higher BMI increases the risk of longer hospital stays and systemic complications. Mediation models indicate that the adverse clinical outcomes associated with obesity are explained by delays in mobility, an intervenable factor. Clinical strategies should be directed at early mobilization to minimize morbidity.

Introduction

With the obesity epidemic expanding in the general population, orthopedic surgeons are encountering an increasing number of obese trauma patients. Caring for the obese trauma population requires tailoring of current practices to optimize care at each stage of management. Conflicting research on the effect of obesity on trauma outcomes impacts standardization of treatment practices for this population [1,2]. In general, obesity is a poor prognostic factor in orthopedic surgery. However, the effect of obesity on specific clinical outcomes after orthopedic trauma is largely unknown, as patients presenting with particular fracture patterns have unique pathophysiology [3–7].

Recently, studies have targeted the obese orthopedic trauma population, presenting accumulating evidence that

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obesity has negative clinical effects in orthopedic trauma. The most notable findings were in acetabular fractures [3], pelvic ring injuries [4], syndesmotic injuries [5], and femoral fractures [6]. Specifically, it has been concluded that obese orthopedic trauma patients involved in a motor vehicle crash suffering lower extremity fractures had a near 10% increase in mortality [8]. Additional findings in a 2015 study showed body mass index (BMI) to be an independent predictor of systemic complications and mortality after femur fracture [6]. BMI has been used as a proxy to categorize obesity, and, according to the Centers for Disease Control (CDC) and Prevention, BMI can be used as a screening tool for body adipose content and individual health [9].

The mechanisms accounting for the relationship between adverse outcomes and obesity are proposed to stem from a chronic inflammatory state and biomechanical stress [10–12]. However, actual bone healing after femur fracture has not been shown to be affected in the obese in a murine model [13]. With prior evidence suggesting a multi-factorial etiology of poor outcomes, we proposed that inferior outcomes in this population may be due, in part, to potentially improvable clinical and surgical factors and enhanced post-operative care. The goal of this study is to explore the mechanisms accounting for the relationship between BMI and clinical outcomes after femur fracture. We will explore our institution's incidence of complications and mortality in the obese after femur fracture relative to their normal-weight counterparts. Additonally, we will investigate the effects that medical comorbidities have on clinical outcomes in orthopedic trauma, as well as explore operative variables as possible mediators of the effect of obesity on outcomes.

Methods

Patient population

Following approval by the local IRB, a retrospective chart review of the trauma registry at our Level I trauma center identified adult patients (age $\geq$ 16) surgically treated for femur fractures over a 6-year period (January 1, 2010 to June 30, 2016). In order to be included in this study, patients had to undergo definitive surgical fixation during index hospitalization. We defined surgical fixation as reamed intramedullary nailing or plate and screw fixation. Fractures treated with only pin or screw placement, and fractures treated non-surgically were excluded. Further exclusion criteria included peri-prosthetic fracture, malleolar-only fracture, femoral neck fracture, other long bone fracture, death before definitive fixation, and if definitive fixation occurred outside of index hospitalization.

Data collection and definitions

From a review of the trauma registry and medical records, demographic data were collected including age, gender, comorbidities, and BMI. BMI is defined as mass in kilograms (kg) per the patient's height in square meters with categories of overweight and obese previously defined by the CDC [9]. BMI was categorized as Normal (BMI $\leq$ 24), Overweight (BMI 25–29.9), and Obese (BMI $\geq$ 30). Patient BMI was recorded from the anesthesiologist preoperative note. Injury specific characteristics including Injury Severity Score (ISS), emergency department (ED) Glasgow Coma Scale (GCS), regional specific Abbreviated Injury Scores (AIS), mechanism of injury (MOI), and fracture location were collected. Fractures were classified according to the AO and Orthopedic Trauma Association (OTA) Fracture and Dislocation Classification System [14].

Operative intervention

The primary type of surgical fixation device, intramedullary nail or plates and screws, was recorded. A single research assistant retrieved operative data from patient electronic medical records including time to definitive fixation, operative time, and estimated blood loss (EBL). Time to definitive fixation was defined as the time in minutes from ED presentation to incision for definitive surgical treatment. In the cases of external fixator application, the time to definitive fixation was from hospital presentation to internal fixation of the fracture, not placement of the external fixator. Operative time was recorded as the time elapsed in minutes from incision to close of the procedure. EBL was the estimated volume of blood, in milliliters, the patient lost during surgery, as recorded in the surgeon's operative note. In the cases where the operating surgeon recorded EBL as minimal, it was determined by the primary investigator that the value of 100 mL would be assigned. Total EBL was defined as the sum of EBL from any temporary fixation operation(s), if applicable, and the definitive internal fixation operation.

Clinical outcomes

Primary outcomes of interest included hospital length of stay (HLOS), in-hospital complications, time first out of bed (TFOB), discharge disposition, and in-hospital mortality. In-hospital complications of pneumonia, sepsis, wound infection, pulmonary embolus (PE), deep vein thrombosis (DVT), respiratory failure, and death were noted. Only complications occurring during the index hospitalization were collected, as follow up data proved to be unreliable and not available for every patient. The diagnosis of any of the pre-specified complications was made by the attending physician throughout the hospital stay and/or at discharge. All complications were first analyzed individually and then in aggregate. TFOB measured the time in hours it took for the patient to be mobilized out of bed, and was defined as the time from ED presentation to first recorded date and time the patient was moved out of bed. Simply sitting on the edge of the bed was not considered mobilization. Physical therapy (PT) and occupational therapy (OT) most often mobilized the patient first, other times mobilization was recorded by the nursing staff. Any documentation of mobilization with adequate details was extracted. Good discharge dispositions were home or rehab, with poor dispositions being nursing facility or death. For the purpose of this study, a discharge disposition to prison was considered home for those patients. Other outcomes investigated included EBL, operative time in minutes, ICU-LOS, days to initial physical therapy session, and ventilator days.

Statistical analysis

BMI was treated as a categorical variable in descriptive analyses, as previously defined, and as a continuous variable for outcome analyses. Bivariate correlations and chi-square tests were used to examine BMI-related differences in baseline characteristics and unadjusted outcomes. Pearson's correlation was performed between BMI and continuous outcomes. Independent effects of BMI were further explored via linear and logistic regression models. Models were adjusted for age, ISS, COPD, and diabetes based on bivariate analyses. A backwards elimination approach was performed to reduce error in the models, with removal of variables based on p-value (>0.05). Precision was maintained as there was narrowing of the confidence intervals. A reduction of bias was obtained as there was <10% change seen in coefficients. Based on these criteria, COPD and Diabetes comorbid conditions were removed from the final models as its inclusion was not

statistically significant in the multiple logistic or linear regression. Removal resulted in minimal change in the coefficients with narrowing of the confidence intervals.

Mediation models, known as path analysis or an extension of a regression, were used to test whether the relationship between BMI and clinical outcomes was mediated by differences in time to mobilization, number of comorbid conditions, or operative factors. Multiple mediation models were compared for fit. SPSS Version 24 was used for all analyses.

Results

Of the 333 patients with femur fractures included in the study, the majority were male (57.4%) with a mean (SD) age of 43.4 (22.7) years. With a mean (SD) BMI of 28.0 (6.0), the study cohort was divided amongst normal weight, overweight, and obese with frequencies of 35.4%, 34.8%, and 29.7%, respectively (Table 1). Predominant MOIs were motor vehicle crashes (43.8%) and falls (34.5%). Distribution of MOIs did not differ significantly between BMI groups. Mean ISS of 12.5 (6.8) reflected mostly extremity injury with an AIS extremity mean of 3.0 (0.2). After extremity injury, abdomen AIS means were the next highest with 0.4 (1.0) and 0.4 (0.9) for the overweight group and the obese group, respectively. Higher BMI was associated with more severe abdominal injuries ($p < 0.05$); 16% and 18% of the overweight and obese cohorts, respectively, had significant abdominal injuries (AIS ≥ 2) compared to 8% of normal weight patients. No significant association existed between BMI category and age, gender, ISS, vital signs in the ED, or ED GCS.

Higher BMI corresponded with a higher incidence of diabetes and pulmonary diseases ($p < 0.05$). Overall complication and mortality rates were 9% and 0.6%, respectively. Mortality in the obese population at 2% was significantly different than the normal and overweight cohorts with a combined mortality of 0% ($p < 0.05$). Additionally, the incidence of complications in the obese cohort (14.1%) was over twice that of normal weight patients (5.9%). Table 2 highlights the correlation beftween higher BMI and inferior outcomes.

In univariate analysis, higher BMI was linked to longer hospital length of stay (HLOS) ($r = .12$), longer intensive care unit length of stay (ICULOS) ($r = .15$) and higher number of total complications ($r = .12$), $p < 0.05$. Higher BMI was also correlated with a longer TFOB ($r = .18$), more mean days to first physical therapy session ($r = .17$), longer operative times ($r = .11$), and greater total EBL ($r = .11$), $p < 0.05$. However, higher BMI was not correlated to an inferior discharge disposition or prolonged time to fixation. Of all measured complications, respiratory failure was most impacted by BMI ($r = .12$), as evidenced by the uptrend in predicted probability of respiratory failure with increasing BMI (Fig. 1). Using logistic regression models controlling for age and ISS, obese patients had 6.66 times the odds of respiratory failure (p = 0.021, 95% CI 1.3,33.3) and a 3.88 odds of any complication (p = 0.020, 95% CI 1.24,12.1) compared to their normal weight counterparts.

HLOS and ICU-LOS averaged 1 and 0.9 days longer, respectively, for the obese group relative to their normal BMI counterparts, $p > 0.05$. TFOB was delayed an average of 12.4 h for overweight patients and 21.7 h for obese patients compared to normal weight patients, $p > 0.05$ (Fig. 2). In a linear regression model controlling for age and ISS, for every one point increase in BMI, time first out of bed was delayed 2.3 h (p < 0.001; 95% CI 1.08, 3.62), ICU-LOS was prolonged 0.24 days (p = 0.019, 95% CI 0.41,0.44), and HLOS increased by 0.16 days (p = 0.013, 95% CI 0.03,0.28).

In path analysis, the effect of BMI on increased risk of complications was accounted for by delayed mobility (longer TFOB), as shown by the significant indirect effects ($a \times b$ paths) in Fig. 3, $p < 0.05$. The nonsignificant direct effect (c' path) indicates no effect of BMI on complication risk after controlling for delayed mobility, $p > 0.05$. Operative time was also a significant mediator to increased complication risk, $p < 0.05$. Indirect effects on complication risk were not significant for other models, including number of comorbidities or EBL as the mediating variables. For a mediation model of HLOS (Fig. 4), significant mediators of the effect of BMI included TFOB, operative time, and EBL. Again, number of comorbidities was not a substantial mediator.

Discussion

The prevalence of obesity continues to rise in the developed world. The increase in medical comorbidities associated with

Table 1
Distribution of Demographic and Clinical Characteristics Overall and as a Function of Body Mass Index (BMI) Category.

	Overall n = 333	Normal Weight n = 118	Overweight n = 116	Obese n = 99	$p^{\pm}$
Age, mean [SD]	43.4 [22.7]	44.1 [25.4]	43.0 [22.9]	43.1 [19.1]	0.750
Male, n (%)	191 (57.4)	62 (52.5)	73 (62.9)	56 (56.6)	0.270
Injury Severity Score, mean [SD]	12.5 [6.8]	12.3 [7.2]	12.6 [6.1]	12.7 [7.0]	0.674
Glasgow Coma Scale, mean [SD]	14.6 [1.7]	14.5 [1.8]	14.5 [1.8]	14.6 [1.6]	0.673
Abbreviated Injury Score, mean [SD]					
Abdomen	0.4 [0.9]	0.3 [0.9]	0.4 [1.0]	0.4 [0.9]	0.128
Extremity	3.0 [0.2]	3.0 [0.2]	3.0 [0.2]	3.0 [0.2]	0.684
Body Mass Index, mean [IQR]	28.0 [18.1-44.8]	22.2 [18.1-24.9]	27.5 [25.1-29.8]	35.4 [30.4-44.8]	<0.001**
Mechanism of Injury, n (%)					
Falls	115 (34.5)	40 (33.9)	45 (38.8)	30 (30.3)	0.137
Motor vehicle collision	146 (43.8)	46 (39.0)	47 (40.5)	53 (53.5)	
Motorcycle collision	40 (12.0)	14 (11.8)	14 (12.1)	12 (12.1)	
Pedestrian vs motor vehicle	12 (3.6)	8 (6.8)	3 (2.6)	1 (1.0)	
Other	20 (6.0)	10 (8.5)	7 (6.0)	3 (3.0)	
Comorbid conditions, n (%)					
Hypertension	89 (26.7)	28 (23.7)	28 (24.1)	33 (33.3)	0.208
COPD*	11 (3.3)	3 (2.5)	1 (0.9)	7 (7.1)	0.034**
Tobacco use	95 (28.5)	36 (30.5)	34 (29.3)	25 (25.3)	0.676
Diabetes	39 (11.7)	7 (5.9)	12 (10.3)	20 (20.2)	0.004**
CHF/CAD*	29 (8.7)	9 (7.6)	8 (6.9)	12 (12.1)	0.349
Major Psychiatric disorder	35 (10.5)	12 (10.2)	8 (6.9)	15 (15.2)	0.143

BMI categories: Normal (BMI $\leq$ 24), Overweight (BMI 25–29.9), and Obese (BMI $\geq$ 30).
* COPD = Chronic Obstructive Pulmonary Disease; CHF = Congestive Heart Failure; CAD = Coronary Artery Disease.
** $p < 0.05$.
$^{\pm}$ p values are estimated with linear regression for continuous variables and χ^2 for categorical variables, omitting overall cohort.

Table 2
Correlation Between Index Hospitalization Clinical Outcomes after Femur Fracture and Higher BMI.

Clinical Outcome	Pearsons Correlation Coefficient, r	Coefficient of determination, r^2	p Value
Hospital Length of Stay	0.12	0.023	0.03*
Intensive Care Unit Length of Stay	0.15	0.014	0.01*
Time First Out of Bed (minutes)	0.18	0.033	0.001*
Days to First Physical Therapy Session	0.17	0.029	0.002*
In-hospital Mortality	0.07	0.005	0.20
Ventilator Days	0.16	0.025	0.31
Number of Complications**	0.12	0.014	0.03*
Operative Time (minutes)	0.11	0.012	0.05
Total Estimated Blood Loss	0.11	0.013	0.04*

* $p < 0.05$.
** Complications included pneumonia, sepsis, wound infection, pulmonary embolus (PE), deep vein thrombosis (DVT), respiratory failure, and death.

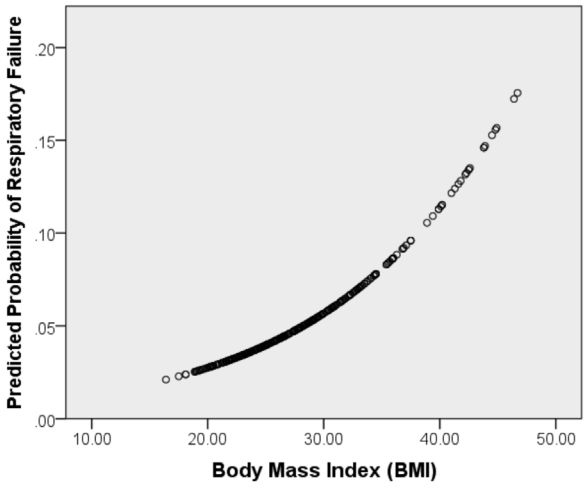

Fig. 1. Predicted Probability of Respiratory Failure with Continuous BMI.

obesity translates to a higher risk of perioperative complications. In published data, morbidly obese trauma patients have in-hospital stays of almost two days longer than non-obese counterparts, in addition to increased odds of disposition to a rehab facility rather than home [15]. This increased length of stay and discharge to long-term care facilities has, and continues to, contribute to rising medical costs associated with obesity. The understanding of the specific characteristics and outcomes of the obese orthopedic trauma population could potentially ease the burden on the healthcare system, and improve clinical outcomes for the obese.

Of the three BMI categories, obese patients were associated with the longest HLOS, which is clinically significant even if not statistically significant. While we did not specifically compute a cost analysis, extended HLOS has previously been correlated with both higher overall hospital expenses and obesity [15]. Our study also concluded mortality rates in the obese are significantly higher than the rate of mortality for normal BMI patients. Conflicting results regarding mortality exist in the literature. Our mortality outcomes reflect similar findings as Murphy et al. [6], but are higher than data from a study conducted by Baldwin et al. [15] which may be accounted for by a higher mean ISS in our study. A lower rate of mortality in the obese population (2%) was found in our study relative to other published studies on the obese trauma population, with mortality rates ranging from 4% to 42% [2,6,16]. Differences in mortalty in the obese population is likely a reflection of the distribution of BMI, with higher BMI conferring a higher risk of mortality, even within the obese population.

Postoperative respiratory complications pose a significant risk for increased morbidity and mortality. The increased incidence of respiratory complications in our obese cohort mirrors prior findings in the general trauma population, who also have a significantly high incidence of respiratory complications [17]. This suggests the trauma population differs from the general non-trauma postoperative population where obesity has not been shown to increase postoperative pulmonary complications [18,19].

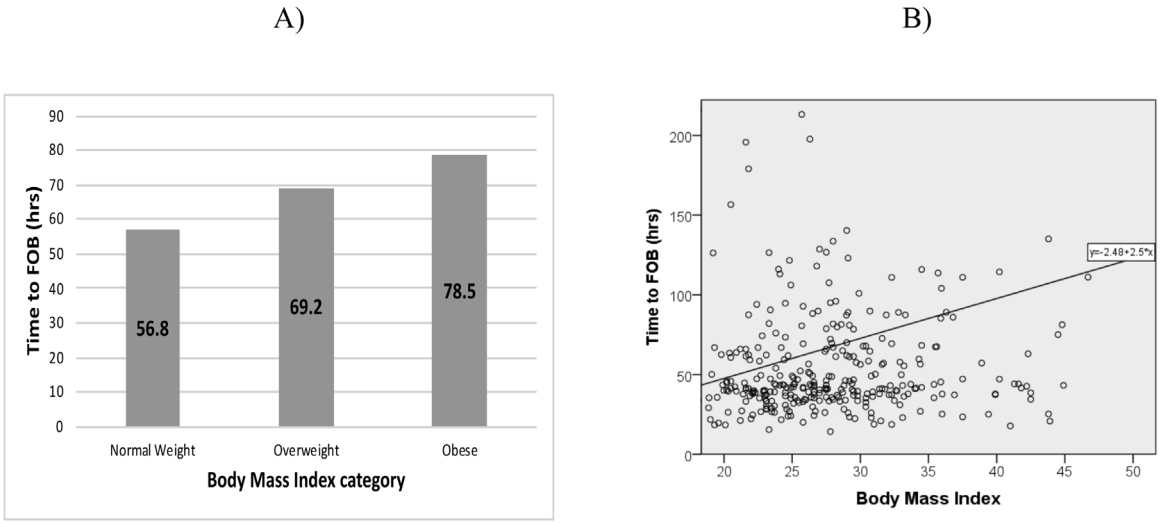

Fig. 2. The effect of BMI on mobility as measured by time to first out of bed (FOB), by A) BMI category* B) as a function of continuous BMI.
*BMI categories: Normal (BMI $\leq$ 24), Overweight (BMI 25–29.9), and Obese (BMI $\geq$ 30)

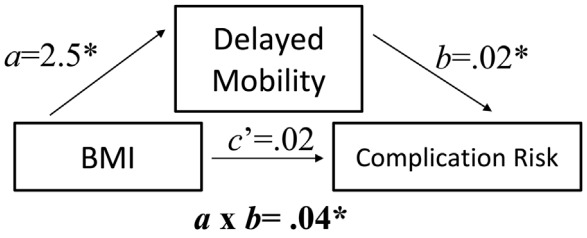

Fig. 3. Mediation model of the effect of BMI on complication risk**, as explained by time first out of bed (TFOB) as a proxy for delayed mobility.
*Significant ($p < 0.05$)
**Complications included pneumonia, sepsis, wound infection, pulmonary embolus (PE), deep vein thrombosis (DVT), respiratory failure, and death.

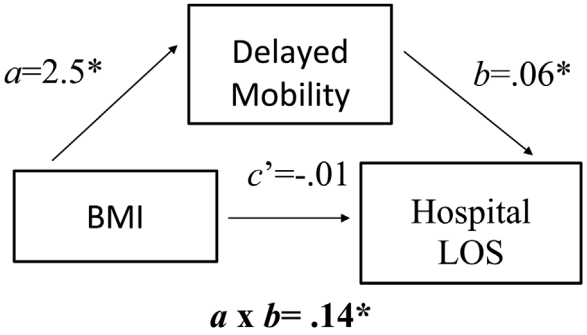

Fig. 4. Mediation model of the effect of BMI on hospital length of stay (HLOS), as explained by time first out of bed (TFOB) as a proxy for delayed mobility.
*Significant ($p < 0.05$)
Note: Other significant mediators for HLOS included operative time and estimated blood loss.

Obese patients did not have a greater chance of requiring rehabilitation services or discharging to poor dispositions. This is contradictory to prior research by Baldwin et al. [15] and Batsis et al. [20], which showed obesity as a risk factor for inferior disposition. Our institution promotes early mobilization through established protocols which may lead to further progress during a patient's inpatient stay and explain the decreased need for rehab after discharge. Regardless, the relationship between HLOS and discharge disposition is complex and likely dependent on other factors such as overall injury, age, and frailty which are variable between study cohorts.

The focus of this study centered on postoperative functional measures that can be improved by protocols for TFOB and time to first PT session. To our knowledge, our study is the first to combine medical complications and postoperative functional measures such as TFOB and first PT session which impacts the recovery trajectory. While this study focused solely on in-patient interventions, early mobility has been shown to improve long-term outcomes in other long bone injuries [21,22] and is an important factor for returning to their functional baseline to reduce the burden of non-fatal injury.

Limitations

Limitations of our study include the inherent error introduced with a retrospective design. The data for BMI was obtained from anesthesia record, which may be prone to error as this measurement is often obtained from a patient's in-bed weighing scale. TFOB and first PT session may have been influenced by presence of other injuries limiting mobility. We did not adjust for polytrauma, as mean ISS was similar across BMI cohorts. Other studies have examined the relationship between operative technique and obesity, which can impact outcomes [6,23]. We did not consider surgical approach (antegrade versus retrograde) or different orthopedic techniques in our study as predictors of outcomes.

Conclusion

Higher BMI puts patients at risk for longer hospital stays and increased rate of systemic complication following femur fracture, which should influence counseling of obese patients after femur fracture. Mediation models indicate that some adverse clinical outcomes associated with obesity are caused by delays in mobility, a preventable non-patient physiologic factor. Clinical strategies could be directed at early mobilization and physical therapy to minimize morbidity.

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