

# Risk factors associated with transport gap bending deformity after bone transport in the treatment of lower extremity bone defects caused by infection

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## Research Article

**Keywords:** Bone transport, external fixator, bone defects, Ilizarov technique, complications

**Posted Date:** April 30th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-468193/v1>

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# Abstract

**Background:** The objective of this study was to observe the efficacy of bone transport using Orthofix external fixator in the treatment of lower limb bone defects caused by infection, and analyze the mechanism and risk factors of transport gap bending deformity (TGBD).

**Methods:** From January 2008 to December 2019, 326 cases of infected bone defects of the lower extremities were treated by bone transport in our medical institution. The location and other relevant information of TGBD were collected, summarized, and analyzed. The Association for the Study and Application of the Method of Ilizarov (ASAMI) standard was applied to assess the bone and functional outcomes.

**Results:** A total of 326 patients have reconstructed the bone defects in the lower extremities successfully, with a mean size of 6.2 centimeters (3.4 - 9.1 cm). TGBD was observed in 42 patients (12.8%) after removing the external fixator, including 32 tibias and 10 femurs, after a mean follow-up of 28.6 months (22 - 47 months). Age>45years, BMI>25kg/m<sup>2</sup>, defect of the tibia, diabetes, osteoporosis, glucocorticoid intake, duration of bone infection>24months, EFT>9months, EFI>1.8months/cm were associated significantly with a higher incidence of TGBD in the binary logistic regression analysis. The independent risk factors associated with TGBD included age>45 years, BMI>25 kg/m<sup>2</sup>, defect of tibia, diabetes, osteoporosis.

**Conclusions:** The bone transport using the Orthofix external fixator is a safe and practical method in the treatment of lower limb bone defects caused by infection. The incidence of TGBD was 12.8%, and the top five risk factors included defect of tibia, BMI>25kg/m<sup>2</sup>, duration of bone infection>24 months, age>45years, and diabetes. Age>45years, BMI>25kg/m<sup>2</sup>, defect of tibia, osteoporosis, diabetes were the independent risk factors. The higher incidence of TGBD may be associated with more risk factors.

## Background

Nonunion caused by infection is a common complication after the treatment of the lower extremity open fracture, where plenty of medical resources are needed to fix it up [1–7]. Similarly, bone defect after the infectious lesion debridement is one of the challenging musculoskeletal problem in orthopedic surgery [5, 6, 8–12]. Bone transport using a unilateral external fixator, which based on the Ilizarov technique, has been used for the past two decades to manage bone defects of the long bone [2, 13]. It allows easier manipulation to achieve compression, distraction, bone lengthening, and deformity correction, compared with conventional circular external fixators. Additionally, the external frame is an effective alternative in the comparison of the internal fixator technique, especially when bone loss, deformity, or failure of previous internal fixation may occur.

Although this technique has been reported by many studies about its efficacy in resolving critical bone defects and limb deformities, there are still some limitations. The occurrence of transport gap bending

deformity (TGBD) after removal of external frame is one of the severe complications in the late period of this treatment. Most previous articles attributed TGBD to the outcome of axial deviation and did not discuss it separately [3, 5, 14–16]. Although  $< 7^\circ$  of axial deformity after bone transport is considered a good bone outcome,  $> 7^\circ$  of axial deformity is likely to affect the limb shape and functional recovery. Pathological fractures, which caused by persistent worsening of malformation sequelae, may occur if not treated. The multi-level Bone transport and long duration of bone infection may also be the reasons of TGBD when the external fixator were removed. Such patients experienced a longer external fixation time during bone transport are brought a higher incidence of immobilization osteoporosis [17, 18], which contributes to the development of TGBD. Besides, the local soft tissue necrosis and other complications may occur easily in the application of correction surgery since the great coverage of scar caused by previous surgery. And a huge medical financial burden and psychological pressure are also placed on patients with TGBD by additional correction surgery. Therefore, it is of great importance for patients to effectively prevent such complications.

In this study, the purpose was to figure out the risk factors associated with the occurrence of TGBD by analyzing our cases after removing the external fixator in the treatment of lower limb bone defects using bone transport.

## Methods

After written informed consent from all patients and approval from the Ethics Committee of our hospital was received, the clinical records and consecutive X-ray photographs were analyzed retrospectively of all patients, who treated with post-traumatic bone defects of the lower extremity using a unilateral external fixator (Orthofix limb reconstruction system, Verona, Italy) from January 2008 to December 2019.

### Inclusion and exclusion criteria

Inclusion criteria: Bone defects after trauma or osteomyelitis debridement of the lower limb; treatment with bone transport using unilateral external fixator; age between 18–60 years; follow-up time  $> 20$  months.

Exclusion criteria: Defects caused by trauma without infection, excision of tumors, congenital defect; without surgical treatment; bone defects at other sites except for lower limbs; incomplete follow-up data; severe cardiovascular and cerebrovascular diseases, mental illness, liver abnormalities, kidney diseases.

### Patients' data

There were 255 males and 71 females with a mean age of 39 years (range, 20–58 years) assessed in this study according to the inclusion criteria. Data regarding patient age, gender, and side of affected, type of initial injury, the interval between initial injury and time of previous surgery were obtained utilizing the admission questionnaire scale. All patients were treated with single-level or double-level bone transport using unilateral external fixator (Orthofix Limb Reconstruction System) after radical debridement, with or without septal filling and soft tissue reconstruction surgery. Defect  $> 6$  cm was considered as the

indication for selecting double-level bone transport. The study was conducted in accordance with the Declaration of Helsinki.

### **Surgical technique**

In the prior stage of bone transport, all necrotic and infected bone and soft tissues are removed from the hardware completely, debrided thoroughly. The bacterial culture and antibiotic sensitivity test were conducted in exudation, to instruct the surgeon to apply appropriate postoperative antibiotics. The defects were filled with antibiotic (5 g vancomycin cement per 40 g gentamicin) PMMA bone cement (Heraeus, Hanau, Germany). Afterward, preoperative anteroposterior and lateral X-rays were used to evaluate the size of the defect and plan the structure of the external fixator. Bone transport surgery could be performed after the infection was controlled completely, which could be determined by laboratory parameters such as white blood cells (WBC), CRP (C-reactive protein), and ESR (erythrocyte sedimentation rate).

When the above preoperative preparation was achieved, we believe that the infection had been successfully eliminated and bone transport surgery was ready to perform. An appropriate number of Schanz screws were inserted into the medial or lateral side of the affected limb, and the clamps were assembled with the individualized external frame, which was designed before operation. Under X-ray perspective, the Schanz screws were adjusted to the best position respectively and tighten the external frame. Afterward, a minimally invasive osteotomy was performed using a Gigli saw with special care to preserve the periosteum as much as possible. Finally, depending on the size of the skin defect, the loss of skin was covered by the designed direct suture with appropriate tension or keystone flap. An X-ray radiograph was arranged on the second postoperative day and intravenous antibiotics were conducted for three days.

Bone transport started after a latent period of seven days. The proximal fragment and the distal fragment were distracted four times per day at a rate of 0.25 mm retrospectively until the two fragments converged. Paid more attention to the pin tract care was recommended, washed the pin tract daily using an alcohol swab with a mass percentage of 75%; the patient was encouraged to carry out weight-bearing activities on crutches 2–4 week after surgery. Subsequently, radiographic examination, WBC, ESR, and CRP were examined at 1, 3, 6, 9, 12, 18, and 24 months after bone transport. Bone grafting at the docking site were performed to promote bone union when the distraction stage ended.

### **Data collection**

The demographics were collected included: age, gender, body mass index (BMI = weight (kg) /height (m<sup>2</sup>)), location of bone defect (femur or tibia), comorbidities (such as diabetes, hypertension, and osteoporosis), glucocorticoid intake, and duration of bone infection.

Postoperative data included defect size (DS), the type of bone transport (single level and double level), time to bone union, external fixator time (EFT/ET), and external fixator index (EFI), and the Association for the Study and Application of the Method of Ilizarov (ASAMI) grade system was applied to assess the

postoperative outcomes. Infection was defined as bone defects associated with sinus drainage, along with positive results of deep bacteriological culture, histological biopsy, radiological and laboratory findings. EFT referred to the time spent before removing the external fixator. EFI is defined as the ratio of EFT months to the distraction regenerate length (cm). Imaging evaluations were performed every 2 weeks during the distraction phase and monthly during the consolidation phase. All patients were followed up closely for at least 20 months after the external fixator was removed.

### **Potential risk factors**

Quantitative variables included age, defect size (DS), the duration of bone infection, time to bone union, external fixator time (EFT), and external fixator index (EFI). And gender, body mass index (normal weight =  $BMI < 25\text{kg/m}^2$ , obesity =  $BMI > 25\text{kg/m}^2$ ), location of bone defect (femur or tibia), comorbidities such as diabetes (yes or no), osteoporosis (yes or no), and the history of glucocorticoid intake (yes or no), and the type of bone transport (single level and double level) were attributed to the categorical variables.

### **Statistical analysis**

T-test or rank-sum tests were used to compare the quantitative data. Pearson's chi-square test or Fisher-exact test were applied to compare categorical data. Multivariate logistic regression analysis was used for associated risk factor analysis. It was statistically significant that  $p < 0.05$ .

## **Results**

A total of 326 patients who met the criteria were enrolled in the study with a mean follow-up time of 28.6 months (22–47 months). There are currently 255 males and 71 females with a mean age of 39 years (20–58 years). The duration of bone infection was 23.7 months (4 months to 47 months) with an average of 3.1 previous failed operations, before bone transport surgery. Of the 326 patients, positive bacteria isolated was observed in 264 cases (80.9%) by the culture test of secretion. Among these, 191 (72.3%) were infected with *S. aureus*, 38 (14.3%) with *P. cuprina*, and 35 (13.3%) with *E. coli*. None of them was infected with methicillin-resistant *S. aureus* (MRSA) or fungi. The bone defect sites included 260 tibias and 66 femurs with a mean size of 6.2 centimeters (3.4–9.1 cm). The mean time to bone union, mean EFT, mean EFI of all cases was 8.07 months (6–10 months), 8.83 months (7–11 months), 1.62 months/cm (1.21–2.77 months/cm) respectively. The rate of excellent and good in the bone outcomes (excellent/good/fair/poor/failure, 76/137/53/60/0) was 81.5%, and 92.3% in the functional results (excellent/good/fair/poor/failure, 92/181/28/25/0) according to the ASAMI grade system.

There was an occurrence of TGBD after bone transport treatment finished in forty-two patients (12.8%), including 35 males, 7 females, 32 tibias, and 10 femurs. Thirty-eight cases were managed wedge-shaped osteotomy correction surgery with fixation, including internal plate fixator in 25 cases, intramedullary nailing in 12 cases, and external fixator in 5 cases. Besides, pin tract infection occurred in 45 cases, delayed union on docking site was presented in 16 cases, axial deviation appeared in 20 cases, and poor regenerate consolidation was observed in 7 cases. Thirty-seven pin tract infections were resolved by local saline washes, occlusive dressings, and oral antibiotic therapy. And eight deep pin tract infections were

managed by surgical replacement of the pin position combined with intravenous antibiotic therapy. Twenty axial deviations were corrected by adjusting the external fixator in the operation room. Sixteen delayed unions on the docking site and seven poor regenerate consolidations were recovered through surgical treatment of autologous bone grafts.

The patients were divided into two groups according to the presence or absence of TGBD (Table 1). After comparing the baseline data of the two groups, the statistically significant variables were entered into binary and multiple logistic regression analysis. There was no significant difference concerning the gender, type of bone transport, hypertension, defect size, and time to bone union > 9months from this cohort. Age > 45years, BMI > 25kg/m<sup>2</sup>, defect of tibia, diabetes, osteoporosis, glucocorticoid intake, duration of bone infection > 24months, EFT > 9months, EFI > 1.8months/cm were associated significantly with a higher incidence of TGBD in the binary logistic regression analysis (Table 2). DS > 5cm was not in a significant association with TGBD. The incidence greater than 50% was found in patients with defects of tibia (76.1%), osteoporosis (73.8%), BMI > 25 kg/m<sup>2</sup> (69.0%), diabetes (59.5%), glucocorticoid intake (54.7%). In the multivariate logistic regression analyses, the following were associated independently with TGBD, included age > 45 years, BMI > 25 kg/m<sup>2</sup>, defect of tibia, diabetes, osteoporosis, and constituted the final model as presented in Table 3.

Table 1  
Baseline characteristics of patients

| Factor   | TGBD             | Not TGBD         | t / $\chi^2$ | P value |
|--|------------------|------------------|--------------|---------|
| Male (%)   | 35(83.3)         | 220(77.4)        | 0.740        | 0.390   |
| Age, mean $\pm$ SD (years)   | 45.58 $\pm$ 6.62 | 38.05 $\pm$ 7.61 | 3.045        | < 0.001 |
| BMI (%)  |                  |                  | 4.315        | 0.038   |
| <25kg/m <sup>2</sup>   | 13(30.9)         | 66(23.2)         |              |         |
| >25kg/m <sup>2</sup>   | 29(69.0)         | 218(76.7)        |              |         |
| Location of defects (%)  |                  |                  | 4.233        | 0.040   |
| Femur  | 10(23.8)         | 56(19.7)         |              |         |
| Tibia  | 32(76.1)         | 228(80.2)        |              |         |
| Type (%)   |                  |                  | 0.201        | 0.654   |
| single level   | 23(54.7)         | 152(53.5)        |              |         |
| double level   | 19(45.2)         | 132(46.4)        |              |         |
| Diabetes yes (%)   | 17(40.4)         | 108(38.0)        | 4.813        | 0.028   |
| Hypertension yes (%)   | 8(19.0)          | 73(25.7)         | 0.868        | 0.351   |
| Osteoporosis yes (%)   | 11(26.1)         | 110(38.7)        | 5.064        | 0.024   |
| Glucocorticoid intake yes (%)  | 23(54.7)         | 142(50.0)        | 8.176        | 0.004   |
| Duration of bone infection, mean $\pm$ SD (month)  | 25.00 $\pm$ 8.02 | 23.61 $\pm$ 7.08 | 0.818        | 0.014   |
| DS, mean $\pm$ SD (cm)   | 6.11 $\pm$ 1.33  | 6.23 $\pm$ 1.30  | 0.940        | 0.340   |
| Time to bone union, mean $\pm$ SD (month)  | 8.60 $\pm$ 0.50  | 7.99 $\pm$ 0.58  | 2.752        | < 0.001 |
| EFT, mean $\pm$ SD (month)   | 9.51 $\pm$ 0.38  | 8.73 $\pm$ 0.65  | 3.668        | < 0.001 |
| EFI, mean $\pm$ SD (months/cm)   | 1.99 $\pm$ 0.28  | 1.58 $\pm$ 0.40  | 2.912        | < 0.001 |
| Follow-up time (months)  | 28.17 $\pm$ 4.29 | 28.64 $\pm$ 3.51 | 0.681        | 0.462   |
| TGBD, transport gap bending deformity. BMI, body mass index. DS, defect size. EFT, external fixation time. EFI, external fixation index. |                  |                  |              |         |

Table 2  
Binary logistic regression analysis of risk factors for TGBD

| <b>Factor</b>  | <b>Odds ratio (95% CI)</b> | <b>Standard error</b> | <b>P value</b> |
|--|----------------------------|-----------------------|----------------|
| Age > 45years  | 0.88(0.82–0.94)            | 0.037                 | 0.001          |
| BMI > 25kg/m <sup>2</sup>  | 2.42(1.01–5.79)            | 0.445                 | 0.047          |
| Defect of tibia  | 2.51(1.16–5.42)            | 0.393                 | 0.019          |
| Diabetes   | 0.46(0.19–0.80)            | 0.357                 | 0.010          |
| Osteoporosis   | 0.40(0.18–0.81)            | 0.363                 | 0.012          |
| Glucocorticoid intake  | 0.36(0.17–0.76)            | 0.380                 | 0.008          |
| Duration of bone infection > 24 months   | 1.07(0.99–1.15)            | 0.036                 | 0.042          |
| DS > 5cm   | 1.16(0.80–1.66)            | 0.186                 | 0.425          |
| Time to bone union > 9months   | 1.77(0.71–4.45)            | 0.468                 | 0.219          |
| EFT > 9months  | 0.10(0.03–0.33)            | 0.594                 | < 0.001        |
| EFI > 1.8months/cm   | 0.06(0.01–0.27)            | 0.731                 | < 0.001        |
| TGBD, transport gap bending deformity. BMI, body mass index. DS, defect size. EFT, external fixation time. EFI, external fixation index. |                            |                       |                |

Table 3  
Multivariate logistic regression analysis of risk factors for TGBD

| Factor  | Odds ratio (95% CI) | Standard error | P value |
|---|---------------------|----------------|---------|
| Age > 45years   | 1.14(1.04–1.24)     | 0.044          | 0.003   |
| BMI > 25kg/m <sup>2</sup>   | 2.71(0.66–4.03)     | 0.715          | 0.012   |
| Defect of tibia   | 2.92(0.91–4.36)     | 0.593          | 0.007   |
| Diabetes  | 0.30(0.10–0.92)     | 0.569          | 0.036   |
| Osteoporosis  | 0.76(0.25–2.29)     | 0.562          | 0.031   |
| Glucocorticoid intake   | 0.97(0.17–0.76)     | 0.380          | 0.683   |
| Duration of bone infection > 24 months  | 1.08(1.00-1.18)     | 0.042          | 0.440   |
| Time to bone union > 9months  | 2.49(0.79–7.83)     | 0.584          | 0.118   |
| EFT > 9months   | 1.85(0.55–3.95)     | 0.688          | 0.276   |
| EFI > 1.8months/cm  | 2.75(1.13–3.52)     | 0.870          | 0.763   |
| TGBD, transport gap bending deformity. BMI, body mass index. EFT, external fixation time. EFI, external fixation index. |                     |                |         |

Regarding the accessorial outcome of bone transport complications, the incidence of TGBD per individual per risk factor was presented (Table 4) and increased substantially in the presence of progressively more risk factors (Fig. 1).

Table 4  
Incidence of TGBD according to the number of risk factors present

| Risk factors(n)* | Patients (n) per risk factor category | Incidence of re-fracture |
|------------------|---------------------------------------|--------------------------|
| 1                | 265                                   | 23(8.6%)                 |
| 2                | 115                                   | 26(22.6%)                |
| 3                | 47                                    | 11(23.4%)                |
| 4                | 13                                    | 5(38.4%)                 |
| 5                | -                                     | -                        |

TGBD, transport gap bending deformity.

\* To categorize patients whether at risk or not, the continuous risk factors were dichotomised: age > 45years vs age < 45years, BMI > 25 kg/m<sup>2</sup> vs BMI < 25 kg/m<sup>2</sup>, femur vs tibia, diabetes vs not diabetes, osteoporosis vs not osteoporosis, glucocorticoid intake vs not glucocorticoid intake, duration of disease > 24 months vs duration of disease < 24 months, EFT > 9months vs EFT < 9months, EFI > 1.8months/cm vs EFI < 1.8months/cm.

## Discussion

The Ilizarov technique has been used for many years to treat bone defects [5, 7–10, 19, 20], and bone transport can be accomplished with many devices, such as circular fixator, unilateral fixator, or intramedullary nail systems. Each device has its advantages and disadvantages [2, 21]. However, to our knowledge, few studies focus on the TGBD after the bone transport treatment finished. In this study, complete electronic medical records and at least 20 months of follow-up data of 326 patients who were managed the bone transport surgery using unilateral external fixator for bone defects were collected and analyzed to figure out the incidence and associated risk factors of TGBD. Briefly, the occurrence of TGBD was in forty-two (12.8%) of 326 patients and the overall cure rate was 87.1%. Furthermore, defect of tibia, BMI > 25kg/m<sup>2</sup>, duration of bone infection > 24 months, age > 45years, and diabetes were the top five risk factors.

Via published researches [1, 2, 5], a higher quality of bone union with the Ilizarov technique using external fixator than internal fixation was noticed. About the characteristics, the external fixator is capable to adjust the direction and angle of bone transport under direct vision, and evaluate the stability of the whole external fixation structure. Moreover, the published study illustrated that the fresh bone formation tissue with differentiation ability was indeed lived in the transport gap when bone union was represented by X-ray graphs [22, 23]. But it still contained hyperplastic fibrous tissue when the transport gap bone tissue section was observed under microscope preview, which indicated that the mineralization of bone tissue was not sufficient [22]. TGBD was in high rate of occurrence if the external fixator was removed at this time. Therefore, one of the challenges faced by orthopaedic surgeons using the bone transport

technique for bone defects was to grasp the standard of transport gap union and avoid axial deviation in distraction stage. Certainly, the equally important was to identify the potential risk factors that patients may have and keep them away from these promptly before such a dreadful outcome occurred.

TGBD may be attributed to many factors, such as the patient's physical function, status of the bone, the mechanism and location of the bone defect, and additional violence [3, 24–28]. Our results showed that patients older than 45 years (OR0.88, CI0.82-0.94) were more likely to acquire the TGBD than the younger. Via published studies [29–32], aging is often considered to be accompanied by the loss of bone calcium, and resulting in osteoporosis, which greatly increases the duration of the consolidation stage, the EFT as well as EFI. Another conjecture is that lower extremity bones in the elder are less able to cope with deformity caused by additional forces than young bones, such as bending and rotation. For instance, the extraosseous morphology of the bone in the elder, the internal trabecular structure, and the connective tissue filled around the trabeculae are degraded in quantity and biological activity [33–35]. These reasons have become the culprit of TGBD in elderly patients gradually. Hence, prophylactic administration of calcium supplementation is recommended when bone transport is managed for patients > 45 years.

Obesity (OR2.42, CI1.01-5.79) and osteoporosis (OR0.40, CI0.18-0.81) are two common diseases with increasing incidence. Fat and bone are connected by many pathways that ultimately serve to provide a skeleton suitable for the quality of the adipose tissue they carrying [18]. Leptin, adiponectin, and insulin/amylin are all associated with this connection [18]. However, excessive body fat, especially abdominal fat, produces inflammatory cytokines, which stimulate bone resorption and reduce bone strength, as has been pointed out by recent studies [18, 36–39]. Despite some studies have shown conflicting results that the resistance of lower limb bones to deformity can be enhanced by obesity, more evidence holds that obesity may be involved in an increased risk of skeletal disorders, as well as the skeletal structure deformity after reconstruction. Similarly, obese patients were nearly 2.7 times more likely to have TGBD than normal-weight in this study. This phenomenon can be explained exactly by the high weight load on the lower limb bones, and abnormal bone metabolism caused by the inflammatory factor pathway of obesity. Then, it is meant to emphasize weight control through a healthy diet and exercise for preventing TGBD when the external fixator was removed.

TGBD occurred in more tibias (OR2.51, CI1.16-5.42) than the femurs in our cohort, after the reconstruction of bone defects. With the view of anatomy, there is better soft tissue coverage in the femur than the tibia, which means a richer blood supply. Thus, nutritional elements required for new bone formation can be accumulated in the femur in a shorter time, which makes the bone union time, EFT, and EFI lower in the treatment of bone defects. There is no such physiological structural advantage in tibial defects, especially in the lower third of the tibia, which is the location of structural changes. A higher rate of nonunion and skeletal structure deformity has been observed to occur here by previous studies [16, 40], since the less blood supply and poor soft tissue coverage. Hence, it is necessary to give a detailed and reasonable postoperative rehabilitation plan to the patients who have completed the bone transport treatment. For instance, non-weight-bearing walking exercise with the crutches for 2–4 weeks after

removal of the external fixator. Gradual resumption of weight-bearing walking is recommended, especially for the tibia, when the radiographs showed that the screw holes were filled with new bone.

At the same time, some causal relations were noticed in our cohort between TGBD and some comorbidities, such as diabetes (OR0.46, CI0.19-0.80). While microvascular and peripheral nerve degeneration is the most common complication of diabetes, the risk of osteoporosis and pathological skeletal structure deformity must also be considered when treating bone defects in diabetic patients [41–44]. The newly generated bone was affected by the unique interactions, given the causes which lead to different types of diabetes [42]. Controversy exists regarding the exact mechanism of bone loss in the diabetic environment, but there is a shred of important evidence to support that high concentrations of glucose are toxic to osteoblasts [44], which are implicated in the formation of bone. Serum osteocalcin levels in diabetic patients also appear to be suppressed by hyperglycemia. High glucose concentrations impair the ability of osteoblasts to synthesize osteopontin for bone formation [43]. Simultaneously, the risk of TGBD caused by falls is also increased by common complications in diabetic patients, such as poor visual acuity, peripheral neuropathy, and reduced balance [41, 44]. As detailed above, there is strong evidence that bone loss and increased risk of pathological skeletal structure deformity can be caused by diabetes and its associated complications, regardless of types. In this study, there were 11 diabetic patients associated with osteoporosis at the same time. And TGBD was observed in all of these patients since their fragile new bone. Therefore, postoperative management is of great importance for diabetic patients to avoid TGBD, including personalized diabetes plans to achieve glycemic control safely, calcium supplementation, and antiresorptive agents.

Radical debridement is a key step in the control of bony infection, especially post-traumatic osteomyelitis [2, 15, 45]. Subsequently, the problem of bone loss after radical debridement have been solved by the bone transport techniques, which based on the principle of distraction osteogenesis. Gradually, these two procedures constitute a systematic protocol for the treatment of infected bone defects [2, 5, 9, 15]. Conversely, bone infection may be concealed by the application of unsystematic treatment plan, which can bring out a long-term bone destruction. The microarchitecture of the bone and the surrounding blood vessels and nerves were destroyed by such prolonged duration of bone infection undoubtedly. For instance, the periosteal and trabecular structure will continue to be threatened when pathogenic microorganisms persist in bone [17, 46]. Bone mineral density was then reduced, resulting in poor bone healing quality and bone degeneration was even aggravated. In this study, unfortunately, each patient in our cohort had a duration of bony infection at least 16 months. The average duration of bone infection (OR1.07, CI0.99-1.15) was up to 25 months in patients who experienced TGBD. This observed phenomenon also validated the mechanism of pathological change described above. Simultaneously, immobilization of osteoporosis occurred during the long period of bony infection, which increased the difficulty of bone transport and reconstruction surgery. Similarly, EFT (OR0.10, CI0.03-0.33) and EFI (OR0.06, CI0.01-0.27) were also risk factors for TGBD during bone transport. One of our conjectures is that the immobilization osteoporosis of the reconstructed bone was also brought about inevitably by the longer EFT and higher EFI when treated patients with a long period of bone infection, especially in the treatment of critical size bone defects (> 4.5cm). Hence, prompt surgical treatment is recommended in the

event of bone nonunion caused by infection. Immobilization osteoporosis can also be avoided effectively by the proper axial load of the lower limb during bone transport treatment. For example, non-weight-bearing walking with crutches was recommended to start on the second postoperative day and gradual normal walking was managed in the second week.

In our study, TGBD was recorded in 42 cases, and the more risk factors patients had, the higher incidence of TGBD they got (Table 4). There are still ways to cope with this complication, including the open reduction and internal fixation (intramedullary nail and internal plate), external fixator after close reduction (unilateral fixator or external locking compression plate) and plaster or splint fixation after manual reduction. Fortunately, bone union were received by patients with TGBD, through treatment with the above methods. Additionally, a satisfactory recovery that the excellent and good rate of the bone result was 81.5%, and the excellent and good rate of function outcome was 92.3% were obtained in our cohort. Amputation surgery was performed on no patient and none of the infection recurrences occurred.

Last but not least, there are some advantages in this study, including a large number of patients, standard techniques, and multi-level data comparison. However, it also has several drawbacks. First of all, this was a retrospective study of a patient with two different bone locations for the osteomyelitis caused by infection in a single medical institution, the results should be considered carefully. Secondly, only one technique was applied to treat infectious bone defects, the ability was then lacked to compare with other techniques. This indicates that (multi-center) collaboration is essential to pool treatment results from individual hospitals into (prospective) clinical studies and subsequently into meaningful analysis.

## **Conclusion**

The bone transport using Orthofix external fixator is still a safe and practical method in the treatment of lower extremity bone defects caused by infection. In this study, the incidence of TGBD was 12.8% after removing the external fixator, and the top five risk factors included defect of tibia, BMI > 25 kg/m<sup>2</sup>, duration of bone infection > 24 months, age > 45 years, and diabetes. Age > 45 years, BMI > 25 kg/m<sup>2</sup>, defect of tibia, osteoporosis, diabetes were the independent risk factors. The higher incidence of TGBD may be associated with more risk factors. TGBD will be effectively avoided, however, when the above risk factors are known.

## **Declarations**

### **Acknowledgments**

Not applicable.

### **Author Contributions**

Kai Liu: Conducted the study. Collected, analyzed, and interpreted the data. Wrote the manuscript.

Yanshi Liu: Designed the study, and interpreted the data, and edited the manuscript.

Feiyu Cai: Planned the project. Interpreted the data.

Chenchen Fan: Interpreted the data.

Alimujiang Abulaiti: Edited the manuscript.

Peng Ren: Edited the manuscript, reviewed the manuscript.

Aihemaitijiang Yusufu: Planned the project. Reviewed the manuscript.

### **Funding information**

This study was sponsored by the Natural Science Foundation of Xinjiang (NO.2020D01C250), and funded by the National Natural Science Foundation of China (NO. 81560357).

### **Availability of data and materials**

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

### **Ethics approval and consent to participate**

This retrospective study was approved by the Ethics Committee of The First Affiliated Hospital of Xinjiang Medical University and carried out in accordance with the ethical standards set out in the Helsinki Declaration. Informed consent was received from all participating.

### **Competing interests**

The authors declare that they have no conflict of interest.

### **Consent for publication**

Not applicable.

### **Disclosure**

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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## Figures

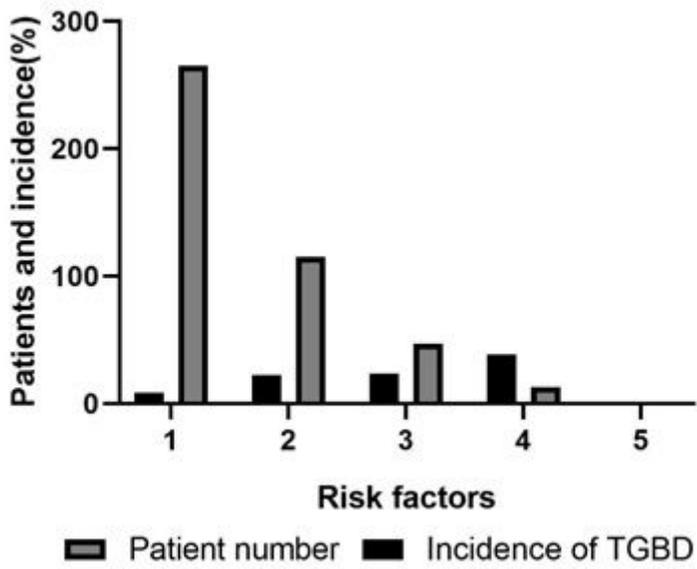


Figure 1

Incidence of transport gap bending deformity (TGBD) according to the number of risk factors.