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REVIEW

SAVE THE SEVERELY ISCHEMIC LIMB: THE JOINT PRACTICAL APPROACHES

The most difficult and painful decision: When there is nothing to do anymore, when is better to do nothing

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ABSTRACT

Chronic limb-threatening ischemia (CLTI) is a state of severe malperfusion of the lower limb. Patients with diabetes, end-stage renal disease, or very elderly, are particularly involved and at risk of a major cardiovascular event, sudden death and amputation. Decision-making in CLTI is based on the initial choice, if attempting limb salvage or proceeding with a major amputation to minimize surgical stress in these fragile patients at risk of perioperative death. It is always important to establish what is their basal functional status, as well as the extent of all their comorbidities, before suggesting a limb revascularization surgery. We should try to understand whether the patient can derive a substantial benefit from a perfectly successful revascularization intervention. Patency or limb salvage should not always be aimed for at any cost: while most patients will benefit from an aggressive limb salvage approach, others will benefit from a primary amputation, and others will benefit from palliative care with no invasive intervention. Therapeutic risk stratification is crucial, and the inability to recover from major stress must be foreseen. We should answer these three questions: Is our patient dying? What is the expected ambulatory capacity of our patient? Is the foot severely infected? Major amputation can also represent the best therapeutic option and, as such, it must be planned and executed with accuracy. Only after this elaborate decision-making process, we can inform our patient to ask for consent to the treatment.

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Chronic limb-threatening ischemia (CLTI) means a state of severe malperfusion of the lower limb, with pain at rest or the appearance of necrosis in the foot, due to severe steno-obstructive arterial disease of at least two anatomical areas (aorto-iliac, femoropopliteal), or of the tibiopedal area. The latter is particularly involved in patients with diabetes, end-stage renal disease, or very elderly. CLTI is a term now preferred over critical limb ischemia, as it is more inclusive of the broad spectrum of hemodynamic impairment (*i.e.* ischemia) and threats to the limb (*i.e.* neuropathy) that are typical of these patients.[1] General and limb prognosis of these patients is adverse: they are at continuous risk of a major cardiovascular event, sudden death, and of course amputation.

Clinical scenario

The enthusiasm linked to the improvement of endovascular techniques and materials has led to a marked increase in revascularization interventions in patients with CLTI, and the satisfactory results of immediate patency have made believe that revascularization is always the best choice. However, Khan *et al.* showed a higher rate of amputation secondary to a previous revascularization

operation, still patent: 38% after bypass and 80% after 3 months after angioplasty.[2]

As we all know, every treatment we carry out should be aimed at improving the general condition of our patient. So, the most important decision in the treatment of CLTI is the initial choice: to attempt limb salvage (LS), or to proceed with a major amputation to minimize the surgical stress due to eventual multiple operations with the consequent risk of perioperative death?

As many as 1/4 of patients with CLTI are now subjected to *d'emblée* major amputation.[3] There is in fact a widespread awareness that major amputation may represent the best treatment in specific subgroups of CLTI patients, but decision-making in CLTI requires a comprehensive evaluation of the patient.

While it is true that CLTI inevitably leads to loss of the limb when left untreated, just as it is true that the best treatment is not always revascularization at all costs, it is also correct to state that the optimal therapy is one that is adapted to the needs of the single patient. It is always important to establish what is the basal functional status of the patient – often very old and in poor general conditions – as well as the extent of all his comorbidities, before suggesting a limb revascularization surgery.

The Trans-Atlantic Inter-Society Consensus (TASC) II[3] and wound-ischemia-foot infection (WIfI)[1] classifications, the identification of a target artery to be revascularized, and the patient's availability of an adequate venous conduit, are all important in quantifying the extent of angiographic lesions, crucial in the endovascular *versus* open revascularization decision-making process, essential to establish the annual risk of major amputation and the wound-healing outcome.[4-7]

In this regard, one of the most recurring questions today is how much to force endovascular treatment in a patient with CLTI considered unsuitable for open surgery. It seems that endovascular treatment in these patients does not give short to medium term advantage over primary amputation, as highlighted by Taylor *et al*. The authors, while demonstrating significantly greater maintenance of walking after revascularization treatment, observed clinical success which did not last beyond a year, as well as a higher mortality compared to the demolition treatment.[8]

We should always think in terms of patient-centered, rather than limb-centered approach: global assessment of the goal of treatment might modify the best treatment option. In other words, we should try to understand whether the patient can derive a substantial benefit from a perfectly successful revascularization intervention, whose technical success we know well does not always correspond to clinical success.

The vascular study group of Northern New England showed that 10% of bypass patients at one year did not receive appreciable clinical benefit.[9]

Taylor *et al*. studied more than 300 patients treated for CLTI at Rutherford stage 5 or 6: only 44% of patients achieved clinical success of the treatment, *i.e.* the simultaneous achievement of the objectives of: bypass patency at least until the trophic lesions healed, LS and walking ability for at least 1 year, survival for at least 6 months. The independent risk variables for failure were: already seriously impaired walking, severe chronic renal failure, the presence of gangrene, and the infrainguinal localization of the steno-obstructive lesions. The coexistence of 2, 3, or all 4 predictive risk factors for failure decreased the probability of clinical success to 33%, 10%, and 5%, respectively.[10]

Other important and non-secondary predictors of failure are the presence of diabetes,[11] constrained living at home or in the nursing home,[12, 13] major amputation of the contralateral lower limb,[14] and the operator's low experience in open and endovascular distal revascularization.[15]

Therefore, patency or limb salvage should not always be aimed for at any cost. While most patients will benefit from an aggressive limb salvage approach (as seen in the previous chapters), some patients will benefit from a primary amputation, and some patients will benefit from palliative care with no invasive intervention.

Therapeutic risk stratification in the CLTI patient is closely related to advanced age. It is often a fragile, vulnerable patient (given the physical and mental impairment), with a reduced physiological reserve, and functionally compromised (given the multiple comorbidities): the inability to recover from major stress must be foreseen.

The goal we must strive for is therefore to try on the one hand to increasingly identify those variables that guide our decision-making in the elderly and frail patient, and at the same time to better define the therapeutic success in the most severely and globally compromised patient with CLTI.[16]

How to proceed

What are the factors to consider helping this patient at best? Of course, the detection of a distal target for revascularization and the availability of adequate venous conduit influences our decision making, but three questions will definitely help us to assess the best options to help our patient.

Is our patient dying?

Being able to detect the patient who is near the end -even if difficult- will help to choose the best option for him/her, avoiding invasive treatment and providing palliative care.

Pharmacological therapy (prostanoids, vasodilators, antiplatelet agents) and hyperbaric therapy do not give comforting results, while the best choice would be to be able to refer this patient to a dedicated Wound Care Center specialized in intensive treatments (negative pressure therapy, debridement, antibiotic-targeted therapy), which may also be able to avoid major limb amputation.[3]

What is the expected ambulatory capacity of our patient?

The one who have not been walking for a long time might not benefit from LS therapy with long healing time. This is the case of a patient who is too ill or debilitated to be able to take advantage of a complex LS program. However, the clinical scenario is varied: from the non-ambulatory patient, very elderly, in a retirement home, with ankylosis in flexion of the knee that would benefit from a thigh amputation to the patient with minimal residual walking capacity – but many comorbidities – in the which the choice of revascularizing the limb or amputating it must necessarily be individualized case by case.

Out of 1000 CLTI patients undergoing revascularization, Taylor *et al*. demonstrated that preoperative walking ability was the main discriminant of postoperative success.[12]

In case of significant infection or persistent pain, amputation might often be the best option, providing quick healing, reduced pain and shorter hospitalization stay with quicker return to better quality of life.

Is the foot severely infected?

In this patient with rapidly evolving sepsis and infected gangrene of the foot, often poorly controlled diabetic, the best option is rapid debridement and amputation to remove the infected extremity. Pus in the devitalized tissue is often found, and guillotine amputation is often the best option in these patients. However, assessment of the level of amputation is essential and can often be limited to the forefoot, allowing for heel preservation.

Only severe septic shock and rapidly evolving infection to the leg will require above knee amputation.

The delayed timing of the intervention, which increases the risk of limb loss, is also part of this scenario. It is due to an educational deficit not only of the patient but also of the physicians, and it is also part of the difficulty of the health system, where access to the operating room is limited.[17, 18]

We must also keep in mind that often our CLTI patient belongs to a low socioeconomic status, has a poor income and a below average educational level: the mechanisms involved in this association could be nutritional, related to psychological stress, and health literacy.[19, 20] Furthermore, it must also be considered that many of these patients develop pain at rest or necrosis in the foot without having suffered in the past from the more tolerable and typical symptoms of peripheral arterial disease. This is explained by the coexistence of peripheral neuropathy, the reduced mobility due to the many comorbidities, or the overlap of an acute event such as a trauma or foot infection.

In all other contexts, *i.e.* a patient with a good prognosis, ambulatory capacity and no widespread severe systemic infection, the vascular surgeon will and should be able to provide lower limb revascularization.

The therapy of amputation

Therefore, although often associated with LS failure, major amputation can also represent the best therapeutic option for our fragile patient. As such, it must therefore be planned and executed with accuracy, always keeping the two fundamental principles of the intervention very clear: 1) to eliminate all necrotic, ischemic or infected tissue, keeping the patient with a residual stump as long as possible, well healed, and functional to a possible prosthetic and rehabilitation program; 2) to seek healing of primary intention, trying not to be forced to carry out a secondary revision of the stump, or more proximal amputation.

Crucial is therefore the initial choice of the level of amputation, which should be unique and definitive. However, as many as 15-25% of patients with subgenicular amputation are re-amputated at the supragenicular level,[17, 21-23] with operative mortality increased to approximately 5%.[11]

If eligible for a rehabilitation program, the leg amputated patient is more likely to walk again than if he were a thigh amputate. In fact, the higher the level of the greater amputation, the greater the effort the patient has to make to walk.[24]

In clinical practice, the choice of the level of amputation is based on a clinical judgment that makes use of data on the local state (none of which is decisive when analyzed individually), an exhaustive analysis of the general condition of our patient with CLTI and, above all, the experience of the surgeon:[25]

- the amputation stump must necessarily be proximal not only to tissues in gangrene, but also to those ischemic or suspected of such;

• the presence of an arterial pulse immediately proximal to the amputation level (major or minor) clearly guarantees total healing of the stump, but it is not always necessary and could bring to an excessive number of too proximal amputations;[26, 27]

• the search for any thermal step and the comparison of the skin temperature with that of the healthy contralateral limb;

• the transcutaneous measurement of the partial pressure of oxygen (tcPo2), generally with a threshold value of 30 mmHg;

• the pre-existence, or not, of walking ability;

• more or less advanced age;

• the extent of the comorbidities;

• the mental state.[28]

It is therefore clear that the choice of the level of amputation cannot be separated from any project of rehabilitation program.

Conclusions

Only after this elaborate decision-making process within our team – and with the help of our colleagues anesthetists, cardiologists, geriatricians, orthopedists, physiatrists – we can inform our patient to ask for consent to the treatment. He must understand the diagnosis of CLTI and be clearly told the purpose of treatment, the risks and benefits associated with it, the alternative therapies, as well as the risks and benefits of not undergoing the treatment we recommend.

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