



Tibial Fractures with Signs of Delayed Union: The Effects of Autogenous Bone Marrow Injection: A Longitudinal Study

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ABSTRACT

Introduction: Tibial fracture union is a lengthy process that begins with the initial trauma and continues for years following clinical and radiological union until the bone regains its previous structure and function. Delayed union and non-union are two typical issues that any surgeon dealing with fracture healing may encounter.

Aim/Objective: To evaluate how autogenous bone marrow injection affects clinical and radiographic evidence of union in tibial delayed union fractures.

Methodology: The study involved patients admitted with tibial shaft fractures that had not healed. Bone marrow is aspirated from the anterior iliac crest under local anesthetic using a specific bone marrow aspiration needle into heparinized syringes to avoid clotting. Bone marrow is aspirated from various locations to avoid aspirating the blood. Under fluoroscopy supervision, the aspirate is injected percutaneously into and around the fracture site.

Results: There were 95 patients with tibial shaft fractures that had not yet healed. There were 66 males and 29 females. The mid-shaft of the tibia was affected in 52 (54.7%) patients, followed by the distal tibia in 25 (26.3%) patients and the proximal tibia in 19 (20%) patients. A total of 36 patients were smokers, while 59 patients were nonsmokers. The right side of the limb was involved in 60 (63.2%) of patients, while the left side was involved in 35 (36.9%). The union rate for delayed tibial fractures was 96.8%.

Conclusion: While the retained hardware appears robust and stable, percutaneous autogenous bone marrow injection is a somewhat invasive, safe and affordable therapeutic option for tibial delayed unions. Smoking is a major controllable risk linked to delay fracture healing. After tibia fractures or documented delayed union, smokers' bones take longer to fuse.

Key Words: Bone marrow, Delayed union, Fracture healing, Non-union, Tibial fractures, Union rate

INTRODUCTION

Tibial fracture union is a lengthy process that begins with the initial trauma and continues for years following clinical and radiological union until the bone regains its previous structure and function.¹ Delayed union and non-union are two typical issues that any surgeon dealing with fracture healing may encounter. A delayed union is described as a failure to achieve a bony union within 6 to 9 months or an

un-united fracture that continues to mend but takes longer than expected period. However, a delayed union does not always result in a non-union.² The tibia is the most commonly involved bone. Delay in the union is caused by systemic and local reasons, including insufficient reduction, inappropriate immobilization, distraction and loss of blood supply due to open fractures, infection and drug consumption.³ There are several options for the therapy of delayed union, each with a distinct level of invasiveness and outcome. Various circum-

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stances can cause delayed healing, but it can also happen for no apparent reason.

Open bone grafting carries the danger of infection, hematoma formation and nerve damage, among other things.⁴ The concept of percutaneous bone marrow injection was born out of a desire to avoid the drawbacks of traditional autogenous open bone grafting. Adult bone marrow contains mesenchymal stem cells, called marrow stromal cells.⁵ MSCs can differentiate into connective tissue cells such as osteocytes, osteoblasts, adipocytes and chondrocytes.⁶ The potential of MSCs to differentiate into bone-producing cells has generated interest in using them in orthopedic injuries to promote fracture repair and treat bone disorders. The marrow is extracted from the iliac crest with a needle and then injected at the fracture site via a percutaneous route under the supervision of an image intensifier.⁷

Non-invasive techniques include low-intensity ultrasound and electromagnetic stimulation. The use of bone morphogenic protein, stem cell therapy, open bone grafting, bone substitutes and Ilizarov, a versatile distraction osteogenesis approach, are all invasive methods.⁸ Because bone marrow is the only tissue that contains both inducible and determined osteoprogenitor cells, it is the transplant of choice. The union was achieved in 75% -90% of reported tibia delayed union case series treated with bone marrow aspirate.⁹ Bone marrow injection enhances healing and provides several advantages over conventional grafting. Problems at the donor and recipient sites are greatly reduced. It is simple to repeat and can be used when open bone grafting is not possible due to bad skin conditions. It uses a bone graft's containing most osteogenic cells. It can be done under local anesthetic, avoiding the hazards of general and spinal anesthesia and it can be done on patients who are allergic to general and spinal anesthesia. It is very economical and performed as an outpatient procedure, which decreases the hospital stays.¹⁰ Percutaneous bone marrow injection with composite graft has shown to be effective in treating simple bone cyst, congenital tibial pseudoarthrosis and managing delayed union in severe clinical situations such as cancer patients, according to certain research.¹ The operation will be conducted on patients as an outpatient procedure because our hospital is a very busy trauma center that receives many patients daily. The technique is appropriate for high-risk patients who are otherwise unfit for spinal and general anesthesia and those who do not want to undergo a second major procedure. This prospective trial aimed to evaluate how well autogenous bone marrow injection affects clinical and radiographic evidence of union in tibial fractures with indicators of delayed union.

Study design: A longitudinal study

Place and Duration: This study was conducted at Sheikh Khalifa Medical City Ajman, United Arab Emirates from April 2019 to April 2021.

METHODOLOGY

The hospital ethical committee accepted the study. A total of 95 patients included in the study who had been operated on with tibial fractures and delayed union. Patients with malnutrition (with a lymphocyte count below 10%), pathological fractures and infected fractures were excluded from the study. The patient's medical history and examination were taken. All operations are performed by experienced orthopedic surgeons with at least five years of expertise. Standard post-operative protocols were followed once the surgery is done. For the next 4-6 weeks, all patients were monitored to see if the clinical and radiological union had occurred. SPSS version 22.0 was used to analyze the data. The average and standard deviation of age were calculated. Gender, surgical indication, smoking, post-surgery alignment and efficacy are all categorical statistics reported as frequency and percentages. The chi-square test was used to compare efficacy < 0.05 level. After stratification of age, gender, smoking and post-surgery alignment, tests were performed, with a p-value of less than 0.05 considered significant. (as shown in Table 5)

RESULTS

A total of 95 patients were included in the study. There were 66 (69.5%) males and 29 (30.5%) females. The average age was 39.2 ± 9.7 years. The majority of the participants in the study were between the ages of 31 and 40 (43.1%), followed by 41-50 years 23 (24.2%) (As shown in Table 1). The mid-shaft of the tibia was affected in 52 (54.7%) patients, followed by the distal tibia in 25 (26.3%) patients and the proximal tibia in 19 (20%) patients. The ratio of smokers was 36 (37.9%), whereas 59 (62.1%) were nonsmokers. After surgery, 57 (60%) patients had a good alignment, while 38 (40%) patients had a poor alignment (As shown in Table 2).

After the injury, the time to interval (length in months) was 7 months in 41 (43.2%) patients, 6 months in 30 (31.6%) patients, 8 months in 21 (22.1%) patients, and 9 months in just 3 (3.2%) patients. Single-shot was received by 27.4% of patients, whereas two injections were received by 72.6% of patients. However, 41 patients followed up once, 30 patients came for the follow-up twice, and 24 patients visited for follow-up thrice, as shown in Table 3.

The right side of the limb was affected in 60 (63.2%) of patients, whereas the left side of the limb was involved in 35 (36.9%). Clinical and radiological effectiveness was found in 73 (76.8%) patients, followed by solely radiological efficacy in 7 (7.4%) patients and clinical effectiveness in 5 (5.3%) patients. After three months of follow-up, 81 patients (85.2%) formed a union and 8 patients (8.42%) formed a union after six months of follow-up. Only 5 (5.3%) patients could not create a union at the end of the six-month follow-up period.

Additional procedures such as open bone grafting or revision surgery were required for these patients. The union rate for delayed tibial fractures was 96.8%, as described in Table 4.

Table 1: Distribution of Age and Gender

Categories		Frequency (%)
Age	Mean $\pm$ SD	39.2 $\pm$ 9.7
	18-30 years	12 (12.6)
	31-40 years	41 (43.1)
	41-50 years	23 (24.2)
	51-59 years	19 (20)
Gender	Male	66 (69.5)
	Female	29 (30.5)

Table 2: Distribution of Fracture site, habits and alignment

		Frequency (%)
Fracture site	Proximal	19 (20)
	Midshaft	52 (54.7)
	Distal	25 (26.3)
Habits	Smoker	36 (37.9)
	Nonsmoker Non-smoker	59 (62.1)
Alignment	Good	57 (60)
	Poor	38 (40)

Table 3: Distribution of No. of Injections, Follow-ups, and Duration

		Frequency (%)
No. of Injections	One	26 (27.4)
	Two	69 (72.6)
No. Follow-ups	One	41 (43.2)
	Two	30 (31.5)
	Three	24 (25.3)
Duration of months	6	30 (31.6)
	7	41 (43.2)
	8	21 (22.1)
	9	3 (3.2)

Table 4: Description of frequencies of limb side, surgery wise, fracture union wise, and effectiveness

		Frequency (%)
Limb Side	Right	60 (63.2)
	Left	35 (36.9)
Fracture union wise	Healed Fracture	91 (95.8)
	Non-union	4 (4.2)

Table 4: (Continued)

		Frequency (%)
Indication of surgery wise	Delayed union	92 (96.8)
	Non-union with implant failure	3 (3.2)
Effectiveness (clinical/radiological/ both)	Clinical	5 (5.3)
	Radiological	7 (7.4)
	Both	73 (76.8)

Table 5: Stratification of surgical effectiveness based on age, gender, smoking status, and surgical indication

		Effectiveness		p-value
		Yes	No	
Gender	Male	72	7	0.78
	Female	11	5	
Age (years)	18-30	13	2	0.69
	31-40	37	4	
	41-50	17	2	
	51-60	13	7	
Habits	Smoker	42	20	0.57
	Non-Smoker	28	5	
Surgery Indications	Delayed Union	81	8	0.59
	Non- Union with implant failure	6	0	

DISCUSSION

Delayed union or non-union of bone fractures has always posed a challenging problem. There is no commonly accepted definition of a fracture's delayed union. Every fracture is known to union once a specific amount of time has passed.¹¹ Delayed union is described as a failure to reach a bony union within six months or an un-united fracture that continues to mend but takes longer than predicted period.^{12,13}

Compared to traditional operative grafting, bone marrow injection improves recovery more quickly and effectively. It provides several advantages over traditional surgery grafting. The advantages include being the donor and recipient sites are much reduced, it can be performed in cases where open bone grafting is not possible due to poor skin condition, it can be repeated, and the use of the most osteogenic cells in bone graft and avoids introducing devitalized tissue (dead bone), allowing it to be utilized in children without causing damage to the growth plate, it can be performed under local anesthesia. It can be employed in some clinical settings when open bone grafting is not appropriate, such as delayed union or fractures that are prone to delay union and risk-free. It is practical and time-saving because it may be done as an

outpatient procedure, reducing hospital stay, and is cost-effective.¹⁴ However, there are significant drawbacks to bone marrow injection, including the lack of instant mechanical stability and the potential of dilution with peripheral blood.¹⁵

In our study, the mean age of the patients was 41.26 years and male (69.5%) cases were higher than females (30.5%) cases. Similar findings were observed by Nazar et al.³ We had 36 smokers and 59 nonsmokers in our study. In tibial shaft fractures, smoking was linked to a higher rate of non-union and delayed union and a long time to union. Smoking is a significant modifiable risk linked to fracture healing delays. After tibia fractures or established delayed union, smokers' bones take longer to fuse.¹⁶ The midshaft of the tibia was implicated in 52 cases in our investigation, whereas the distal tibia was involved in most cases in the study by Kasemet al.¹³ In 60% of patients, post-surgery alignment was satisfactory, but in 40% of patients who had delayed union, alignment was poor. It was similar to Nazar M et al.³ research, in which 30 patients had satisfactory post-surgery alignment, and 12 had poor alignment. In our investigation, two injections were given to 69 patients and one to 26 patients. In contrast, Elsatter TA et al.¹⁷ gave three injections to 11 patients, four injections to seven patients and two injections to two patients. In this study, 41 patients had one follow-up, 30 patients had two follow-ups, and 24 patients had three follow-ups. The study by Akram M et al. had two follow-ups in the highest number of patients.¹⁸ In 60 cases, the right side of the leg was affected, whereas 35 people had the left side affected. It was similar to Nazar M. et al. studies, which found a 3:2 right-to-left ratio.³ In the present study of delayed union of tibial fractures, the union rate was 96.8%. KÜÇÜKALP Aet al. showed union rate of 79%.¹⁹ Although 92% union rate was found in studies by Akram M et al.¹⁸

CONCLUSION

The use of Bone marrow for fracture healing is very good procedure for treatment of non union. Bone marrow aspirates are the major source of osteoinductive factors produced by resident cells such as endothelial cells, MSCs, osteoblasts, platelets and macrophages. It's essentially an autograft without the bone matrix and clinical proof of its ability to mend is accumulating. Our study demonstrated that autogenous BMA extended bone healing. According to the findings, percutaneous autologous bone marrow injection is a little invasive, safe and cost-effective therapeutic option for tibial delayed unions. It should be considered when the retained hardware looks intact and stable. Smoking is a major controllable risk linked to delay fracture healing. After tibia fractures or documented delayed union, smokers' bones take longer to fuse.

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Conflict of interest

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