The Role of Lower Extremity Amputation in Chronic Limb-Threatening Ischemia

Tanner I. Kim, MD[1] Carlos Mena, MD[2] Bauer E. Sumpio, MD, PhD[1,2]

[1] Division of Vascular Surgery, Department of Surgery, Yale University School of Medicine, New Haven, Connecticut
[2] Cardiology Section, Department of Medicine, Yale University School of Medicine, New Haven, Connecticut

Address for correspondence Bauer E. Sumpio, MD, PhD, Department of Surgery, Radiology, and Medicine, Yale University School of Medicine, 330 Cedar Street, BB204C, New Haven, CT 06520 (e-mail: bauer.sumpio@yale.edu).

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Abstract

Chronic limb-threatening ischemia (CLTI) is a severe form of peripheral artery disease associated with high rates of limb loss. The primary goal of treatment in CLTI is limb salvage via revascularization. Multidisciplinary teams provide improved care for those with CLTI and lead to improved limb salvage rates. Not all patients are candidates for revascularization, and a subset will require major amputation. This article highlights the role of amputations in the management of CLTI, and describes the patients who should be offered primary amputation.

Keywords

- amputation
- peripheral artery disease
- chronic limb-threatening ischemia
- artery
- risk factors
- end-stage renal disease

Chronic limb-threatening ischemia (CLTI) represents the end stage of peripheral artery disease and is associated with high rates of limb loss and mortality.[1,2] Surgical and endovascular revascularization are the primary treatment modalities to improve perfusion and avoid amputation. Multidisciplinary teams including vascular surgeons, interventional cardiologists, radiologists, and podiatrists among others provide an opportunity for shared decision-making that improves limb salvage rates and the overall care of patients with CLTI.[3] Not all patients are suitable for revascularization, and major amputation remains an important treatment option in the management of CLTI. Patients may present with severe arterial disease, infections, or tissue loss beyond salvage that will require major amputation. Although often viewed as a failure of treatment, major amputations provide definitive therapy for unsalvageable disease. The use of the grading systems such as the Society for Vascular Surgery (SVS) Wound and Ischemia, Foot Infection (WIfI) classification system help to identify those at high risk for major amputation.[4] In this article, we review the role of amputations in the care of patients with CLTI.

Epidemiology of Lower Extremity Amputations

Major amputations are a common procedure with approximately 60,000 major amputations performed yearly in the United States.[5–7] However, major amputations have been on the decline, with one study in the elderly population showing rates of major amputation, decreasing from 7,528 per 100,000 patients to 5,790 per 100,000 patients from 2000 to 2008.[8] Similar trends have also been observed in countries such as Spain, Germany, Turkey, and the United Kingdom.[9–12] However, there is significant variability in the incidence of major amputations globally, highlighting the importance of standardized methods in reporting to continue to monitor major amputations worldwide.[13]

There is significant variation in the rates of major amputation by ethnicity, socioeconomic factors, and geography. Navajo men have been observed to have particularly high rates of major amputation, attributed primarily to high rates of diabetes.[14] African Americans also have higher rates of major amputation even after adjustment for comorbid

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conditions including diabetes.[15,16] Global studies have also demonstrated significant variation in rates of major amputation, highlighting socioeconomic disparities and limited access to vascular specialists and health care.[14,17,18] In Australia, aboriginal patients and those in rural areas were more likely to present with severe diabetic ulcers and undergo major amputation.[19,20]

Diabetes is the most significant risk factor for major amputation with an eightfold increase risk compared with the general population.[21–23] The lifetime risk of foot infections among diabetic patients is 25% and is the most important cause of major amputation in this group of patients.[24,25] However, aggressive glucose control and medical optimization have been shown to lower this risk.[26] Other important risk factors for major amputation in the setting of CLTI include end-stage renal disease (ESRD), peripheral neuropathy, and smoking.[27–29]

Endovascular procedures have extended the treatment of CLTI to many high-risk patients who were previously not candidates for open revascularization, and have been associated with decreased rates of major amputation.[30] Improvements in medical therapy including antiplatelet therapy and statins in addition to better management of comorbid medical conditions have improved limb salvage rates and mortality.[31,32] However, patients with CLTI still face low rates of overall survival at an average of 3.5 years, which is lower than other serious conditions including heart failure and many cancers.[33–35]

The Role for Amputation

Nearly all patients should be considered for revascularization before amputation. However, it remains an important tool for those with severe forms of CLTI with unreconstructible disease. This was recognized in the recently published Global Vascular Guidelines, which provided recommendations regarding the use of amputations in the management of CLTI.[1] Minor amputations are those that involve the toes or portion of the foot, while major amputations imply more proximal limb loss (e.g., below or above knee amputation [BKA or AKA]). Minor amputations maintain the ability of the patient to bear their weight and seldom require a prosthetic unlike a major amputation. The primary goals of major amputation in the setting of CLTI are the relief of ischemic pain, removal of all diseased or necrotic tissue, and preservation of ambulation if possible. Additionally, major amputations should aim to limit reinterventions and provide an opportunity for rehabilitation or palliation as appropriate.

Indications for Minor Foot Amputation

Minor amputations including toe and forefoot amputations may be necessary for limb salvage and avoidance of major amputation. The indications for minor amputation include infection, osteomyelitis, gangrene, and neurotrophic feet (►**Table 1**). As long as these processes do not extend beyond the forefoot preventing future ambulation, a minor foot amputation can avoid a major leg amputation and help maintain ambulation, functional status, and quality of life. Importantly, perfusion should be assessed to optimize healing following a minor amputation and prevent conversion to a major amputation. When peripheral artery disease is present, revascularization is often required to establish in-line flow distally. For example, transmetatarsal amputations have shown high rates of success when coupled with revascularization procedures.[36,37] Sheahan et al demonstrated a limb salvage rate of 78% at 5 years for patients who underwent transmetatarsal amputation and revascularization.[36]

Table 1 Indications for minor foot amputation

• Infection with adequate perfusion.
• Toe gangrene with small vessel arterial disease.
• Neurotrophic foot with adequate perfusion.
• Osteomyelitis or gangrene with adequate perfusion.

Indications for Major Leg Amputation

The indications for primary amputation in the setting of CLTI are unreconstructible arterial disease, destruction of the major weight-bearing portions of the foot, a nonfunctional lower extremity, severe comorbid conditions or limited life expectancy, and avoidance of a prolonged recovery with multiple high-risk surgical procedures (►**Table 2**). Of these indications, the most common reasons for major amputation include prior failed revascularization, extensive pedal gangrene, and unreconstructible arterial anatomy.[38]

Up to 20% of the patients with CLTI are found to have unreconstructible peripheral artery disease usually due to severe outflow disease with occluded tibial and pedal vessels.[39,40] Unfortunately, this degree of disease is often not amenable to standard surgical or endovascular revascularization, and will often require major amputation. An attempt at revascularization may be attempted although outcomes of both open and endovascular revascularization are significantly worse with poor pedal and tibial outflow.[41–44] Importantly, a proper vascular evaluation with imaging such as angiography or computed tomography angiography is necessary to properly assess all possible treatment options prior to deciding on major amputation for these reasons.

Major amputation also has a role in those with a nonfunctional lower extremity. This may occur in those with paralysis secondary to nerve damage or a stroke, and may be complicated by contractures, which can further limit mobility. Revascularization of a nonfunctional limb has limited utility, and an amputation may provide an opportunity for improved mobility.

Table 2 Indications for major leg amputation

• Unreconstructible arterial disease.
• Destruction of the major weight bearing areas of the foot.
• Nonfunctional lower extremity.
• Severe comorbid conditions or limited life expectancy.
• Prolonged course requiring multiple procedures.

Destruction of major areas of the foot most often occurs in patients with severe foot tissue loss or foot infections. Patients with severe foot infections precluding a transmetatarsal amputation will often require major amputation. This is of particular importance in patients with diabetes and associated peripheral neuropathy given the high incidence of this complication.[24,25] Similarly, patients with osteomyelitis or deep infections or abscesses involving an extensive portion of the foot or calcaneus should also be considered for major amputation. Severe tissue loss involving the foot preventing a transmetatarsal amputation, or extensive tissue loss at the heel should be considered for a major amputation. This includes severe wounds, ulcers, and gangrene extending to the forefoot or midfoot, or involving the heel with possible calcaneal involvement. In some cases, a complex reconstruction with skin flaps following debridement may be possible to avoid amputation.

Patients who have severe CLTI with multiple significant comorbid conditions may benefit from primary amputation. This includes nonambulatory patients or those with dementia due to poor outcomes and minimal improvement in quality of life following revascularization. Oresanya et al used Medicare claims to identify nonambulatory nursing home residents who underwent revascularization for CLTI, and demonstrated little benefits to revascularization in this population with minimal gained function and high rates of mortality over 50% at 1 year.[45]

Similarly, primary amputation has the potential to avoid prolonged reinterventions and wound care regimens. This strategy applies primarily to elderly patients with multiple significant comorbidities, in which repeated high-risk surgical procedures with a low likelihood of success may place them at a high risk for complications.[1,46] Revascularization in this group of patients often includes an extended hospital course or multiple readmissions, placing patients at increased risk for additional complications and a low quality of life.[47,48] Primary amputation can avoid the prolonged immobility and deconditioning associated with a prolonged recovery, and may allow a faster return to independence or baseline functioning.

Patient Selection for Major Amputation in CLTI

A major amputation is an important treatment option in the care of patients with CLTI. A thoughtful and reasoned approach is important to making the decision between revascularization and amputation for those at high risk. The WIfI classification system has been shown to accurately predict the risk of limb loss better than prior grading systems, and is a useful tool to aid in the decision-making process. Robinson et al reviewed 257 patients with CLTI and found that increasing WIfI stage was associated with decreased limb salvage.[49] At 1 year, patients with WIfI stage 4 disease had a 22% rate of major limb loss.

A thorough vascular evaluation including appropriate imaging is essential to proper decision-making. However, multiple studies have documented low rates of vascular evaluations prior to major amputation.[33,50,51] Goodney et al used Medicare claims to show that 54% of the patients with CLTI did not have revascularization within a year of undergoing major amputation.[51]

Identifying which patient should undergo major amputation rather than revascularization can be difficult, as many patients with severe CLTI have significant comorbidities.[52] Suckow et al demonstrated that patients with multiple comorbidities and limited functional status at the time of surgery had higher rates of amputation following lower extremity bypass.[47] Long-term follow-up of patients in the Project or Ex-Vivo vein graft Engineering via Transfection III (PREVENT III) trial found that patients deemed high risk due to multiple comorbidities including ESRD, tissue loss, age greater than 75, anemia, and coronary artery disease were more likely to end up with a major amputation, with rates exceeding 55%.[48] Additionally, a study using the Vascular Study Group of New England (VSGNE) registry found that factors including age, ESRD, diabetes, CLTI, spliced conduit, pedal target, and nursing home status were associated with increased risk of failure with revascularization.[53] Studies comparing primary amputation versus amputation following revascularization among the elderly are mixed, with some finding higher rates of mortality following failed bypass.[54,55]

The decision regarding revascularization versus amputation is a difficult and personal choice. This should involve a thoughtful discussion with the patient regarding appropriate expectations and outcomes. A survey of patients who underwent lower extremity amputation found that physician-controlled factors including timing, shared decision-making, and postamputation support had an important role in the decision-making process and quality of life.[56] Interestingly, a study of amputees noted that several patients expressed a desire for amputation earlier in their clinical course.[57] A high-risk revascularization procedure and wound care regimen with a prolonged course may not align with a patient's overall goals. This emphasizes the importance of shared decision-making and providing patients with the full range of surgical options and potential treatment courses during each step of their treatment.

The Role of Multidisciplinary Teams in the Care of CLTI

A multidisciplinary team approach to the care of patients with CLTI is supported by the SVS and improves outcomes.[3] Specific members of the multidisciplinary team may vary by practice, but typically consist of at least a vascular surgeon and podiatrist. The goals of such a practice include podiatric and wound care, as well as vascular assessments and revascularization if necessary.[3] This is of particular importance for diabetic patients who are at increased risk of limb loss. The inclusion of podiatrists has been shown to significantly reduce rates of major amputation. Integration of podiatrists into a health system in Michigan led to an increase in the diagnosis of diabetic foot ulcers and shifted a significant portion of care to the outpatient setting.[58] The rate of major amputations decreased by 50%, while preventative procedures such as debridement significantly increased. Similarly, the inclusion

of podiatrists in the care of patients with diabetic ulcers in China led to a nearly ninefold reduction in major amputations among patients with severe diabetic ulcers.[59]

Multidisciplinary teams with podiatrists offer additional resources and care for the diabetic foot, and seek to prevent the development of uncontrolled infections and ultimately major amputation. The implementation of multidisciplinary teams has been shown to increase overall procedural volume as well as improve limb salvage rates.[60–62] Our group has investigated the impact of a multidisciplinary team on limb salvage rates in patients with CLTI.[60] The use of a multidisciplinary team led to significant increases in lower extremity revascularizations and minor amputations, and was associated with a significantly lower rate of major amputations. Similarly, Flores et al demonstrated that establishment of a multidisciplinary wound care center increased the volume of lower extremity revascularizations and improved limb salvage rates.[61] An additional benefit observed in multiple studies was an increase in referrals and patient volume.[3,60,61] The use of a multidisciplinary, team-based approach to CLTI increases preventative care and revascularization as opposed to reactive and urgent care, and leads to improved overall outcomes.[63]

Studies across multiple countries have also shown that the implementation of a multidisciplinary team reduced major amputations leading to significant cost savings.[64–66] Using Markov models, diabetic patients treated by multidisciplinary teams with preventative measures lead to savings of $2,900 to $4,442 per patient costs.[67]

The Impact and Outcomes of Major Amputation

Long-term outcomes following major amputation remain poor, with relatively high rates of perioperative and long-term mortality.[54,68] Mustapha et al demonstrated that patients with CLTI treated with primary amputation had significantly lower rates of survival and a higher risk of subsequent amputation over 4 years compared with revascularization.[69] Even after propensity matching, those who underwent primary major amputation had a mean survival of 1.3 years compared with 2.7 and 2.9 years with endovascular and open revascularization, respectively. Jones et al demonstrated similar results among elderly patients, with a 70.9% mortality rate at 3 years.[8] Additionally, proximal amputations, such as AKA, were associated with an even higher risk of mortality.

In addition to the high mortality rates, patients with major amputations will often require revisions and even conversion to a more proximal amputation. Aulivola et al demonstrated a reintervention rate of 18.4% for BKA and 4.7% for AKA.[70] A separate study found that 25% of BKAs ultimately required conversion to an AKA.[71]

Functional outcomes following major amputation are largely dependent on preoperative comorbidities and functional status. Younger, ambulatory patients with fewer comorbidities can generally be expected to have functional outcomes similar to those with successful revascularization.[72] Among those with healed stumps, up to 80% of the patients with a BKA can achieve ambulation, and up to 50% with an AKA may ambulate.[73] However, many patients with CLTI have multiple comorbidities and experience a decline in functional status following major amputation. Taylor et al defined a successful outcome following BKA as wound healing without the need for revision, maintenance of ambulation for at least a year, and survival for at least 6 months postoperatively. The presence of coronary artery disease, cerebrovascular disease, and impaired preoperative ambulatory status decreased the odds of a successful outcome from 67.5 to 10.4%.[74] A study of nursing home patients who underwent major amputation found that the majority of the patients did not return to their preoperative functional status within 6 months.[75] Additionally, higher amputation level, ESRD, and dementia were associated with worse outcomes.

Patients who have a major amputation undergo significant life changes due to the loss of a limb. Quality of life following an amputation has been shown to be largely dependent on the ability to ambulate or return to previous functional status.[76–79] These findings stress the importance of postamputation care and rehabilitation to regain mobility and maintain independence. In addition to quality of life, many studies have found increased rates of depression following amputation.[68,80,81] Depression should be identified and treated promptly as it can slow the rehabilitation process and has been associated with further amputation.[80]

Raviola et al first demonstrated the increased cost of primary amputation compared with bypass surgery in 1988.[82] Since then, multiple studies have supported this finding, even with the use of endovascular interventions.[83–85] Mustapha et al using Medicare claims to demonstrate increased costs associated with primary amputation compared with surgical or endovascular revascularization.[33] After adjusting for follow-up duration, cost per patient year was $49,200 for surgical revascularization, $49,700 for endovascular revascularization, and $55,700 for major amputation.

Conclusion

Amputation remains an important tool in the management of CLTI. Despite improvements in care and treatment, many patients still progress to severe forms of CLTI necessitating a major amputation. However, mortality following major amputation remains high, reflecting the poor health status of this population, and highlights multiple potential areas for improvement in limb salvage.

Conflict of Interest
C.M. is a consultant for Bard, Cook, Cardinal Health, Boston Scientific, and Medtronic. B.E.S. is a consultant for Hypermed.

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