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Limb salvage in Buerger's disease by distraction histogenesis: A prospective study with literature review☆

Ankit Chouhan [a], Devi Sahai Meena [b], Umesh Kumar Meena [b, *], Prateek Behera [c], Lakhpat Yadav [b], Vikas Gupta [d]

[a] Department of Orthopedics, Mewar Hospital Udaipur, India
[b] Department of Orthopaedics, SMS Medical College and Hospital, Jaipur, India
[c] All India Institute of Medical Sciences, Bhopal, Madhya Pradesh, 462020, India
[d] Central Institute of Orthopaedics, VMMC and Safdarjung Hospital, New Delhi, 110029, India

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1. Introduction

Buerger's disease or Thromboangiitisobliterans (TAO) affects small and medium sized blood vessels and is a disease of unknown etiology. Segmental inflammation of blood vessels is seen which then leads to interruption of the distal blood supply.[1] It is a limb-threatening condition and is seen in the young and productive age group. As the exact etiology is still not known, management of TAO is a challenging problem. The disease has a strong association with tobacco smoking.[2].

Treatment options like vasodilator drugs, anticoagulants, prostaglandin therapy etc. have been tried with varying degrees of success.[4] Surgical treatment modalities which have been tried are thrombolytic therapy, arterial reconstruction, bypass vein grafts, lumbar symphathectomy and microvascular omental transfer.[5] Newer modalities like spinal cord stimulation,[6] angiogenesis by autologous bone marrow mononuclear cell implantation[7] and gene therapy[8] have shown promising early results. However, these modalities are expensive and not widely available. Moreover, the ideal modality for treatment of TAO is still undecided[3,4,9] and is debatable.

Ilizarov's method of bone distraction with external fixator has been found to increase the vascularity of the limb by neo-angiogenesis.[3,9,20,and 21] Gradual traction on living tissues can stimulate and maintain regeneration and active growth of tissues (bone, muscle, fascia, nerve, vessels, skin, and its appendages). Both periosteal elevation and distraction osteogenesis have been shown to increase neo-vascularization of bones and the surrounding structures.[3,9]

This study was conceptualized and conducted to evaluate the clinical outcomes of longitudinal tibial corticotomy and horizontal distraction with Ilizarov's ring fixator in Buerger's disease affecting the lower limb.

2. Material and methods

The study was a prospective interventional study and was conducted over a period of two years in the Department of Orthopaedics, Sawai Man Singh Medical College and Hospital Jaipur, Rajasthan. Patients with clinically and radiologically proven Buerger's Disease as per Shinoya's criteria[10,11] were offered to be included in the study and those who provided consent were included. Patients who had been operated previously with any other surgical technique were also included if the index procedure had failed to provide relief to the patient. Patients with highly improbable diagnosis of Buerger's Disease based on Shinoya's criteria, those with gangrenous changes in the foot and leg, co-existing medical conditions and those who refused consent were excluded.

Pre-operative assessment included a thorough history, clinical examination and radiological investigations. Clinical examination included toe pulp temperature, capillary refill time, palpation of femoral, dorsalis paedis and posterior tibial arteries on both sides, examination of ulcer or gangrenous wound (if any) and measurement of claudication distance. All patients underwent CT angiography of bilateral lower limbs before the surgery.

☆ **Study performed at**: Department of Orthopaedics, SMS medical college and hospital, Jaipur, 302004, India.

* Corresponding author. Department of Orthopaedics, SMS medical college and hospital, Jaipur, 302004, India.
E-mail addresses: drankitchouhan@gmail.com (A. Chouhan), sahai.dr.@gmail.com (D.S. Meena), drumesh_meena@yahoo.co.in (U.K. Meena), pbehera15@gmail.com (P. Behera), lakhpatortho@gmail.com (L. Yadav), drvikas@hotmail.com (V. Gupta).

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2.1. Surgical technique

All the patients were operated under spinal anaesthesia on a standard operating table. Tourniquet was not used in any case. A pre-constructed two ring Ilizarov frame was used. The frame consisted of two full rings joined by connecting rods antero-medially and postero-medially and a horizontal distraction assembly on the lateral side. The horizontal distraction assembly consisted of slotted connecting rods mounted on a long connecting plate with male posts.

The surgical steps included a rectangular corticotomy of the antero-lateral cortex of the middle third of tibia. Multiple transverse incisions were used to avoid any wound dehiscence with lateral distraction. The most proximal incision was marked at about 10 cm distal to the tibial tuberosity, 3 cm in length and centered over the anterior crest of the tibia. Thereafter, four more incisions were marked at distances of 3 cm from each other, distal to the first incision. Skin was incised at these sites and the periosteum was also cut. The periosteum over the corticotomy fragment was lifted up. Multiple drill holes were made on the medial surface of the tibia at around 1 cm medial to the crest aiming towards the lateral surface of tibia and exiting about 2 cm below the level of crest. The drill holes were made with 3.2 mm drill bit, which was directed antero-medial to postero-lateral. The corticotomy was then completed with a 5 mm wide sharp osteotome by joining the holes on the medial and lateral surfaces of tibia (Fig. 1). The same osteotome was passed from one incision towards the other to cut the cortex between the incisions. Once the cuts were complete, one osteotome each was inserted into the proximal most and distal most incisions and the corticotomy was pried open.

Once corticotomy was done, the construct was mounted by fixing the proximal ring at the level of head of fibula and the distal ring at around 2 cm proximal to the ankle joint. The fixation was done with Ilizarov wires and Schanz screws following the standard ilizarov techniques and safe zones. Finally three parallel olive wires were passed through the corticotomy into the corticotomised segment of the tibia from antero-medial to postero-lateral direction (Fig. 2). These olive wires were then connected with the horizontal distraction assembly by attaching them with the slotted wires (Figs. 3 and 4).

Gangrenous toes were amputated at appropriate levels to achieve closure. Ulcers or raw areas were extensively debrided.

Post-operatively, patients received intravenous broad-spectrum antibiotic for 48 hours and adequate doses of anti-inflammatory analgesics. Ambulation with walker support with weight bearing as tolerated was started from the second post-operative day. Patients were discharged from the hospital on the fourth post-operative day on oral antibiotics for five days and oral analgesics.

Horizontal distraction was started after a latent period of ten days at the rate of 0.5 mm per day and was continued for six weeks.

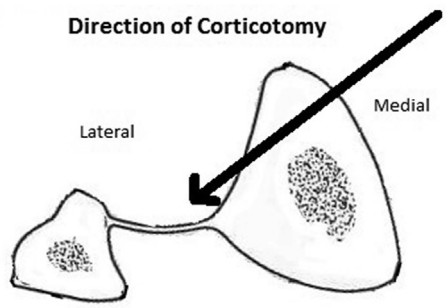

Fig. 1. Schematic diagram showing the direction of drill bit and osteotome insertion.

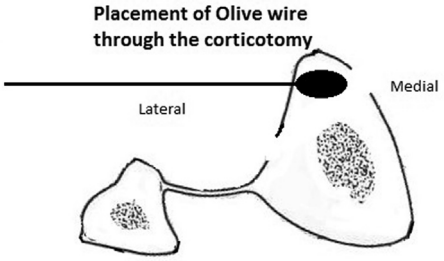

Fig. 2. Schematic diagram showing the placement of olive wires through the corticotomy.

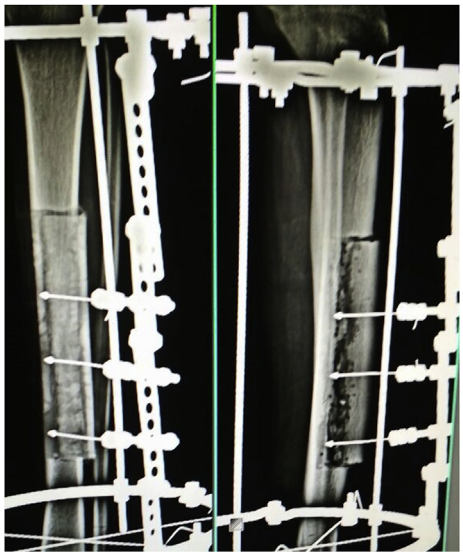

Fig. 3. Immediate post surgery radiographs of a patient showing the corticotomy and the assembly in place.

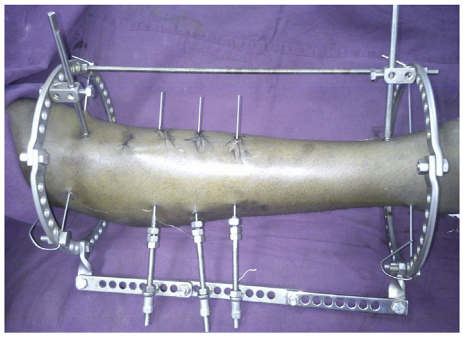

Fig. 4. Clinical photograph of a patient with Buerger's disease with ilizarov frame.

The rhythm of distraction was kept at 0.25 mm twice a day with 12 h interval. After initiation of distraction, the patients were reviewed in out-patient clinic every two weeks till the completion of distraction. During this time radiographs were taken to confirm that the distraction was going on satisfactorily (Fig. 5).

The patients were followed up at three weekly intervals. The healing of the regenerate was monitored on the serial radiographs. The frame was removed after radiological confirmation of sound regenerate healing. All patients were given a patellar tendon bearing cast for 3 weeks after frame removal.

The ischaemic ulcers were examined at each visit and the

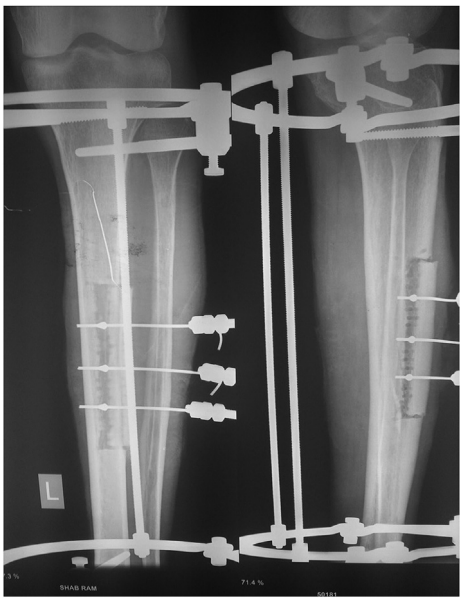

Fig. 5. AP and Lateral radiograph showing longitudinal corticotomy with ilizarov frame.

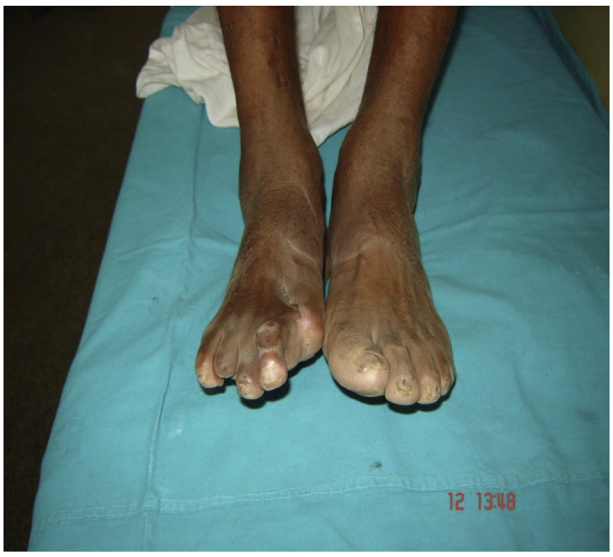

Fig. 6. Clinical photograph at 1 year follow up showing complete healing after treatment with distraction histogenesis and amputation of gangrenous toes.

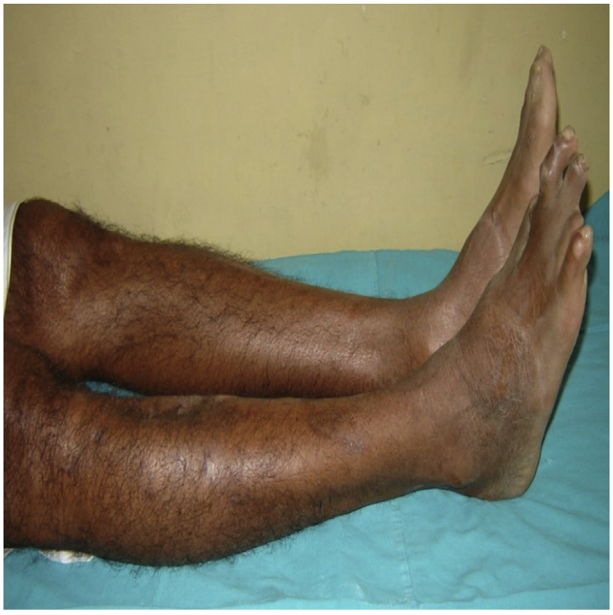

Fig. 7. Clinical photograph at 1 year follow up showing complete healing after treatment with distraction histogenesis and amputation of gangrenous toes.

healing time was recorded (Figs. 6 and 7). The level of rest pain was recorded using Visual Analog Scale (VAS) for pain at 3 months, 6 months and one-year after surgery. Claudication distance was also recorded during these three visits which has been shown in Table 1.

Patients were encouraged to gradually and steadily increase their activity levels. The final goal of the procedure was set to be complete relief of pain and unrestricted ambulation for domestic and vocational purposes. Considering that there is no universally accepted system for grading or scoring in Buerger's disease, the grading system suggested by Patwa and Krishnan[9] was used.

3. Results

A total of 50 patients of Buerger's disease were operated with the described surgical technique. The mean age of patients was 44.44 years(35–55 years). There were only two female patients. While 30 patients had involvement of the right side, 20 had the left side involved. All patients were chronic tobacco smokers, either bidi or cigarettes, with mean duration of smoking of 21.2 years. Eight patients had undergone lumbar sympathectomy prior to this procedure and were referred to us after failure of treatment. Twelve patients (24%) had non-healing ulcers over toes or planar aspect of the foot. In all the patients, healing of ulcers was achieved with distraction over a period of 4–5 weeks. 38 patients had gangrenous changes in one or more toes. Among these, amputation of the gangrenous toes was done at the time of corticotomy in 30 patients and wound was closed primarily in 24 of them. In the remaining 6 patients, delayed closure was done. Wounds healed uneventfully in all of these patients. In rest of 8 patients, amputation of the toes was done after establishment of a clear line of demarcation of gangrene and hence, was operated at a later stage than corticotomy. In none of the patients was a skin graft or flap required for coverage.

Based on the grading system of Patwa and Krishnan,[9] 36 patients (72%) had excellent outcome, i.e. no rest pain, healed ulcer or toe amputation stump, no claudication pain, resumption of previous occupation and unaffected domestic ambulation. Outcome in eight other patients was graded as good, i.e. absence of rest pain, persisting/recurrent ulcers, and claudication distance of 1–2 km but able to continue previous occupation and domestic ambulation affected sometime. Six patients (12%) failed to show relief in pain and the gangrenous necrosis continued to progress, ultimately ending up in below-knee amputation. These six patients were graded as having poor results. These have been summarized in Table 1.

The most frequent complication was superficial infection around the pin sites. A total of 28 patients (56%) had atleast one episode of pin site infection which improved with oral antibiotics. There was comminution of the corticotomy in four patients (8%), with extension of the fracture line into the medial or posterior cortex. In these patients full weight bearing was started after six weeks. One patient had delayed consolidation of regenerate. The fixator in this case was kept for four months and external support in the form of patellar tendon bearing cast was given for four more

Table 1
Postoperative clinical outcome analysis in patients treated with distraction histogenesis.

	Pre-operative	3 months	6 months	1 year
Mean VAS score	9.78	0.98(p value <0.05)	0.45	0.40
Claudication Distance				
Group A(>2 km)	Rest pain in all patients	72%	80%	82%
Group B(1–2 km)		12%	8%	6%
Group C(<1 km)		4%	–	–

weeks after frame removal. There was no relapse of disease or recurrence of symptoms.

In all the patients, CT angiography (CTA) showed infra-popliteal block in the arterial flow along with the typical pattern of the stenosis. 3 months after frame removal, only 16 patients (32%) had definitive changes in the filling pattern. In the rest of 24 patients the changes could not be commented upon due to lack of accurate imaging of distal blood flow in the CTA.

4. Discussion

TAO is a distinct form of non-atherosclerotic vasculitis of unknown etiology affecting small and medium sized arteries.[4] The prevalence of the disease among patients with peripheral arterial disease ranges from values as low as 0.5–5.6% in Western Europe to values as high as 45–63% in India.[3,4]

The etiology is unknown but strongly associated with tobacco use. Genetic factors, cell mediated immunity related factors, HLA predisposition, autoantibodies, low socioeconomic status and poor work environment have also been believed to play a role.[3,4] In this series, poor socio-economic status, chronic tobacco use and lack of education and awareness were the factors common to all the patients.

A number of medical and surgical options have been suggested for management of TAO but the search for an ideal solution to this problem is still continuing. The most effective treatment for Buerger's disease is smoking cessation. Use of tobacco in any form must be absolutely discontinued for any treatment modality to be successful.[4] 76% of our patients completely quit smoking during the duration the treatment. Four other had reported marked decrease in the frequency of smoking but not absolute abstinence. Eight patients did not show any change in their smoking habit. All the cases of failure in the current study were amongst these eight patients.

Medical therapy is of questionable benefit. Vasodilator therapy is not effective because of non-selective vasodilatation, though intravenous Ilioprost has been reported to be effective in one study.[12] Intra-arterial thrombolytic therapy has been tested in acute exacerbation with some success. De-addiction therapies in the form of nicotine patches are used as adjuvant with any treatment regime.[12]

Many surgical modalities have been explored for the treatment of severe TAO. Direct revascularization surgeries are not possible due to diffuse involvement of vessels and absence of a distal target vessel. Graft failure rates are high but can be attempted with impending gangrene.[13] Sympathectomy removes the vasoconstrictor tone thereby improving blood flow and promoting ulcer healing and improving pain. It is one of the most commonly used methods. But, it does not increase flow to ischemic muscles and thus no improvement occurs in claudication distance. Its long-term role in chronically dilated ischaemic vessels is also questionable. And studies have shown that the relapse rate can be unacceptably high.[14,15] Omentopexy is an attractive option. But it has a high learning curve and complication rate. Prolonged ileus, wound infection, closure difficulties and hernia have been reported.[16,17]

Many new methods have been described which have shown promising results in the initial phases of research. Vascular gene therapy may be useful by inducing angiogenesis using vascular endothelial growth factor or basic fibroblast growth factor.[8] Stem cell therapy also offers a promising alternative.[7,18] Stimulation of the spinal cord with implantable devices has been tried by various researchers with claims of success rate of over 90%.[6] But these modalities are in experimental phases. Their efficacy, long term results, safety profiles and cost effectiveness are some issues still under scrutiny. These methods also require highly sophisticated instruments and specially trained personnel. Their cost and availability to commonly affected poor patients remains to be seen.

Distraction osteogenesis by Ilizarov technique has been shown to stimulate neoangiogenesis by stimulating regeneration and active growth of all tissues by the law of tension stress. The gradual distraction forces applied onto the bone segment (following corticotomy) has an indirect effect of distraction of the other tissues which then stimulates new vessel formation. This technique has been shown to have high success rate in ulcer healing, in decreasing the need for major amputation, rest pain, and improving the claudication distance. The complications associated with Ilizarov fixator use are usually preventable and easily manageable.[3] Fokin et al. were the first to use the principles laid down by ilizarov for managing Buerger's disease. In their series of 125 patients they achieved 94.2% good results [20]. Patwa and Krishnan[9] performed the tibial osteotomy in anterior to posterior direction after drilling multiple holes in the same direction. Overdrilling of the medial cortex was required in their technique to allow for the passage of olive wires. We however, used an oblique osteotomy and passed the olive wires through the osteotomy site thereby obviating any requirement of overdrilling the medial cortex. Our technique could be compared to the one followed by Kulkarni et al.[3] The technique used is reasonably easy to learn and does not have a steep learning curve.

In the present series, good to excellent results were achieved in 44(88%) of cases and these results were comparable with those previously published literature (Table 2).[3,9] The only major complication in our series was amputation, required in 12% of cases. Patwa et al. reported the need for amputation in 3.33% of their patients.

Objective assessment of results of TAO treatment has classically been carried out using angiography, measurement of tissue oxygen saturation, digital plethysmography and tread-mill exercise testing.[19] Post-operative angiography was done in all cases of the present series after removal of ilizarov frame and there was definitive change in filling pattern in 32% of cases. Limitations of this study include small number of patients, absence of control group, lack of long term follow up to assess recurrence and absence of definitive objective tool to assess neoangiogenesis. In 32% patients the post operative CT angiography showed improvement in filling patterns. However, the postoperative change in filling pattern could be due to arteriogenesis or conversion of preexistent collateral arterioles into large conductance arteries and not

Table 2
Comparison of present study with previous studies.

Study	N	Follow-up	Results	Complications
Fokin et al.[20]	125	21.6 months	94.2% good results	Local infections – 16 Fractures - 2
Patwa et al.[9]	60	Mean 5.4 years	80% excellent to good	Infections – 30% Fractures- 3.33% Amputations –3.33%
Kulkarni et al.[3]	30	Mean 4.5 years	83.3%excellent to good	Infections – 6.67% Amputations – 13.33%
Present study	50	Mean 12.5 months	88% excellent to good	Pin tract infections – 16% Fractures – 8% BK amputations – 12%

necessarily due to true neo-angiogenesis.[21] Further studies are needed to confirm true angiogenesis due to distraction.

To summarize, Buerger's disease is a limb-threatening disease occurring in young adult males with history of chronic tobacco smoking. There is still no definitive treatment modality which can be recommended as gold standard for the management of this disease. Ilizarov's method of osteotomy and distraction offers a reasonably reliable surgical option to improve distal blood flow. It provides pain relief, improves the healing of gangrenous toes or ischaemic ulcers and improves claudication distance. This method is not technically demanding and is a cost effective to salvage ischaemic limbs from debilitating amputations.

To conclude, in patients with Buerger's disease who are motivated for cessation of smoking and have failed other methods of treatment, longitudinal tibial corticotomy and horizontal distraction with Ilizarov's ring fixator can be offered as a salvage procedure.

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None.

Conflict of interest disclosure

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jcot.2018.08.011.

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