Review Article

Countermeasures against Infection in Critical Limb Ischemia Treatments

Yuichi Izumi, MD, PhD

The preoperative and postoperative infection control measures for critical limb ischemia treatments were described. The treatment strategies for severe ischemic limbs were showed according to the presence and extent of infection. If the treatment strategy for a severe ischemic limb with infection is mistaken, infection will spread and make worse the situation of the ischemic limb, and eventually it can result not only in limb loss but also life threatening. A surgical strategy is very important in the bypass material, the selection of anastomotic site, the use of postoperative antibacterial drugs, and the wound treatment. Infection troubles are the most familiar and indispensable problem for surgeons, the countermeasures against infection especially in critical limb ischemia is the key point along with revascularization. (This is a translation of Jpn J Vasc Surg 2018; 27: 129–132.)

Keywords: critical limb ischemia, infection, bypass, surgical site infection

Introduction

A reliable revascularization is crucial for the treatment of critical limb ischemia (CLI) as the outcome can be significantly affected by concomitant infections of ulcers and necrotic sites. Concomitant diabetes is particularly prone to complicating infections prior to surgery.1 In this paper, we discuss CLI treatment strategies, including pre- and postoperative infection control.

Evaluation of Limb Ischemia

Effective CLI treatment relies on a proper evaluation of the extent of ischemia, the presence or absence of concomitant infections and their degree, and prompt treatment initiation. The extent of ischemia is determined from subjective symptoms, ankle–brachial pressure index, skin perfusion pressure, and size of any skin ulcers or tissue defects. Prompt evaluation of the presence or absence and spread of concomitant infections is also necessary. Even if an infection appears to be confined to a certain area, it should be carefully monitored for unexpected progression and growth of abscesses along the tendons and ligaments and towards the proximal direction of the foot.2 This is related to the anatomical structure of the foot, which is divided into three fascial cavities, inside which blood vessels travel in a mesh pattern (Fig. 1). Once infection spreads to one of these fascial cavities, drainage becomes difficult, facilitating the longitudinal progression (proximal progression) of the lesions (Fig. 2). In some cases, an adequate drainage can only be achieved through metatarsal amputation.

Moreover, this condition often becomes severe in patients with poorly controlled diabetes. It is therefore crucial to manage risk by monitoring the general condition alongside local evaluation. Furthermore, deep ulcers present at the region where the bone is exposed can further complicate osteomyelitis and arthritis, thus requiring confirmation of bone changes through magnetic resonance imaging and computed tomography in addition to angiography.3

Treatment Strategy

Figure 3 shows a CLI treatment strategy that accounts for the presence or absence of concomitant infection as well as its degree.

In the absence of an infection, CLI treatment aims to preserve the limb and improve the patient’s quality of life by performing the minimum required systemic evaluation followed by revascularization. In the presence of an infection, which is confined to one area, the treatment will comprise either revascularization followed by debride-
Izumi Y.

ment or drainage and debridement followed by revascularization. The latter can favor the spread of necrosis and infection, hence exacerbating limb ischemia if the prospect for revascularization time is missed, resulting in the need for excessive debridement. A treatment plan therefore must be devised promptly after diagnosis. It is important to keep in mind that preventing the spread of infection can minimize tissue defects.

Even in patients with spreading infections, the limb can be preserved to some extent through proper preoperative drainage and wound treatment followed by reliable revascularization. However, investigation into the selection of anastomotic sites is needed. Extensive infection that spreads further into the proximal direction of the ankle joint and CLI that causes cellulitis in the lower leg have an extremely poor prognosis and can require major amputation to save the patient’s life without performing revascularization.

The recommended treatment for infection is broad-spectrum antibiotics formulated with carbapenems or beta-lactamase inhibitors. Anaerobic bacteria are particularly prone to being isolated from the deep tissue of ulcers in patients with concomitant diabetes. Cases of mixed infection of methicillin-resistant Staphylococcus aureus and Pseudomonas aeruginosa can also be observed. While no consensus has been reached regarding the systemic administration of antibiotics to patients with local wound infection and no systemic signs of infection, it is recommended to select an antibiotic that acts on the bacterium in question throughout the pre- and postoperative periods in patients where the wound bacterium has been identified preoperatively.

Revascularization and Surgical Site Infection Control

Guidelines for the proper use of antibiotics as postoperative infection prophylaxis, including surgical site infection (SSI) control, have been created by the Japanese Society of Chemotherapy and the Japan Society for Surgical Infection. For the specific case of vascular surgery, guidelines for the use of antibiotics to prevent postoperative infection are presented in Table 1.

A) Anatomy of plantar muscles, digital nerves and arteries. B) Cross-section near metatarsal bases. (From Anderson: Grant’s Atlas of Anatomy. 8th ed.).

Fig. 2 Infection expanded into plantar fascia space.

Fig. 3 Treatment strategy of clinical limb ischemia.
Whenever possible, revascularization for CLI should be performed through the use of a vein graft, making every effort to avoid the use of artificial blood vessels. In patients who require reconstruction of multiple segments, a distal bypass is commonly employed avoiding surgical invasion to the inguinal region as much as possible, where the lymph nodes and vessels concentrate and infection is common. This bypass should be combined with endovascular treatment in the regions of the iliac artery and superficial femoral artery. If an artificial blood vessel is required for an extra-anatomical bypass, expanded polytetrafluoroethylene, which is hydrophobic and presents low histocompatibility and porosity, is advantageous. However, the incidence of infection is high in extra-anatomical bypass, redo surgery, concomitant diabetes, and CLI. Furthermore, old age, obesity, steroid and immunosuppressant use, emergency surgery, prolonged surgery, and other factors pose a high risk for the onset of SSI. In particular, graft sepsis following wound infection can have fatal consequences. Therefore, full consideration must be given when selecting the treatment strategy, surgical procedure, and the perioperative prophylactic antibiotics used.

### Table 1: Perioperative prophylactic anti-biotics usage in vascular surgery (the abstract from ref. 7)

| Surgical procedure                                      | Recommendation grade/evidence level for indication | Recommended antibiotic | Alternative drugs for patients with allergies | Administration period | Recommendation grade/evidence level | Remarks |
|---------------------------------------------------------|---------------------------------------------------|------------------------|-----------------------------------------------|------------------------|------------------------------------|---------|
| Surgery with artificial prosthesis: abdominal aortic surgery | A-1                                               | CEZ                    | VCM, CLDM                                     | 24–48 h                | C1-III                             | Elective surgery should be performed after infection control through antibacterial treatment of infected aneurysm (C1-III) |
| Surgery with artificial prosthesis: Abdominal aortic surgery (high risk of SSI) | A-1                                               | CEZ                    | VCM, CLDM                                     | 72h                    | C1-III                             | *High risk of SSI: emergency surgery for rupture, etc. |
| Surgery with artificial prosthesis: lower limb bypass surgery | A-1                                               | CEZ                    | VCM, CLDM                                     | Single dose–24 h       | A-1                                |                     |
| Endovascular treatment for peripheral blood vessels     | C1-III                                            | CEZ                    | CLDM, VCM                                     | Single dose            | C1-III                             | Selection of an antibiotic susceptible to isolates in the event of lower limb ulceration, etc. (C1-III) |
| Lower limb revascularization (no use of artificial prosthesis) | C1-III                                            | CEZ                    | CLDM, VCM                                     | Single dose (re-administration after a long period of time) | C1-III |                     |

CEZ: cefazolin, VCM: vancomycin, CLDM: clindamycin, SSI: surgical site infection.
Reproduced and partially modified from Reference 7 by permission of Japanese Society of Chemotherapy and the Japanese Association for Infectious Diseases.

![NPWT (Negative Pressure Wound Therapy) after digital amputation.](image-url)
Wound Treatment and Management

Contaminants and deposits on the wound surface inhibit healing. Local wound cleaning is therefore crucial in removing such contaminants and deposits when treating tissue defects. From the infection viewpoint, the wound cleaning solution used (physiological saline, acidic water, tap water, etc.) does not affect the outcome.\textsuperscript{11} The simple use of a topical antibiotic can generate resistant bacteria and thus should be carefully considered.

Once the blood flow has been ensured and the infection has been controlled to a certain degree, treatment to promote granulation is required. In 1997, Morykwas et al.\textsuperscript{12} reported the usefulness of negative-pressure wound therapy (NPWT), after which this practice became widespread for the treatment of refractory wounds. In Japan, from 2010, NPWT is only applied under health insurance coverage and has led to good outcomes when applied to various wounds (Fig. 4).

Conclusion

This paper discussed pre- and postoperative infection control in terms of CLI treatment. For surgeons, infection is the most common and familiar complication and in the specific case of CLI, it is critical for successful treatment alongside revascularization.

Disclosure Statement

There are no conflicts of interest.

Additional Note

The content of this paper was presented at the 26th Educational Seminar of the Japanese Society for Vascular Surgery (October 21st, 2017 in Nagoya).

References

1) Akbari CM, LoGerfo FW. Diabetes and peripheral vascular disease. J Vasc Surg 1999; 30: 373-84.
2) Ishikawa K. The forefront of treatment for diabetic gangrene. Metropolitan Vascular and Endovascular Surgery 1993; 12: 63-6. (in Japanese)
3) Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg 2016; 63 Suppl: 35-21S.
4) Lipsky BA. Empirical therapy for diabetic foot infections. Are there clinical clues to guide antibiotic selection? Clin Microbiol Infect 2007; 13: 351-3.
5) Hunt IA. Foot infections in diabetes are rarely due to a single microorganism. Diabet Med 1992; 9: 749-52.
6) Marston WA. Wound care. In: Cronenwett JL, Johnston KW eds. Rutherford’s Vascular Surgery, 8th ed. Philadelphia: Saunders, 2014: 1221-40.
7) Japanese Society of Chemotherapy, Japan Society for Surgical Infection. Japanese Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery. Tokyo, 2016: 9-18. (in Japanese)
8) Sasajima T. Treatment of artificial prosthesis infection. In: Textbook of Postgraduate Educational Seminar at the 47th Annual Meeting of Japanese Society for Cardiovascular Surgery. Tokyo, 2017: 44-51. (in Japanese)
9) Back MR. Local complication: graft infection. In: Cronenwett JL, Johnston KW eds. Rutherford’s Vascular Surgery, 8th ed. Philadelphia: Saunders, 2014: 654-72.
10) Bandyk DF. Vascular graft infections. Complications in Vascular Surgery. In: Bernhard VM and Towne JB. eds. St. Louis, Missouri: Quality Medical Publishing, 1991: 223-34.
11) Fernandez R, Griffiths R. Water for wound cleansing. Cochrane Database Syst Rev 2012; 2; CD003861.
12) Morykwas MJ, Argenta LC, Shelton-Brown EI, et al. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann Plast Surg 1997; 38: 553-62.