Tibioperoneal (Outflow Lesion) Angioplasty Can Be Used as Primary Treatment in 235 Patients With Critical Limb Ischemia

Five-Year Follow-Up

Gerald Dorros, MD; Michael R. Jaff, DO; Ari M. Dorros, MD; Lynne M. Mathiak, RN; Thomas He, PhD

Background—In a prospective, nonrandomized, consecutive series of tibioperoneal vessel angioplasty (TPVA), critical limb ischemia (CLI) patients’ data were analyzed with regard to immediate and follow-up success.

Methods and Results—TPVA was successful in 270 of 284 critically ischemic limbs (95%), with 167 limbs (59%) requiring dilatation of 333 ipsilateral inflow obstructions to access and successfully dilate 486 of 529 (92%) tibioperoneal lesions. A clinical success (relief of rest pain or improvement of lower-extremity blood flow) was attained in 270 limbs at risk (95%). Clinical 5-year follow-up of 215 of 221 successful CLI patients (97%) with 266 successfully revascularized limbs revealed that bypass surgery occurred in 8% and significant amputations in 9% of limbs; 91% of the limbs were salvaged. The cohort’s probability of survival was 56%: 58% for Fontaine class III and 33% for class IV patients. Class III compared with class IV patients had significantly ($P<0.05$) fewer surgical bypasses (3% versus 16%) and amputations: above-knee, 1% versus 4%; below-knee, 3% versus 12%; and transmetatarsal, <1% versus 21%.

Conclusions—TPVA, often in combination with inflow lesions, is an effective primary treatment for critical limb ischemia. The poor cumulative survival reflects the existence of severe comorbidities, which could potentially be affected by aggressive and effective cardiovascular diagnostic and therapeutic strategies. (Circulation. 2001;104:2057-2062.)

Key Words: angioplasty ■ peripheral vascular disease ■ surgery ■ vasculature
TABLE 1. Patient Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>All CLI Patients</th>
<th>Fontaine Class III</th>
<th>Fontaine Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>235</td>
<td>134</td>
<td>101</td>
</tr>
<tr>
<td>Female</td>
<td>73 (31)</td>
<td>39 (29)</td>
<td>34 (34)</td>
</tr>
<tr>
<td>Male</td>
<td>162 (69)</td>
<td>95 (71)</td>
<td>67 (66)</td>
</tr>
<tr>
<td>Age, y (range)</td>
<td>67 ± 9 (40–86)</td>
<td>67 ± 8 (46–83)</td>
<td>67 ± 10 (40–86)</td>
</tr>
<tr>
<td>First procedures (cases)</td>
<td>284</td>
<td>166</td>
<td>118</td>
</tr>
<tr>
<td>Comorbid state, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior MI</td>
<td>79 (28)</td>
<td>36 (22)</td>
<td>43 (36)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>95 (33)</td>
<td>57 (35)</td>
<td>38 (32)</td>
</tr>
<tr>
<td>CHF, prior</td>
<td>35 (12)</td>
<td>7 (4)</td>
<td>28 (24)</td>
</tr>
<tr>
<td>NYHA Class 3–4</td>
<td>18 (6)</td>
<td>17 (10)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Prior PV surgery</td>
<td>111 (39)</td>
<td>63 (38)</td>
<td>48 (41)</td>
</tr>
<tr>
<td>Coexistent diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>146 (51)</td>
<td>63 (38)</td>
<td>83 (70)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>180 (63)</td>
<td>103 (62)</td>
<td>77 (65)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>77 (27)</td>
<td>29 (17)</td>
<td>48 (41)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>28 (10)</td>
<td>14 (8)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>TIA</td>
<td>20 (7)</td>
<td>13 (8)</td>
<td>7 (6)</td>
</tr>
</tbody>
</table>

MI indicates myocardial infarction; CHF, congestive heart failure; PV, peripheral vascular; and TIA, transient ischemia attack.

CL1 Definitions

CLI was defined as (1) persistent, recurring rest pain requiring analgesia, and an ankle systolic pressure ≤ 50 mm Hg, and/or toe systolic pressure ≤ 30 mm Hg, and/or (2) ulceration, gangrene, or nonhealing wounds of the foot with ankle systolic pressure ≤ 50 mm Hg or toe systolic pressure ≤ 30 mm Hg. The Fontaine classification10 stratified patients as class III (rest pain) or class IV (ulceration and/or gangrene).

Results

Patient demographic data are presented in Table 1. Proximal inflow arterial occlusive disease was often necessary (59% of ischemic limbs) to permit access to diseased infrapopliteal vessels (Table 2). Dilatation was successful in all 337 inflow lesions and in 486 of 529 infrapopliteal lesions (92%); 370 of 376 stenoses (98%) and 116 of 153 occlusions (73%) (Table 3). Complications (Table 4) encountered included 20 episodes of transient contrast-induced acute renal failure (7%), 3 emergency vascular surgeries (0.7%), 1 procedurally related death (0.4%), 1 amputation after popliteal-tibial bypass (0.4%), and 1 compartment syndrome (0.4%). At hospital discharge, 221 patients demonstrated clinical improvement (Table 5), with success attained in 165 of 166 class III limbs (99%) and 105 of 118 class IV limbs (90%).

Clinical 5-year follow-up on 215 of 221 CLI patients (97%) (Table 6) with 266 successfully revascularized limbs revealed that, by use of a hierarchical stratification, bypass surgery occurred in 8% and significant amputation in 9% of limbs. The probability of survival of the cohort (Figure 1) was 56%: 58% for class III and 33% for class IV patients (Figure 2). Class III compared with class IV patients had significantly (P<0.05) fewer surgical bypasses (3% versus 16%) and amputations: above-knee 1% versus 4%, below-knee 3% versus 12%, and transmetatarsal <1% versus 21%. Thus, salvage was attained in 91% of ischemic limbs. The event-free 5-year survival (freedom from death and any repeat vascular procedures) was 31% for the entire cohort (class III, 43% versus class IV, 26%; P<0.05).

Discussion

The definition, pathophysiology, clinical presentation, and sequelae of CLI all may seem intuitively obvious. For these TPVA data to have meaning in attempts to assess their place next to historical data, however, requires an appreciation of the various definitions and their distinctions so as to provide a frame of reference.

CL1 Definitions

Although the definitions of CLI vary within the surgical literature, they all are relatively consistent with the definitions used here. The International Vascular Symposium Working Party14 defined severe rest pain as that which required opiate analgesia for ≥ 4 weeks, and either ankle pressure < 40 mm Hg or ankle pressure < 60 mm Hg in the presence of tissue necrosis or digital gangrene. The Modified International Vascular Symposium Working Party11 defined severe rest pain as that which required opiate analgesia for ≥ 4 weeks and either an ankle pressure < 40 mm Hg or tissue necrosis or...
digital gangrene. The First European Working Group defined severe rest pain as that requiring opiate analgesia for $2$ weeks, or ulceration or gangrene, or ankle pressures $<50$ mm Hg. The Second European Consensus Document defined persistently recurring ischemic rest pain as that which required analgesia for $>2$ weeks and an ankle systolic pressure $<50$ mm Hg, and/or a toe systolic pressure $<30$ mm Hg, or ulceration or gangrene of the foot or toes and an ankle systolic pressure $<50$ mm Hg, or toe systolic pressure $<30$ mm Hg.

**Surgical Approaches**

Femoropopliteal arterial reconstruction for infrainguinal peripheral arterial occlusive disease has better immediate and long-term results in patients with claudication than in those with CLI, and elective bypass surgery to the distal tibial vessels for intermittent claudication has had poor results. Thus, tibial artery bypass surgery to achieve revascularization distal to infrapopliteal obstructions has been reserved for selected CLI patients except in the presence of life-threatening sepsis (until resolved), flexion contractures or paralysis, patients with serious comorbid medical conditions, or patients with markedly reduced life expectancy. Although data on distal bypasses have not been encouraging, Veith and colleagues improved their distal bypass results by using innovative and creative techniques, which resulted in a dramatic decrease in their procedure-related amputation rates (49% to 14%). Their distal bypass procedures, however, had a coincident 30-day mortality of 4% and 90-day graft failure rates of nearly 5%. These data became the standard of care, with success defined as clinical improvement with resolution of rest pain. Yet, the problems of worsening graft patency as a result of distal anastomoses to small diseased vessels, diffuse distal arterial occlusive disease producing poor runoff (outflow), grafts crossing a joint, or graft composition (vein versus synthetic material) make the use of percutaneous interventions even more attractive.

Curiously, not all patients whose first graft occluded required a second operation. Interestingly, the limb did not usually become rethreatened despite the original graft occlusion, and the wound did not recur after having healed. Such observations could be interpreted as indicating “surgical failure.” If the therapeutic aim were to have a patent vessel, however, then graft closures would represent failure, but if the goal were to relieve rest pain or enable wound healing, then despite graft closure the procedure was successful. If this observation were extended to angioplasty, then lesion recurrence or restenosis might not be a major issue if the rest pain were no longer present or wound healing had occurred.

**Surgical Results**

Published longitudinal surgical data provided perspective to the usefulness of these TPVA data; 5 series will be detailed to show the similarities between the surgical and angioplasty data. A 2-year follow-up by the Italian census office of 522 CLI patients (394 men, 76%) detailed demographics of hypertension in 303 (58%), diabetes mellitus in 157 (30%), previous revascularization procedures in 113 (22%), prior myocardial infarction in 98 (19%), previous strokes in 54 (10%), and a lower limb amputation (30 [6%] major and 22 [4%] minor) in 52 (10%). Presenting symptoms included intermittent claudication in 449 patients (86%), rest pain in 200 (38%), and ischemic ulcers or gangrene in 322 (62%). This cohort’s ABI revealed that 4% had an ABI $>0.75$; 6% an ABI $0.51$ to $0.75$; 61% an ABI $0.25$ to $0.50$; and 22% an ABI $<0.25$. Thus, the ABI was often not specific to severe ischemia. In the hospital, 232 patients (44%) had a revascularization procedure and 49 (10%) amputation (30 [6%]

<table>
<thead>
<tr>
<th>Significant Procedural Complications</th>
<th>CLI</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In-hospital deaths</strong></td>
<td>2 (0.7)</td>
<td>0</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td><strong>Procedurally related</strong></td>
<td>1 (0.4)</td>
<td>0</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Emergency vascular surgery</strong></td>
<td>3 (1)</td>
<td>2 (1)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Arterial access repair</strong></td>
<td>2 (0.7)</td>
<td>2 (1)</td>
<td>...</td>
</tr>
<tr>
<td><strong>Bypass</strong></td>
<td>0</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td><strong>Amputation</strong></td>
<td>1 (0.4)</td>
<td>...</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Major infection</strong></td>
<td>1 (0.4)</td>
<td>1 (1)</td>
<td>...</td>
</tr>
<tr>
<td><strong>Compartment syndrome</strong></td>
<td>1 (0.4)</td>
<td>...</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Acute renal failure</strong></td>
<td>20 (7.0)</td>
<td>5 (3)</td>
<td>15 (13)</td>
</tr>
<tr>
<td><strong>Transfusion</strong></td>
<td>1 (0.4)</td>
<td>1 (1)</td>
<td>...</td>
</tr>
</tbody>
</table>

*Amputation followed failed popliteal-tibial graft.*
major and 22 [4%] minor), and after the procedure, 6 (1%) had a myocardial infarction and 8 (2%) had a stroke. During the first year of follow-up, 121 patients (22%) died: 44 (36%) of cardiovascular, 8 (7%) of nonvascular, and 69 (57%) of unknown causes. At 2 years, 30 patients had been lost to follow-up, and 44 of the remaining 401 patients had died (5.5% annualized mortality), with 13 (30%) of cardiovascular, 6 (14%) of nonvascular, and 25 (57%) of unknown causes; their cumulative probability of survival was 68%. Furthermore, data stratification demonstrated significant differences: a 22% mortality for patients 70 years old versus 42% for patients ≥70 years old; a 29% mortality for men versus 44% for women; a 53% mortality if the patient had a major amputation (53%) versus 30% if no major amputation occurred; a 28% mortality for Fontaine class III versus 55% for class IV patients; and a 37% mortality for diabetic versus 31% for nondiabetic patients. The independent 2-year mortality predictors were age ≥70 years (RR 1.93), prior stroke (RR 1.82), and major amputation (RR 1.90). These data are similar to the TPVA data shown here.

Holdsworth and McCollum’s 3-year follow-up of 275 patients (116 women [51%]; mean age 72 years) with severe lower-limb ischemia involving 275 ischemic limbs revealed that rest pain was the clinical presentation in 168 limbs (61%), ulceration in 56 (20%), and gangrene in 51 (19%). Bilateral occlusive severe peripheral vascular disease was common, with 25 patients (11%) having had a previous contralateral limb amputation. The recorded ABIs were 0.40 in 158 patients (66%), 0.50 in 183 (74%), but ≥0.50 in 62 (26%), which again confirms the lack of specificity of the ABI. The therapeutic strategies included arterial reconstruction in 235 limbs (86%), primary amputation in 19 (7%), digital amputation in 6 (2%), and conservative management of 15 (6%). During the 3-year follow-up period, 100 patients

### TABLE 5. TPVA: Discharge Data

<table>
<thead>
<tr>
<th>Length of stay,* d</th>
<th>CLI</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital (range)†</td>
<td>5.6±5.0 (1–29)</td>
<td>4.8±3.9 (2–26)</td>
<td>8.1±6.5 (1–29)</td>
</tr>
<tr>
<td>Procedure to discharge (range)</td>
<td>4.1±3.9 (1–28)</td>
<td>3.5±3.5 (1–25)</td>
<td>5.9±5.0 (1–25)</td>
</tr>
</tbody>
</table>

**Clinical status, n (%)**

- Improved: 221 (94), 133 (99), 88 (87)
- Unchanged: 9 (4), <1 (1), 8 (8)
- Worse: 3 (1), 0, 3 (3)
- Deceased: 2 (0.8), 0, 2 (2)
- Procedure-related: 1 (0.4), 0, 1 (1)

**Successful cases, n (%)**

- 270/284 (94) | 165/166 (99) | 105/118 (90)

*284 class III/IV cases.
†No outliers >30 days.

### TABLE 6. TPVA: 5-Year Clinical Follow-up

<table>
<thead>
<tr>
<th>All Patients</th>
<th>Class III</th>
<th>Class IV</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n (%)</td>
<td>215</td>
<td>128 (60%)</td>
<td>87 (40%)</td>
</tr>
<tr>
<td>Limbs, n (%)</td>
<td>266</td>
<td>160 (60%)</td>
<td>106 (40%)</td>
</tr>
<tr>
<td>Age, y</td>
<td>67±9 (37–86)</td>
<td>68±8 (46–83)</td>
<td>67±10 (37–86)</td>
</tr>
<tr>
<td>Mean follow-up, mo</td>
<td>34±33</td>
<td>39±34</td>
<td>30±30</td>
</tr>
</tbody>
</table>

**Adverse events, n (%)**

- Bypass: 21 (8), 4 (3), 17 (16) <0.05
- AKA: 5 (2), 1 (1) <0.05
- BKA: 18 (7), 5 (3), 13 (12) <0.05
- Transmetatarsal: 23 (9), 1 (<1) 22 (21)

**Survival, %**

- 1 year: 90, 94, 75 <0.05
- 2 years: 86, 89, 60 <0.05
- 3 years: 78, 79, 41 <0.05
- 4 years: 63, 69, 37 <0.05
- 5 years: 56, 58, 33 <0.05
- Event-free survival* 31 43 26 <0.05

Bypass indicates femoropopliteal or popliteal-tibial; AKA, above-knee amputation; BKA, below-knee amputation; and transmetatarsal, transmetatarsal amputation.

*AKA, BKA, transmetatarsal: percentages refer to limbs, not patients.
had died (19 [8%] within 30 days of presentation, and 21 within 30 days of reconstruction [perioperative mortality of 10%]). The cumulative probability of survival was 69% at 1 year, 58% at 2 years, and 48% at 3 years, with causes of death not detailed. The cumulative probability of limb salvage was 94% at 30 days, 83% at 1 year, 73% at 2 years, and 68% at 3 years. Again, these data are comparable to those of TPVA.

Meyers et al^{23} reported on the survival after surgical treatment of 411 patients (249 men [60%]) with 468 severely ischemic limbs: one leg was ischemic in 354 patients and both legs in 57 patients. Surgical procedures included 273 reconstructions, 195 sympathectomies, and 128 amputations (27 primary and 101 after a failed reconstruction or sympathectomy). The operative mortality rates were significant: 5% (27 primary and 101 after a failed reconstruction or sympathectomy). The cumulative probability of limb salvage was 94% at 30 days, 83% at 1 year, 73% at 2 years, and 68% at 3 years. Again, these data are comparable to those of TPVA.

Wolfe and Wyatt’s^{24} collation of 20 lower-leg ischemia publications on 6118 patients stratified these patients into a low-risk cohort (4089 patients) (rest pain and ankle pressure >40 mm Hg) and a high-risk cohort (2029 patients) (rest pain and tissue loss [with or without ankle pressure <40 mm Hg]). The cumulative probability of survival for the entire group was 74% at 1 year, 58% at 2 years, 56% at 3 years, 48% at 4 years, and 44% for 5 years. At 1 year, if conservative treatments were used, 73% of the low-risk patients and 95% of the high-risk patients had lost their limb. When arterial reconstruction was performed on this high-risk group, the outcome resulted in a major amputation in 25%, and 26% of this group would be dead no matter what the treatment.

Finally, a 69-site European registry^{25} followed up 574 patients (431 men, 75%; mean age 71 years), of whom 485 (87.5%) had rest pain and 352 (64%) had ulcers or gangrene. Surgical management included arterial reconstruction in 195 (34%) and sympathectomy in 55 (10%); a major amputation was necessary in 53 patients (9%), a minor amputation in 30 patients (5%), thromboendarterectomy in 44 (8%), angioplasty in 41 (7%), and epidural spinal electrostimulation in 22 (4%). At the 3-month follow-up, 50 patients had died (9%), and 286 patients (50%) were alive, had no ischemic limb, and had not endured any major cardiovascular event; 103 patients (18%) were alive but had persistent CLI, 70 patients (12%) were alive but had endured a major amputation, and 9 patients (2%) were alive but had suffered an infarction or stroke and still had persistent limb ischemia. Thus, surgical reconstruction can be achieved in patients with CLI, but at the cost of significant morbidity and mortality.

**Angioplasty Results**

These TPVA data demonstrate revascularization success rates (94%) similar if not superior to those in recent publications.26–31 These studies must be looked at carefully, however, because the definitions of CLI were often indistinct. Not unexpectedly, TPV disease was often (59% of limbs) preceded by inflow lesion angioplasty so as to gain access to the obstructed tibioperoneal vessels. The patients of Lofberg et al^{31} required this approach in 55 of 94 procedures (59%). The successful inflow lesion angioplasty markedly improved the distal perfusion pressure (as would be attained by femoropopliteal bypass), but in addition, the distal perfusion pressure in the ischemic foot was enhanced by angioplasty of the outflow lesion, not readily achieved with surgery. At 5-year follow-up, 91% of limbs were salvaged, which is significantly higher than and in sharp contrast to those reported, because follow-up extended for 2 years (89%,26 49%,27 80%,28 87%,29), and rarely 3 years (87%,26 72%,28). The 5-year survival statistics were sobering, with only a 56% survival, and these values were supported by the 76% 2-year^{26} and the 75% 3-year^{30} survivals. These TPVA data, with similar patient demographics, and the impressive procedural success demonstrate that this interventional technique is an important therapeutic option. The TPVA procedural and follow-up results were superior to those of the historical surgical series; the differences in endovascular and surgical survival rates, however, are even more dramatic when the surgical procedural operative mortality is considered. Endovascular procedures offer a significant alternative to surgical procedures.

**Conclusions**

Endovascular therapy has an important and definitive role for patients with infrapopliteal arterial occlusive disease and CLI by easily revascularizing inflow and outflow lesions with minimal morbidity and mortality, which significantly improved distal extremity perfusion pressure. This more complete restoration of blood flow than can be attained by bypass surgery in the presence of the outflow lesions resulted in immediate relief of rest pain and enhancement of wound healing, often in conjunction with transmetatarsal amputation. TPVA produced improved patient outcomes, and the 5-year follow-up data showed that the need for subsequent surgical bypass or amputation was acceptable considering the

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**Figure 1.** Actuarial analysis of CLI patient.

**Figure 2.** Actuarial analysis of CLI patients stratified into Fontaine class III and IV cohorts.
patient populations. Although the survival statistics were sobering, they direct us toward the need for much more aggressive diagnostic and therapeutic approaches for these patients. These patients have advanced, diffuse coronary heart and/or cerebrovascular disease. This issue requires our immediate attention. This communication raises other issues that must be addressed: is stent-supported angioplasty with or without adjunctive use of glycoprotein inhibitors superior to balloon angioplasty? Does brachytherapy have a therapeutic role, especially with regard to restenosis? These data, however, provide evidence that angioplasty is the primary therapy for patients with CLI.

Acknowledgments

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References

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