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ORIGINAL ARTICLE

Does obesity affect diaphyseal femoral fracture healing treated with intramedullary locking nail?

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ABSTRACT

Objectives: This study aims to evaluate the effect of obesity on radiological fracture union in diaphyseal femoral fractures (DFFs) treated with intramedullary nailing (IMN).

Patients and methods: Between January 2017 and December 2018, a total of 120 patients (101 males, 19 females; mean age: 35.1±3.0 years; range, 18 to 72 years) treated with IMN for closed DFFs were retrospectively analyzed. Data including age, sex, location, weight, height, comorbidities such as diabetes mellitus, hypertension or kidney injury, date of injury, mechanism of injury, type of femoral fractures (AO classification), date of surgery, duration of surgery, IMN length and diameter used, date of radiological fracture union and complications of surgery such as nonunion, delayed union, and infections were recorded.

Results: Of the patients, 63 had obesity and 57 did not have obesity. There was a statistically significant difference in fracture configuration among patients with obesity; they sustained type B (p=0.001) and type C (p=0.024), the most severe fracture configuration. The nonunion rate was 45%. Obesity had a significant relationship with fracture nonunion with patients with obesity having the highest number of nonunion rates (n=40, 74.1%) compared to those without obesity (n=14, 25.9%) (p=0.001). Fracture union was observed within the first 180 days in 78.9% of patients without obesity, while it developed in the same time interval in only 38.1% of patients with obesity (p=0.001).

Conclusion: Fracture union time for the patients with obesity was longer, regardless of the fracture configuration. Obesity strongly affects fracture union time in DFFs treated with an IMN. Obesity should be considered a relative risk in decision-making in the choice of fixation while treating midshaft femoral fractures.

Keywords: Femur fracture, fracture healing, intramedullary locking nail, obesity.

Obesity has reached epidemic proportions globally with high mortality.[1] These inherently have caused a surge in healthcare costs due to higher relative mortality rates and the increased risk of developing coronary artery disease, hypertension, and diabetes mellitus. Given the ongoing pandemic of obesity, orthopedic surgeons should expect to treat an increasing number of these patients. Treating fractures in this patient population may present unique challenges and difficulties.[2,3]

Tucker et al.[4] conducted a multi-center, prospective study to evaluate differences in operative

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time and functional outcome of patients with and without obesity undergoing intramedullary nails (IMNs) for femoral fractures. The operation time was significantly prolonged in patients with obesity. Numerous factors were described, including delay in entry point localization, technical know-how, complication rates, bleeding, and increased length of hospital stay.[5,6]

Numerous reports exist on the fixation technique of IMN in patients with obesity, but there has been little focus to identify the effects of obesity on fracture union.[7] Based on the available literature, obesity affects bone metabolism through several mechanisms. Previously, it was thought that obesity had a positive effect on bone healing; however, recent studies have shown that excess fat mass is not protective and is associated with lower bone mineral density and bone mineral content.[8,9] Obesity may decrease bone formation (osteoblastogenesis) while increasing adipogenesis, as adipocytes and osteoblasts are derived from a common multipotential mesenchymal stem cell.[10] Besides, obesity may increase bone resorption through upregulating proinflammatory cytokines such as interleukin (IL)-6 and tumor necrosis factor-alpha (TNF-α), which can stimulate osteoclast activity.[10]

In the present study, we aimed to investigate the effect of obesity on the average time for radiological fracture union in DFFs treated with an IMN.

PATIENTS AND METHODS

This single-center, descriptive, retrospective, cross-sectional study was conducted at Tertiary Centre in Central Malaysia, Kuantan Orhtopaedics Department between January 2017 and December 2018. A total of 120 patients (101 males, 19 females; mean age: 35.1±3.0 years; range, 18 to 72 years) treated with IMN were included. Data were obtained from medical records and anteroposterior (AP)-lateral view plain radiographs of patients treated with an IMN in our center. All selected patients met the following inclusion criteria: ≥18 years of age, closed DFF (AO type 32A-C), and available for follow-up for 12 months. Exclusion criteria were an immature skeleton, ipsilateral fracture of the hip, tibia/fibula, open femoral fractures, pathological fractures, fractures with vascular injuries, and previous femoral fractures on the same side, and missing follow-up data for at least 12 months.

Based on a power of 80% (β=0.2), α of 0.05, and radiological union difference of three weeks and standard deviation (SD) of 4.86 between the two study groups (those with and without obesity), based on a retrospective study of the effects of body mass index (BMI) on the clinical and radiological outcomes of Pilon fractures by Çeçen et al.,[11] the calculated sample size for each group was 42 patients. Allowing for a 20% dropout, a final sample size of 50 per group was used.

The data were collected by using a proforma that covered all the measurement parameters of interest, including demographics of patients, weight, and height, BMI >30 kg/m^2, comorbidities such as diabetes mellitus, hypertension or kidney injury, date of injury, mechanism of injury, type of femoral fractures, date of surgery, duration of surgery, IMN length and diameter used, date of radiological fracture union and complications of surgery. The BMI of patients was calculated based on the weight and height of patients documented in the anesthesia forms.

Surgery was performed by a single surgical team who are experienced in the nailing system. The patient was placed supine with the affected limb in traction on a fracture reduction table. Antegrade IMN was performed for all cases (T2 Recon Nailing System; Zimmer, USA). Reaming was performed for all cases. Proximal locking screws were used in the antegrade femoral mode for all cases. Distal locking screws with both static and dynamic holes were used. Patients were, then, initiated on physiotherapy and ambulation with crutches.

The radiological union was defined as bridging callus in three of four cortices in the AP and lateral view.[12] Postoperatively, a femur X-ray was done and subsequently repeated during follow-up. X-rays were repeated every six weeks, until fracture union was achieved. All radiographs were reviewed separately by two independent reviewers on two separate occasions. Both reviewers had more than five years of service as orthopedic medical officers. Each patient's radiograph was reviewed, the date of union was documented, time to union was calculated twice, and an average between the two readings was taken for each reviewer. The final value was the average between the two reviewers' readings, which was attempted to reduce potential bias.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean ± standard deviation (SD) or median (min-max), while categorical variables were expressed in number and frequency. The Pearson chi-square test, Fisher chi-square test, and continuity correction chi-square test were used to compare categorical variables in independent groups. The conformity of continuous variables to normal distribution was evaluated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Normality analysis revealed that all data sets were non-normally distributed. The Mann-Whitney U test was used to compare data sets that were not normally distributed for the variables. Relationships between variables were examined using regression analysis. Multiple linear regression analysis was used to identify the predictors of union of the bone. A *p* value of <0.05 was considered statistically significant.

RESULTS

A total of 63 patients with obesity and 57 without obesity were included in the study. The majority of the patients (n=81) were between 18 and 30 years and 19.2% (n=23) patients were between 31 and 40 years. There was no statistically significant difference in demographic data, fracture characteristics, or duration of surgery between those with and without obesity. The nonunion rate was 45% in our study, and obesity had a significant relationship with fracture nonunion, with patients with obesity having the highest number of nonunion rates (n=40, 74.1%) compared to those without obesity (n=14, 25.9%) (p=0.001).

Regarding fracture union, two patients without obesity achieved radiological union in less than 90 days. Fracture union was observed within the first 180 days in 78.9% of patients with obesity, while it developed in the same time interval in only 38.1% of patients with obesity (p=0.001). There was a statistically significant difference in the fracture configuration and obesity, particularly in type B (p=0.001) and type C (p=0.024), the most severe fracture configuration. Of 51 patients with type C fractures, 30 (58.8%) had obesity (Tables I and II).

Based on our data, of 72 smokers, 39 (54.2%) patients did not have obesity, and 33 (45.8%) patients had obesity, and no statistically significant relationship was identified. Based on the data collected, the number of patients with obesity living in the urban area was more (67.2%), compared to those living in the rural area (38.7%) (Table II). Our study had no reported cases regarding postoperative complications, such as wound breakdown and surgical site infection.

Multiple linear regression was used to determine the predictors of union of the bone. Four variables were included in the preliminary model. The variables were BMI (obesity), location (rural), Orthopaedic Trauma Association (OTA) Fracture Classification (B), and OTA Fracture Classification (C). All the variables were categorized into two groups. Reference groups were identified. All the variables were analyzed using the forward method. Assumptions for multiple logistic regression were checked. An inverse relationship was identified between the union of the bone and obesity in the multiple logistic regression analyses (B=-1.56, p=0.001) (Table III). Other remarkable variables that had an inverse relationship with the union of the bone in the regression analyses were high-energy trauma (B=-2.25, p=0.035) and severe stages of fracture classification (B=-1.41 p=0.007 for type B - B=-1.15 p=0.010 for type C). The only variable

TABLE I
Patient demographics and baseline data of patients

	Frequency	Percent
Age group (year)		
18-30	81	67.5
31-40	23	19.2
41-50	7	5.8
51-60	5	4.2
>60	4	3.3
Nail diameter (mm)		
8-10	54	45.0
11-12	64	53.3
>13	2	1.7
Nail length (mm)		
320-360	48	40.0
361-400	70	58.3
401 above	2	1.7
OTA fracture classification		
Type A	42	35.0
Type B	27	22.5
Type C	51	42.5
Body mass index		
Non-obese	57	47.5
Obese	63	52.5
Status of union		
Nonunion	54	45.0
Union	66	55.0
Location		
Rural	62	51.7
Urban	58	48.3

OTA: Orthopaedic Trauma Association.

TABLE II
Comparison of the relationship between categorical variables and union status

	Nonunion		Union			
Factors	n	%	n	%	χ^2	*p*
Age group (year)						
8-40	45	83.3	59	89.4	0.94	0.331
>41	9	16.7	7	10.6		
Location						
Rural	18	33.3	44	66.7	13.22	0.001*
Urban	36	66.7	22	33.3		
Duration of surgery (min)						
0-120	22	40.7	31	47	0.47	0.494
>121	32	59.3	35	53		
Nail length (mm)						
320-360	27	50	27	40.9	0.99	0.319
>360	27	50	39	59.1		
Extra procedures						
Bone grafting	29	58.7	3	4.5	62.48	0.001*
Dynamization	8	14.8	0	0		
None	17	31.5	63	95.5		
Body mass index						
Non obese	14	25.9	43	65.2	18.33	0.001*
Obese	40	74.1	23	34.8		
OTA fracture classification						
Type A	11	20.4	31	47		
Type B	16	29.6	11	16.7	9.83	0.007*
Type C	27	50	24	36.4		
Side						
Left	22	40.7	29	43.9	0.12	0.724
Right	32	59.3	37	56.1		
Smoking						
No	26)	48.1	22	33.3	2.72	0.099
Yes	28	51.9	44	66.7		
Diabetes mellitus						
No	48	88.9	63	95.5	1.85	0.174
Yes	6	11.1	3	4.5		
Hypertension						
No	49	90.7	61	92.4	0.11	0.740
Yes	5	9.3	5	7.6		
Kidney disease						
No	54	100	65	98.5	0.83	0.364
Yes	0	0	1	1.5		
Type of trauma						
Low energy	1	1.9	10	15.2	6.31	0.012*
High energy	53	98.1	56	84.8		

OTA: Orthopaedic Trauma Association; * Significant p<0.05, Chi-square test was used for analysis.

TABLE III
Effect of independent variables on bone union and multiple logistic regression analysis results

Risk factors	B	Wald	*p*	OR	95% CI Lower	95% CI Upper	Cox & Snell R square	Nagelkerke R square
Body mass index (Obese)	-1.56	12.07	0.001*	0.21	0.09	0.51	0.26	0.34
Location (rural)	1.12	6.55	0.010*	3.06	1.30	7.21		
OTA fracture classification (B)	-1.71	7.77	0.005*	0.18	0.05	0.60		
OTA fracture classification (C)	-1.09	4.80	0.028*	0.34	0.13	0.89		
Constant	1.35	6.38	0.012	3.84				

OTA: Orthopaedic Trauma Association; Dependent: Union, Yes = 1, *Significant $p<0.05$, Multiple logistic regression method forward conditional prediction model Union, Yes= 1.35 + (-1.56 × BMI [Obese]) + (1.12 × Location[rural]) + (-1.71 × OTA fracture classification[B]) + (-1.09 × OTA fracture classification[C])
Where the change of each significant factor ($p<0.05$) will have an effect/influence/increase of union by 34% (Nagelkerke R Square= 0.34) statistically.

showing a positive effect on the union of the bone was the place of residence, and living in a rural area could have positive effects on union (B=1.12, p=0.010).

DISCUSSION

The risk and promotive factors for nonunion in the past two decades have been extensively studied, including open fracture, delayed weight-bearing, tobacco use, fracture classification, and diabetes.[13,14] Still, there is little information about the relationship between obesity and nonunion in the literature. Intramedullary nailing is the first choice for managing femur shaft fracture with low complication rates (4.9%) and an excellent option for aseptic nonunions of non-comminuted femoral shaft fractures with union rates reported to range from 72 to 100%.

Bostman[15] reported that obesity was a significant risk factor for the severity of fracture patterns. It has been also postulated that obesity affects bone metabolism by decreasing bone formation and increasing bone resorption by osteoclast.[8] The main finding of the current study is that the union time for the patient with obesity was longer regardless of fracture configuration.[16]

Besides, conflicting data have been shared about the effect of obesity on bone healing in animal experiments. Previously, it was thought that body mass could act as a barrier, thereby reducing the impact of aging and hormones on bone quality.[17] Still, as seen in the current study, the excess body fat and weight increased the force acted on the bone; thus, the severity of the fracture was worse and delayed union was more. Nonunion was observed to be significantly higher in patients with obesity. Gao et al.[18] reported that fracture healing slower in obese mice, while Histing et al.[19] reported the opposite.

Operative time is one of the crucial variables to consider while choosing between different surgical options. Although not of primary importance, increased operative time may expose a patient to increased surgical complications and costs.[20] Time in the operating room is expensive, adding to the already burdened healthcare system.[21] Operative time for each case showed no statistically significant difference (p=0.59) between both groups of patients. Tucker et al.'s[4] study showed that antegrade nailing in patients with obesity was 50% more time-consuming than retrograde nailing in those without obesity.

Our study had no reported cases regarding postoperative complications such as wound breakdown and surgical site infection. Our data showed that 40 of 54 patients in the nonunion group had obesity and underwent secondary procedures to enhance bone healing, such as dynamization of the implant and bone grafting. These additional procedures lead to increased costs to the healthcare system and delayed patient recovery, leading to loss of income for patients. This further increases the socioeconomic burden on the patient and the already strained healthcare system. Our patients had no reported cases of reoperation due to implant failure or infection.

Smoking affects fracture unions. Collinge et al.[22] reported that smoking could increase complication rates in Pilon fracture recovery, requiring further interventions. Our data showed no statistically significant results to confirm this, possibly due to a small sample size of 120 patients; 72 were smokers, and of that, 39 (54.2%) had obesity, and 33 (45.8%) did not have obesity.

Nonetheless, there are some limitations to this study. It is a retrospective study with a relatively limited sample size. The outcome of the nonunion and delayed union can result from the type of fracture, but not obesity alone. One of the main reasons for very high nonunion rates in this study is that we used AO classification, which did not mention complexity and type of fracture or the degree of comminution. Most of our fractures were complex fractures with comminution that involved soft tissue injury. We believe that the disparity of soft tissue injury, time to surgery, and the level of surgeon experience as some of the reasons for the high nonunion rate, and all these factors are contributing factors to the limitations of this study. We suggest using the Winquist classification instead of AO in future studies. In addition, the surgical procedure was standardized; however, the procedure was performed by a variety of trained senior residents and surgeons and was not standardized to a fixed group of surgeons. Also, no BMI analysis was done, and a BMI of >30 kg/m^2 was taken as a cut-off. Another potential limitation in this study is that only piriformis entry nails of a single brand were used. In a multi-center, large-scale, prospective study, the significance of the study could have been magnified. It would have allowed it to be a critical reflector of obesity in the DFF union. While this is a stepping-stone for a more comprehensive study to reflect the multiracial Asian population in the future, the conclusions obtained from this study can be applied by our primary healthcare workers on the frontlines to educate the population about obesity.

The population's health would continue to deteriorate as the human population continues to age. Therefore, there is a need to develop a global strategy to combat excess weight gain, both diet and activity. We must spread awareness about the impact of obesity and reduce the burden and cost on healthcare systems that are already strained. Although the relationship of obesity with the delayed union, nonunion, and fracture patterns was found in the present study, it is still challenging to make a final decision on the subject due to the current limitations. Dynamic compression plating could be used as an alternative or an addition for these patients.

The current study provided preliminary information for further prospective, randomized-controlled studies on this subject. To the best of our knowledge, it is one of the few studies in the literature on the subject. In this respect, this study contributes to the literature.

In conclusion, in patients with obesity, more nonunions were seen, and it took longer for union regardless of fracture configuration treated with an IMN in our study. Obesity should be considered a relative risk in decision-making in the choice of fixation while treating midshaft femoral fractures.

Ethics Committee Approval: The study protocol was approved by the Medical Research and Ethics Committee (date: 10.07.2019, no: NMRR-19-1317-48054 [IIR]). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Idea/concept and design: S.R., N.S.; Data collection and/or processing: S.J.I., N.S., R.S.; Analysis and/or interpretation and control/supervision: S.R., N.S., M.A.T.; Literature review: S.J.I., N.S., M.A.T.; Writing the article: All authors; Critical review: S.R., A.J., M.A.T., N.S.; References and fundings: R.S., M.A.T., S.J.I.; Materials: S.J.I., R.S., N.S.

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