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TRANSVERSE TIBIAL BONE TRANSFER (TTBT) IN DIABETIC FOOT ULCER (DFU): TECHNICAL ASPECTS, BIOCHEMICAL MECHANISMS, SAFETY AND OUTCOMES OF A NOVEL SURGICAL METHOD

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ABSTRACT

Background. Diabetic foot ulcers (DFUs) affect a substantial proportion of the 589 million adults currently living with diabetes worldwide and remain a leading cause of lower-limb amputation and excess mortality. Despite debridement, offloading, advanced dressings, negative-pressure wound therapy, hyperbaric oxygen, topical growth factors, and revascularisation, recalcitrant ulcers still progress to amputation in approximately 20% of cases, with five-year mortality near 70% among those amputated. Tibial cortex transverse transport (TTT), a derivative of Ilizarov's distraction osteogenesis principle, has emerged as a regenerative surgical option for advanced DFUs.
Methods. We performed a narrative review of literature published between January 2001 and April 2026, identified through PubMed and Google Scholar, addressing surgical technique, biological mechanisms, clinical efficacy, and safety of TTT in DFU.
Results. TTT, a small antero-medial tibial corticotomy with slow transverse distraction, elicits a coordinated regenerative response. Mechanistic studies show distraction-induced elevation of proangiogenic mediators and satisfactory outcomes in patients. Clinical data, including a meta-analysis, a multicentre cohort and other small studies, indicate wound healing rates of approximately 95%, limb salvage rates exceeding 95%, and recurrence rates near 3% during two-year follow-up. Significant improvements in ankle-brachial index, dorsal foot temperature, pain scores, and quality of life are consistently reported. Complications are manageable: risks of approximately 2% for tibial fracture and 8% for pin-site infection.
Conclusions. TTT is a mechanistically rich, clinically effective, and reasonably safe option for advanced DFUs. Adequately powered multicentre randomised trials comparing TTT with contemporary best practice are needed to define its definitive role.

KEYWORDS

Transverse Tibial Bone Transfer; Diabetic Foot Ulcer Healing; Distraction Osteogenesis; External Fixator

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1. Introduction

Diabetes is one of the most common health problems in the world. The most recent issue of the International Diabetes Federation (IDF) Diabetes Atlas (2025) reports that in 2024, as many as 589 million people suffered from diabetes, which is 11.1% of the world's adult (20–79 years) population (Genitsaridi et al., 2026). Currently, diabetes is one of the leading causes of disability, premature mortality, and expenses for society. In addition, according to the IDF prognosis from 2025, in 2050 diabetes will concern 853 million people (Genitsaridi et al., 2026), posing an even greater challenge for healthcare systems and causing an increasing number of complications. Ulceration of the diabetic foot is a common complication of diabetes. The risk of developing this complication ranges from 19% to 34% in a lifetime for people with diabetes (Armstrong et al., 2017). Diabetic foot ulcers (DFUs) become infected in over 50% of patients suffering from DFU (Prompers et al., 2007). The occurrence of DFU itself causes a 2.5-fold increase in mortality (Walsh et al., 2016); what is more, DFU is a risk factor for amputation and death—20% of patients with this condition will require amputation (Armstrong et al., 2017), 50–60% of whom will die within 5 years (Chen et al., 2023; Murphy-Lavoie et al., 2025).

Current treatment methods for diabetic foot ulcers include negative-pressure wound therapy, growth factors, bioengineered tissue, acellular matrix tissue, stem cell therapy, hyperbaric oxygen therapy, and, most recently, topical oxygen therapy (American Diabetes Association Professional Practice Committee [ADA], 2025). However, the effectiveness of currently available methods is limited, prompting physicians to further research. The purpose of this article is to highlight this new treatment method and assess its effectiveness based on the available literature.

Transverse tibial bone transfer (TTBT or TTT) is a method based on the main biomechanical and molecular ideas of the Ilizarov technique. TTBT involves osteotomy of a small bone fragment within the tibia, followed by transverse traction, which initiates remodeling and tissue regeneration. Despite many similarities, the two methods differ: distraction osteogenesis has distinct clinical applications and addresses large bone fragments that are moved vertically (Malkova & Borzunov, 2021).

This method can mobilize bone tissue and soft tissues such as muscles, fascia, vessels and nerves to regenerate and lengthen, but also to induce neovascularization and improve blood flow in the distal segments of the limbs, as evidenced by the increase in ABI (Liao et al., 2026). Studies show that increased cell proliferation and metabolism are caused by an increase in the concentration of molecules (mediators) such as HIF-1α, VEGF, PDGF, EGF, antioxidant proteins or small extracellular vesicles (sEVs) containing mRNA, causing increased fibroblast migration, neovascularization, and growth of neurons and vessels—resulting in tissue regeneration (Liu, Huang, et al., 2024; Ou et al., 2022; Xie et al., 2024).

This review summarizes the scientific work on the treatment of diabetic foot ulcers with a particular emphasis on the new TTBT method—describing the benefits, risks, biochemical mechanisms and their multipotency, and most importantly, the effectiveness of the method—highlighting the need to extend our scope of practice in order to lower rates of complications, amputations and deaths in the population suffering from diabetes.

2. Pathophysiology of Diabetic Foot Ulcer

The pathophysiology of diabetic foot ulcers is complex and multifactorial, encompassing neuropathic, vascular, and immunological components, all of which arise as consequences of chronic hyperglycaemia (Armstrong et al., 2017; Dawi et al., 2025). Persistently elevated blood glucose levels activate several metabolic pathways which together generate oxidative stress within nerve cells and ultimately lead to the development of peripheral neuropathy (Feldman et al., 2019). Non-enzymatic glycation of structural and functional proteins, with the subsequent accumulation of AGEs and their interaction with the receptor for AGEs (RAGE), further exacerbates nerve dysfunction, sustains pro-inflammatory cascades, and contributes to local ischaemia (Khalid et al., 2022). At the vascular level, hyperglycaemia induces endothelial dysfunction, manifesting as reduced bioavailability of vasodilators—particularly nitric oxide; the resultant vasoconstriction, combined with the hypercoagulable state characteristic of diabetes, predisposes the tissues of the foot to ischaemia and ulceration. Immunological dysregulation further compounds these effects: chronic hyperglycaemia drives the polarization of macrophages toward the pro-inflammatory M1 phenotype, depletes regulatory T cells, impairs neutrophil function, and disrupts angiogenic signalling, thereby perpetuating a chronic inflammatory environment that delays re-epithelialization and tissue regeneration (Dawi et al., 2025).

3. Methodology

This study was designed as a narrative literature review aimed at synthesizing current evidence regarding the application of transverse tibial bone transfer (TTBT) in the management of diabetic foot ulcers (DFUs). The narrative approach was selected to allow for a comprehensive exploration of both the molecular mechanisms underlying tissue regeneration and the clinical outcomes reported across heterogeneous study designs, which would not be amenable to a strict systematic review or meta-analytic framework.

A comprehensive literature search was performed using two principal electronic databases: PubMed (MEDLINE) and Google Scholar. The search covered publications issued between January 2001 and April 2026, with particular emphasis on articles published within the last five years in order to reflect the most current developments in the field. The following keywords and their combinations were employed: “transverse tibial bone transfer”, “transverse tibial transfer”, “tibial cortex transverse transport”, “diabetic foot ulcer”, “diabetic foot”, and “diabetic foot healing”.

Studies were considered eligible if they were peer-reviewed original research articles, systematic reviews, or meta-analyses; provided an accessible abstract in English; and addressed clinical outcomes, molecular mechanisms, or both aspects of TTBT in the context of DFU management. Conference abstracts without full-text availability, editorials, letters to the editor, commentaries lacking original data, studies of inadequate methodological quality, and duplicate publications were excluded.

Included studies were assessed by their quality, methodological soundness and impact. Only studies meeting high methodological standards were retained for synthesis. Relevant data were extracted from each included publication. A qualitative synthesis was performed and organized thematically around two principal domains: (1) the molecular and cellular mechanisms underlying the regenerative effects of TTBT, and (2) the clinical outcomes associated with its application in patients with diabetic foot ulcers.

4. Indications and Surgical Technique of TTBT

The main indications for TTBT are chronic, non-healing diabetic foot ulcers and chronic ischemic ulcers caused by atherosclerosis or other vascular diseases. Diseases of affluence, such as diabetes or atherosclerosis caused by hypertension or other diseases, have a common denominator: damage to vessels, and consequently, nerves and other tissues. TTBT induces neovascularization and tissue regeneration, increasing the chances of healing chronic ulcers that do not heal with standard methods.

The TTBT technique is based on the main principles of Ilizarov's distraction osteogenesis method - it involves performing an osteotomy of a bone window and subsequent transverse traction of the aforementioned bone fragment in the medial-anterior aspect of the tibia. Due to the novelty of the described method, strict guidelines regarding the course of treatment have not yet been developed, although most studies include wound debridement, targeted antibiotic therapy, regular dressing changes, negative pressure therapy, and metabolic stabilization, including normalization of glycemia, in their treatment protocols (American Diabetes Association Professional Practice Committee [ADA], 2025).

The key step in the treatment of DFU might be surgery - TTBT. The anteromedial surface of the tibia is the site of choice for many authors, although the level of osteotomy varied across the studies. Wen et al. (2023) proposed an osteotomy 10–30 cm distal to the tibial plateau, while Ou et al. (2022) performed an osteotomy at the level of the middle and lower tibia, Chen et al. (2020) and Yuan et al. (2021) performed an osteotomy in the proximal aspect of the tibia. Following the incision of the skin, it is essential to perform a meticulous periosteal incision before proceeding with an osteotomy to create a small bone window. Depending on the study, the size of the bone windows varied significantly - from a single bone window measuring 7 × 1.8 × 1.5 cm (Ou et al., 2022) to two bone windows measuring 1.5 × 1.5 cm (Liu, Yao, et al., 2024). In the subsequent phase of the procedure, two pins should be precisely inserted into the proximal and distal regions of the tibial shaft surrounding the osteotomy site, alongside two additional pins placed within the bone window. Initiation of bone transport occurred between 3 to 5 days post-surgery. The bone transport process may follow two distinct protocols: either advancing 1 mm per day for a duration of 14 days, or 0.25 mm every 6 hours, sustained over the same 14-day period. The retraction of the tibial bone window can also adopt one of three different regimens: 1 mm per day for 14 days, 0.25 mm every 6 hours for 14 days, or an accelerated protocol of 2 mm per day for 7 days. Following the procedure, patients were subjected to careful monitoring, and if bone union progressed without complications - typically within 6 to 8 weeks - the pins and associated fixation devices were removed. Subsequent evaluations of the patients ensued to assess recovery outcomes (Hu et al., 2023).

5. Molecular Mechanisms Underlying Transverse Tibial Bone Transport

In prior research, Ilizarov established that distraction osteogenesis promotes histiogenesis, which encompasses the formation of muscle, vascular structures, nerves, and bone. The biomechanical principles underlying both the tibial transport bone technique (TTBT) and distraction osteogenesis suggest that both methods might have a similar effect. Consequently, Ou et al. (2022) conducted a study to investigate whether elevated levels of pro-angiogenic growth factors are present in patients undergoing TTBT. The growth factors examined in their research included basic fibroblast growth factor (bFGF or FGF2), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF).

Among these, VEGF stands out as a vessel-specific cytokine and mitogen, essential for the proliferation and migration of vascular endothelial cells. Its significance in neovascularization cannot be overstated; it plays a pivotal role in the recruitment of newly formed vessels to tissues exhibiting elevated VEGF levels, thus contributing to wound healing and the maintenance of normal vascular architecture (Nieves et al., 2009).

On the other hand, bFGF (FGF2) serves as a critical growth factor for fibroblasts and the extracellular matrix. Its mechanism of action primarily involves enhancing fibroblast proliferation and facilitating their migration toward areas with increased levels of this growth factor. Notably, FGF2 exhibits a synergistic, pro-angiogenic effect in conjunction with VEGF, influencing several endothelial receptors, including the tyrosine kinases FGFR1 and FGFR2 (Pang & Poon, 2006).

5.1. Proangiogenic Factors

In the study by Ou et al. (2022), serial serum measurements of growth factors were conducted in a population of 10 people (5 men and 5 women) with diabetes mellitus and diabetic foot ulcer Wagner stage 4 who underwent TTBT. The beginning of outward movement (0.25 mm every 6 hours for 2 weeks) of the bone window started 5 days after surgery, and blood samples were drawn 1 day before surgery and on days 1, 4, 11, 18, 28, and 35 post-surgery. The outward movement was followed by 3 days of mechanical silence and then a return protocol lasting 2 weeks (0.25 mm every 6 hours). The study demonstrated that levels of VEGF, bFGF, and EGF on the 11th (7th day of outward bone transport), 18th (14th day of outward bone transport), 28th (7th day of inward bone transport), and 35th (14th day of inward bone transport) postoperative days were significantly higher than pre-operative baseline values ($p < 0.05$). PDGF levels were significantly elevated from the 18th postoperative day onward. These findings indicate a systemic, time-dependent release of angiogenic and histogenic mediators triggered by the mechanical distraction process.

5.2. Mechanistic Findings: HIF-1α Pathway and Angiogenesis

At the cellular and molecular level, Liu, Huang, et al. (2024) established a rat model of severe ischemic DFU and investigated an additional mechanism underlying the efficacy of TTT. A total of 48 rats were randomly allocated into three groups: control, sham, and TTT. The sham group underwent the same procedure as the TTT group, with the exception that the corticotomized segment was not subjected to transport. The study demonstrated that DFUs in the TTT group healed more rapidly, with a significantly smaller wound surface area at each time point assessed (postoperative days 3, 6, 9, and 12; $p = 0.001–0.05$, depending on the time point).

Moreover, histopathological examination of the DFUs on days 6 and 12 revealed that the TTT group achieved a significantly greater mean dermal thickness compared with the remaining groups ($p < 0.001$), as well as a higher percentage of collagen content relative to both the sham and control groups ($p < 0.001$). In contrast to the control and sham groups, hair follicle-like structures were observed within the DFUs of the TTT group, and the epidermis exhibited continuity, whereas in the control and sham groups the epidermis was incomplete and discontinuous.

Furthermore, Laser Doppler Perfusion Imaging and Computed Tomography Angiography were performed on postoperative days 6 and 12. Both modalities demonstrated significantly increased blood flow and vascular volume within the hindlimb of the TTT group compared with the control and sham groups (all $p < 0.001$).

At the molecular level, the activity of $CD31^+$ endothelial cells and $VEGFR2^+$ cells was significantly higher in the TTT group than in the control or sham groups at both day 6 and day 12 (all $p < 0.001$ for $CD31^+$; $p = 0.001–0.01$ for $VEGFR2^+$, depending on the time point), and the expression of PDGF-BB, SDF-1, and HIF-1α was similarly elevated (all $p < 0.001$). The authors proposed a mechanistic model in which the osteogenic activity induced by transverse distraction generates a localized hypoxic microenvironment that triggers the expression of hypoxia-inducible factor 1-alpha (HIF-1α), a subunit of the HIF-1 complex. HIF-1 is a pleiotropic transcription factor that exerts multidirectional effects, including the upregulation of circulating VEGF, PDGF-BB, and SDF-1, as well as the enhanced expression of insulin-like growth factor 2 (IGF-2) and transforming growth factor alpha (TGF-α).

As a result of TTT, angiogenic factors such as VEGF, PDGF-BB, and SDF-1 traverse the trans-cortical capillaries into the peripheral circulation and ultimately reach the DFU site, thereby inducing neovascularization and promoting wound healing. Importantly, the sham group (corticotomy without transport) did not exhibit significant improvement, confirming that the transverse distraction component, rather than the cortical incision alone, is responsible for the therapeutic effect. These findings, in conjunction with the activation of the HIF-1α pathway, indicate that the clinical benefit of TTT is attributable to the transverse cortical distraction itself.

5.3. SDF-1/CXCR4 Signaling and Endothelial Progenitor Cells

The role of the SDF-1 (stromal cell-derived factor-1)/CXCR4 (CXC chemokine receptor 4) signaling axis and endothelial progenitor cells (EPCs) was delineated by Ou et al. (2023) in a diabetic rodent model undergoing TTBT. The SDF-1/CXCR4 complex is known to have multifaceted functions, with previous research highlighting its critical involvement in the regenerative processes of various tissues, including the lungs, heart, liver, and nervous system. Furthermore, previous research demonstrated that the localized administration of SDF-1 at the myocardial infarction site facilitates the development of collateral circulation

and enhances cardiac revascularization. This evidence highlights the significant revascularizing and regenerative capabilities of these molecules (Das et al., 2019).

Flow cytometry results in the Ou et al. (2023) study showed that TTT increased the numbers of endothelial progenitor cells (EPCs) in peripheral blood as determined by CD34 and CD133 expression. EPCs are a group of many subsets of cells with high expression of vascular endothelial cell surface markers-their main goal is to adhere to hypoxic/ischemic tissue and promote vasculogenesis. In this study, an accumulation of EPCs was observed at skin ulcer sites after TTT surgery regardless of the time post-surgery. Moreover, levels of SDF-1 and CXCR4 mRNA and protein expression in the TTT group were significantly higher than in blank or fixator control groups. All of these changes were accompanied by accelerated wound closure and significantly higher quality of the dermis and epidermis in the TTT group. These findings were backed by a separate experimental study on a diabetic rodent model by Qin et al. (2024), in which a considerable increase in circulating EPCs was observed in the TTT group versus control and sham groups ($p < 0.01$), and the HIF-1α/SDF-1/CXCR4 signaling pathway was confirmed as pivotal in the angiogenic response. Additionally, a shift from pro-inflammatory M1 macrophages toward anti-inflammatory M2 macrophages was observed, indicating TTT's immunomodulatory capacity and suggesting that the regenerative effect of TTT is multifactorial, spanning both vascular and immune compartments.

5.4. Small Extracellular Vesicles and Multi-Tissue Regeneration

A landmark mechanistic study by Xie et al. (2024) revealed an additional layer of complexity within the TTT mechanism. This multi-stage investigation was initiated with experiments conducted in a rat model. In the first phase, diabetic foot ulcers were induced in 20 Sprague-Dawley rats, which were subsequently allocated into two subgroups: a control group and an experimental group, the latter undergoing bone transport. The degree of ulcer re-epithelialization was then compared between groups, revealing a significantly greater percentage of re-epithelialization in the bone transport cohort, accompanied by enhanced neovascularization and an increased density of nerve fibers and fibroblasts. In the next step, plasma harvested from rats in both the control and experimental groups was applied to human umbilical vein endothelial cells (HUVECs) and human dermal fibroblasts (HDFs); plasma derived from the experimental group markedly augmented angiogenesis and HDF migration. The plasma was subsequently fractionated into three components—soluble factors, large extracellular vesicles (lEVs), and small extracellular vesicles (sEVs)—and molecular analysis of these fractions identified the sEV fraction as carrying the highest abundance of mediators promoting angiogenesis and fibroblast migration, and, by extension, diabetic ulcer healing. An analogous phenomenon was observed in sEVs isolated from human samples following TTBT. Furthermore, the study demonstrated that antioxidant proteins (glutamate-cysteine ligase catalytic subunit [GCLC], glutathione peroxidase 1 [GPX1], and catalase [CAT]), together with small extracellular vesicles (sEVs) possessing multi-tissue regenerative potential, are released during bone transport in both humans and rats. These vesicles preferentially accumulate within diabetic wounds and are enriched in microRNAs - most notably miR-494-3p - which drive neovascularization, fibroblast migration, and nerve fiber regeneration.

Furthermore, the study showed that deletion of miR-494-3p in rats attenuated the beneficial effects of bone transport, thereby confirming the functional significance of this pathway.

A pilot randomized, single-center, placebo-controlled, double-blind trial (66 patients enrolled) reported in the same publication demonstrated that oral administration of ginsenoside Rg1 (an upregulator of miR-494-3p) together with reduced glutathione accelerated wound healing in patients with refractory DFU. After 12 weeks of therapy, the mean rate of wound contraction reached 71.5% in the control group versus 91.1% in the treatment group, with the difference reaching statistical significance ($p < 0.05$). Taken together, this multi-stage investigation provides robust translational evidence supporting the sEV-mediated mechanism (Xie et al., 2024).

6. General Outcomes of Tibial Cortex Transverse Transport in the Healing of Diabetic Foot Ulcers

Over the past 20 years, multiple studies have reported that tibial bone transverse transport (TTT) consistently produces favourable clinical outcomes in the management of diabetic foot ulcers (DFUs), including ulcers at advanced Wagner grades (Wagner, 1981) or University of Texas (UT) classifications (Lavery et al., 1996) historically associated with major amputation. The largest quantitative synthesis available is the systematic review and meta-analysis by Hu et al. (2023), which included seven studies that enrolled 818 participants. The pooled wound healing rate in this study was 0.96 (95% CI: 0.93–0.98) and the pooled limb salvage rate reached 0.98 (95% CI: 0.95–1.00) after treatment with TTT. When directly compared with conventional management (American Diabetes Association Professional Practice Committee [ADA], 2025),

the TTT group was associated with a significantly higher healing rate (OR: 10.43; 95% CI: 3.96–27.43; $p < 0.001$) and a statistically significant higher limb salvage rate (OR: 9.65; 95% CI: 3.30–28.20; $p < 0.001$) (Hu et al., 2023).

This data is supported by the largest available prospective dataset (Chen et al., 2022)—a seven-centre cohort study of patients with recalcitrant DFUs (UT 2-C to 3-D, unresponsive to prior treatment for at least 8 weeks). The study enrolled 1175 patients; after exclusion of deceased patients (85, 7.2%) and patients lost to follow-up (18, 1.7%), a group of 1072 patients was left for analysis. The mean ulcer size was 41.0 ± 8.5 cm² and 16.6% of ulcers extended above the ankle. During 2-year follow-up, 1019 (94.9%) patients healed in a mean time of 12.4 ± 5.6 weeks, 53 (4.9%) underwent major amputation, 33 (3.1%) experienced recurrence of the ulceration and 23 (2.1%) suffered from pin-site infections. For comparison, conventional surgical treatment of DFUs demonstrated varying healing rates of 46–77% and limb salvage rates of approximately 82% with a follow-up period of 12 months (Forsythe et al., 2020).

Smaller prospective and retrospective series confirm this consistency across different procedural modifications. In the study by Chen et al. (2020), 136 patients were enrolled in a study group that underwent TTBT and 137 patients were treated with standard surgical treatment. Transverse tibial bone transport substantially increased healing rates (OR 10.40 [95% CI 3.96 to 27.43]; $p < 0.001$) and lowered the rate of major amputations (OR 0.10 [95% CI 0.04 to 0.30]; $p < 0.001$) and also decreased the recurrence of severe and recalcitrant diabetic foot ulcers in the 2-year follow-up (OR 0.20 [95% CI 0.05 to 0.45]; $p < 0.001$) with relatively minor complications such as pin-site infections or corticotomy-site fracture that were treated with closed reduction. In the prospective study by Wen et al. (2024) of 52 consecutive DFU patients, the wound healing rate was 92.3% (48 patients) at the 1-year follow-up, with a significant reduction in VAS pain scores and a significant increase in dorsal foot skin temperature, ankle-brachial index, and dorsal foot blood flow at the 4th postoperative week ($p < 0.001$).

Modifications of the original technique have been introduced to reduce surgical morbidity. The most widely used modification (mTTT) replaces corticotomy of a single large block with two smaller bone windows of 1.5 × 1.5 cm. In a retrospective analysis by Liu, Yao, et al. (2024), the investigators included 98 patients with Wagner grade ≥ II ulcers in the study. Patients were followed up for 3 months; 2 patients died due to perioperative complications, so only 96 patients were included in the statistics. The postoperative wound healing rate was 95.83% (92 patients) and the average healing time was 53.18 ± 20.18 days. Modified tibial transverse bone transport resulted in significant improvements in ankle-brachial index, WIfI (Wound, Ischemia, Foot Infection) classification, and VAS pain scale at three months postoperatively compared to preoperative evaluation, with all these differences being statistically significant ($p < 0.05$). In another retrospective mTTT study by Yuan et al. (2021), the DFU wounds (University of Texas Score from 2C to 3D) of all patients ($n = 201$) healed completely with a mean healing time of 4.6 ± 1.6 months. Another great benefit of mTTT was improvement in ABI and ankle skin temperature comparing preoperative versus postoperative evaluation ($p < 0.001$). What is even more important is that there were 0 cases of complications such as recurrence of ulcer, amputations, pin-site infections, surgical wound infections or corticotomy-site fractures.

TTT is responsible not only for improved DFU healing but also for higher quality of life. In the multicentre cohort study conducted by Chen et al. (2022), improvement in patient-reported quality of life after treatment was found: compared to preoperative status, patients had higher physical (26.2 ± 8.3 versus 41.3 ± 10.6, $p = 0.008$) and mental (33.6 ± 10.7 versus 45.4 ± 11.3, $p = 0.031$) component summary scores at the 2-year follow-up than at baseline. Adverse events were limited and clinically manageable: closed tibial fracture at the corticotomy site occurred in 8 (0.7%) patients and was treated successfully with external fixation, while pin-site infections occurred in 23 (2.1%) patients and resolved with dressing changes. These complication rates are as low as the pooled estimates from the meta-analysis (2% fracture risk, 8% pin-site infection risk) (Hu et al., 2023) and may reflect differences between pin-care protocols across the studies. What is more, the biomechanical safety is supported by finite element analysis demonstrating that TTT does not compromise the overall stability of the tibia (Su et al., 2025).

Taken together, the available evidence indicates that TTT achieves wound healing rates of approximately 95%, limb salvage rates above 95%, and recurrence rates of approximately 3% in patients with advanced or recalcitrant DFUs, while simultaneously improving distal perfusion, neuropathic symptoms, pain scores, and overall quality of life—with a complication profile that remains acceptable in routine clinical practice.

7. Safety of the Tibial Cortex Transverse Transport Procedure

The clinical introduction of tibial cortex transverse transport (TTT) as a limb-salvage option for recalcitrant diabetic foot ulcers (DFUs) has been accompanied by close scrutiny of its safety profile, given that the technique requires an iatrogenic tibial corticotomy in a population frequently affected by impaired bone quality, peripheral neuropathy, microvascular disease, and compromised wound healing. The most comprehensive safety assessment to date is provided by the systematic review and meta-analysis conducted by Hu et al. (2023), which evaluated both the effectiveness and the safety of TTT in patients with DFUs.

Three categories of complications emerged as the principal safety concerns associated with the TTT procedure: fracture at the transportation site, infection at the pin channels, and necrosis of the skin overlying the anterior tibia.

The pooled risk of fracture at the transportation site was 0.02 (95% CI: 0.00–0.04), corresponding to five tibial fractures recorded among 178 patients across the included studies. Although this incidence is low in absolute terms, a fracture at the osteotomy site may necessitate revision surgery, prolong rehabilitation, and delay ulcer healing. In patients of short stature, narrowing of the bone window has been recommended, and in postmenopausal women or other patients with severe osteoporosis, referral for standard osteoporosis treatment prior to surgery has been advocated to mitigate the risk of fracture at the osteotomy site (Fan et al., 2020; Hu et al., 2023).

The pooled incidence of pin-site infection was 0.08 (95% CI: 0.00–0.22). The authors emphasized that perioperative antibiotic prophylaxis and meticulous daily pin-site disinfection are essential to reduce the risk of pin-channel infection (Hu et al., 2023).

Although less frequently quantified, necrosis of the soft tissues overlying the anterior tibia represents an additional concern associated with the procedure. This complication is primarily attributable to prolonged continuous pressure on the skin overlying the anterior tibia during the transport phase. Surgeons are accordingly advised to preserve the blood supply of the skin flap, avoid excessive interference with the soft tissues, and monitor the skin status closely in the postoperative period; the transport process should be terminated if signs of ischaemia or necrosis become apparent (Hu et al., 2023; Zhang et al., 2020).

A particularly important safety-related outcome concerns the long-term durability of healing. The recurrence rate of DFUs in the TTT group was significantly lower than that observed in non-TTT controls, with a risk ratio of 0.18 (95% CI: 0.06–0.49; $p = 0.001$, Hu et al., 2023). This finding indicates that, despite the procedural risks intrinsic to TTT, the long-term protective effect against ulcer recrudescence substantially outweighs the perioperative complications—an important consideration when balancing the risk-benefit profile of the technique against more conservative interventions.

In addition to the recommendations summarized above, broader guidelines have been proposed to enhance the safety of TTT. The 2020 Expert Consensus on the Treatment of Diabetic Foot Ulcers Using Tibial Transverse Transport, published in China, has emphasized the importance of further simplification of the external fixator, preserving the periosteum, and narrowing the incision and bone window dimensions with the aim of reducing complication rates. Furthermore, the consensus recommends against the use of a tourniquet in order to preserve blood supply to the lower limb.

8. Discussion

This review aimed to synthesise current evidence on transverse tibial bone transport (TTT/TTBT) for diabetic foot ulcers (DFUs), spanning biological mechanisms, surgical technique, clinical efficacy and safety. The most important observation is the consistency between preclinical and clinical data: the neovascularising cascade characterised at the molecular level is mirrored by the high rates of wound healing and limb salvage reported in patients.

Mechanistically, TTT does not act through a single pathway but elicits a coordinated, multi-level regenerative response. One of the underlying mechanisms is the HIF-1α axis, activated by controlled local hypoxia generated during cortical distraction (Liu, Huang, et al., 2024). As a pleiotropic transcription factor, HIF-1α drives the release of VEGF, PDGF-BB, bFGF, EGF and SDF-1 (Liu, Huang, et al., 2024; Ou et al., 2022), counteracting the endothelial dysfunction and impaired angiogenic signalling typical for chronic DFUs. In parallel, the SDF-1/CXCR4 axis mobilises $CD34^{+}/CD133^{+}$ endothelial progenitor cells toward ischaemic tissue (Ou et al., 2023; Qin et al., 2024), while the observed M1-to-M2 macrophage shift (Qin et al., 2024) reverses the very inflammatory mechanism that perpetuates delayed re-epithelialisation. The identification of small extracellular vesicles enriched in miR-494-3p and antioxidant proteins (Xie et al., 2024) adds a further

layer, linking the vascular effect to nerve and fibroblast regeneration. Crucially, deletion of miR-494-3p attenuated the benefit of bone transport (Xie et al., 2024), confirming its effect.

Clinically, convergence across independent sources is striking. The meta-analysis of 818 patients reported pooled healing of 0.96 (95% CI: 0.93–0.98) and limb salvage of 0.98 (95% CI: 0.95–1.00), with a large effect versus conventional care (OR 10.43; 95% CI: 3.96–27.43; Hu et al., 2023). This data is confirmed by the largest prospective cohort (1072 analysed patients), in which 94.9% healed in a mean of 12.4 ± 5.6 weeks (Chen et al., 2022), contrasting with the results of conventional therapy. Consistent improvements in ankle-brachial index, dorsal foot temperature, VAS pain and quality of life (Chen et al., 2022; Wen et al., 2024; Yuan et al., 2021), together with a low recurrence rate (≈3%; RR 0.18; Hu et al., 2023), suggest that TTT modifies the ulcer biocenosis rather than merely closing the wound.

The safety profile is acceptable in a population burdened by osteoporosis and microangiopathy, with pooled risks of 0.02 for fracture and 0.08 for pin-site infection (Hu et al., 2023). Modified TTT with two smaller bone windows appears to reduce complication rates further (Yuan et al., 2021), though zero-complication single-centre series may reflect favourable selection.

9. Conclusions

Strengths of this narrative review must be weighed against limitations. As a narrative review, this work risks selective citation and precludes formal quantitative synthesis. The evidence derives almost exclusively from one geographical region, relies heavily on observational or retrospective designs, and is marked by protocol heterogeneity (osteotomy level, window size, distraction regimens). Publication bias favouring positive results cannot be excluded.

Accordingly, adequately powered, multicentre randomised trials comparing TTT with contemporary best practice - conducted in diverse populations with blinded outcome assessment - should be performed, alongside protocol standardisation and pharmacological approaches reproducing the TTT effect (e.g., ginsenoside Rg1; Xie et al., 2024). In summary, TTT offers a mechanistically grounded, clinically effective option for recalcitrant and chronic DFUs, needing more high-quality evidence with diversified populations.

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