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ORIGINAL ARTICLE

TIBIAL CORTICOTOMY AND PERIOSTEAL ELEVATION FOR CHRONIC CRITICAL LOWER LIMB ISCHAEMIA

By
Saleh El-Awady, Ayman Ali,[1] Osama Kumbar,[2] Seid Abd El-Maksoud[3]
[1]Surgery, Orthopedics, [2]Diagnostic Radiology, [3]Medicine, Mansoura University Hospital, Egypt

Correspondence to: Saleh Elawady, Email: zadarm@yahoo.com

Aim: *Estimating procedure's safety, efficiency, efficacy and cost/benefit.*
Methods: *Thirty six patients were enrolled. Preoperative demographic data, ankle systolic pressure, and magnetic resonance angiography were obtained. Early results (1st month) included skin perfusion and pain, late results involved wound healing, pain, Kelker score, procedure morbidity, patient satisfaction and quality of life.*
Results: *Mean age ±SD was 68.03 ±5.5, males were 23(63.9%), twenty (55.6%) patients had ankle systolic pressure ≤50 mmHg and 29 (80.5%) with infrainguinal disease .Within the 1st month; skin perfusion and rest pain improved in 91.7%, 86.1%, patients respectively. Magnetic resonance angiography at the 2nd month declared vascular response for all patients. By the end of 1st year 34(94.4%) patients achieved complete wound healing, also rest pain and claudication relief occurred in 86.1% & 55.6% patients, with20 (55.6%) patients had excellent score. Procedure morbidity was (17.7%).Satisfaction measures at six and twelfth months were "mean ±SD" 7.1 ±1.3, 8.7 ±1.7 respectively. Twelfth month quality of life improved (overall score P = 0.05, mental health scale < 0.05 and pain/anxiety domain P < 0.001).*
Conclusion: *The procedure represents an invaluable tool to be evaluated in randomized study.*

Keywords: *Clinical trial, amputation, revascularization.*

INTRODUCTION

Chronic critical limb lower ischaemia (CCLLI) is a persistent relentless problem that impairs functional status and quality of life (QoL),[1] representing the progressive evolution of peripheral arterial occlusive disease "PAOD",[2] on annual base one in every 200.000 population had the disease.[3]

Despite major advances, the disease carried dismal prognosis,[4] the yearly mortality rate (independent of treatment efforts) ranging from 19% to 54%.[5,6] Also, one third of survivors required major amputation within 12 months[7] and 20% of those with intact limbs suffers continuous disease.[8]

Not only the disease carried narrow therapeutic window, [conservative medical treatment had only little relief,[9] therapeutic angiogenesis is of limited outcome,[10] for revascularization; about 20-30% of patients have unreconstructable arterial tree with 70% success rate,[11] lastly amputation (primary and secondary) had poor QoL and outcome,[12] but also it had a high health economics "failed technique-co-morbid disease, rehabilitation".[8]

The distraction histogenesis (DH) after Ilizarov was used to improve the vascular response in CCLLI.[13] It is a vascular dependent process[14] based on stress tension principle,[15] deriving pleuripotent cell differentiation "coupling angiogenesis with osteogenesis,[16] in a temporospatial manner"[17] improving the vasculature of the ischaemic extremity.[18] However, the patients may suffer temporary deterioration and late reappearance of revascularization, also the process had its morbidity related to purulent complications, fracture, distal segment osteoporosis, pinhole infection and bulky framework.[13,19,20]

Recently Kelker devised trap-door corticotomy and periosteal elevation aiming to surgical controlled inflammation,[21] with consequent inflammatory angiogenesis crosstalk. This controlled inflammation is a biologic process that is dependable and predictable gaining neovascularity[22] and acts as endogenous bypass conduits improving the circulatory status.[23]

In this pilot study; the Kelker technique was evaluated with CCLLI patients regarding secondary major amputation as a primary outcome measure. Both patient centered outcome; pain, wound healing, satisfaction, QoL and procedure related morbidity; fracture, wound complication as secondary outcome measures. Procedure efficiency; "angiogenesis" using Magnetic Resonance Angiography "MRA" with contrast enhancement was documented. The Finite end points were death or major amputation. The follow up period was one year.

PATIENTS AND METHODS

This study was conducted in Mansoura University Hospital, Department of Surgery, Sector 8 as of June 2005 to January 2008.

Patients with CCLLI according to European Working group on CCLLI[24] were included in the case of medical treatment failure (smoking abstinence – Pentoxifilline – opiates analgesia) with neither surgical nor radiologic options of revascularization, failure of surgical treatment (failed sympathectomy ± revascularization) or failure of both. Patients exclusion criteria were patients had impaired inflammatory response "steroid & immune-compromised", patients refusal, patients not candidate for MR study, patients with massive secondary infection and patients candidates for primary amputation according to Trans-Atlantic inter-Society Consensus document on management of peripheral arterial disease (TASC) guidelines.[8]

Preoperatively; patients' demographic data, co-morbid diseases and previous operative intervention and limb evaluation (vascular, neurological, and ulcer type "ischemic & neuro/ischaemic") were documented. Also ankle systolic pressure was documented using Pocket Doppler and routine laboratory investigations were done.

Finally, patients were grouped according to Le riche-Fontaine,[25] and preoperative MR angiography(whole body-1.5-TMR system – Vision, Siemens, Erlagen. Germany) with contrast (Gadodiamide - Omniscan, Nycomed, Oslo, Norway) was performed to detect anatomic vessel occlusion.

The procedure was done under spinal anesthesia without tourniquet. Two gm cefotaxime "IV" were administrated as prophylactic antibiotic. The procedure involved (a) periosteal elevation on the medial and lateral sides of the tibia from its chin till the medial malleoleus "interspaced (3-4) wounds". (b) trap-door tibial corticotomy (10 cm below knee – 5cm length – rectangular – vertically based-lateral side width), done as follow (1) curved lateral incision over tibia (2) multiple drill holes "1 cm apart" guided with "k-wire" are made from anteromedial surface passing to posterior cortex along the endosteal side (anterior side of window) (3) drill holes at its upper and lower margins are made to complete the rectangle sides (4) the osteotome (2 mm width) connect the drill holes together first "anterior", second "margins" forming three-sided corticotomy (5) the posterior perforated cortex of the three-sided cortictomy is broken manually like a hinge using two wide osteotomes inserted through the anteromedial cortical cut and resting along the lateral cortex (6) periosteal closure at corticotomy site using Vicryl 00 (Ethicon) (7) wounds suturing using Silk 00 (Assut Sutures). (Fig 1).

The procedure was ended by ulcer desloughing and gangrenous areas ablation.

Postoperative; on the 2nd day plain x-ray was obtained to assess fracture tibia(Fig 2a) and I.V. antibiotic was administrated for 7 days, the only analgesic was paracetamol, neither limb elevation nor dependency, early mobilization of nearby joints and early ambulation were encouraged (Toe-touch weight bearing for 2 weeks, gradual foot bearing after that and full weigh bearing when radiographic evidence of fracture healing is obtained (Fig 2b,c,d) (Fig 3b); MRI findings), neither antiplatelets nor anticoagulants were used. Wounds are to be rechecked after 4 days and patients were discharged after 7 days.

Follow up: Clinical outcome was assessed every two weeks in the first two months; then every month until the end of the study. In each visit the ankle systolic pressure was measured, both photo documentation for wound healing and X-ray leg were obtained. By the end of second month MRA with contrast was performed to detect the "vascular response" manifested as changes in the visualization {defined as a subjective impression of recognition of collateral vessels on an image} of collateral vessels from proximal calf to the ankle ,their assessment protocol

[unchanged, increased, decreased] of small and large collaterals .The large collaterals was defined when occupied third the studied length, or 25% of the infrapopliteal artery width, vascular leash and arterial enhancement.

The outcome measures were ***First:*** Clinical; the main clinical outcome measure was secondary major amputation (below or above knee). The secondary clinical outcome measures were both: (A) Patient related outcome: (1) pain; ischaemic rest (time dependent) & claudication (condition related) graded stage I absent, IIA none disabling and IIB disabling, IIA & IIB on domestic or occupational activity.[25] (2) Wound healing was assessed as "healed" complete cover with epithelium, "healing" cover with viable granulation tissue, "resistant" enlarged size with infection and "recurred" ulcer recurrence.[26,27] (3) Global score after Kelker 2003[21] graded as; Excellent: neither ischaemic rest pain nor claudication but healed wounds. Good: relief of rest pain, none disabling claudication and healed wounds. Fair: relief of rest pain but disabling claudication. Poor: major amputation. (4) Patient satisfaction,[28] the visual analogue score was used [0- not satisfied & 10 maximum satisfaction] (5) Quality of life, the 36 item short form health survey (SF-36) was applied.[29] (B) Procedure related morbidity: (1) fracture, (2) wounds infection, ulcer and haematoma. ***Second:*** Radiological assessment of the vascular response.

The study protocol was approved to local institutional review board. All patients signed written informed consent.

RESULTS

In this study group (36 patients); the mean age ± SD was 68.03 ± 5.5 years (55 – 78 years), of them twenty three (63.9%) were male and thirteen (36.1%) were female. Twenty (55.6%) patients were Diabetics, 27 (75%) patients had hypertension and 21 patients were smoker. Lumbar sympathectomy was done for 7 (19.6%) and revascularization for 2 (5.8%) patients.

Twenty (55.6%) patients had the ankle systolic pressure (ASP) ≤50 mmHg and 13 (36.1%) patients with ASP above 50 mmHg. In three (8.3%) patients the cuff couldn't be applied (all patients had trophic skin changes, ischemic or neuroischaemic ulcer, gangrenous toes, gangrenous skin patches hence they were stage" IV" Leriche-Fontaine).

The pre operative MRA study defined no major arterial obstruction candidate for endoluminal or surgical bypass and detected 7 (19.4%) patients with aortoiliac disease, 10 (27.8%) patients with superficial femoral artery disease {fig-3-A}, 3 (8.3%) patients with popliteal disease and 16 (44.4%) patients with tibioperoneal disease.

Early results (within the first month) highlightened 33 (91.7%) patients with improved skin perfusion (venous refill- warm skin -skin brightness) on the 4th postoperative (PO) day and 31 (86.1%) patients with absent rest pain on the 7th PO day.

The postoperative MRA study after "8" weeks documented 20patients with collateral arteries [small, 70 %-large,30 %] {fig-3-D-E- F} ,32 patients gained better enhancement of the vessels {fig-3- G}and16patients had acquired new vascular leash (Fig 3h).

Over time from the second month thirty one (86.1%) patients were relieved from ischaemic rest pain after the 2nd month (Table 1a). Also wound healing scale (recurrent – resistant – healing – healed) was progressively improved over 2nd, 4th, 6th, 12th months (Table 1c), the data were photo documented for dry gangrene of digits and skin patch(Fig 4), heel ulcer associated with plantar foot secondary infection (Fig 5), neuro-ischaemic ulcer overlying the third metatarsal head{fig 6& also MRI documented; (Fig 3c) Similarly claudication pain was improved over 2nd, 6th, 12th months Table 1b.

The later results scored as Kelker 2003 declared that twenty patients (55.6%) had excellent score, ten patients (27.8%) were good, five patients (13.9%) got fair score and one patient (2.9%) suffered poor results Table 1c.

Patient satisfaction measures at the 6th month and the 12th month were mean ±SD, range (7.1 ±1.3, 4 – 10 "6th month" & 8.7 ±1.7, 7 – 10"12th month").

When comparing the QoL preoperative to the 12th month PO. The latter achieved marginally overall improvement (P=0.05), only in the mental health scale (P< 0.05), specially the pain (P = 0.001), emotional (P = 0.001) and social domains (P = 0.001) Table 2.

There was no perioperative mortality and the morbidity rate was 6 (17.7%) [fracture tibia 1 (2.8%) (Fig 2e,f), wound ulcer 1 (2.8%), haematoma 1 (2.8%) and wound infection 2 (5.8%)].Only one patient (2.8%) required above knee amputation (life threatening secondary infection on healing wound) Table 3.

Table 1. Later results (from the second month) of the studied patients.

		2nd month		4th month		6th month		12th month	
		No	%	No	%	No	%	No	%
A- Ischaemic rest pain	Present	5	13.9						
	Absent	31	86.1						
B- Claudication pain	Absent	11	30.6			16	14.4	20	55.6
	Non-disabling	12	33.3			12	33.3	10	27.8
	Disabling	13	36.1			8	22.2	6	16.7
C- Wound healing	Healed	19	52.8	24	66.7	33	91.7	34	94.4
	Healing	11	30.6	10	27.8	1	2.8	0	0
	Resistant	6	16.7	2	5.6	1	2.8	1	2.8
	Recurrent	0	0	0	0	1	2.8	1	2.8
D-Overall Kelker sscore	Excellent							20	55.6
	Good							10	27.8
	Fair							5	13.9
	Poor							1	2.9

Table 2. Patients' quality of life.

	Pre-op	12th month post-op	P Value
Emotional domain	33.4 ±3.4	72.9 ±9.4	0.0001
Limitation to social activity	28.5 ±6.4	57.5 ±9.8	< 0.05*
Pain/anxiety domain	37.92 ±6.51	74.56 ±8.8	0.0001*
Limitation to physical activity	51.3 ±6.5	52.1 ±6.6	> 0.05
Social domain	28.5 ±6.4	57.5 ±9.6	< 0.05*
Physical domain	41.9 ±5.7	44.7 ±6.5	> 0.005
Vitality domain	35.4 ±3.9	39.6 ±6.1	> 0.05
General health domain	37.5 ±4.1	39.7 ±5.9	> 0.05
Physical health score	41.9 ±6.5	42.1 ±7.5	> 0.05
Mental health score	53.0 ±6.4	57.9 ±6.1	< 0.05*
Overall score	46.4 ±6.4	48.9 ±7.1	0.05*

Student t-test was used -P value ≤0.05* is significant.

Table 3. Patients' morbidity.

Morbidity	No	%
Fracture	1	2.8
Wound haematoma	1	2.8
Wound ulcer	1	2.8
Wound infection	2	5.6
Major amputation	1	2.8

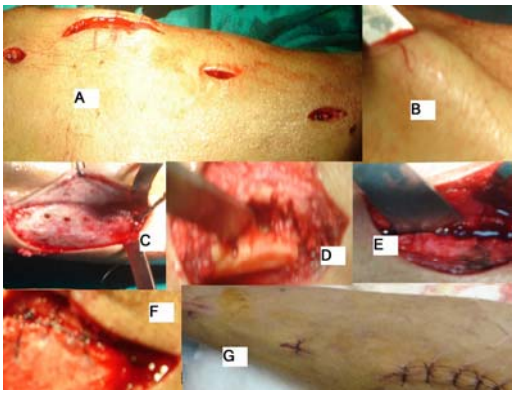

Fig 1. Procedure steps; (a)incisions, (b) periosteal elevation,(c) drilling, (d) holes connection, (e) posterior cortex fracture, (f) periosteal repair at corticotomy site ,(g) wound suturing.

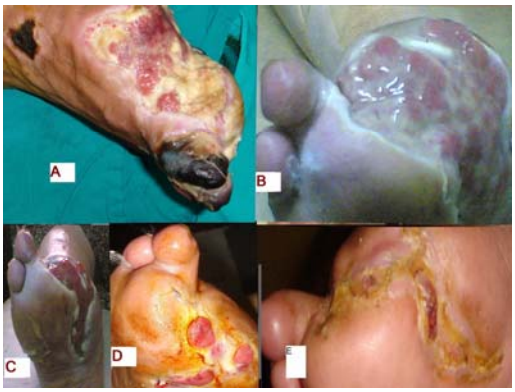

Fig 4. dry gangrene (a) preoperative gangrenous skin patch &toe (B-c-d) healing over 2,4,6.weeks. (e) healed, 8weeks.

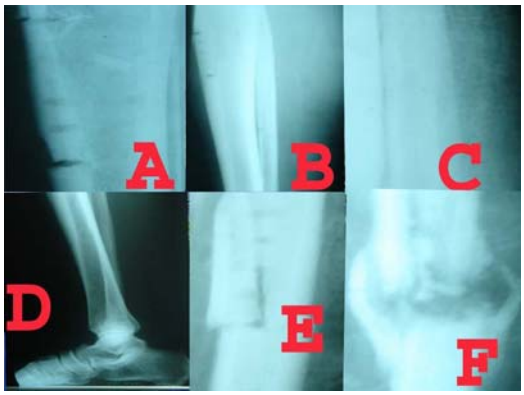

Fig 2. plain x ray study; (a) second day postoperative (b) healing corticotomy (c) healed corticotomy (d) early ambulation (e) fracture site (f) callus formation.

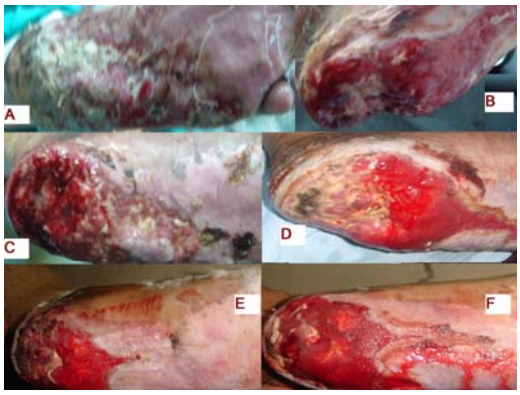

Fig 5. heel ulcer with foot infection, (a) preoperative,(b c d e f) healing over 2,4,6,8,10,weeks.

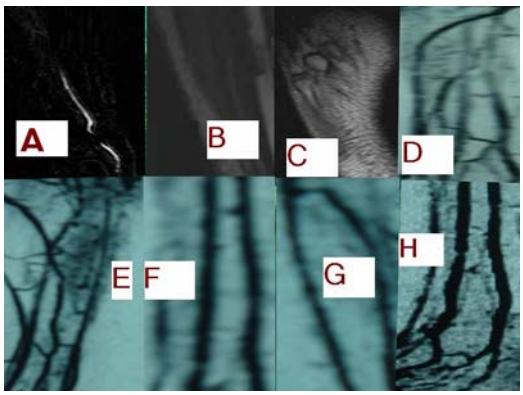

Fig 3. M R A study (a) multiple vessel occlusion (b) corticotmy site (c) healed ulcer (d)&(e) large collaterals (f) small collaterals (g) enhanced vessel(h) vascular leash.

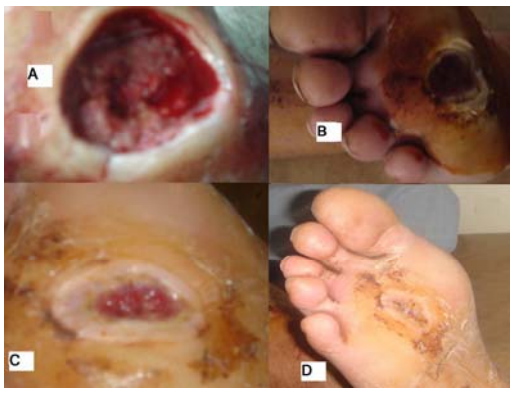

Fig 6. neuroischaemic ulcer (a) immediate postoperative, (b,C) healing over 2,4,weeks.(d)healed 8 weeks.

DISCUSSION

Chronic critical limb lower ischaemia (CCLLI) represents microcirculatory dysfunction[8] and impaired angiogenesis (exhausted or abnormal ultra structure),[30] most CCLLI patients are unsuitable for surgery (revascularization or angioplasty) and the current pharmacotherapy has little effect.[31]

Corticotomy (preserve periosteal and endosteal vessels)[32] and periosteal elevation improve CCLLI vasculature through many ways; ***firstly:*** induction of surgically controlled local persistent (the blood vessels are blocked and the periosteum is repaired) inflammation.[21] That inflammation once reached critical surface/volume ratio induces angioswitch[33] resulting in bidirectional paracrine integrated network.[23,34] In inflammation the triggering factors for angioproteins secretion are (i) inflammation hypoxia,[35] (ii) plasma extravasations of kinins,[36] (iii) the macrophages secrete the angioproteins directly[37] and stimulate the fibroblasts and endothelial cells to secrete the angiogenic proteins.[38] The angiogenesis sustain inflammation through (i) O2, nutrient supply& waste products removal,[39] (ii) the new vessels are leaky,[40] (iii) the endothelial cells express endothelial cell adhesive molecules (ECAM) which are inflammatory cells chemo attractants.[41]

The second scale is (i) fracture induced angiogenesis as the fracture haematoma is inherently angiogenic being rich in both Vascular Endothelial Growth Factor (VEGF)[42] and platelets that secrete platelet derived endothelial cell growth factor "PD,ECGF" resulting in osteoblast "VEGF" secretion.[43] (ii) fracture induced vasculogenesis as the fracture mobilizes the bone marrow pleuripotent cell that differentiate into endothelial cells,[44] (iii) fracture induced arteriogenesis mediated through shear stress changes of the arterioles caused by endothelial cell changes in shape and phenotype,[45] (iv) increased blood supply due to fracture induced haematopoietic pronounced function.[46]

The third scale is osteogenesis and angiogenesis crosstalk;[47] the endothelial cells secretions (cytokines & growth factors) stimulate osteoblast secretion of (i) VEGF,[48] (ii) bone morphogenetic proteins "BMP",[49] both stimulate osteogenesis & angiogenesis.

The fourth scale is neural dependent as fine unmyelinated nerve fibres grow with neoangiogenesis (neurite extension–arborization)[50] secreting neuropeptites facilitating inflammation,[51] angiogenesis[52] and act as sensory innervation,[50] to be neurologically studied later on.

The fifth scale is periosteal stripping (the periosteum is rich in sensory nerve fibres and osteoprogenator cells),[53] its elevation interrupted the sensory nerves decreasing pain resulting in early ambulation,[21] with consequent treadmill running improved vascularity).[54]

Significantly, many patients presented with trophic skin lesions despite ASP above 50 mmHg, so the strongest indicator of failed collateral circulation and CCLLI presence is the skin perfusion as[55] documented. Implicit in the observation the ASP didn't change postoperatively as the current method didn't open the arterial blockage, so the Rutherford et al.[56] criteria for successful revascularization procedures must be changed.

In this study the immediate results; the improved skin perfusion is attributed to inflammatory reflex vasodilatation and the leaky immature new vessels,[57] and the immediate pain relief is mostly related to periosteal nerves stripping.[21]

The progressively favorable ulcer healing in contrast to distraction histogenesis "only 17 weeks"[53] is related to variable revascularizations scales resulted in improved skeletal fatigue loading preserving the new vasculature as treadmill running.[54]

The current study proved procedure effectiveness related to (i) improved pain, both time dependent (ischaemic rest pain) and condition related (claudication) (ii) wound healing (iii) global Kelker score.

In contrast to amputee poor QoL overall score, reduced physical health scale,[58] and impaired pain/anxiety domain in revascularized patients,[1] this technique achieved significantly improved total score, mental health and the general health domain.

Significantly, the improved QoL, success of limb preservation and function and early ambulation resulted in better patient satisfaction.

The procedure morbidity was no high, however one diabetic patient required major amputation, that amputation was likely to the biologically compromised diabetic foot status[59] and diabetus prevent new vascular leash remodeling due to "PD,ECGF-B" deficiency,[60] hence the procedure is safe.

Compared with revascularization high health economics[8,61] and poor outcome of amputation,[58] this procedure not only had better cost/benefit but also, it didn't prevent revascularization if required later on.

Lastly, the radio logically documented variable vascular

response was attributed to MRA limitation as vessels more than 180 µm in diameter were only detected.[62] The discrepancy of vascular response with the clinical Kelker score grades are related to the clinical course of the disease (hypertension-heart failure-local capillary dysfunction-endotheliopathy), or the collateral flow may not be accompanied with improved nutritive flow,[63] so perfusion study and functional assessment of angiogenesis using radiolabelled VEGF monoclonal antibodies may be significant than MRA study to detect restoration of circulation. However the documented vascular response (vascular leash, collaterals and enhanced vasculature) proved procedure efficiency.

In conclusion, the procedure is an invaluable tool in managing CCLLI being safe, efficient and effective with better satisfaction and quality of life.

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