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A comparison of percutaneous transluminal angioplasty versus amputation for critical limb ischemia in patients unsuitable for open surgery

Spence M. Taylor, MD, Corey A. Kalbaugh, MS, Dawn W. Blackhurst, DrPH, Dwight C. Kellicut, MD, Eugene M. Langan III, MD, and **Jerry R. Youkey, MD,** *Greenville, SC*

Background: **Percutaneous transluminal angioplasty (PTA), although not the traditional therapy, seems to be a safe alternative for patients with critical limb ischemia who are believed to be unsuitable candidates for open surgery. However, the efficacy of PTA in this setting has not been analyzed. The purpose of this study was to compare the outcomes of PTA for limb salvage with outcomes of major limb amputation in physiologically impaired patients believed to be unsuitable for open surgery.**

Methods: **From a prospective vascular registry, 314 patients (183 underwent amputation, and 131 underwent complex PTA for limb salvage) were identified as physiologically impaired or unsuitable for open surgery. This was defined as having at least one of the following: functional impairment (homebound ambulatory or transfer only), mental impairment (dementia), or medical impairment (two of the following: end-stage renal disease, coronary artery disease, and chronic obstructive pulmonary disease). Patients undergoing PTA were compared with patients undergoing amputation by examining the outcome parameters of survival, maintenance of ambulation, and maintenance of independent living status. Parameters were assessed by using Kaplan-Meier life-table curves (log-rank test and 95% confidence intervals [CIs]) and hazard ratios (HRs) from the Cox model.**

Results: **PTA resulted in a 12-month limb salvage rate of 63%. Thirty-day mortality was 4.4% for the amputation group and 3.8% for the PTA group. After adjustment for age, race, diabetes, prior vascular procedure, dementia, and baseline functional status, PTA patients had significantly lower rates of ambulation failure (HR, 0.44; *P* = .0002) and loss of independence (HR, 0.53; *P* = .025) but had significantly higher mortality (HR, 1.62; *P* = .006) than amputees. However, when life tables were examined, the maintenance of ambulation advantage lasted only 12 months (PTA, 68.6%; 95% CI, 59.6%-77.7%; amputation, 48%; 95% CI, 40.4%-55.5%) and was not statistically significant at 2 years (62.2% [95% CI, 48.8%-71.5%] and 44% [95% CI, 35.8%-52.2%], respectively). Maintenance of independent living status advantage lasted only 3 months, with no statistically significant difference at 2 years (PTA, 60.5%; 95% CI, 45.4%-75.6%; amputation, 52.6%; 95% CI, 40.4%-64.9%). Although mortality was high in both cohorts, patients who underwent amputation had a survival advantage for all time intervals examined (at 2 years: PTA, 29%; 95% CI, 19.9%-38.1%; amputation, 48.1%; 95% CI, 39.2%-56.9%).**

Conclusions: **Patients who present with critical limb ischemia and physiologic impairments that preclude open surgery seem to have comorbidities that blunt any functional advantage achieved after PTA for limb salvage. PTA in this setting affords very little benefit compared with amputation alone. (J Vasc Surg 2007;45:304-11.)**

As the population ages, the overall physiologic condition of patients presenting with critical limb ischemia (CLI) will undoubtedly become more debilitated. Consequently, the degree of physiological impairment will influence the type of treatment offered. Patients who are bedridden and nonambulatory will continue to receive expectant therapy and primary limb amputation when necessary. Patients with milder physiologic impairment, capable of realizing benefit from limb salvage, will most likely receive the preferred procedure for multisegmental arterial disease: open surgical bypass. However, there is a growing number of patients who, although functional, are significantly debilitated and have substantial physiologic impairment. Despite the presence of CLI, these patients possess physical debilities that most vascular surgeons would consider contraindications to open bypass surgery. Examples include patients who present with multiple medical comorbidities and limited life expectancy; patients with minimal ambulatory capability, who function independently by using their limbs for short distance walking or for transfer but depend on a wheelchair for the activities of daily living; and patients who have functional dementia but do not require institutionalization. These individuals pose a dilemma to the practicing vascular surgeon. If left untreated, the CLI will most likely progress to limb loss and further disability.[1] However, these patients usually do not have the physiologic reserve for meaningful functional recovery after open surgical bypass even when it is technically successful. Although this is a subjective judgment, these patients are believed to be too sick for a large operation and are, simply stated, unsuitable for open surgery.

From the Academic Department of Surgery, Greenville Hospital System University Medical Center.

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Reprint requests: Spence M. Taylor, MD, Academic Department of Surgery, Greenville Hospital System University Medical Center, 701 Grove Rd, Greenville, SC 29605 (e-mail: staylor2@ghs.org).

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Percutaneous treatment of peripheral arterial disease has gained increasing acceptance as an alternative to open bypass in various clinical situations. For example, most would consider the initial best interventional treatment for claudication to be percutaneous transluminal angioplasty (PTA) if technically feasible.[2] Indeed, some have advocated angioplasty as an acceptable treatment for certain cases of CLI.[3-14] The most obvious advantage to this minimally invasive therapy is the low morbidity and mortality associated with treatment.[3,15,16] Considering this, peripheral angioplasty would seem a logical alternative for the aforementioned patient group with CLI who are unsuitable for open bypass. Most of these patients are capable of surviving an angioplasty procedure. Furthermore, the poor long-term patency of angioplasty when used for CLI usually has little relevance to these patients. Consequently, clinical expectations in these cases are limited, and success is usually measured as the ability to improve peripheral circulation enough to allow healing and limb salvage. Goals are generally geared toward maintaining the functional status quo. Angioplasty creates no leg incisions that might jeopardize the level of subsequent limb amputation, and thus this would seem to be a no-lose proposition for patients with amenable arterial lesions. Despite this logic, it can be argued that peripheral angioplasty is an expensive modality in a financially failing health care system and that it should be used only if clinical benefit can be demonstrated. In reality, functional benefit after treatment with PTA for limb salvage in debilitated patients believed unsuitable for open surgery has not been examined. Therefore, the purpose of this study was to answer this clinical question: When a patient with CLI is judged unsuitable for open surgery, will he/she alternatively achieve functional benefit from a treatment strategy using PTA and aggressive wound management to attain limb salvage?

METHODS

To examine the proposed study question, we retrospectively identified a group of patients who were deemed unsuitable for open surgery and who underwent PTA of the lower extremities for CLI. To measure the success of this treatment, the functional outcomes of these patients were compared with those of a cohort of medically and physiologically impaired patients who had undergone primary major limb amputation consequent to CLI without vascular intervention before amputation. Functional end points measured included survival and postoperative maintenance of ambulatory and independent living status as compared with the preoperative state.

The lower extremity database and data collection process. Since 1992, a prospective vascular registry of all cases performed on the Vascular Surgery Service at Greenville Hospital System University Medical Center has been maintained. However, since 1998, the year our endovascular program was initiated, a subset of patients with lower extremity peripheral arterial disease has been closely followed up with Institutional Review Committee approval. Each procedure is entered on an Excel spreadsheet (Microsoft Corp, Redmond, Wash). Preoperative demographics are obtained at presentation and entered into the database. Functional information (ambulatory status and living situation) are also included. Follow-up information has been recorded at each postprocedure visit. The type of treatment (PTA, open bypass, or amputation) is left to the judgment of the treating physician. For patients receiving open infrainguinal bypass, minimum follow-up consists of noninvasive duplex scan–derived graft flow velocities at 1 month, every 3 months for the first 18 months, and then every 6 months thereafter. Patients with endovascular intervention are followed up at a minimum with a patient visit and a noninvasive vascular study at 1 month and then at 6-month intervals thereafter. The database (to include functional information) is updated at each visit. Also, the database has been scrutinized each summer by independent research workers completing missing data points (especially with amputees) or missing patients. Sources used to attain follow-up include the hospital computerized Lifetime Clinical Record, the computerized radiology Picture Archiving Communication System (PACS), and the online obituary services of all statewide newspapers.

To date, more than 1700 revascularizations and 700 major lower extremity amputations have been entered into the database, and patients have been followed up for functional outcome and living status. All endovascular procedures entered into the registry were performed by vascular surgeons or an interventional-trained vascular internist. Using the above-described database, we identified 314 patients with CLI (rest pain or tissue loss with an ankle pressure <50-70 mm Hg or toe pressure <30-50 mm Hg) who were medically, functionally, or mentally unsuitable for open vascular surgery and who underwent either PTA or major limb amputation. For the purpose of this study, all surgically unsuitable patients were defined as (1) medically impaired (at least two of the following active clinical diagnoses: dialysis-dependent end-stage renal disease and/or high-risk coronary artery disease as defined by the Eagle criteria[17] and/or clinically treated chronic obstructive pulmonary disease), (2) functionally impaired (homebound ambulatory [defined as being able to walk around the home with assistance but unable to actively walk outside the home] or nonambulatory transfer only [defined as using the lower extremities to help transfer from wheelchair to bed or wheelchair to commode only]), or (3) mentally impaired (defined as having clinical dementia not requiring institutionalization). In our database, independent living status is classified as independent (able to perform activities of daily living without assistance, whether it be in an independent domicile or in an assisted-living environment) or nonindependent. Ambulatory status is classified as ambulatory out of home, homebound ambulatory, nonambulatory transfer only, or bedridden. When considering the functional state before surgery, the status was graded as according to baseline ambulatory classification before the onset of ischemia. Impaired functional status was, therefore, usually a consequence of pre-existing chronic medical conditions such as arthritis or advanced age and not that of acute-on-chronic foot ischemia. For the purpose of this study, all patients who were bedridden and nonindependent at initial presentation were excluded from analysis. With these definitions, there were 63 medically impaired patients (amputation, n = 34; PTA, n = 29), 226 functionally impaired patients (amputation, n = 119; PTA, n = 107), and 129 mentally impaired patients (amputation, n = 90; PTA, n = 39). Multiple causes of impairment were present in 104 patients.

Of the 314 patients, 183 underwent 206 major limb amputations (90 above-knee amputations, 6 through-knee amputations, 64 below-knee amputations, and 23 bilateral amputations), and 131 underwent PTA of 148 lower extremities for limb salvage. Of the procedures performed, 47 were performed on the aortoiliac vessels, and 101 were performed on the infrainguinal vessels. The pattern of aortoiliac occlusive disease treated was classified as Trans-Atlantic Inter-Society Consensus (TASC) A or B (n = 32) and TASC C or D (n = 15). The pattern of infrainguinal occlusive disease treated was classified as TASC A or B (n = 44) and TASC C or D (n = 57). Primary stents were generally used in cases for which stand-alone angioplasty resulted in arterial dissection or residual stenosis and a measurable pressure gradient. All 206 amputees experienced successful clinical healing of their amputation site, and all 148 angioplasty procedures were believed to be technically successful (defined as an adequate cosmetic result at the end of treatment and either an increase of at least 0.15 in posttreatment ankle-brachial index or an increase in great toe pressure of at least 15 mm Hg). A demographic comparison of amputees vs patients undergoing endovascular PTA is shown in the Table.

For the purpose of this study, preoperative ambulatory and independent living status were compared with postoperative ambulatory and independent living status. Deterioration in ambulatory status was defined as a change from the preoperative ambulatory classification (ie, from ambulatory out of home to homebound ambulatory or to nonambulatory transfer only). Similarly, deterioration in independent living status was defined as a permanent change in status from living independently to living nonindependently. Temporary admission to an assisted living or a rehabilitation facility for the purpose of recovery was not counted as deterioration in living status. Within the 314-patient cohort, there were individuals who were classified as nonindependent but ambulatory before intervention or amputation (n = 98; 76 who underwent amputation and 22 who underwent PTA). These patients were included in the analysis for survival and maintenance of ambulatory status after treatment but were excluded in the analysis for maintenance of independent living status.

Statistical analysis. Kaplan-Meier survival curves were used to assess limb salvage, survival, maintenance of ambulatory status, and maintenance of independent living status over time. The proportional hazards assumption was tested for each plot and found to be appropriate. The log-rank test was used to assess differences in the curves between the two study groups, which also underwent variable adjustment (age, race, presence of diabetes, prior vascular procedure, dementia, and baseline functional status) by using a Cox proportional hazards model. Hazard ratios (HRs) and 95% confidence intervals from the final model were used to describe the time risk. All analyses were conducted by using SAS software (version 8; SAS Institute, Cary, NC). *P* values <.05 were considered indicative of statistical significance.

Table. A demographic comparison of 314 patients unsuitable for open surgery who underwent either PTA or primary amputation for critical limb ischemia

Variable	*Amputation (n = 183)*	*PTA (n = 131)*	P *value*
Age (y)			
<65	68 (37.2)	20 (15.3)	
65-79	75 (41.0)	63 (48.1)	<.0001*
≥80	40 (21.8)	48 (36.6)	
Sex			
Male	99 (54.1)	69 (52.7)	.8027
Female	84 (45.9)	62 (47.3)	
Race			
White	118 (64.5)	101 (77.1)	.0164*
Black/Hispanic	65 (35.5)	30 (22.9)	
Diabetes mellitus			
No	53 (29.0)	52 (39.7)	.0468*
Yes	130 (71.0)	79 (60.3)	
Smoke			
No	79 (43.2)	52 (39.7)	.5381
Yes	104 (56.8)	79 (60.3)	
ESRD			
No	108 (59.0)	83 (63.4)	.4370
Yes	75 (41.0)	48 (36.6)	
Prior vascular procedure			
No	80 (43.7)	92 (70.2)	<.0001*
Yes	103 (56.3)	39 (29.8)	
Living status			
Independent	107 (58.5)	109 (83.2)	<.0001*
Nonindependent	76 (41.5)	22 (16.8)	
CAD			
No	69 (37.7)	40 (30.5)	.1881
Yes	114 (62.3)	91 (69.5)	
Dementia			
No	93 (50.8)	92 (70.2)	.0006*
Yes	90 (49.2)	39 (29.8)	
Functional			
Ambulatory	64 (35.0)	24 (18.3)	.0012*
Impaired	119 (65.0)	107 (81.7)	
Medical impairment			
No	149 (81.4)	102 (77.9)	.4376
Yes	34 (18.6)	29 (22.1)	
Single impairment	130 (71.0)	93 (71.0)	.9929
Multiple Impairments	53 (29.0)	38 (29.0)	

PTA, Percutaneous transluminal angioplasty; *ESRD,* end-stage renal disease; *CAD,* coronary artery disease.
Factors significantly associated with treatment were age, race, diabetes mellitus, prior vasc procedure, preoperative living status, dementia, and preoperative functional status.

RESULTS

Follow-up was complete for all 314 patients (amputation group: median, 283 days; average, 459 days; PTA group: mean, 311 days; median, 386 days). The 30-day mortality was 4.4% for the amputation group and 3.8% for

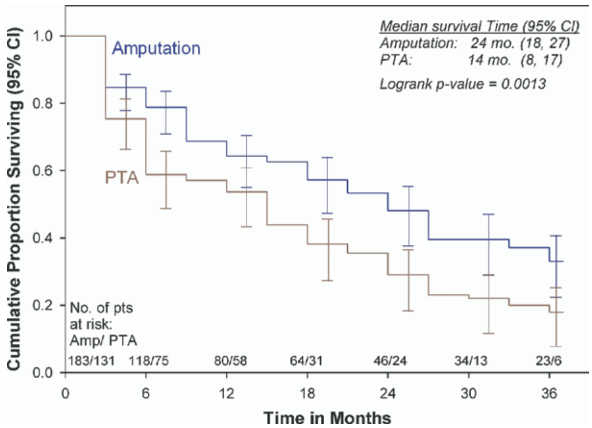

Fig 1. A survival comparison of 314 patients unsuitable for open surgery who underwent percutaneous transluminal angioplasty *(PTA)* or primary amputation *(amp)* for critical limb ischemia. *CI,* Confidence interval.

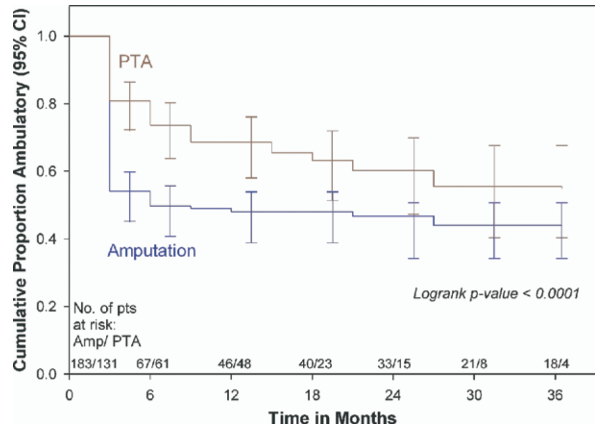

Fig 2. A comparison of maintenance of ambulation in 314 patients unsuitable for open surgery who underwent percutaneous transluminal angioplasty *(PTA)* or primary amputation *(Amp)* for critical limb ischemia. *CI,* Confidence interval.

the PTA group. PTA along with appropriate wound and foot care was associated with a 63% 12-month limb salvage rate as determined by Kaplan-Meier life-table analysis. Overall, 42 patients (6 ambulatory out of home, 28 homebound ambulatory, and 8 nonambulatory transfer only) in the PTA group subsequently received a major limb amputation at some point during the study. Five of these patients ambulated with the use of a prosthetic device after surgery. Figures 1, 2, and 3 show comparisons by using Kaplan-Meier life-table analysis of amputation vs PTA for overall survival, maintenance of ambulatory status, and maintenance of independent living status, respectively. There was a statistically significant survival advantage for patients undergoing major limb amputation when compared with patients receiving PTA (48% vs 29% at 24 months; log-rank; $P = .0013$). The median survival time for patients undergoing amputation was 24 months, compared with 14 months for those undergoing PTA. There was a statistically significant advantage in maintenance of ambulatory status for patients undergoing PTA when compared with patients receiving major limb amputation (60.2% vs 44% at 24 months; log-rank; $P < .0001$). Likewise, there was a statistically significant advantage in maintenance of independent living status for patients undergoing PTA when compared with patients receiving major limb amputation (60.5% vs 52.6% at 24 months; log-rank; $P = .046$).

When stratifying the type of treatment (amputation vs PTA) by the type of physiologic impairment (functional impairment vs medical impairment vs mental impairment), functionally and mentally impaired amputees demonstrated a survival advantage when compared with PTA patients (44.4% vs 30.1% at 24 months [log-rank; $P = .0203$] and 47.5% vs 36.7% at 24 months [log-rank; $P = .0140$], respectively). However, there was no statistically significant survival advantage for either treatment group for medically impaired patients (62.6% [amputation] vs 51.7% [PTA] at 24 months; log-rank; $P = .0668$). Although functionally

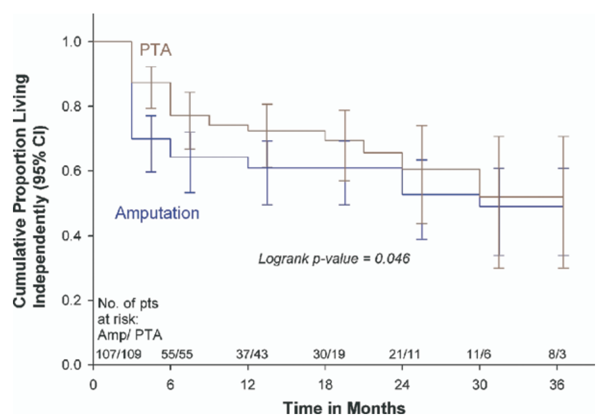

Fig 3. A comparison of maintenance of independent living in 314 patients unsuitable for open surgery who underwent percutaneous transluminal angioplasty *(PTA)* or primary amputation *(Amp)* for critical limb ischemia. *CI,* Confidence interval.

impaired PTA patients demonstrated an advantage in maintenance of ambulatory status compared with amputees (60.8% vs 44.4% at 24 months; log-rank; $P = .0003$), there was no statistically significant advantage in maintenance of ambulation for medically (43% [amputation] vs 58.2% [PTA] at 12 months; log-rank; $P = .1463$) or mentally (43.5% [amputation] vs 54.5% [PTA] at 24 months; log-rank; $P = .0625$) impaired patients. Likewise, although functionally impaired PTA patients demonstrated an advantage in maintenance of independent living status compared with amputees (59.9% vs 42.1% at 24 months; log-rank; $P = .0043$), there was no statistically significant advantage in maintenance of independence for medically (57.1% [amputation] vs 67.1 [PTA] at 12 months; log-rank; $P = .5618$) or mentally (62.1% [amputation] vs 50.9% [PTA] at 12 months; log-rank; $P = .4794$) impaired patients.

As shown in the Table, there is a great deal of heterogeneity in the demographics of patients grouped by treatment (amputation vs PTA). Considering this, Cox proportional hazards models were used to adjust the treatment outcomes for age, race, diabetes mellitus, prior vascular intervention, dementia, and baseline functional status. After adjustment, the type of treatment was the most consistent predictor of outcome and was statistically significant for every outcome parameter measured. PTA was the only independent predictor of mortality (HR, 1.62; $P = .0064$). Diabetes mellitus and type of treatment were the only statistically significantly independent predictors of ambulation deterioration. In the latter case, PTA patients had significantly lower rates of ambulatory failure (HR, 0.44; $P = .0002$) when compared with patients undergoing amputation. The presence of dementia, impaired preoperative functional status, and type of treatment were all statistically significant independent predictors of living status deterioration. Regarding treatment, PTA patients had significantly lower rates of living status deterioration (HR, 0.53; $P = .0245$) compared with patients undergoing amputation.

Finally, a Kaplan-Meier comparison of cumulative survival, cumulative maintenance of ambulation, and cumulative maintenance of independent living status rates showed that, although there was an advantage in maintenance of ambulatory status and maintenance of independent living status in the patient group treated with PTA, the increment of benefit was quite modest. When considering maintenance of ambulation, the benefit derived from PTA lasted only 12 months (Fig 2), and when considering maintenance of independent living status, the benefit derived from PTA lasted only 3 months (Fig 3). After 1 year, the two treatments seemed to have equivalent outcomes. In contrast, these short-lived benefits of functional outcome with PTA seemed to be offset by a more sustained clinical survival disadvantage for patients undergoing percutaneous treatment and aggressive limb salvage (Fig 1).

DISCUSSION

There is a growing body of literature advocating an expanded role for PTA in the treatment of CLI.[3-14] Most of the studies report small numbers of patients who, for usually technical reasons, are not candidates for open surgery. Patients usually are cited as having no distal arterial targets for bypass or no veins for a conduit. The end points of success are typically quite broad and include healing of ischemic ulcers, resolution of rest pain, improvement of the ankle-brachial index, or healing of a minor amputation site. One contemporary series recently reported data by using the reporting standards of the Society for Vascular Surgery and the International Society for Cardiovascular Surgery in which patency data and limb salvage were measured.[5] In summarizing the reported data, limb salvage and, more commonly "clinical success rates" ranged from 55% to 90%. It is interesting to note that in essentially every report, historical controls are implied.[3-6,8-11,13] The clinical outcomes achieved with PTA are typically compared with the expected results after bypass. The conclusions are fairly consistent. Each report usually concedes that although outcomes are not as good as those with surgical bypass, they are usually better than expected and are certainly better than doing nothing. What is implied in "doing nothing" is, of course, primary limb amputation. The limitations of all of these studies are the same. The patients included in the trials are usually heterogeneous, and the clinical successes, when they occur, are generally attributed to the treatment by PTA. In reality, because the studies usually have no real controls, successes may occur with simple medical management alone and no PTA. Most of the reports also imply, again with no proof, that the outcomes reported are superior to outcomes that occur after major limb amputation.

Our study made no such assumptions. It looked at PTA in patients with CLI determined to be unsuitable for open surgery and measured meaningful functional outcomes: survival, the ability to maintain preoperative ambulation status, and the ability to maintain preoperative independent living status. These end points were chosen because they could be measured against outcomes of doing nothing—namely, primary amputation. In trying to answer a simple, but important, question—does PTA benefit patients with CLI who are unsuitable for open bypass?—we objectively defined characteristics that most would accept as being consistent with surgical unsuitability and then retrospectively studied functional outcomes from our prospective database after treatment. Despite being able to salvage most limbs, we found 3-year maintenance of ambulatory status and maintenance of independent living status to be 55% and 51%, respectively. Survival was a sobering 18% at 36 months. To provide a frame of reference, we compared these data not with outcomes achieved from a comparable cohort of medically and physiologically impaired patients after successful bypass, but with a similar population that underwent primary major limb amputation. As might have been anticipated, we found that after adjusting for demographic differences in the populations, patients treated with PTA had superior rates for maintenance of ambulation and independent living status compared with amputees. What was not anticipated was that these advantages were very short lived: only 3 months for maintenance of independence and 1 year for maintenance of ambulation. Taking a critical perspective, therefore, it can be concluded that after 1 year, PTA used to attempt limb salvage afforded no more functional benefit than primary limb amputation alone. Given these findings, the treatments after 1 year seem to be equivalent.

However, an additional unanticipated finding occurred: patients who underwent PTA and treatment for aggressive limb salvage experienced a significant survival disadvantage when compared with amputees. This disadvantage occurred essentially across all time points measured. The reason for these findings is unclear. It was originally speculated that there may have been some type of selection bias inherent to the retrospective design of the study. However, when adjusting for all other factors in the

Cox model, type of treatment was the most clinically and statistically significant variable found to explain the survival difference. Thus, we are left to believe that these findings are real. In these cases, patients often had chronic foot wounds associated with their chronic ischemia. Prolonged wound care was usually necessary after PTA to achieve limb salvage. This often resulted in repeat doctor visits, recurrent bouts of cellulitis, and multiple rounds of antibiotics. The clinical stress incurred as a result of this treatment course, no doubt, may have taken its physiologic toll on our debilitated patients. It therefore can be postulated that poorer long-term survival was the result of this chronic illness and treatment. Regardless of the cause, these findings suggest that aggressive limb salvage comes at a cost not previously realized.

In this study, we chose not to emphasize results attained by subgroup analysis. Surely critics will cite that it is unfair to compare patients with technically focal arterial lesions (TASC A or B) with patients with technically complex arterial lesions (TASC C or D) or patients who attain limb salvage with patients who eventually require amputation or even patients who are able to achieve a below-knee amputation with patients who undergo above-knee amputation. We concede that there may be subgroups in the PTA cohort that performed superior to subgroups in the amputation cohort. Also, we concede that a superior 12-month maintenance of ambulation may be significant for this population with limited life expectancy. However, we chose to approach this from the perspective of the clinician at the bedside who is forced to make a clinical decision as to the type of therapy to be performed given the results of the physical examination and vascular laboratory study obtained. The physician usually does not have the luxury of knowing into which subgroup this patient might later fall. The surgeon must decide whether the next step in the process is to proceed with an arteriogram and possible catheter-based intervention or not. What this study demonstrated was that, when taken in aggregate, patients unsuitable for open surgery had physiologic comorbidities that offset any possible functional benefit achieved by PTA for limb salvage. Although further study examining factors associated with successful outcome, including the anatomic pattern of disease, may be helpful, PTA resulted in no functional advantage to primary amputation alone. The implications of these findings are obvious to the clinician at the bedside of the physiologically impaired patient.

We found the results of this study to be enlightening. We have moderated our enthusiasm for percutaneous intervention in the debilitated patient. This is particularly true in the cohort of patients who are functionally impaired. Whereas traditional wisdom has recommended pursuit of an aggressive course of limb salvage for patients who use their limbs only to ambulate around the home or to transfer from chair to bed, the findings of this report suggest that early amputation may provide a better long-term outcome. Further study is needed before a recommendation to abandon PTA for all patients with functional, medical, or mental impairments can be accepted. However, this study makes it clear that PTA should be used quite selectively. Frank discussion with families should occur in which realistic goals and expectations with a clear emphasis on palliation should be clearly outlined and understood before any treatment. Our findings suggest that major limb amputation is not only reasonable palliation, but also better therapy in some instances.

In summary, patients who are physiologically unsuitable for surgery and who present with CLI have a very modest functional advantage after treatment with PTA compared with patients undergoing primary lower extremity amputation—an advantage that lasts no longer than a year and is offset by a sustained and significant survival disadvantage. From this, it can be postulated that these patients have medical comorbidities that blunt any potential functional advantage achieved by limb salvage, regardless of the method used for revascularization. According to these findings, we conclude that PTA should not routinely be used for patients with CLI who are medically and physiologically unsuitable for open bypass.

AUTHOR CONTRIBUTIONS

Conception and design: SMT, CAK, DWB
Analysis and interpretation: SMT, CAK, DWB, DCK, EML, JRY
Data collection: CAK
Writing the article: SMT
Critical revision of the article: SMT, CAK, DWB, DCK, EML, JRY
Final approval of the article: SMT, CAK, DWB, DCK, EML, JRY
Statistical analysis: DWB
Overall responsibility: SMT

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INVITED COMMENTARY

Joseph L. Mills, MD, *Tucson, Ariz*

The Greenville group has addressed an important issue concerning patients with critical limb ischemia (CLI). All would agree that, when possible, ambulatory and functional patients with CLI should undergo revascularization for limb salvage and that demented, nonambulatory, nursing home–confined patients with fixed contractures should undergo primary major limb amputation. An increasingly common problem is what to do with the frail patient who fits somewhere in the middle of these two extremes of the CLI patient spectrum. Many practices have moved toward endoluminal therapy for such patients, on the basis of the yet-unproven but logical premise that percutaneous therapy, although less durable, may be less morbid and still permit limb salvage for patients with limited life expectancies without incurring excessive risk.

The authors conclude, on the basis of their nonrandomized, retrospective study, that CLI patients who appear "physiologically unsuitable for surgery have a very modest functional advantage after treatment with PTA [percutaneous transluminal angioplasty] compared to patients undergoing primary amputation" and that "PTA should not be routinely employed for patients with CLI who are medically and physiologically unsuitable for bypass." Although this is partially correct, I believe that the authors overstate their case and fail to consider important factors needed to make a decision in such patients.

The authors actually report that "there was a statistically significant advantage in maintenance of ambulatory status for patients undergoing PTA when compared to patients undergoing primary amputation (60.2% versus 44% at 24 months, $P < .001$)." PTA patients also exhibited a significant advantage in maintenance of independent living status at 2 years (60.5% vs 52.6%; $P < .046$) and lower rates of ambulatory failure ($P < .002$) and lower rates of living status deterioration ($P < .025$) than primary amputees. An alternative interpretation of the authors' own data, then, would be that for whatever time frail CLI patients have left in the world, PTA is in fact beneficial with respect to maintenance of ambulatory and independent living status but that in such patients who actually live more than 2 to 3 years, the benefits wane. The cost of PTA in these patients was an apparently increased mortality compared with primary amputation, but the two groups were not randomized and differed in several important respects (table 1). Lack of randomization resulted in major differences between the PTA and primary amputation groups; the most important difference was that nearly twice as many amputation patients (56.3%) as PTA patients (29.8%) had undergone previous vascular reconstruction ($P < .0001$). The obvious inference is that the majority of patients in the primary amputation group had already failed reasonable revascularization attempts (and also survived those attempts), whereas the PTA group more likely included the truly physiologically and functionally impaired and not just those with "anatomic impairment" (no conduit, no outflow, and so on). The 4.4% mortality rate for amputees is also much lower than expected mortality rates for major limb amputation in high-risk patients and leads one to question their degree of physiologic impairment.

What factors need further study? First, the patients should have been stratified both by Trans-Atlantic Inter-Society Consensus (TASC) classification and degree of ischemia. TASC classifications for aortoiliac and infrainguinal disease are clear-cut, and one would expect interventions for proximal and A/B lesions to be simpler and more durable than more distal or complex (C/D) interventions. Certainly the authors would not deny a frail patient presenting with a small, nonhealing toe ulcer an iliac angioplasty and stent for a 90% TASC A lesion. However, for an unsuitable surgical candidate with complex infection extending into the forefoot and multilevel TASC C/D disease, primary amputation may be the better part of valor. The authors did not report how many subsequent foot debridements and local amputations were required to achieve limb salvage. This factor—repeated infections and debridements after successful PTA—may have been the straw that broke the camel's back, and not the PTA itself. Such considerations may have contributed to the reported 3-year survival of only 18% in PTA patients compared with 33% in primary amputees. Unfortunately, CLI is somewhat of a black hole; we still lack clear definitions of degree of ischemia (trivial nonhealing toe ulcer, simple toe gangrene, extensive forefoot necrosis, heel necrosis, osteomyelitis, and so on), and the authors admittedly provided no clinical information concerning the patients' presentation. Without examining each patient to assess the degree of difficulty of proposed limb-salvage efforts, it is impossible to interpret the data in a meaningful way.

The authors have appropriately recognized that treatment of the frail patient with CLI who is not believed to be an open-surgical candidate is complex; injudicious PTA and multiple aggressive foot debridements to effect limb salvage attempts at all costs are unwarranted. However, we still do not have enough data to deny all such patients revascularization. The issues facing the vascular surgeon are nearly insurmountable and will likely always require careful clinical judgment and individualized care. In addition to the numerous physiological, psychological, and social factors that require consideration, the complexity and expected durability of the intervention, as well as the degree and extent of forefoot infection and ischemia, will need to be carefully assessed before embarking on amputation or revascularization. A third