JAMA Network Clinical Guideline Synopsis

Review of the Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia

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GUIDELINE TITLE: Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia

RELEASE DATE: June 2019

PRIOR VERSION(S): None

DEVELOPER: Global Vascular Guidelines Initiative

FUNDING SOURCE: Society for Vascular Surgery, European Society for Vascular Surgery, and World Federation of Vascular Societies

TARGET POPULATION: Clinicians directly involved in treatment of chronic limb-threatening ischemia.

MAJOR RECOMMENDATIONS (quality/evidence ratings):

- Limb staging
  - Use a threatened limb classification system (1/C) and limb-based anatomic staging system (good practice statement).
- Medical management
  - Antiplatelet monotherapy (1/A).
  - Moderate-intensity or high-intensity statin (1/A).
  - Consider clopidogrel as the single antiplatelet agent of choice (2/B).
  - Consider low-dose aspirin and rivaroxaban, 2.5 mg, twice daily (2/B).
- Revascularization
  - Aorto-iliac disease:
    - Endovascular-first approach for moderate to severe disease (1/B).
    - Surgical reconstruction for average-risk patients with extensive disease or after failed endovascular intervention (2/C).
  - Femoral artery disease:
    - Common femoral artery endarterectomy with patch angioplasty for significant disease (1/C).
    - Consider common femoral artery endarterectomy with concomitant iliac stent placement if aorto-iliac disease is also present (2/C).
  - Infrainguinal disease:
    - In average-risk patients, endovascular or open-based on severity of limb threat, disease anatomy, and availability of autologous vein (1/C).
    - In high-risk patients, endovascular-first approach (2/C).

Summary of the Clinical Problem

In 2010, it was estimated that more than 200 million people worldwide were living with peripheral arterial disease. Chronic limb-threatening ischemia (CLTI) represents the end stage of peripheral arterial disease, which, left untreated, incurs a risk of major amputation, approaching 25% at 1 year. Despite the global scale and severe clinical consequences of CLTI, it has been poorly defined and variably managed. Prior guidelines, such as the Trans-atlantic Intersociety Consensus Document on the Management of Peripheral Arterial Disease (TASC II), have offered treatment recommendations based on disease anatomy alone.[1] A more contemporary, nuanced definition of the problem and thorough understanding of the state of evidence are required to guide medical treatment, revascularization strategies, and future study.[2]

Characteristics of the Guideline Source

Three vascular societies formed the global vascular guideline initiative: the European Society for Vascular Surgery, the Society for Vascular Surgery, and the World Federation of Vascular Societies. The writing group was composed of 58 individuals from 24 countries and multiple medical and surgical specialties. Although the 3 sponsoring societies primarily represent vascular surgeons, these guidelines were endorsed by multiple international groups representing medical and interventional specialties. All funding for the guidelines was from the sponsoring societies. Direct industry funding of the guidelines was prohibited, and industry consultants were excluded from both the writing and reviewing groups. Strict limits were set for contributing authors on industry income during work on the guidelines, and conflicts of interest were reported in detail. An open comment period was observed prior to publication.

Evidence Base

Authors used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methods to rate recommendation strength and quality of evidence. Final grading was determined by the guideline developers and a methodologist. Four systematic reviews were commissioned, subjected to peer review, and published in the *Journal of Vascular Surgery*, focusing on the natural history of CLTI,[3] nonrevascularization-based treatments,[4] and outcomes associated with revascularization.[5,6]

The guidelines were published in the June 2019 issue of the *Journal of Vascular Surgery* and the July 2019 issue of the *European Journal of Vascular and Endovascular Surgery*. The guidelines clearly indicate which studies were used as the basis for recommendations. An addendum was included on the safety of paclitaxel-eluting devices for the treatment of CLTI, instigated by concerns over potential increased mortality risk associated with these devices.

Benefits and Harms

Chronic limb-threatening ischemia is a manifestation of systemic atherosclerosis, and as a result, concurrent cardiovascular disease is often seen, contributing to a 1-year mortality rate of 22%.[3] In

Table. Institution of Medicine: Standards for Developing Trustworthy Clinical Practice Guidelines

Standard	Rating
Establishing transparency	Good
Management of conflict of interest	Good
Guideline development group composition	Fair
Clinical practice guideline–systematic review intersection	Good
Establishing evidence foundation for and rating strength of recommendations	Good
Articulation of recommendations	Good
External review	Fair
Updating	Fair
Implementation issues	Fair

addition to improving limb salvage through revascularization, treatment of patients with CLTI offers an opportunity to reduce cardiovascular morbidity and mortality through risk factor modification. The medical management of CLTI is a focus of the guidelines, and these recommendations in particular can be applied widely with minimal risk (Table).

With regard to revascularization, there is wide variability in practice patterns, especially as they pertain to endovascular and open surgical approaches. Revascularization strategies can be influenced by a variety of factors, including training/expertise, resource availability, and referral patterns. The guidelines emphasize the importance of appropriate patient selection (based on patient characteristics, limb staging, and disease anatomy) as the best way to manage the heterogeneous population of patients with CLTI. Optimal treatment of these patients requires expertise in both open and endovascular revascularization techniques as well as familiarity with risks associated with each approach.

Discussion

The guidelines make several meaningful recommendations, reframing the problem of CLTI and how to approach its treatment. They argue for abandoning the term *critical limb ischemia* because it is nonspecific and imprecisely defined.

Once patients are diagnosed as having CLTI (based on presence of atherosclerotic PAD and rest pain or tissue loss), the severity of the clinical problem should be determined first by applying a threatened limb classification system (such as the Wound, Ischemia and Foot Infection system [WIfI]). The guidelines then introduce the Global Limb Anatomic Staging System (GLASS) to stratify the anatomic pattern of disease. This approach emphasizes the importance of choosing a treatment strategy based on clinical findings in addition to anatomy of arterial disease. A major limitation of the TASC II[1] guidelines was that they recommended treatments based only on the anatomy of isolated arterial segments, with no clinical context. Although decisions regarding revascularization are often complex, a 3-step approach that takes into account patient risk, limb staging, and anatomic pattern of disease is recommended.

Areas in Need of Future Study or Ongoing Research

The prognostic value of the WIfI system has been supported by multiple observational studies; however, GLASS has yet to be studied in practice. The Best Endovascular vs Best Surgical Therapy for Patients with Critical Limb Ischemia (BEST-CLI) trial is an important ongoing trial that will help to provide more robust evidence for revascularization strategies (A. F. is a co–principal investigator of BEST-CLI).[7] Revascularization recommendations are addressed by the guidelines but generally not supported by high-quality evidence.

ARTICLE INFORMATION

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