Critical Limb Ischemia and Intermediate-Term Survival*

Joshua A. Beckman, MD, Mark A. Creager, MD

Peripheral artery disease (PAD) affects 7 to 8 million persons living in the United States and over 200 million persons worldwide (1,2). In approximately 2% to 3% of patients with PAD, arterial perfusion is inadequate to sustain basal metabolic requirements, resulting in critical limb ischemia (CLI), typically affecting the most distal segments of the leg and manifested as rest pain, skin ulceration, and/or frank gangrene.

Patients with CLI are at risk for 2 important sequelae: first, the severity of leg blood-flow reduction forebodes a high rate of amputation in the absence of revascularization (3). Second, the presence of CLI is indicative of a large systemic atherosclerotic burden, which increases the likelihood of adverse cardiovascular events, including myocardial infarction, stroke, and death. Thus, 2 competing considerations must weigh in the analysis when balancing the potential benefits of revascularization: the expected limb salvage versus the expected cardiovascular outcome of the patient. It is at this nexus of palliation and survival that CLI sits and represents a good example of health care in the present day: In the setting of competing risks, when is the risk of a palliative procedure of value?

The discussion regarding which patients with CLI would benefit from revascularization becomes even more compelling when taking into account the aging of the population that significantly increases the number of elderly patients at high mortality risk, both from complications of limb-saving procedures, adverse cardiovascular events, and other noncardiovascular comorbidities. Recently, the perioperative mortality risk of revascularization has diminished, lowering the threshold to consider surgery or percutaneous procedures. For example, in the PREVENT III (Prevention of Intrainguinal Vein Graft Failure III) study of a novel molecular therapy to reduce vein graft failure in 1,404 patients, 30-day mortality was <3% (4). Similar observations were made in the BASIL (Bypass versus Angioplasty in Severe Ischaemia of the Leg) trial (5) and National Surgical Quality Improvement Program data (6). Yet, over the last 15 years, intermediate-term survival, defined as 1- to 2-year mortality, has not changed appreciably. In 1997, the I.C.A.I. Group (Gruppo di Studio dell’Ischemia Cronica Critica degli Arti Inferiori) reported a 31% 2-year mortality in patients with CLI. Two-year mortality in the BASIL trial was 26.8% (7). In the Swedish national experience, the mortality rate was 27.7 and 13.4 per hundred person-years for those with and without diabetes, respectively (8). Thus, the difficulty in determining who will benefit from a surgical or endovascular procedure rests less on the procedural morbidity and mortality than on the expectation of survival long enough to accomplish recovery and enjoy its effects.

It is in this aspect that Soga et al. (9), in this issue of JACC: Cardiovascular Interventions, have improved the process of patient selection. The authors retrospectively evaluated 995 patients who were followed for more than 2 years after endovascular revascularization for CLI. The mortality rate, as expected, was high at 41%, and cardiovascular death was the most common cause of death. Using this cohort, the authors determined the demographic and medical factors that associated most strongly with 2-year mortality and devised a scoring system to estimate survival at 2 years. Patients with 8 points, for example with Rutherford class 5 disease, age 81 years, who cannot walk, and whose left ventricular ejection fraction is low, should be considered for revascularization.

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fraction is 40% to 49%, have a 50% 2-year survival rate. Awareness of the likelihood of intermediate-term survival better informs the discussion with patients about the benefits of a procedure, its attendant risks, and the patient’s intermediate-term outcomes.

There have been other published risk assessment tools for patients with severe PAD who are under consideration for revascularization (Table 1). Most of the studies supporting these tools have focused on factors similar to Soga et al. (8-14). Moxey et al. (7) compared the BASIL survival prediction model to the FINNVASC (Finland National Vascular) registry and the PREVENT models. In this study, the ability of each model to predict mortality is performed by comparing the area under the curve (AUC) for each receiver-operating characteristic curve. The AUCs for 2-year mortality derived from these studies ranged from 0.533 to 0.664, which are considered poor to good for a prediction model. Soga et al. (9) did not report an AUC for their receiver-operating characteristic curve. As can be seen in the table, many of the factors in each model are similar to each other and rely heavily on demographic and medical factors. Combining these datasets to generate a most accurate survival model would be helpful for physicians and surgeons who care for these patients.

Still, demographic and medical factors do not provide the whole story, and other factors must be taken into consideration when pondering the benefits of revascularization for CLI. For example, although the primary purpose of revascularization in patients with CLI is limb salvage, an important extended goal is the restoration of ambulation. Other important factors, such as nursing home residence, inability to leave the home, and dementia, are potent predictors of an inability to ambulate after revascularization, and should also be incorporated into the decision-making analysis (15,16). Thus, we believe appropriate decision making requires, not only an understanding of the periprocedural and intermediate-term risks for cardiovascular events, including death, and the likelihood of limb salvage, but also the impact of the procedure on sustained functional recovery, independence, and quality of life.

Soga et al. (9) have provided new information to assist in understanding intermediate-term outcomes. The challenge will be to study populations large enough to integrate patient characteristics and comorbidities with all of these outcomes together to improve clinical decision making in patients with CLI.

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**TABLE 1 Intermediate-Term Risk Prediction Models**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Points</th>
<th>FINNVASC</th>
<th>Points</th>
<th>PREVENT III</th>
<th>Points</th>
<th>BASIL</th>
</tr>
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<tbody>
<tr>
<td>Nonambulatory status</td>
<td>2</td>
<td>Diabetes mellitus</td>
<td>1</td>
<td>Dialysis</td>
<td>4</td>
<td>Tissue loss</td>
</tr>
<tr>
<td>Rutherford class</td>
<td>1.5-3.0</td>
<td>Gangrene</td>
<td>1</td>
<td>Tissue loss</td>
<td>3</td>
<td>Body mass index</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>1</td>
<td>Coronary artery disease</td>
<td>1</td>
<td>Age &gt;75 yrs</td>
<td>2</td>
<td>Creatinine</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2</td>
<td>Urgent operation</td>
<td>1</td>
<td>Coronary artery disease</td>
<td>1</td>
<td>Bollinger score</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.0-2.0</td>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.5-3.0</td>
<td>Smoking</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>2</td>
<td>Coronary artery disease</td>
<td></td>
<td>Ankle pressure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Method of use:
- Total score indicates risk
- Risk categories divided at 3 and 8 points
- Model available for download

Adapted from Moxey et al. (7) with addition of the Soga et al. data (9).

BASIL = Bypass versus Angioplasty in Severe Ischaemia of the Leg; FINNVASC = Finland National Vascular registry; PREVENT III = Prevention of Infragenual Vein Graft Failure III.


KEY WORDS amputation, critical limb ischemia, peripheral artery disease, peripheral revascularization