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A Pioneer's Perspective on Endovascular Therapy as it Has Evolved from the Aorta to the Tibial Arteries

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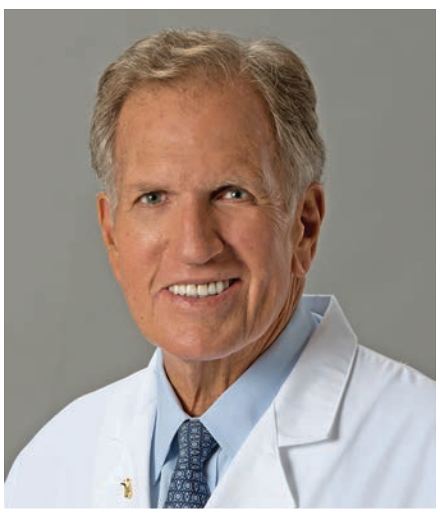

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Endovascular therapy finds its roots in the first angioplasty performed in 1963 by Charles Dotter, MD, known as "the Father of Interventional Radiology." In his initial description of this procedure, Dotter predicted many of the subsequent procedures and technologies that would emerge, but I doubt even he could have imagined the extent to which endovascular therapy would develop over the last 50 years. The early procedures of angioplasty were performed with relatively simple devices by today's standards. They included early guidewires and progressive dilatation devices that were basically Teflon tubes passed over these guidewires. Nonetheless, the concept of treating atherosclerosis and occlusive disease of the arterial system was established and its expansion predicted.

An interesting side note to this landmark procedure was that it was done in a patient who suffered from critical limb ischemia (CLI) with a non-healing ulcer of her foot. Given the current epidemic of CLI, and a building professional and public health interest in this disease state, it seems only fitting that the very first vascular intervention was performed in this clinical setting.

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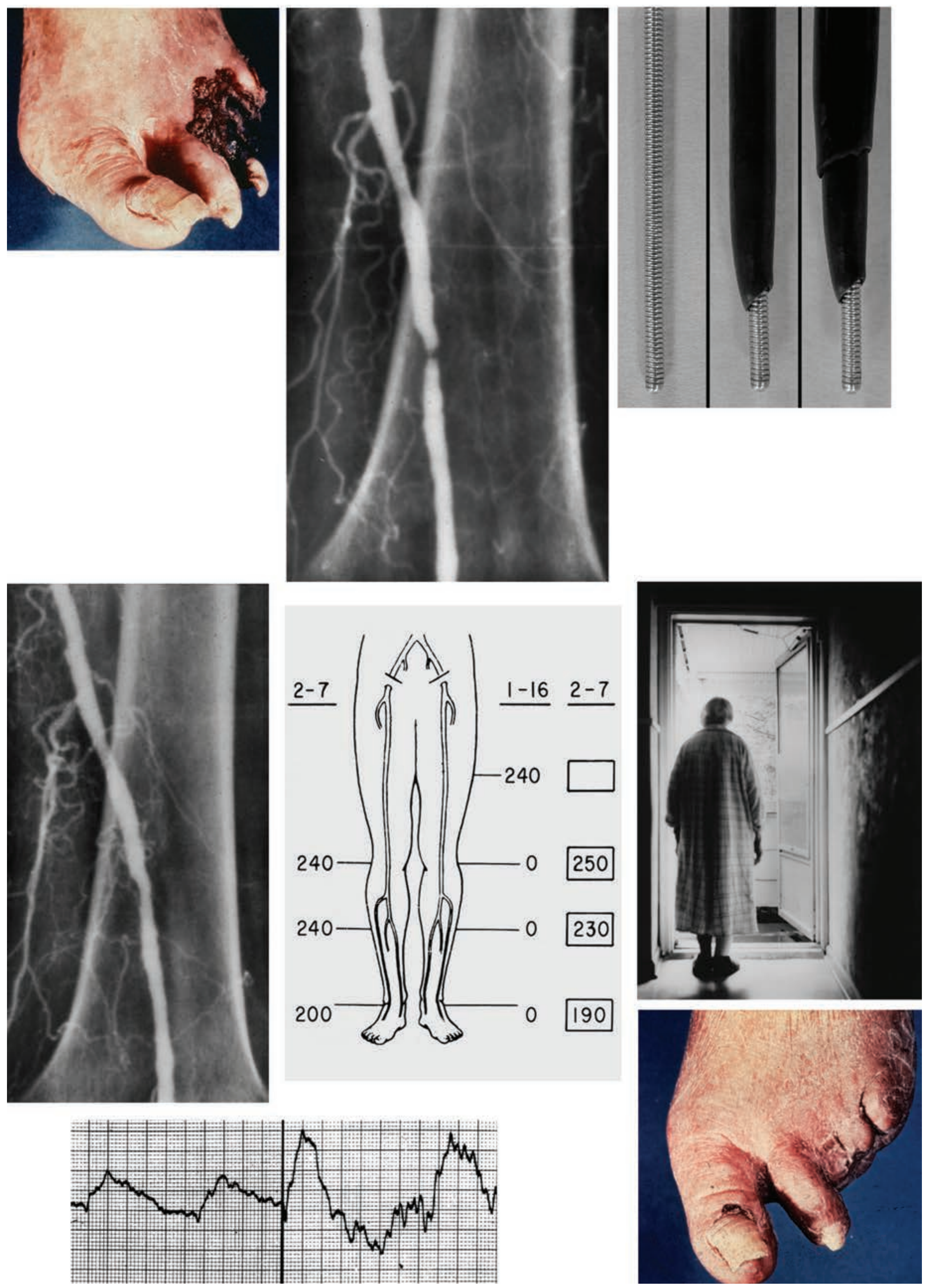

Figure 1. The first percutaneous transluminal angioplasty (PTA), performed by Charles Dotter, MD, in Portland, OR in January 1964. The procedure was performed on an 82-year-old women with painful leg ischemia and gangrene who refused leg amputation. PTA, utilizing a guidewire and coaxial Teflon catheters, successfully opened a stenotic superficial femoral artery (SFA) lesion. The dilated artery stayed open until her death from other causes more than 2 years later. *Images courtesy of John Kaufman, MD.*

Lack of Association Between Limb Hemodynamics and Response to Infrapopliteal Endovascular Therapy in Patients With Critical Limb Ischemia

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ABSTRACT: Background. Non-invasive limb hemodynamics may aid in diagnosis of critical limb ischemia (CLI), although the relationship with disease severity and response to endovascular therapy is unclear. **Methods and Results.** This prospective, single-center study enrolled 100 CLI patients (Rutherford class 4-6) who underwent infrapopliteal endovascular revascularization (175 lesions) in the Peripheral RegIstry of Endovascular Clinical OutcoMEs (PRIME) registry. Hemodynamic measures included ankle-brachial index (ABI), toe-brachial index (TBI), and toe pressure (TP). Procedure success following revascularization was defined as stenosis ≤30%. Hemodynamic success was defined as an increase >0.15 in ABI or TBI relative to baseline. Freedom from amputation was defined as no major or minor amputation during follow-up. Clinical success was defined as a decrease of at least one Rutherford class during follow-up. Treatment success was defined as procedure success, freedom from amputation, and clinical improvement. Median baseline hemodynamic values were 0.90 for ABI, 0.39 for TBI, and 54 mm Hg for TP. Twenty-nine patients (29%) did not meet the common hemodynamic diagnostic criterion for eligibility in CLI trials (ABI ≤0.5, TBI ≤0.5, or TP <50 mm Hg). Main outcomes included 96% procedure success, 95% freedom from amputation, 64% clinical success, and 62% treatment success. There was no relationship between baseline (or with the pretreatment to posttreatment change) limb hemodynamic values and the response to infrapopliteal endovascular therapy. **Conclusion.** Non-invasive hemodynamic studies may have limited clinical usefulness in patients with CLI. The usefulness of these parameters to confirm eligibility and to assess response to therapy in interventional CLI clinical trials should be re-evaluated. ***Reprinted with permission from J INVASIVE CARDIOL 2017;29(5):175-180.***

Jihad A. Mustapha, MD

Symptomatic peripheral artery disease affects 15%-20% of older adults and is associated with a 4-fold increase in all-cause mortality risk and an 8-fold increase in cardiovascular mortality risk.[1] Peripheral artery disease may insidiously progress to critical limb ischemia (CLI), defined as the presence of rest pain requiring analgesia and/or ischemic tissue loss.[2] Prognosis following CLI diagnosis is grave, with 1-year mortality and major amputation rates ranging from 20%-50%.[3-5] These statistics underscore the importance of early diagnosis and intervention to improve tissue perfusion, relieve pain, and promote wound healing.[6-10]

The diagnosis of CLI is routinely based on clinical symptoms and confirmed by measurements of non-invasive limb hemodynamics such as ankle-brachial index (ABI), toe-brachial index (TBI), and/or toe pressure (TP).[11] Limb hemodynamic measures are often used to confirm eligibility in CLI clinical trials where ABI ≤0.5, TBI ≤0.5, and/or TP <50 mm Hg are required for

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Editor's note: Articles in this supplement to *Cath Lab Digest* did not undergo peer review.

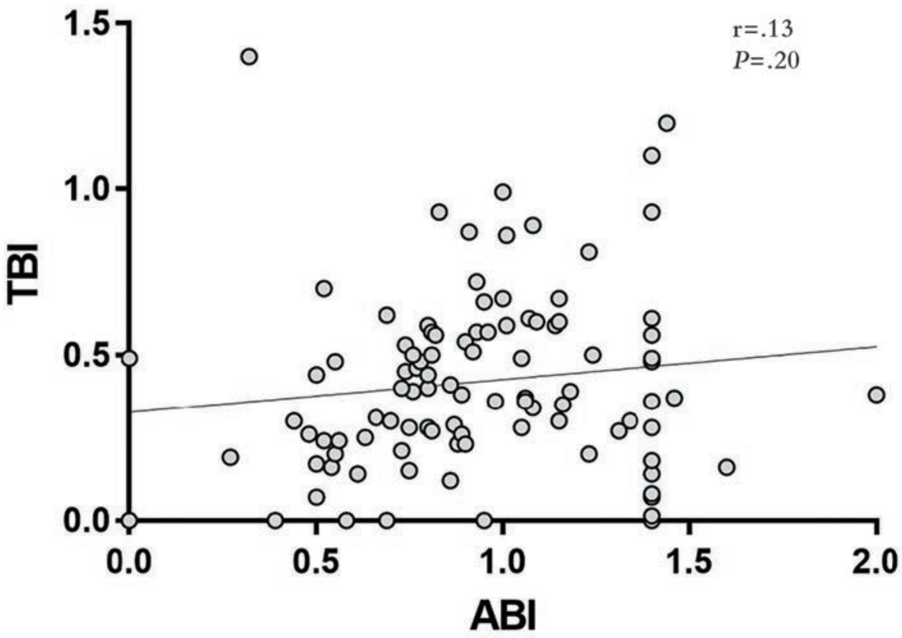

Figure 1. Relationship of ankle-brachial index (ABI) and toe-brachial index (TBI) prior to endovascular therapy in patients with critical limb ischemia.

Table 1. Baseline patient characteristics.

Variable	n = 100
Demographics	
Age (years)	75 ± 10
Male sex	67 (67%)
Body mass index (kg/m²)	29 ± 5
Medical history	
Dyslipidemia	92 (92%)
Hypertension	89 (89%)
Diabetes	68 (68%)
Smoking history	61 (61%)
Coronary artery disease	46 (46%)
Coronary artery bypass graft	23 (23%)
Congestive heart failure	21 (21%)
Myocardial infarction	15 (15%)
Cerebrovascular disease	12 (12%)
Dialysis	3 (3%)
Chronic kidney disease stage	
1	7 (7%)
2	40 (40%)
3	44 (44%)
4	7 (7%)
5	2 (2%)
Rutherford class	
4	42 (42%)
5	53 (53%)
6	5 (5%)
Blood chemistry	
Creatinine (mg/dL)	1.1 (0.9-1.5)
GFR (mL/min/1.73 m²)	59 (44-76)
Hemoglobin (g/dL)	12.4 ± 1.9
Diameter stenosis	
100%	28 (28%)
70%-99%	23 (23%)
<70%	49 (49%)
Limb hemodynamics	
Ankle-brachial index	0.90 (0.73-1.16)
Toe-brachial index	0.39 (0.24-0.57)
Toe pressure (mm Hg)	54 (32-85)

Data provided as mean ± standard deviation, number (%), or median (interquartile range). GFR = glomerular filtration rate.

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enrollment.[6,11-16] These measures are also used to quantify response to therapy in CLI clinical trials where ABI or TBI increases >0.15 are taken as evidence of hemodynamic success.[17,18] However, recent studies have shown that many CLI patients do not meet these diagnostic hemodynamic criteria.[6,11,19] Furthermore, the association between changes in these hemodynamic parameters and clinical outcomes following endovascular therapy is unclear. The purpose of this study was to assess the relationship of limb hemodynamics with response to infrapopliteal endovascular revascularization in patients with CLI.

METHODS

Patients. This is a prospective, single-center study of consecutive CLI patients who underwent infrapopliteal endovascular revascularization in the Peripheral RegIstry of Endovascular Clinical OutcoMEs (PRIME) registry. Institutional review board approval and patient consent were obtained prior to any procedures or data collection. Eligible patients were adults ≥18 years with symptomatic CLI (Rutherford class 4-6) and angiographically confirmed infrapopliteal disease that required endovascular revascularization. Patients underwent clinical examination and noninvasive limb hemodynamic measurements, including ABI, TBI, and TP prior to revascularization and within 3 months post intervention on the affected limb.

Procedures. Hemodynamic measures were obtained after subjects rested supine for 5 minutes. Systolic pressures were measured in both arms (brachial artery) and at the dorsalis pedis and posterior tibial arteries using a MultiLab Series 2-CP (Unetixs Vascular) or Dopplex D900 Doppler waveform analyzer (Huntleigh). *ABI* was calculated as the ratio between the higher of the ankle pressures and the higher brachial pressure. *Systolic TP* was evaluated at the hallux using a MultiLab Series 2-CP (Unetixs Vascular) or Vista Doppler waveform analyzer (Wallach Surgical Devices) by photoplethysmography. *TBI* was calculated as the ratio between toe pressure and the higher brachial pressure.

Endovascular revascularization was attempted on all study subjects. Intervention included angiographic evaluation of arterial stenosis of the infrainguinal and infrapopliteal arteries by physician estimate, prior to infrapopliteal intervention of the target lesions. Revascularization method was determined by the treating physician and included one or a combination of the following: atherectomy, percutaneous transluminal angioplasty, drug-coated balloon angioplasty, and/or bare-metal or drug-eluting stent placement. Angiography was performed to assess procedure success post revascularization.

Outcomes and definitions. *Procedure success* following revascularization was defined as stenosis ≤30% determined by physician visual estimate. *Hemodynamic success* was defined as an increase >0.15 in ABI or TBI relative to baseline following endovascular therapy. *Freedom from amputation* was defined as no major (above the ankle) or minor (below the ankle) amputation during follow-up. *Clinical success* was defined as a decrease of at least one Rutherford class during follow-up. *Treatment success* was a composite endpoint that comprised procedure success, freedom from amputation, and clinical improvement.

Data analysis. Continuous data were reported as mean and standard deviation or median and interquartile range, depending on normality assumptions. Categorical data were reported as frequencies and percentages. Group comparisons were performed with independent samples t-test for normally distributed continuous data, Mann-Whitney U-test for non-normally distributed continuous data, or Fisher's exact test for categorical data. Longitudinal changes in clinical outcomes were assessed with paired t-tests or Wilcoxon signed-rank test, based on normality. Univariate logistic regression assessed the relationship of baseline characteristics on treatment success. Variables that loaded into the univariate model at $P<.10$ were evaluated in a multivariable model using backward elimination (likelihood ratio method). A P-value $<.05$ was considered statistically significant. Data were analyzed using Predictive Analytics Software version 22 (SPSS, Inc).

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> "The purpose of this study was to assess the relationship of limb hemodyanamics with response to infrapopliteal endovascular revascularization in patients with CLI."

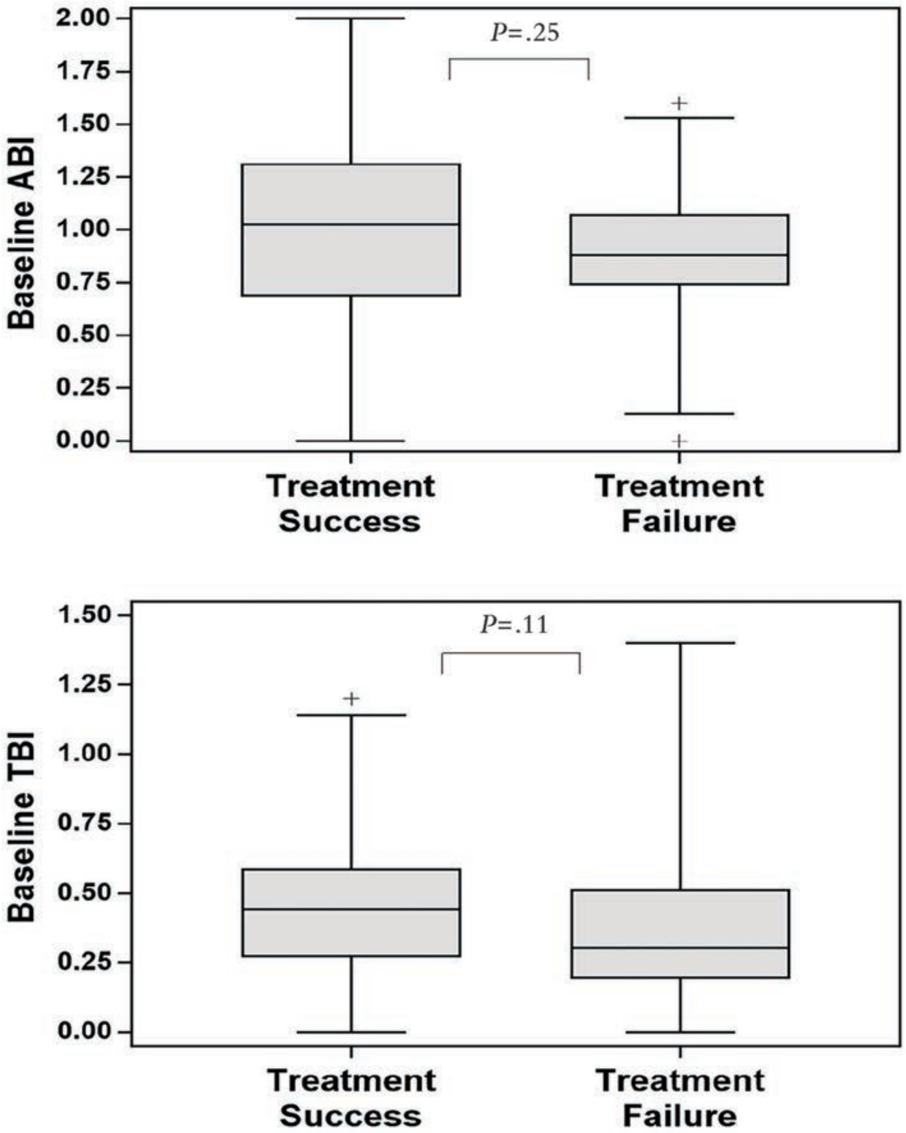

Figure 2. Box-and-whisker plot of baseline ankle-brachial index (ABI; top) and toe-brachial index (TBI; bottom) values by short-term treatment outcome following infrapopliteal endovascular therapy. The horizontal line inside a box represents the median, the ends of the box represent the first and third quartiles, the whiskers extend to the 2.5th and 97.5th percentiles, and "+" symbols represent outliers. Treatment success was defined as procedure success, freedom from amputation, and clinical success.

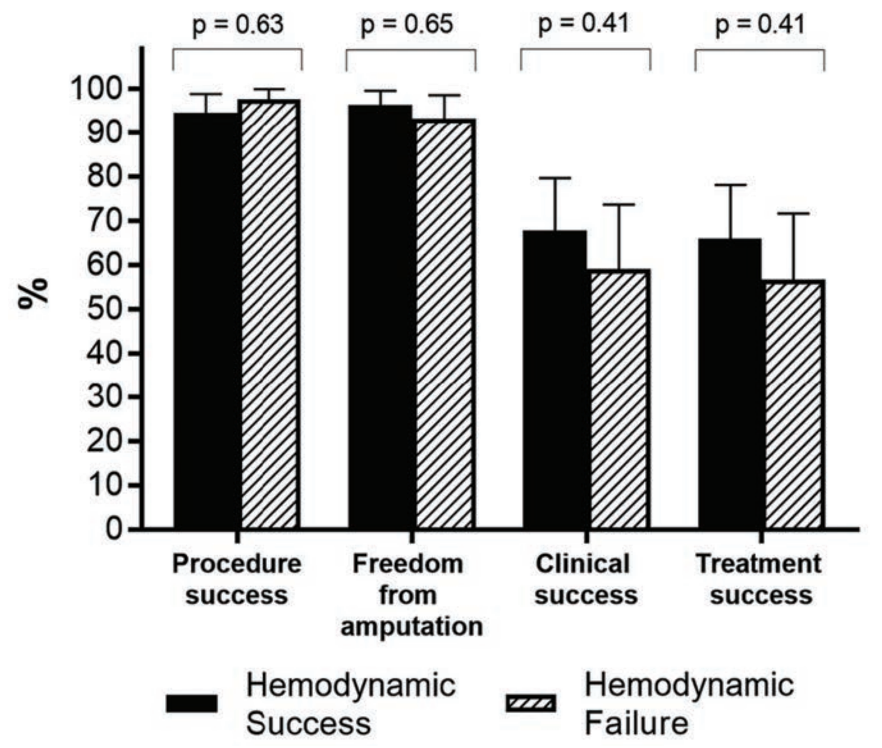

Figure 3. Short-term outcomes following infrapopliteal endovascular therapy by hemodynamic outcome. Hemodynamic success was defined as ankle-brachial index increase >0.15 or toe-brachial index increase >0.15. Procedure success was defined as stenosis ≤30% determined by physician visual estimate. Clinical success was defined as Rutherford improvement ≥1 class. Treatment success was defined as procedure success, freedom from amputation, and clinical success.

Table 2. Comparison of key patient characteristics and outcomes following infrapopliteal endovascular therapy by common diagnostic hemodynamic thresholds.

Variable	Eligible (n = 71)	Not Eligible (n = 29)	*P*-Value
Baseline characteristics			
Age (years)	75 ± 10	75 ± 9	.91
Male sex	49 (69%)	18 (62%)	.64
Body mass index (kg/m2)	28 ± 5	30 ± 5	.12
Diabetes	50 (70%)	18 (62%)	.48
Smoking history	43 (61%)	18 (62%)	>.99
CKD stage 3-5	37 (52%)	16 (55%)	.83
Rutherford class 5/6	43 (61%)	15 (52%)	.50
Endovascular therapy outcomes			
Procedure success	68 (96%)	28 (97%)	>.99
Freedom from amputation	66 (93%)	29 (100%)	.32
Clinical success	42 (59%)	22 (76%)	.17
Treatment success	41 (58%)	21 (72%)	.26

Data provided as mean ± standard deviation or number (%).
Eligible = baseline ankle-brachial index ≤0.5, toe-brachial index ≤0.5, or toe pressure <50 mm Hg; procedure success = stenosis ≤30% determined by physician visual estimate; clinical success = Rutherford improvement ≥1 class; treatment success = procedure success, freedom from amputation, and clinical success.

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RESULTS

A total of 100 patients clinically diagnosed with CLI (Rutherford class 4-6) underwent infrapopliteal endovascular revascularization between January 2013 and January 2016. Mean age was 75 years and 67% were male. The most common comorbidities were dyslipidemia (92%), hypertension (89%), and diabetes mellitus (68%). Over 50% of patients presented with at least chronic kidney disease stage 3 (glomerular filtration rate <60 mL/min). Median baseline hemodynamic values were 0.90 for ABI, 0.39 for TBI, and 54 mm Hg for TP (Table 1). There was no significant association between baseline ABI and TBI values (Figure 1). Twenty-nine patients (29%) did not meet the common hemodynamic diagnostic criterion for eligibility in CLI trials (ABI ≤0.5, TBI ≤0.5, or TP <50 mm Hg).

Revascularization was performed in 175 infrapopliteal lesions. Treated segments included the popliteal artery (P3 segment) (25%), anterior tibial artery (24%), tibioperoneal trunk (15%), peroneal artery (15%), posterior tibial artery (13%), dorsalis pedis (3%), lateral plantar artery (2%), medial plantar artery (1%), lateral calcaneal artery (1%), and pedal loop (1%). Main outcomes included 96% procedure success, 95% freedom from amputation, 64% clinical success, and 62% treatment success.

When comparing patients based on hemodynamic diagnostic eligibility, there were no observable differences in baseline characteristics or in response to infrapopliteal endovascular therapy (Table 2). Baseline ABI (Figure 2A) and TBI (Figure 2B) were not different in patients with treatment success or treatment failure. In the univariate logistic regression model, lower Rutherford class, absence of diabetes, higher glomerular filtration rate, and higher hemoglobin were associated with treatment success and subsequently included in the multivariate model. Notably, neither ABI (P=.20), TP (P=.23), nor TBI (P=.31) predicted treatment success after endovascular therapy. In the multivariate logistic regression model, only lower Rutherford class (odds ratio, 19.8; 95% confidence interval [CI], 5.5-71.6; P<.001) was associated with treatment success (Table 3).

Despite the high procedure success rate following endovascular therapy, only minimal (albeit statistically significant) increases in limb hemodynamics were observed. Hemodynamic success was 56%, ABI increased from 0.93 ± 0.35 to 1.06 ± 0.26 (P<.001), TBI increased from 0.42 ± 0.25 to 0.49 ± 0.25 (P=.04), and TP increased from 61 ± 38 mm Hg to 71 ± 37 mm Hg (P=.04). When comparing patients with hemodynamic success vs hemodynamic failure, there were no statistical differences in procedure success, freedom from amputation, clinical success, or treatment success (Figure 3).

DISCUSSION

Data regarding the effectiveness of endovascular modalities for the treatment of infrapopliteal disease in patients with CLI are beginning to emerge with variable outcomes. The results of this study demonstrated a lack of association of non-invasive limb hemodynamic measures with baseline patient characteristics, disease severity, and response

Table 3. Logistic regression: predictors of treatment success (defined as procedure success, freedom from amputation, and clinical success).

Variable	Unit of Measure	Odds Ratio	95% CI	*P*-Value
Univariate model				
Rutherford class	4 vs 5/6	19.8	5.5-71.6	<.001
Diabetes	No vs Yes	3.9	1.4-10.5	<.01
Glomerular filtration rate	Per 10 mL/min/1.73m^2 increase	1.3	1.1-1.6	.01
Hemoglobin	Per 1 g/dL increase	1.3	1.0-1.7	.02
Ankle-brachial index	Per 0.1 unit decrease	1.1	1.0-1.2	.20
Toe pressure	Per 10 mm Hg increase	1.1	1.0-1.2	.23
Age	Per 5 year increase	1.1	0.9-1.4	.24
Toe-brachial index	Per 0.1 unit increase	1.1	0.9-1.3	.31
Smoking	No vs Yes	1.4	0.6-3.2	.44
No. diseased vessels	Per 1 vessel decrease	1.1	0.7-1.8	.64
Body mass index	Per 5 kg/m^2 increase	1.0	0.7-1.4	.81
Sex	Male vs female	1.1	0.5-2.6	.84
Final multivariate model				
Rutherford class	4 vs 5/6	19.8	5.5-71.6	<.001

CI = confidence interval.

to infrapopliteal endovascular therapy among patients with CLI. Therefore, the clinical usefulness of these measures in patients with CLI is questionable.

The accuracy of non-invasive hemodynamic testing to identify patients with CLI with compromised infragenicular run-off has been studied by several authors. Bunte and colleagues[6] showed that 29% of patients with CLI and abnormal infrapopliteal run-off had normal or mildly abnormal ABIs (defined as ABI >0.7 and <1.4), and that low TBI was not associated with abnormal infrapopliteal run-off. However, TBI values were somewhat higher with improved pedal perfusion, questioning the utility of these indices to assess limb hemodynamics in CLI patients with abnormal infrapopliteal anatomy. Shishehbor et al[19] reported only 16% of CLI patients had abnormal ankle pressures and that abnormal TP had better specificity in CLI diagnosis. Still, 40% of patients in this study had normal TP values and neither ABI nor TP were associated with disease severity. Vallabhaneni et al[20] reported that CLI patients with TP ≤10 mm Hg had higher amputation rates relative to those with TP of 31-50 mm Hg (60% vs 18%, respectively; P<.001); however, patients did not have exclusive infrapopliteal disease, as in our current study. Our results suggest only a weak association between limb hemodynamics and response to infrapopliteal endovascular therapy; instead, Rutherford class was the sole predictor of treatment success in multivariate analysis.

"Clinicians should maintain a high index of suspicion and a low threshold to proceed with repeat revascularization when dictated by clinical judgement..."

Commonly utilized non-invasive limb hemodynamic assessments can be misleading and unreliable in CLI, as they frequently failed to identify patients with severe disease and limb-threatening angiographic anatomies in the current study. No differences were observed in outcomes after endovascular therapy among patients with CLI regardless of baseline ABI, TBI, or TP, many of which would have been otherwise considered "normal" and possibly resulted in denial of therapy that could have otherwise proven beneficial. Ongoing studies designed to identify patients with CLI who would benefit from specific methods of endovascular therapy have used ABI, TBI, and TP values of ≤0.5, ≤0.5, and/or <50 mm Hg, respectively, as inclusion criteria (and hence as surrogate diagnostic criteria for CLI). Results from the current study suggest that the use of limb hemodynamic measures as inclusion/exclusion criteria in studies of infrapopliteal therapies is questionable, since many appropriate patients are excluded using these thresholds. Furthermore, this study questions the necessity of performing non-invasive studies as surveillance tools after infrapopliteal revascularization procedures in patients with CLI given the lack of association between hemodynamic success and clinical outcomes. Clinicians should maintain a high index of suspicion and a low threshold to proceed with repeat revascularization when dictated by clinical judgment regardless of the information provided by the aforementioned tests. Emerging modalities such as evaluation by skin perfusion pressure, transcutaneous oxygen pressure, fluorescent angiography through the use of indocyanine green dye, subcutaneous implantation of oxygen microsensors, or use of two-dimensional perfusion imaging software are promising, and given further study, may prove useful in diagnosis and prognosis of patients with complex peripheral arterial disease and CLI.[21-25]

Study limitations. There were several limitations of this study that may impact interpretability. First, patient outcomes were reported through 3 months post treatment. Therefore, the relationship of limb hemodynamics with longer-term clinical outcomes after endovascular therapy in patients with infrapopliteal disease cannot be evaluated in this study. Second, physicians involved in patient follow-up were not blinded to the intervention and the results of the preprocedural non-invasive limb hemodynamics. Finally, the study represents a single-center experience, where patients were not randomized and were treated by experienced operators specifically trained in CLI therapy.

CONCLUSION

Non-invasive hemodynamic studies may have limited clinical usefulness in patients with CLI. The use of these measures to confirm eligibility and to assess response to therapy in interventional CLI clinical trials should be re-evaluated. ■

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CLI Perspectives

How to Approach the "Desert Foot" in the CLI Patient

J.A. Mustapha, MD, (Metro Health Hospital, Wyoming, Michigan) interviews Luis Mariano Palena, MD, from the Interventional Radiology Unit, Foot and Ankle Clinic, Policlinico Abano Terme, Abano Terme Padova, Italy.

Luis Mariano Palena, MD

INTRODUCTION

J.A. Mustapha, MD

Critical limb ischemia (CLI) remains a mysterious disease and it is difficult to pinpoint a universal definition to describe its aggressive nature. Clinically, many of us may refer to a patient as having CLI if they present with rest pain and in the same breath, we may refer to a patient as having CLI if they present with black foot. Clearly, there is a broad spectrum of presentation and unfortunately a narrow description of it. The same broad spectrum also exists in the invasive nature of CLI. A patient with rest pain and single-vessel runoff will be defined as CLI just as much as a patient with rest pain and/or skin breakdown with absent flow to the foot, usually referred to as desert foot. Patients with CLI and desert foot tend to land on the spectrum of a no-option patient more often than required. In this issue, Dr. Luis Mariano Palena will be sharing with us the most current available options for patients with desert foot.

J.A. Mustapha, MD: **What is your angiographic definition of desert foot?**

Luis Mariano Palena, MD: Desert foot is an infrequent vascular condition that affects diabetic patients with CLI and frequently those with chronic renal failure and hemodialysis. This condition is defined as "the occlusion of all the main foot arteries." It means occlusion of the dorsalis pedis, lateral tarsal artery, both plantar arteries, and occlusion of the plantar arch. The angiography only shows collateral vessels of the foot.

Dr. Mustapha: **Considering the significant lack of target vessels in the foot, what was the driving factor for you to venture into creating treatment options for these patients?**

Dr. Palena: These patients often arrive to our care with ischemic and infected ulcers in the foot. Due to their baseline vacular conditions, they are at high risk for major amputation. On the other hand, these patients are poor candidates for distal bypass or for any surgical revascularization, because of the lack of flow through any of the main vessels in the foot. For these reasons, these patients do not have anything to lose and allow us to try, sometimes in an aggressive way, to save their limbs.

Dr. Mustapha: **What is your current clinical and invasive assessment strategy for a patient with desert foot?**

Dr. Palena: All these patients arrive at our cath lab with a precise clinical indication. Complete assessment of the ulcers (presence of ischemia and/or infection) and assessment of the deepness of the ulcer (involvement of the soft tissue, the bone, etc.) is usually done using the Texas University Classification (TUC). The invasive

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Figure 1. Diabetic patient with CLI, in Rutherford class 6.

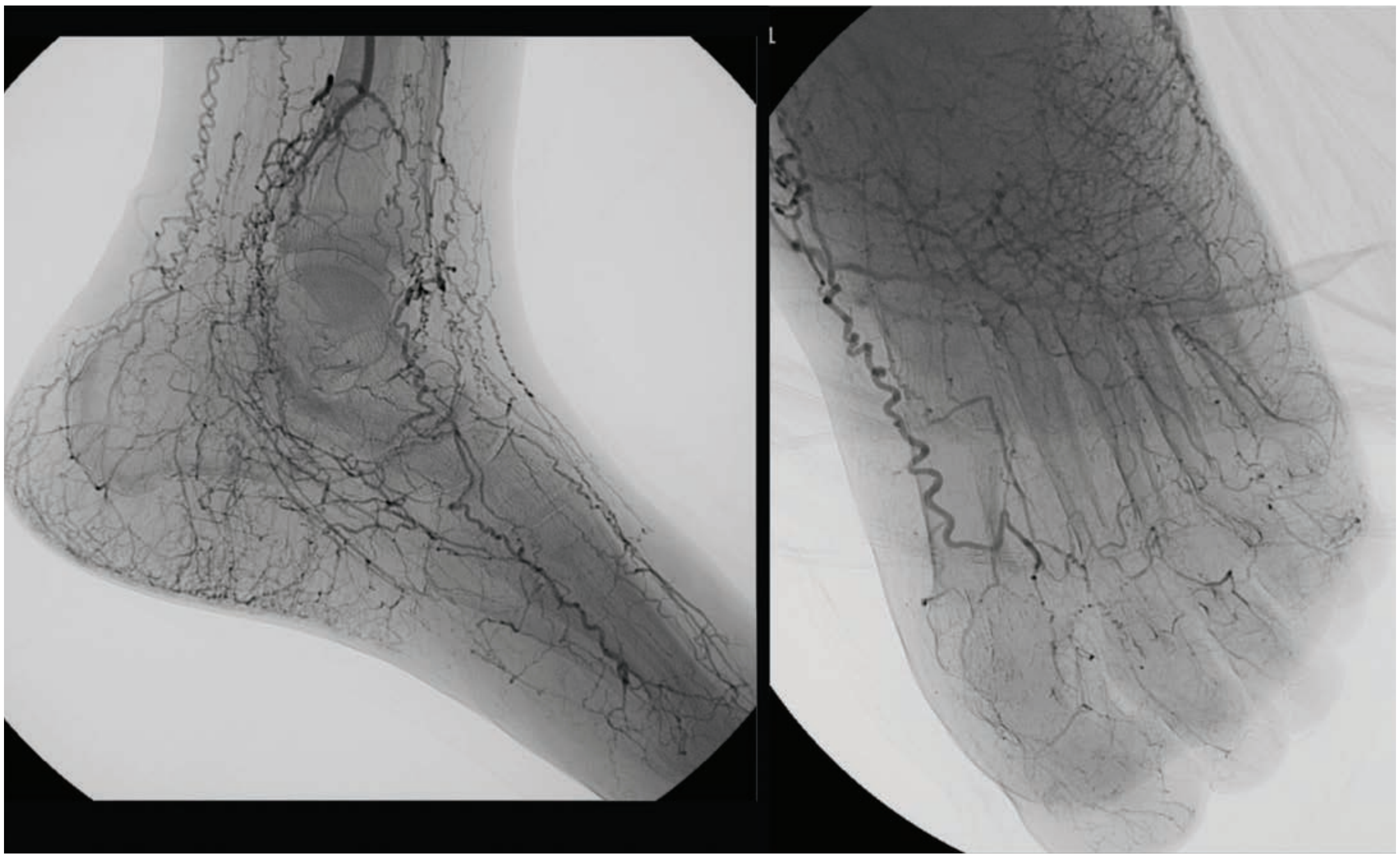

Figure 2. No patent main vessels.

A Peek Into Latin American CLI Statistics and Flow of Therapy in Colombia

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Critical limb ischemia (CLI) is a significant issue in Colombia, a South American country with a population of 48.2 million. While there is a lack of hard statistics on CLI in Colombia, there is information on the prevalence of diabetes and cigarette smoking, two important factors that contribute greatly to CLI.

Approximately 18 million people in Central and South America have diabetes. By 2030, it is estimated that the number will increase by 65%. Therefore, 30 million people will be living with the disease in this region.[1] In Colombia, some estimates suggest the potential morbidity and mortality caused by this disease. The International Diabetes Federation (IDF) reports a national prevalence of 4.8% in people 20-79 years of age, which would correspond to a total of 1,427,300 people diagnosed. According to the National Health Survey (ENS 2007), the prevalence of diabetes by self-report in the population aged 18-69 is 3.51%.[2]

SMOKING RATES ON THE RISE

Tobacco is one of the greatest threats to public health. It kills six million people per year, of which more than five million are direct consumers and more than 600,000 are non-smokers exposed to secondhand smoke. Almost 80% of the world's more than one billion smokers live in low- and middle-income countries, where the burden of morbidity and mortality associated with tobacco is higher.[3]

The prevalence of cigarette smoking in Colombia is 17.1% — 23.8% among men and 11.1% among women. Among young people, the prevalence is 27.6%. Each year, 26,460 people die from smoking cigarettes (72 per day), and 221,112 are ill. Attention to the latter group costs 4.3 billion pesos per year (equating to $13 million in United States currency) and smoking causes 674,262 years of healthy life to be lost in the country.

Multiple studies at the international and national levels concur that the age of onset of cigarette consumption has been decreasing. The most recent survey conducted by the Rumbos program of the Presidency of the Republic of Colombia found that 65% of young people consume this substance for the first time between 10 and 14 years of age, followed by young people between the ages of 15 and 19.[4]

> **"The positive results achieved during the last four years at Hospital Universitario Clinica De San Rafael have been due to a comprehensive care program for patients with CLI led by the vascular surgery service."**

Figure 1. Ultradistal angioplasty in a CLI patient.

In countries such as Colombia, the epidemics of diabetes and smoking generate many patients with arterial disease. The great majority of them lead to the need for emergency medical services for CLI, unlike in developed countries, where claudication leads to more timely medical care.

I perceive the causes of this problem are fourfold:

1. Lack of early diagnosis of arterial disease and recognition of CLI as an urgent condition;
2. Lack of available centers that specialize in limb salvage;
3. Lack of integrality in the management of patients with CLI;
4. Lack of knowledge of limb salvage technologies and programs among patients, physicians, insurance companies and government.

COMPONENTS OF A SUCCESSFUL PROGRAM

Hospital Universitario Clinica De San Rafael is a private institution in Bogota and a national reference center for vascular disease. The facility conducts an average of 80 surgical, endovascular or hybrid procedures per month for limb salvage, with a salvage rate of more than 70%.

The positive results achieved during the last four years at Hospital Universitario Clinica De San Rafael have been due to a comprehensive care program for patients with CLI led by the vascular surgery service. The team offers all available treatment options with the ultimate goal of preventing major amputation. The philosophy at the hospital is that limb salvage is not simply the placement of stents and obtaining a satisfactory angiographic image. Successful limb salvage involves much more.

Strategies established for patients with CLI include:

1. **Early diagnosis and treatment with the mindset of "tissue is time."** All patients admitted with ulcerations of the lower extremities of any origin are assessed first by vascular surgery, which determines the diagnostic and therapeutic process.

Figure 2. Ultradistal bypass for CLI.

The vascular surgeon becomes the lead member of the multispecialty team caring for the CLI patient. Internal medicine, infectology, and nephrology services are integral parts of the care team. Orthopedic surgery is only consulted when vascular surgery concludes that the patient requires a major amputation. All patients with CLI are taken to diagnostic arteriography and the course of care is determined by the vascular surgery team.

2. **Speed and opportunity.** The vascular surgery service responds to the call of patients with CLI immediately, including procedures at night and on weekends, with a rapid response by the endovascular suite team.
3. **Different revascularization procedures.** Patients with critical ischemia are evaluated by the vascular surgery group. Based on the angiographic study, the characteristics of the lesion and the state of the limb, the best method of revascularization is established —surgical, endovascular and hybrid are all considered. In the first instance, we consider the endovascular procedure, whether it is percutaneous angioplasty with flat balloon, drug-coated balloon, bare metal peripheral stents, thrombolysis, percutaneous thrombectomy, or ultra-distal angioplasty (Figure 1). If these procedures fail or are not the first indication, endarterectomy, profundoplasty, or distal and ultradistal bypass (Figure 2) is performed. The autologous vein is utilized in most bypass cases.
4. **Tissue management.** Patients with CLI enter a tissue management program that includes periodic surgical debridement of necrotic tissues, minor amputations (digital, transmetatarsal, Syme's, Chopart), wound care with vacuum therapy, and specialized wound dressings. These procedures are performed by the same group of vascular surgeons and are initiated at the time of revascularization procedures. The wound care plan is established and followed by the vascular surgery team.
5. **Comorbidity management.** Internal medicine, nephrology, and infectology act as support services for the management of patients with diabetes, coronary disease and other medical pathologies, optimizing the metabolic, nutritional and infectious status of CLI patients.
6. **Alternative medical therapies.** When the patient cannot be revascularized in any way, we have two last-line options: prostaglandin analogs and stem cell therapy.
7. **Follow-up.** Following revascularization, CLI patients are followed over time. Monitoring is more frequent during the first year, occurring every three months. Patients are monitored for patency of reconstructions and risk factors that may cause a return of CLI.

"Patients with CLI enter a tissue management program that includes periodic surgical debridement of necrotic tissues, minor amputations (digital, transmatatarsal, Syme's, Chopart), wound care with vacuum therapy, and specialized wound dressings"

HOLISTIC CARE IS CRITICAL

In Colombia, CLI is a preponderant manifestation of arterial disease. Holistic management is critically important to counteract its effects, integrating both new and old technologies to reach the ultimate objective of limb salvage. ■

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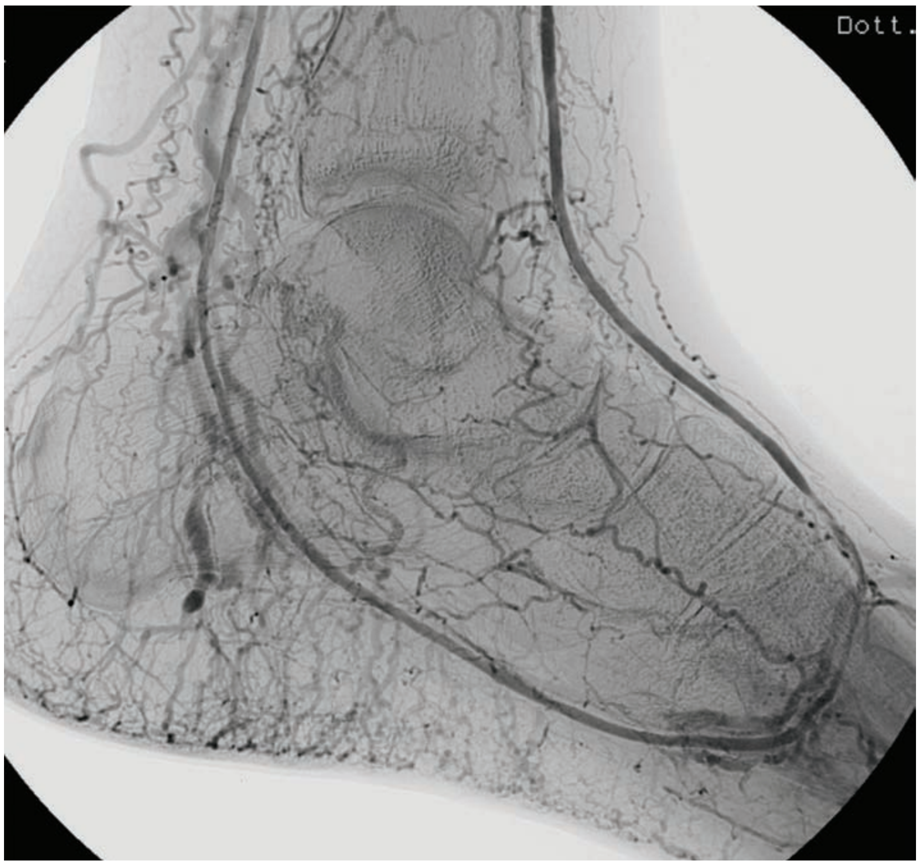

Figure 3. Complete foot revascularization after subintimal recanalization of the dorsal and plantar circulation, including the plantar arch.

Figure 4. Transmetatarsal amputation, which healed and was maintained for 3 years.

PALENA from page 8

assessment includes selective and super-selective angiography. Two-dimensional perfusion imaging is used when trying to understand if we can improve perfusion of the foot when treating the proximal vessels.

Dr. Mustapha: **Do non-invasive hemodynamics play a role throughout the course of therapy?**

Dr. Palena: The only non-invasive hemodynanic measure we use is the transcutaneous oxygen ($TcPO_2$) value that demonstrates the presence of ischemia, but does not show us the desert foot condition. I believe it is very difficult for these patients to achieve any clinical improvement without revascularization.

Dr. Mustapha: **Do you have guidelines in your institution to define which patients will require primary major amputations, or do all of your patients get at least an attempt at revascularization?**

Dr. Palena: Primary major amputation is indicated in patients with deep infections that involve not only the foot bones, but also the tibial and fibular bones, without any possibility to save the leg where revascularization could increase the risk for septicemia, as related to the presence of the infection. Clearly, this situation is very infrequent.

If the patient does not meet this clinical scenario, in all other cases, we believe in bringing these patients for at least an attempt at revascularization, with the aim of saving and maintaining a functional limb.

Dr. Mustapha: **What is the average time required for you and your team to revascularize a desert foot?**

Dr. Palena: It depends patient by patient. However, as a good rule, we try to not work more than 2 hours, which is often enough time to successfully treat complex multilevel and multivessel arterial disease.

Dr. Mustapha: **Please share a case with us.**

Dr. Palena: I will describe a case of desert foot in a diabetic patient with CLI. You can see he was in Rutherford class 6 (Figure 1) and there were no patent main vessels on the foot (Figure 2). After subintimal recanalization of the dorsal and plantar circulation, including the plantar arch, we were able to restore the blood flow to the foot, achieving a complete foot recanalization (Figure 3). The patient underwent transmetatarsal amputation that healed and was maintained for 3 years (Figure 4).

Dr. Mustapha: **Do patients with desert foot receive additional follow-up in comparison to patients without desert foot?**

Dr. Palena: No specific follow-up. Our idea is to obtain an ulcer or surgical incision healing and we always regularly follow up with those patients in trying to achieve this goal.

Dr. Mustapha: **What is your medical cocktail for CLI patients with desert foot after revascularization?**

Dr. Palena: It is the same as for all patients with CLI: dual antiplatelet therapy for 3 months and then aspirin for life.

Dr. Mustapha: **Do you feel more operators will be able to perform similar procedures with the proper training?**

Dr. Palena: I truly believe so. I think that actually many operators are able and are increasing the necessary skills to successfully treat this kind of situation. The learning curve is, in my opinion, the same that every vascular specialist undergoes to treat the foot vessels in CLI patients. This means every vascular specialist dedicated to CLI treatment should be able to treat this complex and extreme situation.

Dr. Mustapha: **Do you see CLI becoming its own specialty, with a team-focused approach to achieve the highest safety and efficacy?**

Dr. Palena: In the near future, I think we will have greater dispersion of this concept. Actually, in Italy as well as in many other countries, there are dedicated CLI centers that work in a multidisciplinary way. I hope this concept will spread to achieve safe and efficient treatment.

Dr. Mustapha: **What is your advice to global operators who are willing to take on desert foot revascularization?**

Dr. Palena: My advice, if I can give it, is to always try to recanalize the foot arteries of those patients affected by desert foot, following the clinical indications and considering that these patients do not have anything to lose. ■

"I think that actually many operators are able, and are increasing the necessary skills, to successfully treat this kind of situation."

KATZEN from page 1

Like many important innovations, adoption of this new procedure was slow for many reasons. From a technical point of view, it was difficult and challenging. Remember, we did not even have vascular sheaths at that time, so blood loss was a significant part of early angioplasty. In addition, there was significant resistance to the application of these procedures by vascular surgeons of that day, who were concerned about direct intervention on plaque, and perhaps other things as well.

Fortunately, European physicians read Dotter's work, came to visit Portland, Oregon, and learned how to perform this new procedure of angioplasty. European pioneers such as G.J. van Andel, MD, and Eberhard Zeitler, MD, among others, began performing this procedure and rapidly increased their experience. Throughout the late 1960s and early 1970s, thousands of patients were treated in Europe while only hundreds of patients were treated in the United States. Clearly, the concept of percutaneous treatment of vascular disease was beginning to get traction, particularly overseas. In Europe, this procedure became known as Dottering or progressive dilatation of stenosis and occlusions.

EVOLUTION OF EARLY ADVANCES IN TREATING LARGER ARTERIES

From these early experiences, slow development occurred in the 1960s with various shapes of catheters/dilators emerging in an attempt to make the procedure more effective. However, everyone involved in expanding this technology understood there was a significant need for devices that could open arteries to a diameter bigger than the device itself. The maximum diameter of these progressive dilators was relatively small in the 5.0 to 6.0 mm range. As a result, treatment of larger vessels, including the iliac arteries, could not be performed. A number of investigators, such as Werner Porstmann, MD and others, developed solutions to treat larger arteries including the Porstmann or "caged" balloon.[1] In fact, the very first patient that I personally treated was at the University of Rome. The patient had iliac stenosis and a porcelain cage balloon in 1974 (yes it is true), with a great result, which proved to be incredibly durable. This experience crystallized my own vision for the future as I became highly focused on improving less invasive therapies.

In early papers, Dotter predicted the use of splints that subsequently became known as stents. However the concept of placing a scaffolding to maintain patency was actually described in the early 1960s by Dotter himself. Another important aspect of endovascular therapy in regard to using the catheter as a surgical instrument was the use of catheters for drug delivery. In the case of thromboembolic disease, the concept of low-dose thrombolytic therapy was proven and advocated by Dotter, and became an important mainstay of managing vascular occlusive disease.[2] Thousands of patients have been treated based on the concept that one can reduce risks of thrombolytic therapy by delivering lower doses of an agent directly into the clot.

TECHNOLOGICAL DEVELOPMENTS WITH BALLOON ANGIOPLASTY

The development of peripheral angioplasty was the stepping stone to the application of angioplasty to other parts of the circulation. It was only a matter of time, however, and very dependent on the development of appropriate technology and improvement of existing technology. One of the next major milestones came from polymer technology developed by Andreas Gruentzig, MD and his colleagues in making the so-called "rigid" balloon.

Prior to this development, the use of balloons in the circulation was associated with rupture because of the inability to contain the outer diameter. In addition, the balloons were not particularly effective for remodeling of plaque. However, with technological advances, balloons were first applied in the peripheral and renal circulation. This began to shine a light on the real potential of endovascular therapy and provided significant steps in reaching the potential defined by earlier pioneers. As balloon angioplasty advanced in the periphery, renal circulation, and finally the coronary circulation, true excitement began to develop with more wide dissemination of endovascular approaches to atherosclerosis.

IN SEARCH OF IMPROVED DATA-DRIVEN OUTCOMES

The pressure on data-driven outcomes was also a byproduct of these technology developments. A significant shift from anecdotal publications to series including outcomes was a result. The number of physicians becoming engaged and committed to less invasive vascular therapy was growing rapidly, increasing the idea pool and enthusiasm. As a result of the more simplified procedures, and reduction in morbidity, wider application of the technologies occurred. Another byproduct during this period was a synergy developing between physicians with ideas and technology companies interested in implementing those ideas. This collaboration soon led to a rapid explosion in devices and approaches to solve important clinical challenges.

As more was learned about peripheral angioplasty, it became apparent that the procedures had an inherent failure rate both acutely and long-term. Investigators such as Dotter, Hans Wallstén, MD, and Julio Palmaz, MD developed different approaches to providing intravascular scaffolding to maintain arterial patency acutely and improve long-term outcomes. These stents became widely used in the late 1980s and early 1990s, greatly improving outcomes and acceptance of vascular intervention. While these procedures initially required large delivery devices, the concept of miniaturization and reduction in profile leading to reduction in morbidity began to drive technology development.

This period of time also demonstrated that all new technology does not necessarily add value to a patient from an economic point of view. As more disciplines of medicine became involved, there was increasing involvement by vascular surgery and interventional cardiology, bringing new ideas to vascular solutions. Some of these ideas were successful, and others were not. Looking back, ideas such as hot tip lasers, first-generation directional atherectomy, and direct excimer laser angioplasty did not contribute to improved outcomes, but did serve to increase interest in the field of endovascular therapy.

HOW ONE TECHNOLOGICAL ADVANCE LED TO THE NEXT INNOVATION

One of the concepts that we can observe throughout this developmental period is that one technological advance became the foundation for the next one. Straight catheter angioplasty led to balloon angioplasty. Balloon angioplasty led to the development of stents. Stent development integrated with fabrics and other types of coverings brought to bear the concept of endovascular grafting. While some of the initial applications of what are now called endografts were for trauma and acute emergencies, pioneers were again thinking of solving an important clinical problem, namely the treatment of aortic and other aneurysms. Interestingly, some of the early covered stents included devices that were covered with silicone, fabric, and vein grafts, all of which were manufactured in the hands of operators trying to create unique solutions for patients in distress.

Improved technology provided the foundation for pioneers to begin addressing less invasive therapy for abdominal aortic aneurysms. The concept of using a stent as an anastomotic alternative, to which fabric was sewn, proved to be a successful way of excluding an abdominal aortic aneurysm. These landmark advances by numerous investigators leading to pioneering first case experiences showed that no mountain should present an obstacle in the advancement of our field. The successful treatment of aneurysms as a secondary byproduct led to the rapid involvement of vascular surgery in endovascular therapy. Prior to the first aneurysm therapy, most vascular surgeons had looked askance at what was going on in the field of vascular intervention and remained "traditional." Following this milestone, however, a rapid movement of vascular surgery into the space created conflict that affected the field for over a decade.

IN CONCLUSION

Today, endovascular therapy represents a field that includes multiple disciplines in general, working collaboratively to advance this important area of less invasive therapy. In our own institution, from another organizational point of view, we look at "endovascular therapy" in the broadest sense, looking at all aspects of accessing and treating the heart and circulation less invasively from a transcatheter approach. By merging the similarities clinically, organizationally, and architecturally, we take the advantage of aligning similarities for operational and clinical benefit. As a result, present procedures as diverse as transcatheter aortic valve replacement (TAVR) and pedal access are all part of endovascular therapy from an organizational point of view.

Over the past decade, the field has grown even more rapidly and has, in fact, matured. The rapid advancement of numerous technological solutions to similar clinical problems, aligned with increasing cost pressure on the healthcare system, has brought about the need for improved clinical science, data collection, and proof of benefit. This rings true not only in comparing various endovascular techniques to each other, but to surgery and conservative management as well. These are important signs of a mature discipline.

Importantly, in regard to this publication, and the CLI Global Society, it is somewhat ironic that the very first vascular intervention was performed in a patient with CLI and that today, the field of endovascular therapy is becoming increasingly focused on disease that is increasing in almost epidemic proportions, and is a significant public health crisis in many countries around the world. We are on the cusp of truly making a difference through the society's efforts in collecting data, defining CLI as a disease state, and employing many advanced techniques to reduce both amputation rates and mortality from this devastating problem.

In reflecting back on the pioneering efforts, with such limited resources available to accomplish therapy and comparing it with today's technology, better trained physicians, and greatly improved technology, I can only say what an exciting time it is to be involved in this field. ■

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Case Study: Endovascular Reconstruction of the Pedal Loop; Illustrating Challenges and Strategy

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Peripheral arterial disease (PAD) characterized by narrowing of the arteries of the extremities, affects over 8 million people in the U.S. and over 200 million worldwide.[1,2] PAD has emerged as a public health challenge alongside the epidemics of diabetes, and kidney disease that contribute to the development of PAD. Of these patients, 1-2% will develop critical limb ischemia (CLI), the final common pathway of PAD characterized by non-healing ulcers on the extremities, and rest pain that may result in limb amputation. Patients diagnosed with CLI have a morbid prospect, particularly after amputation.[3] This serves as the impetus to attempt to salvage the limb by correcting the underlying vascular insufficiency through endovascular or surgical approaches. While improvements in endovascular technology have led to significant advances in the treatment options available to these patients. Effective treatment requires a combination of having adequate endovascular tools, physician skill, and patience.

A number of key technical considerations must be taken into account when treating CLI. First, these patients often present with below-the-knee disease. Treating these lesions can be challenging because of the distance from the traditional contralateral femoral access site and the paucity of devices with adequate working length. In addition, lesions below the knee have a smaller diameter and are more prone to restenosis and remain the achilles heel of this era of endovascular intervention. Second, chronic total occlusions (CTOs) are more common in below-the-knee lesions. These are difficult to treat and require interventionalists to be familiar with a variety of techniques and devices in order to achieve procedural success.

Here we present a case that illustrates the inevitable hurdles associated with treating CLI and strategies to navigate these successfully.

CASE STUDY

A 53-year-old male with a past medical history of tobacco use and PAD requiring left below the knee amputation presented to the CLI clinic with discoloration of his distal foot and associated rest pain. A 2+ posterior tibial pulse was palpable on exam and vascular ultrasound confirmed blood flow to the level of the ankle. However, due to past history of PAD in the left leg and

Continued on page 16

"Treating these lesions can be challenging because of the distance from the traditional contralateral femoral access site and the paucity of devices with adequate working length."

Figure 1. Posterior tibial artery patent throughout proximal and mid sections, extends distally before occluding at the ankle.

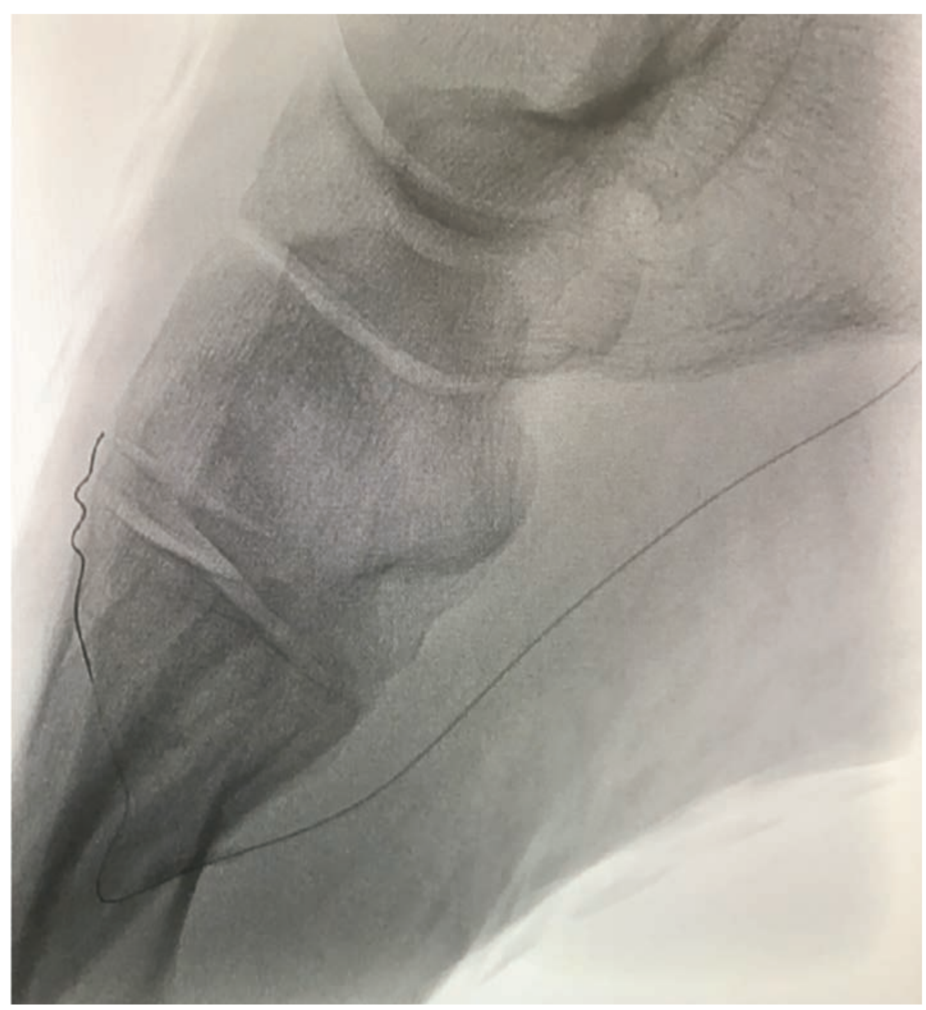

Figure 2. Traversing wire from posterior tibial artery extending through the lateral plantar branch to the dorsalis pedis artery.

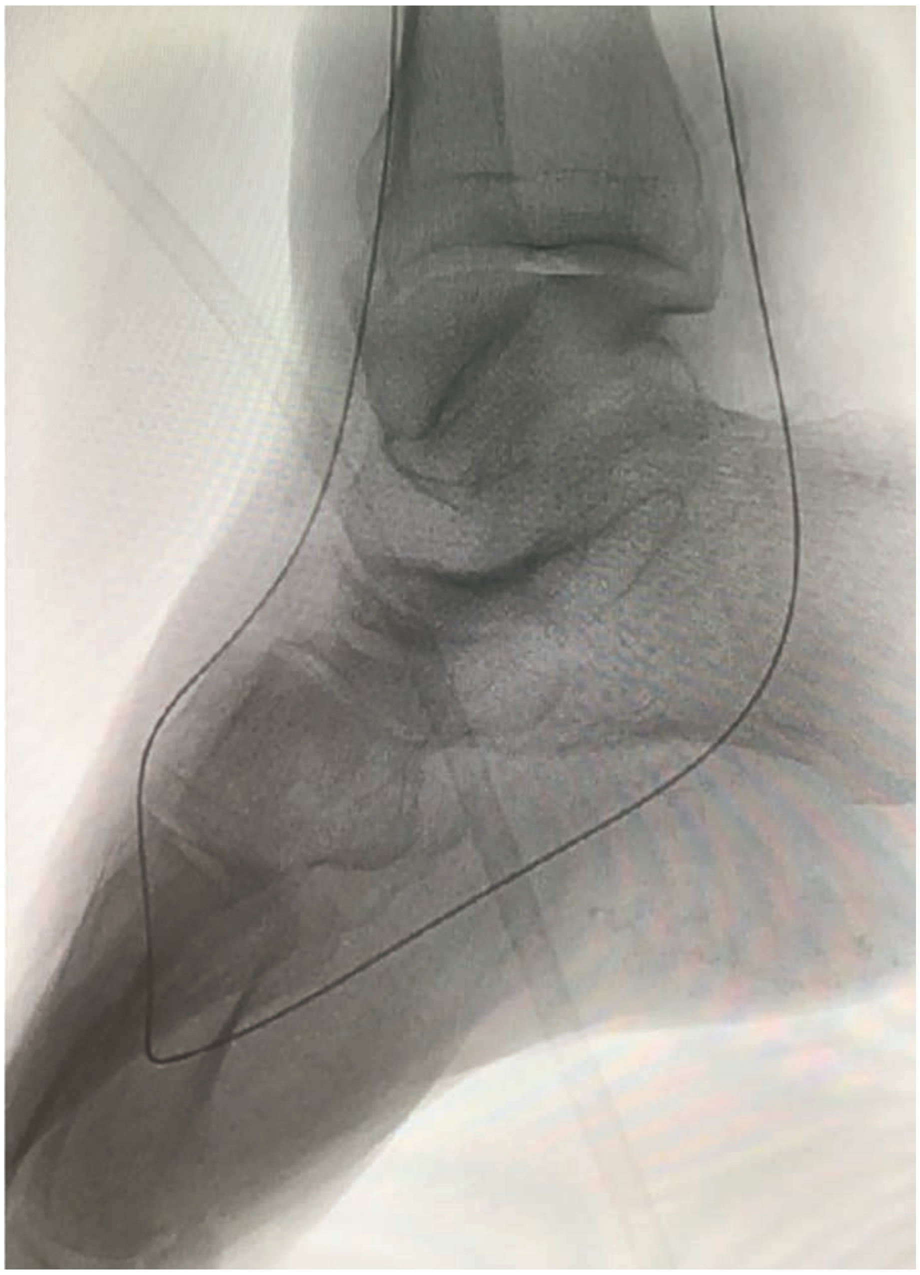

Figure 3. Successful connection of anterior tibial and posterior tibial arteries with wire extending through the pedal loop.

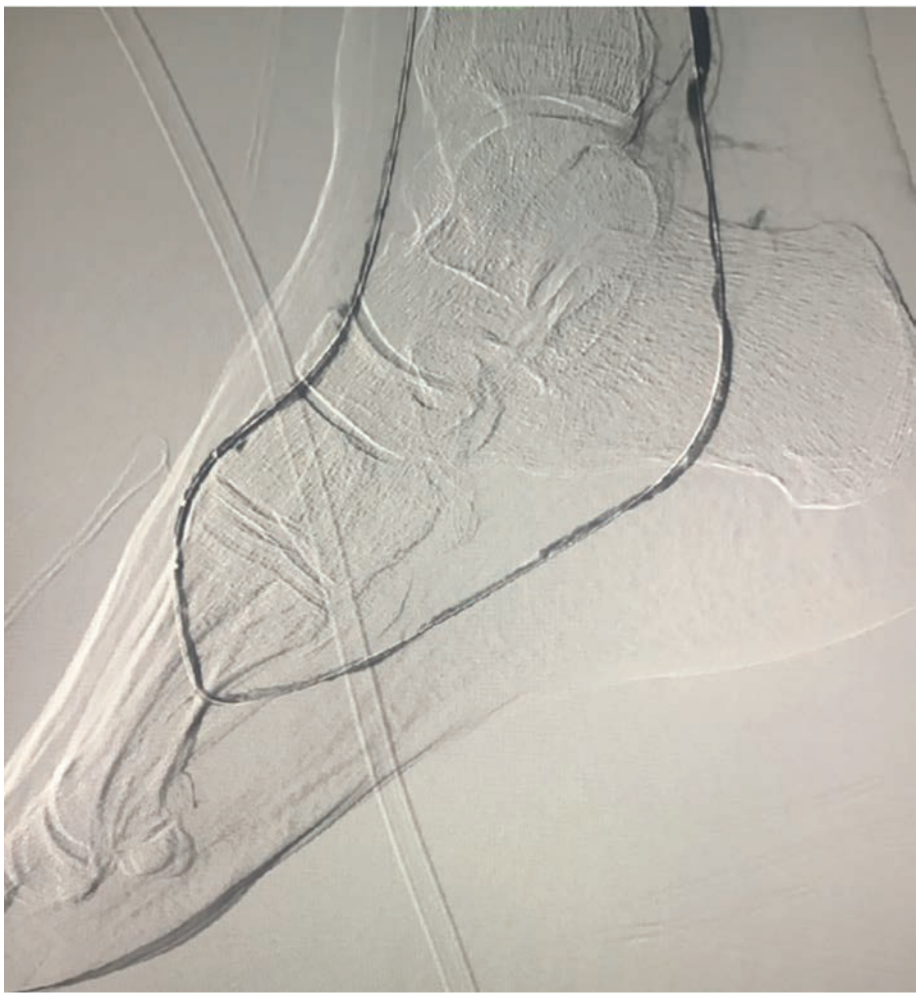

Figure 4. Successful revascularization of the right lower extremity following percutaneous transluminal angioplasty of the distal posterior tibial, dorsalis pedis and anterior tibial arteries.

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symptoms strongly suggestive of vascular insufficiency (rest pain and discoloration of toes), a peripheral extremity angiogram was performed. This revealed a widely patent right superficial femoral artery and popliteal artery. The right anterior tibial artery (ATA) was occluded proximally with no obvious distal reconstitution. The right peroneal artery was widely patent to the foot and the right posterior tibial artery (PTA) was occluded at the level of the ankle (Figure 1).

A contralateral retrograde approach was attempted to cross the distal posterior tibial occlusion using a Runthrough wire (Terumo Medical), however the wire was unable to cross. Next, an 0.18 gm Victory wire (Boston Scientific) along with a Corsair crossing catheter (Asahi Intecc) were used successfully to cross the lesion. The wire followed by the Corsair was extended through the lateral plantar branch back into the dorsalis pedis artery (DPA) (Figure 2). Angioplasty with a 1.50 mm x 15.0 mm over the wire coronary balloon was performed in the segment extended from the PTA to the DPA. This was then followed by a 2.0 mm x 80 mm peripheral balloon resulting in approximately 30% residual stenosis. Considering restrictions from the inadequate length of the equipment needed to extend into the ATA from a retrograde approach, the patient was repositioned on the table and antegrade access was obtained.

A Runthrough wire was then reinserted into the PTA to the level of the DPA. Through the Corsair, the Runthrough wire was exchanged for an 0.18 gm Victory wire and extended to the mid ATA. Considering significant resistance, a second 0.18 gm Victory wire was then inserted in an antegrade fashion into the proximal occluded ATA to the level of the DPA. Using a "wrapping wire technique," with the second wire wrapping the retrograde wire, the two wires rendezvoused in the same plane. Percutaneous transluminal angioplasty was performed in the occluded ATA down to the DPA utilizing a 2.0 mm x 120 mm balloon (Cook Medical), a 2.5 mm x 250 mm Sleek dilatation catheter (Cordis Corporation), and 4.0 mm x 50 mm balloon (Cook Medical) resulting in an approximate 30% residual stenosis. This resulted in connecting the pedal loop from the ATA to the PTA supplying flow to the digits (Figures 3 and 4).

DISCUSSION

Patients diagnosed with CLI are faced with a particularly morbid prognosis with the prospect of amputation, disability, and high mortality rates. This case illustrates the challenges of treating multiple lesions below the knee to restore blood flow to the distal extremity to avoid amputation. In addition, the anatomical and device-related constraints that an interventionalist must keep in mind while treating CLI are apparent. Physicians should be well versed in advanced interventional techniques in order to give the patient the best chance of avoiding limb amputation. While there have been significant advances in the devices available for treating PAD, there is still a paucity of the types of devices needed to address the unique challenges faced when treating CLI and, particularly, lesions below the knee, such as wires of adequate length and related treatment tools. While these cases can be challenging and laborious, they can make a significant impact on the quality of life and independence of the patient by staving off limb amputation. Ultimately, success is determined by the skill and patience of a provider as well the comfort in using a variety of tools and techniques. ■

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"Physicians should be well versed in advanced interventional techniques in order to give the patient the best chance of avoiding limb amputation."

In Memoriam

ALAN T. HIRSCH, MD, MSVM 1954 – 2017

The recent passing of Alan Hirsch, MD, MSVM, left a legacy of the highest commitment in the field of vascular medicine. Dr. Hirsch was a pioneer in the field of vascular medicine. After studying at Harvard and the University of California, San Francisco (UCSF), he went on to serve as a Professor of Medicine and director of the Vascular Medicine program of the Lillehei Heart Institute at the University of Minnesota. He was deeply dedicated to improving public health.

Dr. Hirsch was the loving father of Jonathan Hirsch and Rebecca Hirsch, a dear brother of Gail (Bill Neiman) Hirsch Neiman, an adored uncle of Brent (Yael Aufgang) Neiman and Leigh (Jeremy Weisz) Neiman Weisz, a beloved companion of Sue Duval and loving father figure of Alex Duval.

Among numerous leadership roles, Dr. Hirsch was a founding member and past president of the Society for Vascular Medicine and vice president of the CLI Global Society.

Dr. Hirsch epitomized that one person can make a difference in this world. He was a force of nature and the voice of PAD research. He enthusiastically urged each of his colleagues to do the right thing, even if it wasn't the easy thing. Dr. Hirsch was a strong advocate for patients and vascular medicine. He balanced an amazing schedule of work, teaching, speaking and advocacy with unwavering high energy, a positive attitude and passion for his work. Dr. Hirsch was greatly respected by his peers, students and patients, and will be missed by many.

In honor of Dr. Hirsch, the Amputation Prevention Symposium (August 9-12, 2017 in Chicago) will open with the Alan T. Hirsch Memorial Keynote Address, which will be delivered by Barry T. Katzen, MD, FACR, FACC, FSIR, from 8:35 a.m. to 8:55 a.m. on August 9. For more information, visit www.amptheclimeeting.com. ■

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July 24-27, 2017
Chicago Endovascular Conference (CEC) 2017
Location: Chicago, IL
Website: www.cvcpvd.com

August 9-12, 2017
Amputation Prevention Symposium (AMP)
Location: Chicago, IL
www.amptheclimeeting.com

September 11-14 , 2017
Vascular InterVentional Advances (VIVA 17)
Location: Las Vegas, Nevada
Website: www.vivapvd.com

September 16-20, 2017
Cardiovascular and Interventional Radiological Society of Europe Annual Congress (CIRSE)
Location: Copenhagen, Denmark
Website: www.cirse.org

October 29-November 2, 2017
Transcatheter Cardiovascular Therapeutics (TCT) 2017
Location: Denver, Colorado
www.tctconference.com and www.crf.org/tct

November 14-18, 2017
VEITH Symposium
Location: New York, New York
www.veithsymposium.org

February 3-7, 2018
International Symposium on Endovascular Therapy 2018 (ISET)
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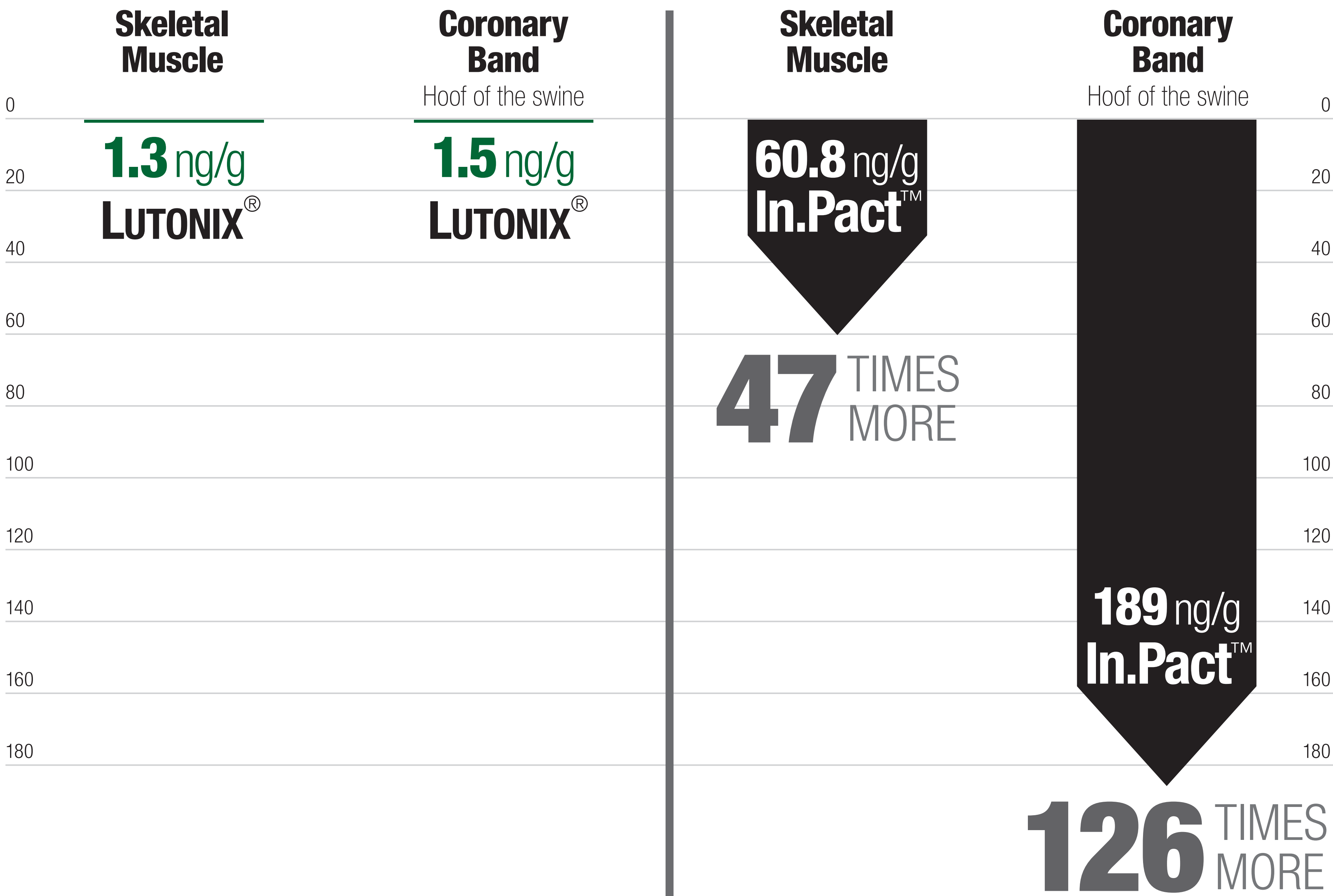
1. Jetstream Calcium Study
CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Please see reverse for Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

PRE-CLINICAL DOWNSTREAM Paclitaxel Levels*

Downstream Paclitaxel Tissue Concentration Levels 1x dose at 28 Days



LUTONIX® 035
Drug Coated Balloon PTA Catheter

In.Pact™ Admiral™

BARD

*Journal of Vascular and Interventional Radiology: Comparison of Particulate Embolization after Femoral Artery Treatment with In.Pact Admiral versus LUTONIX® 035 Paclitaxel-Coated Balloons in Healthy Swine. Limitations associated with this pre-clinical study include: Pathologic findings are limited to healthy swine and do not account for the fact that human PAD presents with co-morbidities; and transferring pre-clinical findings in healthy animal arteries to humans with peripheral arterial disease is complex, as lesions can be complicated by fibrosis, necrosis and calcification. This study was funded by Lutonix, Inc. (New Hope, Minnesota). Article available at: http://dx.doi.org/10.1016/j.jvir.2016.06.036. Kolodgie et al, JVIR D-15-01131R1. **Please consult product labels and instructions for use for indications, contraindications, hazards, warnings and precautions.** Rx Only Bard and Lutonix are trademarks and/or registered trademarks of C. R. Bard, Inc., or an affiliate. All other trademarks are property of their respective owners. Bard Peripheral Vascular, Inc.1625 W. 3rd Street | Tempe, AZ 85281 | 1 800 321 4254 | www.bardpv.com **BPV/LTNX/0816/0086h**