

'No-Option Chronic Limb-Threatening Ischaemia: What Can We Do To Save Limb?'

Florio A¹, De Chiara MS¹ and Sallustro M^{2*}

¹Department of Translational Medical Sciences, Vascular Surgery Unit, University of Campania "Luigi Vanvitelli", Medical School, Naples, Italy

²Vascular and Endovascular Surgery Unit, Department of Public Health, University of Naples Federico II, Naples, Italy

*Corresponding author:

Marianna Sallustro,
Vascular and Endovascular Surgery Unit,
Department of Public Health, University of
Naples Federico II, Naples, Italy

Received: 19 May 2023

Accepted: 26 June 2023

Published: 04 July 2023

J Short Name: COS

Copyright:

©2023 Sallustro M, This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

Abstract

The aim of this study is to describe the characteristics, the management and the outcome of a series of patients with no-option critical limb ischemia (CLI) treated with a conservative multidisciplinary combined approach including best wound care, NPWT and dermal substitutes. The primary end was limb salvage and 1-year amputation-free survival. The secondary end was mortality and healing time of lesion. Between January 2016 and January 2021, 76 patients with no options CLI were admitted. In 14 patients, there was a failure in distal revascularization with a persistent CLI after the procedure. In 58 patients, revascularization was not feasible. Despite the persistent CLI, a group of patients of this cohort obtained no progression of CLI, complete wound healing treated with surgical debridement or distal amputation and application of NPWT in association with dermal substitute. Any superimposed infection was treated with antimicrobials. Pain was controlled with analgesics. Overall limb was saved in 72 % of the cases. A 1-year survival was 84%. Use of NPWT, dermal substitutes combined with a conservative foot surgery with an approach with minor amputation in patients with no-option CLI may save patient limb and life

Keywords:

Limb ischaemia; No-option CLTI;
Amputation, limb salvage; Revascularization

Citation:

Sallustro M, Florio A, De Chiara MS. 'No-Option Chronic Limb-Threatening Ischaemia: What Can We Do To Save Limb?'. Clin Surg. 2023; 9(6): 1-4

1. Introduction

Chronic limb-threatening ischaemia (CLTI) may be regarded as the advanced severe stage of peripheral arterial diseases (PAD) and causes pain, leg ulcers and/or gangrene with the additional risk of superimposed infections. Severe pain, progression of gangrene and of infection, alone or in combination, are clinical settings leading to major amputation most frequently. Amputation is risky and carries a 5-year mortality as high as 45% [1]. For all the above-mentioned reasons the disease impairs quality of life (QOL) greatly. Moreover, patients are at increased risk of morbidity and death also because CLTI is often associated with myocardial infarction and stroke [2, 3]. Health, economic and social burdens are considerable. Epidemiological data indicate that the risk of CLTI increases with the increasing age and depends on the presence and severity of additional factors and/or comorbidities such as hypertension, diabetes, overweight, hyperlipidemia, sedentary daily life, renal failure, smoking [2, 3].

Revascularization is the first line option and it is of fundamental importance in order to optimize limb salvage and patient survival [4]. However when a previous revascularization fails or there is no indication to surgical or endovascular approach for anatomic reasons, CLTI may be considered a no-option one [5]. The management of these patients is challenging, and major amputation appears as the only way to go through. However, when lesions or gangrene do not progress and pain is bearable and can be handled a conservative treatment may be considered. In these settings, a well-planned and tailored therapeutic strategy may contribute to save limb or to lower the level of amputation

In the present study, we wanted to report our therapeutic approach to CLTI no-option patients because we realized that major amputation could be avoided in several instances.

2. Patients and Methods

In our retrospective study we included in 76 patients seen for no-option chronic limb ischaemia (CLI) at our Vascular Surgery Unit January 2016 to January 2021. Cases were considered no-op-

tion as they were not suitable for revascularization or had failed it. Of the 76 cases 39 were males (51 %), aged 75 (68-85) years, and 37 were females (49 %) aged 73 (66-84) years. Demographic, clinical, laboratory and imaging data were recorded. Imaging included Eco Doppler, AngioTC/MR and Angiography. We also recorded characteristics of lesion, non-healing minor amputations of the index limb, treatment performed and outcome. Our treatment approach had been as follows. Patients not eligible for revascularization presenting stable ulcers and non-extensive, non-evolving gangrene were considered for conservative treatment (Figure 1a, 1b). This included local debridement, antibiotic therapy of superimposed infection and drainage of abscess whenever present, NPWT in order to remove exudate and application of Dermal Substitutes (DS). Among these biomaterials PELNAC® (Gunze Medical Materials Center, Kyoto, Japan) is a porcine-derived dermal substitute (PDDS) which proved to promote ulcer healing in several clinical settings (6). In several instances use of PDDS was followed by the application of Suprathel® (Polymedics Innovation GmbH, Germany), which is an Alloplastic Skin Substitute (ASS). Distal gangrene was treated with minor amputation .If tissue or flap was unable to cover surgical site application of PDDS was performed in order to accelerate healing. Patients with severe pain and/or progression of gangrene and/or of superimposed infection underwent major amputation. Anticoagulants, anti-platelet drugs and statins were used .Medical therapy of comorbidities was always given. Patients were monitored for 12 months post-treatment. The primary endpoint was limb salvage and 1-year amputation-free survival. The secondary endpoint was mortality and healing time of lesion. Study was conducted in full respect of Helsinki Declaration and of principles of Good Medical Practice.



Figure 1a: Wide, deep and infected ulcer of ischemic lower leg before treatment.

3. Results

A total of 76 patients with no-option CLTI were included in the study and their characteristics are given in (Table 1). Proportion of males and of females was similar and 10% of patients were older Than eighty years. Percentages of risk factors in decreasing order were tobacco, 54% followed by dyslipidemia , 51% and diabetes, 49%.More than a half of patients had vascular involvement with hypertension and/or carotid plaques and/or ischemic heart disease. Out of 76 subjects, 15 had chronic kidney failure and three of the 15 were on hemodialysis. CLTI was associated with systemic lupus erythematosus (SLE) in three cases, with scleroderma (SD) in 2 and with rheumatoid arthritis (RA) in 2.Data of treatment are reported in Table 2. Ten patients underwent above knee amputation due to one or more of the following: extensive gangrene, severe infection, uncontrolled pain, deterioration of clinical conditions. Six out of the 10 subjects who had received a major amputation died within the following 12 months.

For eight subjects we lowered level of amputation from above to below knee even in presence of amputation stump dehiscence.

Fifty-eight patients received either a minor amputation and/or an individualized local therapy. For this subgroup of cases local debridement, NWPT and DS, alone or in combination were performed as needed. Ischemic lesions healed in 54 of the 58 patients (95%).



Figure 1b: The ulcer after multistep treatment including the application of Dermal Substitutes.

Table 1: Characteristics of 76 patients with no- option CLTI.

Males N(%)	39(51%)
Median age ,yrs range	75 (68-85)
Smoking,N (%)	41(54%)
Diabetes ,N (%)	37(49%)
Dyslipidemia,N (%)	39(51%)
Hypertension ,N (%)	43(57%)
Carotid artery disease, N(%)	30(39%)
Ischemic heart disease,N(%)	40(53%)
Chronic renal failure,N(%)	15(20%)
Autoimmune disease,N(%)	7(9%)

Table 2: Treatment outcome of 76 patients with no-option CLTI

Above knee amputation	10(13%)
Amputation lowered to below knee ^a	8(11%)
Minor amputation and/or local therapy ^a	58(76%)

4. Discussion

We evaluated 76 patients that we had seen for no-option CLTI. Criteria for selecting no-option cases that we used are consistent with a categorization proposed recently [6]. Patient population included in the study is challenging for one or more of the following: no indication to or failure of revascularization, old age, and high percentage of risk factors and of metabolic, cardiovascular, renal and autoimmune comorbidities, the need of a multidisciplinary approach.

Uncontrolled pain, deterioration of clinical conditions, worsening of gangrene and infection, alone or in combination demand major amputation aimed at saving patient life .However no-option CLTI does not always require major amputation [7]. Indeed in our series the index limb was amputated in 10 of the 76 subjects only .In order to save patient life avoidance of major amputation is of utmost importance since survival of amputated subjects is very poor [8], 6 of 10 cases in our series . Data available in the literature also point to an ominous prognosis of CLTI treated with major amputation that was shown to be an independent predictor of mortality at multivariate analysis [1, 5, 9].

For eight patients we were successful with lowering the level of amputation from above to below knee. In this respect we feel that every effort should be made in order to lower level of amputation and heal stump dehiscence should it occur .Indeed lowering level of amputation below knee offers many advantages: QOL improves, walking with the prosthesis is easier and this improves collateral flow, rehabilitation is made easier, both wheel chair and bed mobility get better [10].

Fifty-eight patients presented with a distal gangrene which appeared to be non-progressive, dry and well demarcated. Therefore these subjects received a less aggressive treatment that included debridement and minor amputation. Surgical or chemical debridement was used according to status of wound bed. NPWT was nec-

essary to remove exudate and promote wound healing especially in deep lesion. Application of DS and ASS represented the last stage of our protocol to cover large tissue defect resulting for atypical minor amputation in order to save the limb (Figure 2 a, 2b), We used porcine-derived dermal substitutes that proved well tolerated and effective [6]. The 58 cases all did better as pain was relieved, clinical course was favorable and amputation-free survival was maintained.

We want to emphasize that all efforts to save an ischemic limb are to be made .These attempts are of utmost importance although clinical presentation of CLTI is often challenging and surely demanding. In some instances, wounds are considered incurable at first glance and surgeon rushes into amputation. However if one does not rush through the above decision, lesions might improve and even heal with an appropriate conservative treatment and amputation may be avoided It is relevant to remember that saving an ischemic limb is an ethical issue.

According to our experience, we suggest that important practical points are 1) Diagnosis of no-option CLTI has to be appropriate; 2) Amputation is necessary when patient life and/or limb salvage are at high risk; 3) Necrotic tissue has to be removed only when circumscribed; 4) A well-conducted therapy may avoid amputation or substantially lower amputation level.

No-option CLI patients who received a successful attempt to limb salvage showed a significantly longer survival and a better QOL than those treated with major amputation [11].

Finally, a consensus on which are the criteria to define no-option” CLTI are not established as yet .In turn therapeutic approach may differ from one surgical team to another and data of various patient series are not comparable.



Figure 2a: The ulcer after a multistep treatment including negative pressure wound therapy and application of dermal and skin substitutes. pre treatment.



Figure 2b: Dramatic tibio-tarsal deep wound with osteomyelitis of ischemic leg in patient with T2DM. Post-treatment.

5. Conclusions

The data presented indicate that limbs of patients assumed to have no-option CLTI can be saved. An appropriate therapy may achieve unexpected benefits and amputation can be avoided. Patients with distal gangrene and/or ulcer, and with control of pain are more likely to avoid major amputation. Limb salvage is associated with a higher one-year amputation-free survival and a better QOL. Attempts to lower level of amputation from above to below knee should always be pursued. CLTI-related pain may be relieved and innovative effective therapeutic tools such as DS and ASS may improve healing of wounds. Treatment of PAD plays a key role in order to prevent CLTI from occurring and to decrease morbidity and mortality. Treatment of CLTI is expected to move a step forward in order to improve clinical benefits further.

References

1. Ying AF, Tang TY, Jin A, Chong TT, Hausenloy DJ, Koh WP. Diabetes and other vascular risk factors in association with the risk of lower extremity amputation in chronic limb-threatening ischemia: a prospective cohort study. *Cardiovasc Diabetol.* 2022; 21(1): 7.
2. Bertelè V, Roncaglioni MC, Pangrazzi J, Terzian E, Tognoni EG. Clinical outcome and its predictors in 1560 patients with critical leg ischaemia. Chronic Critical Leg Ischaemia Group. *Eur J Vasc Endovasc Surg.* 1999; 18(5): 401-10.
3. Reinecke H, Unrath M, Freisinger E, Bunzemeier H, Meyborg M, Lüders F, et al. Peripheral arterial disease and critical limb ischaemia: still poor outcomes and lack of guideline adherence. *Eur Heart J.* 2015; 36(15): 932-8.
4. Goodney P, Shah S, Hu YD, Suckow B, Kinlay S, Armstrong DG, et al. A systematic review of patient-reported outcome measures patients with chronic limb-threatening ischemia. *J Vasc Surg.* 2022; 75(5): 1762-75.
5. Kim TI, Vartanian SS, Schneider PA. A Review and Proposed Classification System for the No-Option Patient With Chronic Limb-Threatening Ischemia. *J Endovasc Ther.* 2021; 28(2): 183-93.
6. Sallustro M, Polichetti R, Florio A. Use of Porcine-Derived Dermal Substitutes for Treatment of Nonhealing Vascular Leg Ulcers: A Case Series. *Int J Low Extrem Wounds.* 2022; 21(3): 332-336.
7. Dalla Paola L, Cimaglia P, Carone A, Scavone G, Boscarino G, Bernucci D, et al. Limb salvage in diabetic patients with no-option critical limb ischemia: outcomes of a specialized center experience. *Diabet Foot Ankle.* 2019; 10(1): 1696012.
8. Thorud JC, Plemmons B, Buckley CJ, Shibuya N, Jupiter DC. Mortality After Nontraumatic Major Amputation Among Patients With Diabetes and Peripheral Vascular Disease: A Systematic Review. *J Foot Ankle Surg.* 2016; 55(3): 591-9.
9. Malyar NM, Freisinger E, Meyborg M, Lüders F, Gebauer K, et al. Amputations and mortality in in-hospital treated patients with peripheral artery disease and diabetic foot syndrome. *J Diabetes Complications.* 2016; 30(6): 1117-22.
10. van Reijen NS, Hensing T, Santema TKB, Ubbink DT, Koelemay MJW. Outcomes of Conservative Treatment in Patients with Chronic Limb Threatening Ischaemia: A Systematic Review and Meta-Analysis. *Eur J Vasc Endovasc Surg.* 2021; 62(2): 214-24.
11. Duff S, Mafilios MS, Bhounsule P, Hasegawa JT. The burden of critical limb ischemia: a review of recent literature. *Vasc Health Risk Manag.* 2019; 15: 187-208.