Does Obesity Affect Fracture Healing in Children?

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Abstract

Background Obesity is a risk factor for various orthopaedic diseases, including fractures. Obesity's influence on circulating hormones and cytokines and bone mineralization ultimately influences the body's osteogenic response and bone mineralization, potentially increasing the risk of fracture and impacting fracture healing.

Questions/purposes Does obesity delay fracture recovery in overweight or obese children as measured by the time to release to normal activity? Is this average time for return to activity influenced by the mechanism of the injury? Does obesity's effect on mineralization and loading in overweight or obese children lead to a greater proportion of upper extremity fracture versus lower extremity fracture?

Methods We prospectively followed 273 patients with nonpathologic long bone fractures treated from January

2010 to October 2011. Patients were stratified into obese/overweight, normal weight, and underweight groups. All patients were followed until release to regular activities (mean, 41 days; range, 13–100 days).

Results Release to regular activities occurred sooner in obese/overweight than in normal weight patients: 39 and 42 days, respectively. A greater proportion of obese/overweight patients had low to moderate energy mechanisms of injury than did normal weight patients, but we found no difference between the groups in terms of return to activity when stratified by mechanism. There was also no difference in the proportion of upper extremity injuries between the two groups.

Conclusions Obese/overweight children did not have a delay in release to activities compared with children of normal weight.

Level of Evidence Level II, prognostic study. See Guidelines for Authors for a complete description of levels of evidence.

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Introduction

Obesity, defined by the Centers for Disease Control and Prevention (CDC) [7] as a body mass index (BMI) at or above the 95th percentile for children of the same age and sex, has become an increasing public health problem in the United States. According to the CDC, 17% of children and adolescents aged 2 to 19 years are obese [5]. Of particular concern is the youngest segment of the population; the CDC report that nearly one-third of low-income children, aged 2 to 4 years, are obese or overweight [6]. Obesity is a risk factor for childhood onset of a variety of health issues: obese children are more likely than normal weight children to have high blood pressure, high cholesterol, and Type 2

diabetes, all of which are risk factors for heart disease [6]. Furthermore, obese children are more likely to become obese adults [6], which further magnifies the importance of preventing and treating childhood obesity.

Among musculoskeletal conditions, obesity has been associated with issues involving the growing skeleton such as slipped capital femoral epiphysis and Blount's disease [9, 27]. More recently obesity is reportedly a risk factor for an increased incidence of fractures in children [10, 18, 20, 34, 35, 37, 38]. Potential contributors to the increased fracture risk in obese children include poor mobility [38], poor balance [20], poor nutrition [18], and inherent mechanical disadvantage [10, 37]. When surveyed, overweight children reported a greater prevalence of fractures and musculoskeletal discomfort [38]; in motor vehicle crashes, obese children are at a higher risk of extremity injury [34]; and at trauma centers, childhood obesity is a risk factor not only for extremity fracture, but also for complications (such as decubitus ulcers and deep venous thrombosis) and the need for operative intervention [35].

The overall effect of obesity on the musculoskeletal system is complex. On a cellular level, adipocytes and osteoblasts are derived from the same mesenchymal stem cell line. Therefore, it has been hypothesized [4] that obesity promotes differentiation of this reserve of mesenchymal stem cells into adipocytes, leaving decreasing numbers of cells available to differentiate into osteoblasts. This switching of lineages from bone progenitors to fat progenitors would theoretically be expected to have a negative effect on bone formation [4]. Obesity also influences the upstream imprinting process of stem cells: human mesenchymal stem cells' osteogenic response to strain reportedly inversely correlates with the donor's BMI and with leptin and estradiol levels within the bone microenvironment [17]. Although that study suggested a blunting of osteogenic response with obesity, it showed the altered milieu of cytokines was a likely factor that could theoretically reduce fracture healing if what occurred in vivo was similar to what had happened in vitro [17].

To make the situation even more complicated, some reports indicate that at least one cytokine upregulated in obesity [4, 30], leptin, has both a positive [1, 14, 23] and negative [15, 26, 29, 33] influence on bone metabolism and formation. Leptin has been reported to have receptors in the central nervous system and on peripheral targets [3, 31]. With receptors on the hypothalamus, it is a regulator of appetite and reproductive function [31]. Peripherally, it influences bone metabolism through receptors on osteoblasts, chondrocytes, bone marrow stromal progenitor cells, and hematopoietic precursor cells [3]. In vitro, it is an anabolic factor, stimulating osteoblast and chondrocyte proliferation, and inhibiting osteoclastogenesis [8, 19, 25, 39]. Despite these findings, the effects of elevated leptin

levels in obesity and the resulting bone phenotype are unclear. Mouse models that ablate the leptin-signaling pathway have not produced uniform results. Leptin-deficient mice and leptin receptor knockout mice have both been reported to have high [1, 14, 23] and low [15, 26, 29, 33] bone mass. Whether these alterations at the cellular level translate to an overall delay in fracture recovery in the setting of childhood obesity is to be determined.

On a macroscopic level, again the overall effect of obesity on the musculoskeletal system is complex. Wolfe's law would suggest the increased loading of the lower extremities and spine would result in stronger bones. Although some studies have reported that bone mineral capacity is higher in obese and overweight than in normal weight individuals [16, 24, 28, 38], other studies have reported decreased bone mass relative to bone size and body weight [21, 22], and some studies have reported no difference [12, 32]. Without encountering increased weightbearing forces as seen by the lower extremity in obesity, the upper extremity may be more susceptible to fracture.

We therefore asked (1) whether childhood obesity is associated with a delay in release to normal activities as a result of presumed delay in healing; (2) whether this delay in release to normal activity is influenced by the proportion of fractures resulting from low- to moderate-energy mechanisms; and (3) whether childhood obesity is associated with a greater proportion of upper extremity fractures.

Patients and Methods

From January 2010 to October 2011, we prospectively followed 474 patients 2 to 16 years old who presented to our institution's outpatient clinic, emergency room, or trauma bay with nonpathologic fractures. The 2-year age cutoff reflected the fact that the CDC's BMI percentile for age charts are not available for children from birth to 2 years of age. For the purpose of this study we culled the 374 fractures involving long bones: humerus, radius, ulna, femur, tibia, and fibula. We then excluded patients with insufficient height and weight data for calculating BMI (23), delayed or incomplete followup (76), and who died (two). Therefore, 273 patients formed our study group. All patients were followed until release to activities (mean, 41 days; range, 13–100 days); no further patients were lost to followup. No patients were recalled specifically for this study; all data were obtained from medical records and radiographs.

At the time of presentation, we obtained demographics, a standard history and physical, and appropriate radiographs. We used height and weight data to calculate BMI and BMI percentile for age. By definition, obese patients

were at or above the 95th percentile for age, overweight patients were below 95th percentile for age and at or above the 85th percentile for age, normal weight patients were below the 85th percentile for age and at or above the 5th percentile for age, and underweight patients were below the 5th percentile for age. Stratifying by weight, there were 61 (23%) obese patients and 38 (14%) overweight patients, together comprising 36% of our study group; these patients formed our obese/overweight group. There were 154 (57%) normal weight patients and 17 (6%) underweight patients.

Mechanism of injuries was defined for the purposes of our study as one of three types: (1) high energy; (2) moderate energy; or (3) low-energy injury. Injuries from motor vehicle collisions, pedestrians struck, gunshot wounds, assault, and falls from height greater than 10 feet were classified as high energy. Injuries from playground equipment or sports participation were classified as moderate energy, and falls from a stationary position or tripping on an object on the ground were defined as low energy. This continuum of moderate- and low-energy mechanisms was evaluated as a single group as a result of the propensity for single extremity involvement without extensive soft tissue injury. The obese group sustained a smaller proportion of ($p = 0.025$) fractures from high-energy mechanisms (9% [nine of 99]) than the normal weight group (20% [30 of 154]) (Table 1). We found no difference ($p = 0.92$) in fracture locations between the two groups. In the obese/overweight group, 67 (68%) patients sustained upper extremity injuries and 32 (32%) sustained lower extremity injuries. In the normal weight group, 105 (68%) patients sustained upper extremity injuries and 49 (32%) sustained lower extremity injuries (Table 1).

Patients were treated by operative or nonoperative means, taking into account the nature of the injury, whether the fracture was open, the overall health status of the patient, and the preference of the treating physician.

Subsequent outpatient clinic followup varied and was adjusted per preference and affected by patient adherence. A clinic visit generally occurred 1 to 4 weeks after the initial injury with subsequent visits in the 1- to 4-week interval as necessary. Standard orthogonal radiographs of

the fractured long bone were obtained at each visit. The treating physician documented progression of release to full activity. All patients in the study group had complete intake and followup data.

We determined differences in time to release to activities between the obese/overweight group and the normal weight group using the Mann-Whitney test. We determined differences in the proportion of low to moderate and high energy of injury mechanism between the obese/overweight group and the normal weight group using the chi square test and stratified the two weight groups by energy mechanism and analyzed the difference again with the Mann-Whitney test. We determined differences in the proportion of upper extremity fractures between the obese/overweight group and the normal weight group using the chi square test. To avoid excluding the underweight patients, a second set of statistical analyses was performed as described previously, this time comparing all patients at or above the 85th percentile BMI for age with the patients below the 85th percentile BMI for age (Table 2). We removed three patients from our analysis. One underweight patient sustained a refracture at the original fracture site. This patient was removed from statistical analysis, because the prolonged time to release to activities reflected a second injury as opposed to a biological delay in healing. Two normal weight patients had prolonged periods of activity restriction resulting from a progressive malunion in one and nonunion in the other. These patients were removed from statistical analysis, because they required serial interventions and procedures over the course of 6 to 9 months. No obese patients had refracture, malunion, or nonunion. Statistical analysis was performed using VassarStats.net (Richard Lowry, PhD, Poughkeepsie, NY, USA).

Results

The obese/overweight group had a shorter ($p = 0.035$) mean time to release to activity compared with the normal

Table 1. Percentage/number by fracture location and energy of injury mechanism

Fracture location/ energy of injury mechanism	Normal weight	Overweight/ obese	p value
Total	154	99	
UE fracture	68% (105)	68% (67)	0.92
LE fracture	32% (49)	32% (32)	
High	19% (30)	9% (9)	0.025
Moderate/low	81% (124)	91% (90)	

UE = upper extremity; LE = lower extremity.

Table 2. Percentage/number by fracture location and energy of injury mechanism

Fracture location/ energy of injury mechanism	BMI < 85th percentile	BMI ≥ 85th percentile	p value
Total	171	99	
UE fracture	69% (118)	68% (67)	0.82
LE fracture	31% (53)	32% (32)	
High	20% (35)	9% (9)	0.014
Moderate/low	80% (136)	91% (90)	

BMI = body mass index; UE = upper extremity; LE = lower extremity.

Table 3. Days to release to regular activities by energy of injury mechanism

Energy of injury mechanism	Normal weight	Overweight/obese	p value
All	42	39	0.035
High	47	49	0.5
Moderate/low	41	38	0.072

Table 4. Days to release to regular activities by energy of injury mechanism

Energy of injury mechanism	BMI < 85th percentile	BMI ≥ 85th percentile	p value
All	42	39	0.055
High	46	49	0.46
Moderate/low	41	38	0.095

BMI = body mass index.

weight group, averaging 39 days (range, 15–96 days) and 42 days (range, 13–100 days), respectively. We found no difference between obese/overweight groups and normal weight groups in terms of return to activity when stratified by low- to moderate-energy injuries ($p = 0.072$) or high-energy injuries ($p = 0.5$) (Table 3). We also found no difference between patients at or above the 85th percentile BMI for age and patients below the 85th percentile BMI for age in terms of return to activity when stratified by low- to moderate-energy injuries ($p = 0.46$) or high-energy injuries ($p = 0.095$) (Table 4).

Discussion

Childhood obesity is a national health problem, putting the obese child at risk for many medical conditions, including an increased risk of fracture. Obesity alters skeletal loading and circulating hormone and cytokine levels, which in turn change bone morphology and metabolism. This overall interaction between fat and bone has many layers; the net effect is difficult to quantify. However, from a clinical standpoint, the question of whether obesity negatively affects fracture recovery is an important one. We therefore sought to determine if childhood obesity is associated with a delay in release to normal activities as a result of a presumed delay in healing and if any difference is the result of differing proportions of low- to moderate-energy injury mechanisms. We also sought to determine if there is a greater proportion of upper extremity fractures resulting from a relative decrease in bone strength relative to the increase in weight.

Our study had some limitations. First, the end point of fracture healing was determined subjectively by the treating orthopaedist. The orthopaedist's interpretation of the patient and clinical picture, including the patient's preinjury and anticipated postinjury activity level, could favor an aggressive, early release versus a conservative, delayed release. Therefore, we can definitively state only that in our study, patients in the obese group were released to activities more quickly after fracture than were patients in the normal group. Obese and overweight children, who may have a more sedentary baseline activity level, could be released earlier. However, the time at which weightbearing and activities can be resumed, rather than the time at which a fracture is radiographically healed, is the more clinically relevant end point. Second, there was heterogeneity between the different patient populations, which could bias our results. There was a difference in the mechanisms of injury with more children in the normal weight group sustaining high-energy injuries. Nevertheless, our subpopulation analysis showed no difference in average time to release to activities between the groups when comparing high- and moderate/low-energy injuries. Third, we did not have a standardized followup protocol, and therefore the duration between visits and repeat radiographs varied according to the clinician's interpretation of what was required for the injury and the patient. Lastly, although we tried to capture all patients coming to our department, there were certainly patients who were not captured because of insurance restrictions requiring followup elsewhere or failure of participation in the study among providers. None of these failures to enroll patients in our study would have been likely influenced by the weight of the patient.

Our data suggest obese/overweight children have a faster time to fracture recovery and release to activities compared with their normal weight counterparts and no difference in release to activity when stratified by energy of injury mechanism. By demonstrating a lack of a delay in the recovery process, it suggests the detrimental effects of obesity and adiposity on the musculoskeletal system are potentially balanced with the beneficial ones in the post-fracture period. With our current understanding of obesity and the musculoskeletal system, there is evidence suggesting that obesity has a positive effect on fracture healing. On a cellular level, there are alterations in the circulating hormones and cytokines. Recent studies have supported the idea of leptin, a cytokine upregulated in obesity, being an anabolic bone factor. Its deficiency reduced cortical bone volume and reduced trabecular bone volume, thickness, and numbers [40], reduced total serum osteocalcin, and resulted in decreased strength in three-point bend testing. Injection of leptin showed increased gene expression associated with osteogenesis, increased osteocalcin, increased bone mineral density, increased bone mineral content, and decreased genes associated with osteoclastogenesis, adipogenesis, and

adipocyte lipid storage [2]. There was also an increase in the mineral apposition rate. Although no study directly addressed the role of leptin in fracture healing, they showed the anabolic influence leptin has on bone.

Our findings show that obese/overweight children have no difference in the proportion of upper extremity fractures when compared with normal weight children. Again the net effect of obesity and increased mechanical loading during a fall versus the benefit of increased bone strength did not result in a detectable difference in fracture locations. From a mechanical standpoint, obesity and the accompanying increased skeletal stress are beneficial to bone strength [11, 13, 28, 36]. For example, in adults, increased BMI protects against osteoporosis and hip fractures, suggesting increased bone strength [11, 13, 36], and in childhood and adolescence, obesity is associated with increased vertebral bone density and mass [28]. However, a contrasting study showed girls who sustain forearm fractures tend to be overweight [37]. These girls have actually decreased cross-sectional bone dimensions [37]. Our hypothesis, that the benefits of increased weight on bone remodeling would not be realized in the nonweightbearing upper extremities, leading to a greater proportional of upper extremity fractures in obese children, was not correct.

We found obese/overweight children with fractures returned to activity without any delay compared with normal weight children. Increased BMI percentile for age did not negatively affect return to activity, and therefore obesity is not identified as a risk factor for delayed healing of fractures in children. Although the precise mechanism and interaction for this finding is not yet understood, it seems that in this one instance, the negative impact of obesity on bone is outweighed by the positive. Still, one must consider the negative influence of obesity on increased fracture risk, increased need for surgical fracture intervention, and increased complication rates after treatment when advising patients. Additional study in this area is required, which may yield not only more insight into the biology of fracture healing, but new areas for modulation of fracture healing.

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