

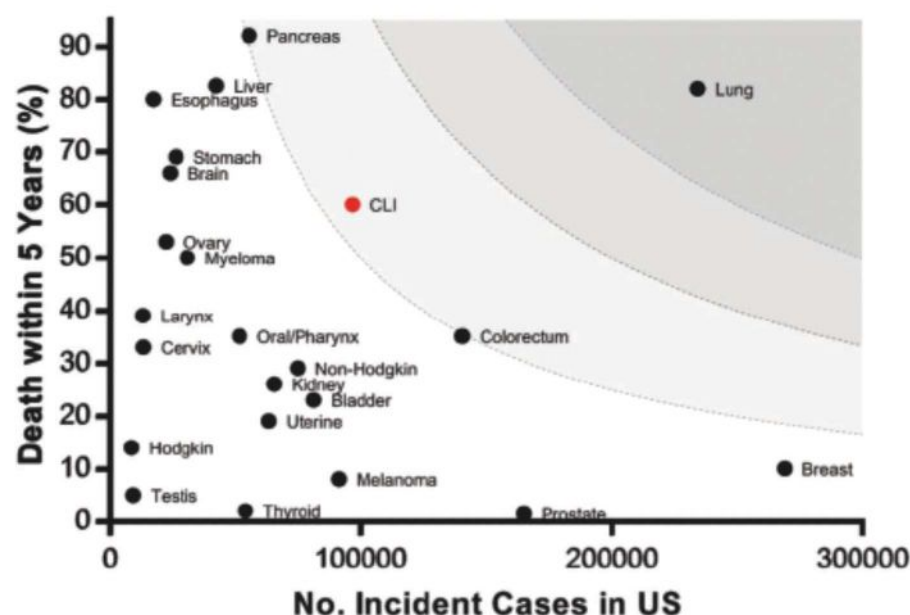
## Critical Limb Ischemia is a Threat to Life and Limb

J. A. Mustapha, MD; Barry T. Katzen, MD; Richard F. Neville, MD; Robert A. Lookstein, MD; Thomas Zeller, MD; Larry E. Miller, PhD; Vickie R. Driver, MD; Michael R. Jaff, DO

A recent publication on behalf of the CLI Global Society confirmed that CLI is an underdiagnosed and undertreated deadly disease that requires proper diagnostic imaging and increased awareness.<sup>1</sup>

Worldwide, 202 million adults have peripheral arterial disease (PAD) which has a higher prevalence than ischemic heart disease, heart failure, Alzheimer's disease/dementia, cancer, HIV/AIDS and opioid addiction.<sup>2</sup> Among 9 to 20 million adults with PAD in the United States, 11% suffer from CLI.<sup>3,4</sup> This is likely considered an underestimation. CLI prevalence is typically estimated from administrative claims databases using ICD clinical diagnosis codes. Although use of administrative diagnosis codes yields high sensitivity when patients with a CLI diagnosis code likely have the disease, there is a corresponding loss of specificity when patients, who may actually have the disease, do not have the corresponding CLI diagnosis code. Validation studies suggest that use of administrative codes for CLI diagnosis may underestimate the true prevalence by 25%.<sup>5</sup> Given these factors, it can be estimated that between 1 to 3 million Americans have CLI.

When an individual receives a first diagnosis of CLI, the mortality risk is 24% at 1 year and 60% over 5 years.<sup>6</sup> Fewer diseases have a higher mortality rate. Among 22 different types of malignancy, only six have a 5-year mortality rate higher than that of CLI.<sup>7</sup> CLI is even more deadly than this statistic suggests. When viewed in isolation, 5-year mortality rates fail to convey the disease-specific mortality burden from a population perspective. Many cancers with high mortality rates are relatively rare, so the overall mortality burden to the population is modest. Conversely, the mortality burden associated with some of the most common cancers is blunted due to relative low mortality rates. Consequently, several deadly cancers, such as melanoma or ovarian cancer, are actually less common and less deadly than CLI. A helpful metric for quantifying the overall mortality burden of a disease is the 5-year incident mortality. That is, among all patients who receive a first-time disease diagnosis in a given year, how many will die sometime during the next 5 years?<sup>1</sup> The annual incidence and 5-year mortality rates for CLI was derived from a Medicare



**Figure 1.** The relationship of 5-year mortality and annual incident cases of CLI and 22 common cancers. Plotted is the absolute number of deaths within 5 years among patients in the United States who received their first diagnosis during a 1-year period. The number of deaths is > 150,000 for diagnoses plotted in the dark gray background, > 100,000 in the gray background, > 50,000 in the light gray background, and < 50,000 in the white background.

Excerpted from Mustapha JA, Katzen BT, Neville RF, Lookstein RA, Zeller T, Miller LE, Driver VR, Jaff MR. Critical Limb Ischemia: A Threat to Life and Limb. *Endovasc Today*. 2019;18(5):80-82.

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## CLI Global Society Coalition Submits ICD-10 Proposal for 2021 Update

As part of its mission to raise awareness and better define CLI disease, the CLI Global Society is leading a multi-specialty medical society task force to differentiate CLI disease from peripheral arterial diseases in the medical coding and billing nomenclature, beginning with ICD-10 CM diagnosis codes.

The goal is to support the myriad of coding professionals, educators, compliance staff, and physicians to identify and define CLI in order to track and monitor patient treatments and outcomes in the future.

The CLI Global Society's proposal is being considered by the CDC ICD-10 CM Coordination & Management Committee for addition to the 2021 update. This effort is a first step in building awareness among public and commercial payers of the complexity associated with caring for patients who experience critical limb ischemia.

The hard work and effort of the members of the multi-society task force is greatly appreciated. ■

SOCIETY	TASK FORCE MEMBERS
Critical Limb Ischemia Global Society	Barry Katzen, MD Robert Lookstein, MD
Society for Cardiovascular Angiography & Intervention	Mehdi Shishehbor, DO
Society for Vascular Medicine	Mitchell Weinberg, MD
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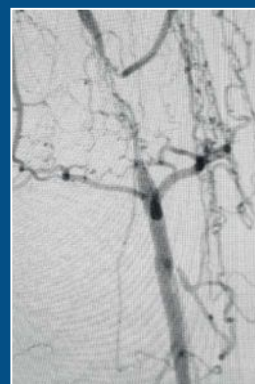


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# Intravascular Imaging in Infrainguinal Intervention

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The limitations of angiography in assessing the degree of atherosclerotic change in the vasculature are well known. In coronary procedures, the use of intravascular (IV) imaging [intravascular ultrasound (IVUS) or optical coherence tomography (OCT)] is an accepted adjunct to angiography that offers both diagnostic and therapeutic guidance.

IV imaging is underused in coronary procedures in the U.S. with estimates showing only 5% to 7% of coronary interventions utilizing OCT or IVUS.<sup>1,2</sup> Two recent large scale trials in coronary literature show that the use of IV imaging improves patient outcomes.<sup>3,4</sup> The IVUS-XPL trial demonstrated significantly lower rates of target revascularization when IVUS was used compared to angiography alone in long coronary lesions ( $\geq 28$  mm).<sup>5</sup> This was followed by the ULTIMATE trial (Intravascular Ultrasound Guided Drug Eluting Stents Implantation in “All-Comers” Coronary Lesions), which also demonstrated superior outcomes with IVUS compared to angiography alone (HR, 0.530; 95% CI: 0.312–0.901;  $P=.019$ ). Despite these data, the use of IV imaging has been slow to be adopted for lower-extremity intervention. A retrospective analysis of the Nationwide Inpatient sample from 2006 to 2011 showed that use of IVUS during lower extremity endovascular procedures

## Despite studies examining its use in endovascular procedures showing that IV imaging was associated with improved outcomes, IV imaging has been slow to be adopted for lower-extremity intervention.

was as low as 1.4%. Similar to the coronary IVUS trials, IV imaging in endovascular procedures was associated with improved outcomes in the form of lower complication (12.0% vs 14.9%;  $P<.001$ ) and amputation rates (5.3% vs 9.8%;  $P<.001$ ).<sup>6</sup>

The use of IV imaging in peripheral endovascular interventions is not a new concept. In patients undergoing endovascular intervention in the early to mid 1990s, it was demonstrated that up to 40% of aortoiliac interventions that appeared satisfactory by angiography had underexpanded stents when evaluated with IVUS. Furthermore, patients whose interventions were evaluated by IVUS upfront did not require re-intervention, whereas 25% of the patients without initial IVUS imaging required reintervention.<sup>7</sup> More recently, a propensity matched analysis showed improved 5-year primary patency rates (65% vs

35%;  $P<.01$ ) with the adjunctive use of IVUS compared to angiography alone in femoropopliteal interventions.<sup>8</sup>

### APPLICATIONS OF INTRAVASCULAR IMAGING

**Intravascular ultrasound.** IVUS is useful to determine vessel sizing, minimal lumen area, and the composition of plaque in the arterial wall. Color flow imaging can also aid in the diagnosis of dissection. Several IVUS catheters are available for clinical use. Lower frequency IVUS catheters (10 MHz) provide imaging diameters up to 60 mm and are appropriate for evaluation of large vessels such as the aorta and IVC and iliac arteries and veins. Higher frequency catheters (20–60 MHz) are appropriate for imaging infrainguinal vessels (imaging diameters 6 mm–8 mm) and are able to provide superior spatial resolution when compared with lower frequency catheters (150

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

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# Potential Role for Edetate Disodium-based Infusions as Adjunctive Treatment for Limb Salvage in Patients With Critical Limb Ischemia

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Gervasio A. Lamas, MD

The most severe form of peripheral artery disease (PAD) is critical limb ischemia (CLI). It leads to an increase in morbidity, procedural interventions, hospital admissions, poor quality of life, amputation, and mortality risk. Despite a decrease in the rates of amputations in patients with PAD, 75,000 major amputations occur each year. Thus, additional interventions are needed in the battle against CLI to further decrease amputations and improve quality of life. In 2018, several very large studies reported the association of low-level lead exposure with atherosclerotic death, and of low level cadmium exposure with PAD. Both metals are chelated by edetate disodium. Both toxic metals are known to cause endothelial dysfunction, increase inflammation, and have pro-atherosclerotic properties, potentially increasing the risk of PAD.

Edetate disodium is a chelator with high affinity to toxic metals such as cadmium and lead, and an association with cardiovascular disease.<sup>1</sup> Chelation therapy with edetate disodium has been in use for more than 60 years as a treatment for atherosclerosis, but without definitive trials until 2012.<sup>2</sup> The Trial to Assess Chelation Therapy (TACT) demonstrated a benefit in reducing major adverse cardiovascular events in post-myocardial infarction patients with diabetes. A post-hoc analysis of 162 TACT patients with diabetes and PAD demonstrated a 48% relative reduction ( $P=.0069$ ) of the TACT primary endpoint.<sup>3</sup> Although the results were



Figure 1. Evolution of non-healing and dry gangrene in patient at baseline and at completion of his chelation regimen.<sup>5</sup>

positive, the study did not address the mechanism of action. A follow-up study by Arenas et al quantified the affinity of edetate disodium-based infusions to toxic metals, and inferred toxic metal excretion as a possible mechanism of benefit.<sup>1</sup> The study enrolled 26 post-MI patients with diabetes and administered a single infusion of edetate disodium-based chelation, with measurement of urinary levels of metals at baseline and overnight after infusion. The study demonstrated an increase in toxic metal levels compared to baseline, urine lead excretion increased by 3,835% and cadmium by 633%.

Due to the potential for benefit in patients with diabetes and PAD,<sup>4</sup> we offered a regimen of 50 TACT infusions to 10 patients with CLI. This review will present one previously reported patient,<sup>5</sup> with initial angiographic findings, the outcome after completion of the chelation regimen extending beyond what was

previously reported, and discuss possible mechanisms of action. There was no follow-up angiography as our study was not funded for it. This patient is being presented as a hyper-responder.

## CASE PRESENTATION

An 81-year-old male former smoker (20 pack-years), with longstanding type 2 diabetes, and vascular disease in multiple distributions presented to our facility for treatment. He had coronary bypass surgery 15 years earlier. He first developed symptomatic PAD 4 years before presentation, and 7 months before that date we saw that his symptoms had progressed to CLI with dry gangrene of the left first digit and approximately 50% gangrene of the second digit. Three years after diagnosis of CLI, along with completion of multiple procedures, he still had dry gangrene in his left foot (Figure 1). A lower extremity angiogram was performed,

which demonstrated complete occlusion of the common femoral artery extending to the origins of the superficial femoral artery (SFA) and profunda femoris, complete occlusion of the distal SFA and popliteal artery extending to involve all three infrapopliteal arteries with single vessel runoff via a reconstituted posterior tibial artery (Figure 2). The patient underwent a left femoral thrombo-endarterectomy and patch angioplasty followed by a left ilio-femoral endarterectomy with vein patch repair of the left common femoral artery by vascular surgery. Despite the revascularization attempt, non-healing ulcers and dry gangrene progressed even with ongoing supportive therapy with hyperbaric oxygen therapy. The patient was scheduled for below-the-knee amputation. His wife heard of our edetate disodium-based chelation pilot study, and

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# Independent Adjudication Found Zero Deaths Attributable to LUTONIX® 035 DCB

Syntactx clinical research organization, using a medical advisory committee consisting of an interventionalist and oncologist, adjudicated patient deaths across LUTONIX® 035 DCB trials. If in disagreement, an oncologist was used to break the tie. The conclusion: **none of the deaths were attributed to paclitaxel.**<sup>1</sup>

Independent Analysis  
2 + 1 Adjudication = 0 Paclitaxel  
Interventionalist & Oncology + Oncologist Related  
Deaths<sup>1</sup>

**LUTONIX® 035**  
Drug Coated Balloon PTA Catheter

<sup>1</sup> Analysis conducted by an independent clinical research organization, Syntactx LLC for which it was compensated by BD. 173 deaths in LEVANT 1 and LEVANT 2 (including patients from Continued Access arm of LEVANT 2), with 151 occurring in LUTONIX® 035 DCB patients (14.0%) and 22 in PTA patients (10.4%). Data on file. Bard Peripheral Vascular, Inc. Tempe, AZ.

The LUTONIX® 035 Drug Coated Balloon PTA catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions up to 300 mm in length in native superficial femoral or popliteal arteries with reference vessel diameter of 4-7 mm.

In March 2019, the U.S. Food and Drug Administration (FDA) issued a letter noting an increased risk in long-term mortality with paclitaxel-coated devices when used to treat peripheral arterial disease in the femoropopliteal artery. In June 2019, the FDA Circulatory System Devices Panel of the Medical Devices Advisory Committee acknowledged this potential increase in mortality, noted the strong evidence of benefit regarding paclitaxel-coated device use, and recommended additional efforts to evaluate long-term safety. BD will continue to work collaboratively with FDA and industry for additional safety data collection and inform labeling as appropriate. These communications as well as information about the FDA Panel meeting can be found at: <https://www.fda.gov/medical-devices/letters-health-care-providers/update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting>



# Minimal Arterial Access for Lower Extremity Intervention (MáLEI) in Patients with Critical Limb Ischemia

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Imraan Ansaarie, MD

Various methods of peripheral revascularization, such as percutaneous transluminal angioplasty (PTA), stenting, and atherectomy, are the cornerstone procedures for peripheral artery disease. Transfemoral access is the most common access used for these peripheral procedures due to their high success rates. However, due to an increased risk for complications and extended length of stay post-revascularization, it can be undesirable and costly to patients. Therefore, considerations such as quality of life and cost have become increasingly relevant in choosing between femoral artery access and alternative revascularization access points, such as transradial/transulnar with or without transpedal access or minimal arterial access lower extremity intervention (MáLEI).

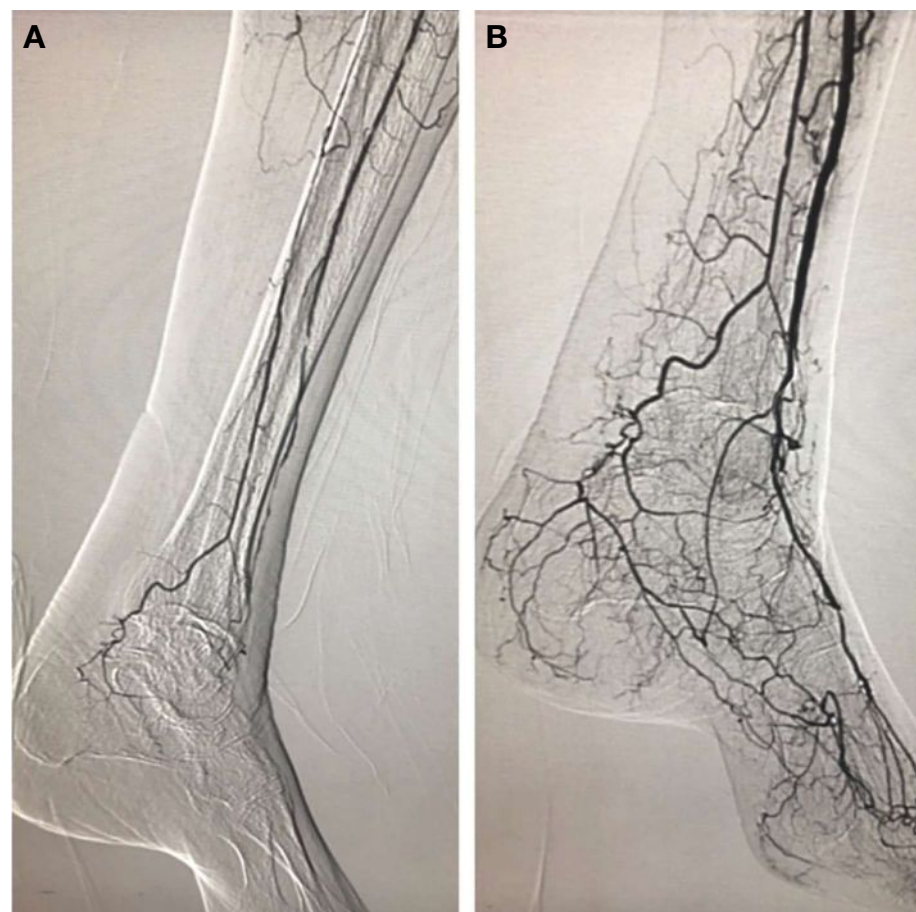
This procedure has now been completed more than 90 times, utilizing every MáLEI access site including radial, ulnar, and pedal, in nearly every Rutherford-Becker class in every TASC II lesion. Our success rate is greater than 95%, defined as completion of the procedure without requiring access secondarily via the femoral, popliteal, or brachial artery. The medium vessel size and area of the access site leads to fewer complications, faster recovery time, and earlier ambulation time compared with the larger vessel access. Here we will discuss two case reports where MáLEI intervention was beneficial due to the patient's "difficult aortic bifurcation" with advanced comorbidities and a patient who had previous femoral access site complications and advanced comorbidities.

## CASE 1

JH is an 85-year-old female with a past medical history of hypertension,

congestive heart failure, and dyslipidemia. She presented to the emergency department with gangrene of the left foot, involving all the toes. On admission, she was also in congestive heart failure. After appropriate diuresis and optimization, she was brought to the interventional radiology suite for her initial angiogram done via left radial artery access. The access was obtained via ultrasound guidance and a 5-Fr Glidesheath Slender (Terumo). The angiographic evaluation found multiple high-grade lesions noted in the entire left SFA, left popliteal artery, left anterior tibial artery, and diffuse disease in the left peroneal artery. The TP segment and the left posterior tibial artery were 100% occluded. After the initial angiogram, over a stiff 0.035-inch, 1.5-mm J-tip 400-cm Glidewire (Terumo), a R2P Destination Slender Guiding Sheath 6 Fr, 119 cm (Terumo) was placed via the left radial artery and advanced into the left external Iliac artery under radiographic guidance. The patient was then fully anti-coagulated in the standard fashion. The lesions, in the left SFA, popliteal artery, and the anterior tibial artery, were crossed with the help of a NaviCross 0.035-inch angled tip 150-cm support catheter (Terumo) and a 0.014-inch Viper Wire. Once the wire was successfully placed in the left dorsalis pedis artery, atherectomy and angioplasty of the left superficial femoral artery, left popliteal artery, and the anterior tibial artery was performed using a 1.50 solid Diamondback 360 Extended Length Peripheral Orbital Atherectomy Device (OAD) from Cardiovascular Systems, Inc. (CSI).

The balloon angioplasty of the anterior tibial artery was performed using a 2.0 x 200 mm Ultraverse Rx balloon (Bard). The left popliteal artery and the left superficial femoral artery balloon angioplasty was performed using a R2P Metacross RX PTA balloon 5.0 x 200 mm (Terumo). After successful atherectomy and balloon angioplasty, the final angiogram showed an excellent result, with no major side branch compromise, no flow limiting dissection, and no distal embolization. At this time, the procedure was deemed complete and the R2P Destination Slender guiding sheath 6 Fr, 119 cm was removed over the stiff 0.035-inch, 1.5-mm J-tip 400-cm Glidewire, under radiographic guidance with no complications. Homeostasis was achieved using the standard TR Band (Terumo). The patient was successfully discharged home and instructed to return in 6 weeks for a formal trans-metatarsal amputation, which healed uneventfully.



**Figure 1.** (A) Initial angiogram of the left foot via (L) radial artery showing CTO of the peroneal artery in its mid-body with absent dorsalis pedis artery. CTO = chronic total occlusion. (B) Final angiogram showing Atherectomy and balloon angioplasty of Peroneal, anterior tibial, and Dorsalis pedis arteries via (L) Radial artery showing successful revascularization of the left foot.



**Figure 2.** (A) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the left SFA. (B) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the mid left anterior tibial artery. (C) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the left dorsalis pedis artery.

## CASE 2

A 67-year-old male presented with a non-healing wound of the right lower extremity. His past medical history was notable for hypertension, diabetes with complications of peripheral vascular

disease, coronary artery disease, and dyslipidemia. His surgical interventional history included a prior coronary artery bypass graft. On his physical examination,

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# CLI in Women: Have We Done All We Can to Ensure Treatment Equality?

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Peripheral arterial disease (PAD) affects between 5 to 10 million individuals in the United States and is associated with significant morbidity, mortality, and healthcare costs.<sup>1</sup> While the incidence of PAD may be similar in women versus men, as women outlive men, the burden of PAD is higher in the aging female population.<sup>2</sup> Despite these circumstances, PAD is under-diagnosed in women, and women are under-represented in PAD clinical trials.<sup>3</sup>

Several sex-related differences exist with respect to PAD. The traditional cardiovascular risk factors are more commonly present in men with PAD compared to women with PAD.<sup>3</sup> For example, women with PAD are more likely to suffer from depression compared to women without PAD. Other conditions such as hypothyroidism, arthritis, osteoporosis, and inflammation can occur more often in women with PAD compared to women without PAD.<sup>4</sup> Awareness of these women-specific comorbidities can help with earlier diagnosis of PAD.

The clinical presentation of women with PAD is also different from men with PAD. Women tend to present with PAD at an older age and with more advanced disease, including femoropopliteal and multi-level infrainguinal disease and critical limb ischemia (CLI).<sup>5</sup> In fact, the female gender has been shown to be an independent predictor for severe and diffuse atherosclerotic disease.<sup>6</sup>

Women also have higher rates of asymptomatic and atypical presentations of PAD. In one study of 933 women, 35% had an ABI less than 0.91, consistent with PAD. However, 63% of these women had no exertional leg pain, instead presenting with atypical symptoms of slower walking velocity, poorer standing balance

scores, slower time to arise five times consecutively from a seated position, and fewer blocks walked per week.<sup>7</sup> In addition, women with CLI have higher readmission rates compared with men.<sup>8</sup> However, at least one study suggests that men have overall worse amputation-free survival than women.<sup>9</sup>

Although the current literature is lacking with regard to the investigation of sex-specific treatment outcomes for PAD and CLI, existing evidence suggests that there is no sex-based difference with regard to the benefit of conservative management with a supervised exercise regimen and medical therapy with cilostazol when women are compared with men.<sup>10,11</sup>

The advanced age observed in women with PAD and CLI may be due to the late onset of PAD resulting from a potential protective role of hormones before menopause.<sup>12,13</sup> PAD may also progress at a more rapid pace in the post-menopausal state, once again explaining the common presentation of CLI in women.<sup>14</sup> Advanced age may contribute to the increased rate of women with CLI. If elderly women are living alone or in nursing facilities or not getting proper clinical care, it is plausible that their PAD would advance to the point of CLI.

The multi-level disease associated with occlusions in women with CLI may require open surgical revascularization.<sup>6</sup> There are conflicting reports regarding the outcomes of revascularization in women with CLI.<sup>6,15</sup> Some studies suggest that women have a higher incidence of graft failure, wound infection, bleeding complications, limb loss, and mortality compared with men.<sup>16-18</sup> However, at least one study suggests this difference may relate to higher use of autogenous grafts in women than men. In patients

Summary of PAD/CLI Findings in Women vs. Men (Current Limited Data)	
Asymptomatic PAD	More common in women
Atypical PAD presentation	More common in women
Supervised exercise outcomes	Same
Cilostazol outcomes	Same
Readmission rates (CLI)	Higher in women
Amputation free survival	Higher in women
Surgical revascularization complications	No consensus
Surgical revascularization outcomes	Same
Endovascular revascularization success	Higher in women
Endovascular revascularization complications	Higher in women
Endovascular revascularization outcomes	Same
Amputation rates (DFU)	Same
Inpatient mortality	Higher in women
Wound healing rates (arterial ulcers)	Same

who receive prosthetic conduit, acute graft failure was higher for women than men.<sup>19</sup> A recent meta-analysis suggests that, with regard to open surgical revascularization, women have significantly increased risk of 30-day mortality, amputation, early graft thrombosis, embolization, incision site complication, cardiac events, stroke, and pulmonary complications. However, long-term outcomes were similar.<sup>20</sup> Recently, data suggest that men are more likely to undergo surgical rather than endovascular revascularization, and also have higher amputation and mortality rates post-intervention compared with women.<sup>21</sup> Consequently, the data in the literature are conflicting with regard to sex-based differences in complication rates following open surgical revascularization.

In recent years, with the advent of newer devices, there has been a shift toward more endovascular treatment for the management of PAD, including CLI. The literature is conflicting regarding the outcomes of endovascular interventions in women with CLI compared to men.

At least one study suggests technical success rates are higher in women, although higher rates of embolic events were also seen.<sup>22</sup> Another study indicates improved patency rates after endovascular intervention in women, though limb loss was also higher for women in that study.<sup>23</sup> One study demonstrated the female sex was related to a five-time greater risk of treatment failure.<sup>24</sup> More recent literature suggests that the 5-year clinical outcomes following endovascular revascularization are similar in men and women, with no statistically significant difference in MACE (major adverse cardiac events) and MALE

(major adverse limb events) at 5 years.<sup>25</sup> Yet another study demonstrated that following intervention, women with CLI may have a higher rate of major adverse cardiovascular events.<sup>26</sup>

In patients with diabetic foot ulcers, at least one study suggests amputation rates do not appear to differ between men and women.<sup>27</sup> However, regardless of open or endovascular revascularization, women with lifestyle-limiting claudication or CLI admitted after intervention to having higher inpatient mortality than men.<sup>15</sup> There is limited evidence with regard to the effect of sex on arterial ulcer lower extremity wound healing rates, although at least one study suggests healing rates are significantly related to skin perfusion pressure and not sex.<sup>28</sup>

CLI is the most advanced presentation of PAD and is a growing epidemic.<sup>29</sup> Further investigation is needed to determine the sex-related differences that contribute to PAD development and presentation with CLI. Despite unanswered questions, more efforts are needed to educate patients and clinicians about the occurrence of PAD in women with the hope of earlier diagnosis. Despite the lack of robust data, it seems endovascular treatment of CLI in women remains a viable option and should be considered, despite the old age of the patient and her comorbidities. Finally, more women need to be represented in PAD clinical trials such that better data-driven outcomes analysis can be performed to optimize the management of women with PAD and CLI. In summary, we have not done everything to ensure treatment equality, but we can start today! ■

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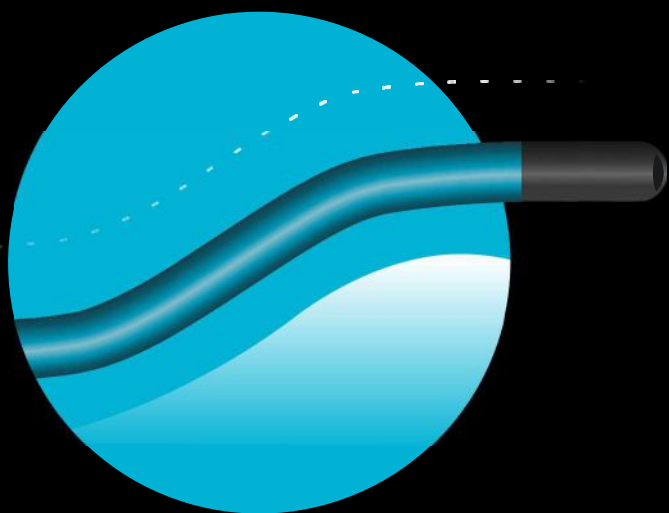
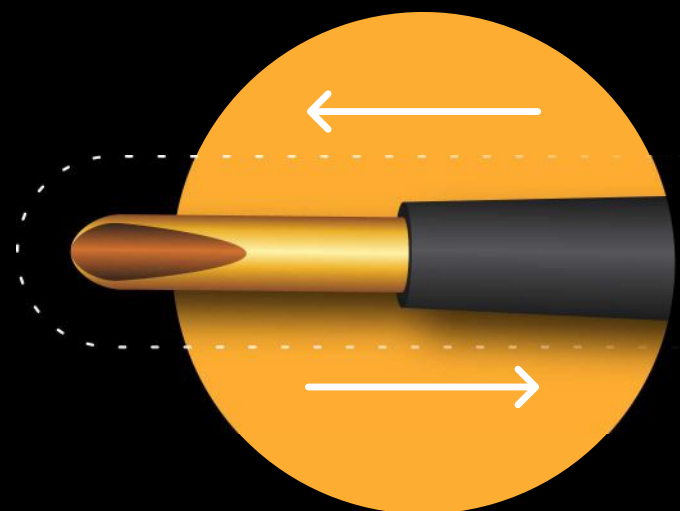
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# The Importance of Establishing Flow in Metatarsal Branches in CLI Patients

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## CASE DESCRIPTION

A 79-year-old male presented with severe worsening shortness of breath. Medical history included severe peripheral vascular and coronary artery disease, hypertension, dyslipidemia, and type 2 diabetes. Medical therapy consisted of aspirin, amlodipine, losartan, statin, and oral hypoglycemic therapy. The patient was not able to perform daily activities without shortness of breath. He has severe intermittent claudication when he walks a few steps and pain at rest in his left leg. This has limited his daily activities.

Ankle brachial index (ABI) at rest was performed and revealed ABI 0.73 on the right and 0.55 on the left. Doppler waveform revealed monophasic distal waveforms on the right and blunted monophasic waveforms on the left. The pulse volume on the left was greatly diminished. Computed tomographic angiography (CTA) of the abdominal aorta and bilateral iliofemoral runoff revealed severe scattered atheromatous plaquing involving the superficial femoral artery (SFA) with occlusion in the mid-segment. There was tandem stenosis of the left popliteal artery above the knee with collateral reconstitution of a severely diseased popliteal artery below the knee. There was a single vessel runoff of the left peroneal artery, which was severely diseased proximally and reconstitution of the posterior tibial artery at the distal ankle.

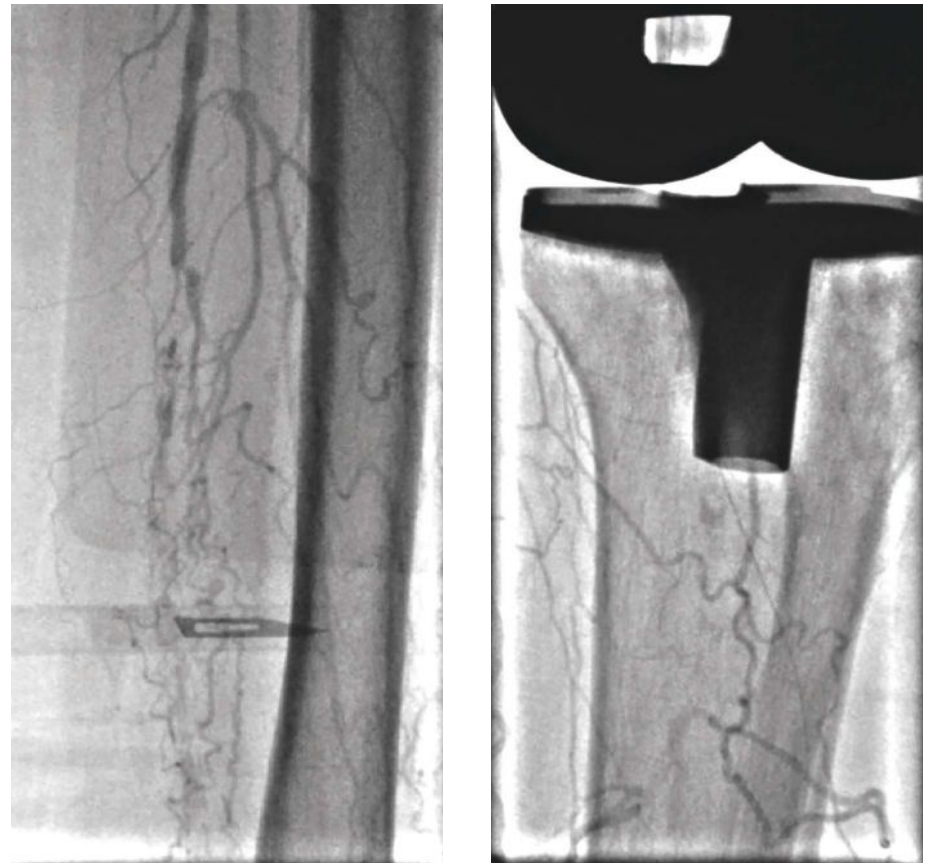
The patient was referred for peripheral angiography and intervention of the left leg. After obtaining retrograde access in the right common femoral artery, initial angiography of the left leg revealed 50% disease in the superficial femoral artery (SFA) with severe popliteal and

below-the-knee disease. The patient had a knee prosthesis which rendered visualization of the popliteal and tibioperoneal trunk impossible. The popliteal artery appeared to be occluded, however, without proper visualization of arteries below that level. Intervention of the occluded popliteal and percutaneous transluminal angioplasty (PTA) was attempted.

A 0.014-inch Corsair crossing catheter (Asahi) and a 0.014-inch Confianza Pro 12 wire (Asahi) were advanced to the distal popliteal artery. Hand injection through the Corsair catheter revealed distal reconstitution of the posterior tibial artery at the level of the ankle via collaterals. However, the tibioperoneal trunk and the ostium of the posterior tibial artery were not seen. Therefore, a pedal access under ultrasound guidance of the posterior tibial artery was attempted without success due to the burden of calcium and the very short reconstituted segment from collateral flow. Antegrade intervention of the posterior tibial artery was attempted again but was impossible at this time. The procedure was stopped at this point, a staged intervention with pedal access of the left posterior tibial artery was scheduled.

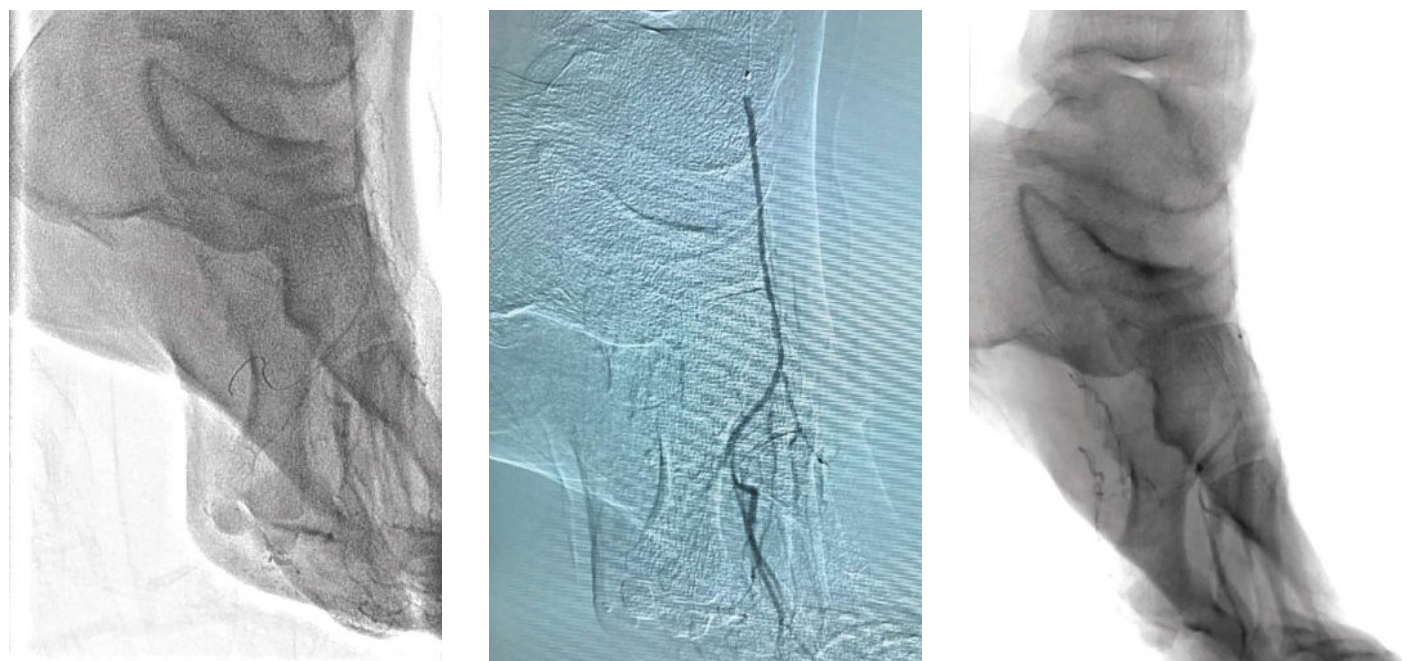
The patient was brought to the lab for a staged PTA of the left posterior tibial, anterior tibial, and popliteal arteries. Under ultrasound guidance, retrograde

*Continued on page 11*



**Figure 1.** Diagnostic angiography revealed 50% SFA disease with 100% occlusion of the popliteal. Small collaterals filled the lower leg. SFA, superficial femoral artery.

**“The high degree of calcium and total occlusion of the arteries rendered pedal access impossible.”**



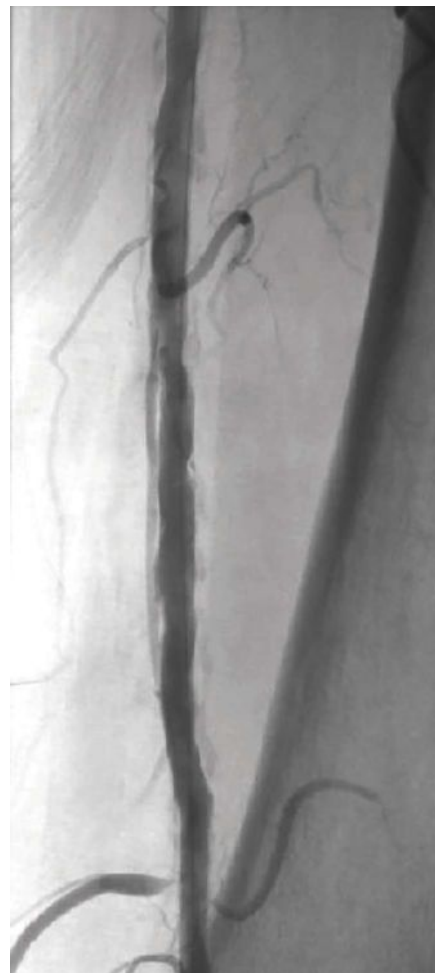
**Figure 2.** Angiography of the anterior tibial artery revealed brisk flow in the first and second metatarsal arteries and hyperemia throughout the foot and metatarsals.



access of the left posterior tibial and anterior tibial arteries was attempted without success. The high degree of calcium and total occlusion of the arteries rendered pedal access impossible. Therefore, the right femoral artery was accessed in the retrograde fashion with a 5-Fr femoral sheath (Merit Medical). A 5-Fr diagnostic catheter (internal mammary tight shape) was used to cross to the contralateral left leg. Angiographic findings revealed 50% superficial femoral artery stenosis that becomes 100% occluded distally at the Hunter's canal with collateral filling of the popliteal artery which in turn is 100% occluded. Beyond this point there was virtually no flow other than small collaterals into the peroneal artery. There was no flow in the anterior and posterior tibial arteries.

We proceeded with intervention of the left lower leg arteries. A 6-Fr x 65-cm Destination sheath (Terumo Corporation) was advanced to the left SFA. The SFA lesion was ballooned with a Pacific Extreme 4.0-mm x 300-mm balloon (Medtronic). A 0.035-inch Glidewire Advantage wire (Terumo) was advanced to the tibioperoneal trunk. A 0.014-inch Pilot 50 wire (Asahi) and a Corsair Pro catheter (Asahi) were advanced to the chronically occluded anterior tibial artery. After crossing the proximal ATA segment, a 0.014-inch Fielder XT (Asahi) was used to cross into the distal segment. A 2.0-mm x 120-mm Armada balloon (Abbott) was inflated multiple times in the ATA. Then, a 0.014-inch Sion Blue (Asahi) was used to access the first and second metatarsal arteries. A 2.0-mm x 40-mm Pacific Plus balloon (Medtronic) was inflated in the first, then second, metatarsal arteries. This resulted in brisk flow to the metatarsals with hyperemia throughout the foot.

The anterior tibial artery and popliteal artery were then further ballooned with a 3.5-mm–3.0-mm x 210-mm Ev3 balloon (Medtronic). Next, the SFA was ballooned with a 6.0-mm x 120-mm



**Figure 3.** Final angiography revealed 0% residual stenosis and brisk flow throughout the left leg and foot.

**“This case demonstrates the importance of peripheral intervention on below-the-knee arteries as well as pedal and metatarsal arteries for limb salvage procedures.”**

Armada balloon (Abbott). This resulted in 0% residual stenosis and brisk flow throughout the left leg with hyperemia throughout the sole of the foot.

On the follow-up visit, the patient had significant improvement. There is no claudication on exertion and no pain at rest. The patient has no ulcers and skin appearance is warm and pink. As a result

of this successful percutaneous intervention, he will start rehabilitation.

#### CONCLUSION

This case demonstrates the importance of peripheral intervention on below-the-knee arteries as well as pedal and metatarsal arteries for limb salvage procedures. Complete revascularization to the foot

and toes can ensure limb salvage in CLI patients. In CLI, both inflow and outflow disease have to be treated to reduce the risk of amputation. ■

*Disclosures:* None.

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#### MUSTAPHA from cover

claims analysis.<sup>8</sup> Values were compared to those 22 different types of cancer derived from the Cancer Statistic Center of the American Cancer Society.<sup>9</sup>

Because CLI is both common and deadly, more incident cases die over 5 years after a CLI diagnosis than with any type of cancer, except for lung cancer (Figure 1).<sup>1</sup>

#### CLI MORTALITY IN CONTEXT

When comparing incident cases of CLI and 22 types of cancer, the diseases responsible for the most deaths over 5 years in the US are:<sup>1</sup>

- Lung cancer (192,000)
- Critical limb ischemia (58,000)

- Pancreatic cancer (51,000)
- Colorectal cancer (49,000)
- Liver cancer (35,000)

#### CLI PATIENTS BELONG TO AN UNDERSERVED POPULATION

Adding to the poor prognosis after diagnosis of CLI, patients with this disease remain underserved from diagnosis to medical therapy and utilization of revascularization. Society guidelines recommend that all individuals diagnosed with CLI undergo an imaging study to assess the viability of endovascular or surgical revascularization.<sup>1</sup> Despite this, angiography is only performed in approximately one of four patients, despite the fact that patients who undergo angiography have a 90% lower risk of major amputation than patients who do not undergo angiography.<sup>8</sup>

Patients with CLI typically present with extensive atherosclerotic disease and multiple comorbidities. Therefore, optimal medical therapy focusing on diabetic control, antihypertensive medications, and anti-lipids is crucial to lowering the risk of cardiovascular complications, major amputation, and mortality. However, less than one-third of patients with CLI are prescribed optimal medical therapy.<sup>9</sup>

Limb amputation is too often the primary treatment for CLI, without first considering whether revascularization is feasible, which is a concerning disservice to these patients.<sup>1</sup> Among patients with CLI who underwent revascularization or major amputation in a recent study, 8.5% were subjected to above-the-ankle amputation as their initial treatment.<sup>6</sup> Even more perplexing, 30% of patients

who underwent major amputation presented with rest pain or ischemic ulcer but not gangrene.<sup>1</sup>

Compared to vascularization, amputation doubles the risk of death over the next year, even after controlling for important confounders such as age, disease severity, diabetes, and chronic kidney disease. Furthermore, in patients with gangrene in whom many healthcare providers may believe major amputation is the only viable first-line therapy, endovascular and surgical revascularization double patient survival compared to amputation.<sup>1</sup>

#### AWARENESS IS IMPERATIVE

In 2013, the Recalcitrant Cancer Research Act was signed into law by

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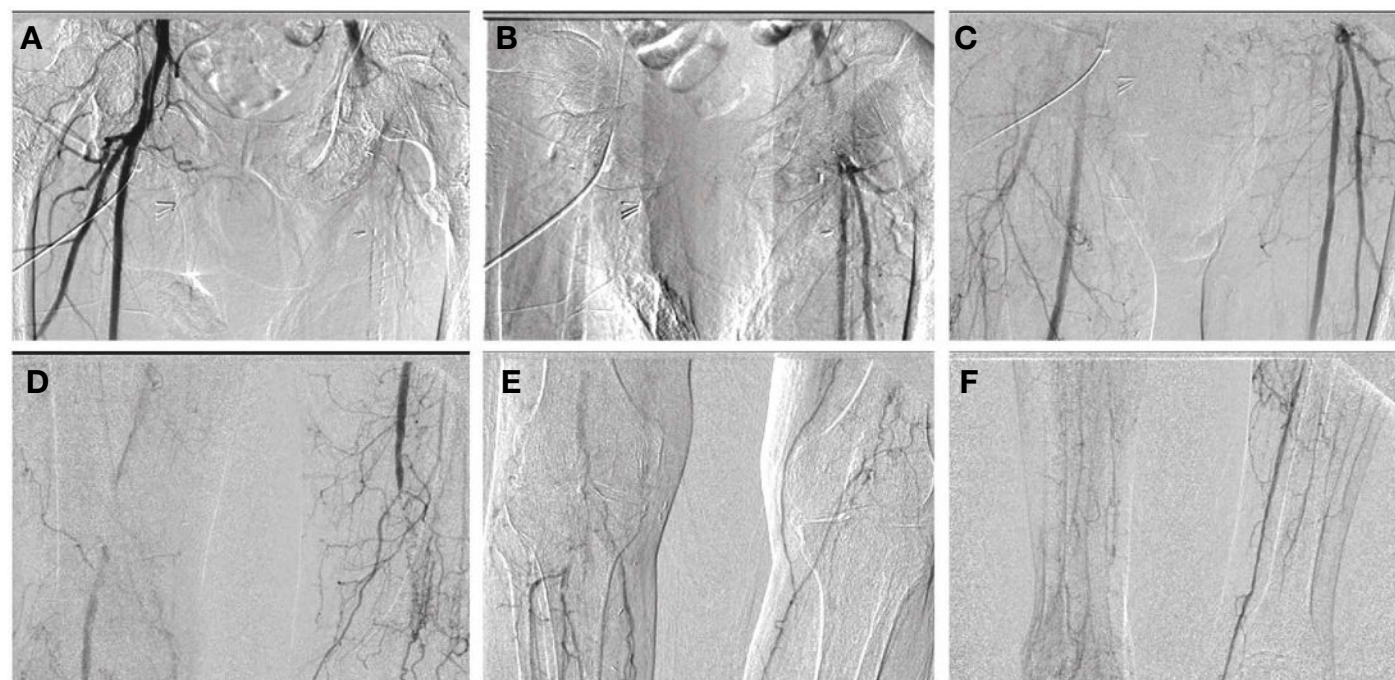
## UJUETA from page 4

the patient elected to undergo treatment within the trial protocol as a final option before major amputation.

The patient noted a reduction in ischemic pain between infusion 5 and 10. By infusion 20, there had been significant healing of long-established gangrene. He completed the 50 planned edetate disodium infusions without any side-effects or complications. No major adverse cardiovascular events were encountered. Quality of life and physical limitation measured by the PAD Questionnaire improved by 250% and 1,785%, respectively. The SF-36 questionnaire demonstrated an improvement in pain scale of 900% and general health by 50%. The measurement of urinary cadmium and lead were increased by approximately 400% and 3,000%, respectively. Most importantly, the patient was able to avoid any amputations during the treatment phase of 210 days (30 weeks). At the completion of the treatment regimen, all ulcers and gangrene were healed (Figure 1). Skin perfusion pressure (Sensilase®) in the target vascular bed (left dorsal foot) demonstrated an improvement of 73%.

## DISCUSSION

Although improvement was seen after completion of the 50 planned infusions of edetate disodium-based chelation, there is a possibility that our observations may have been due to play of chance. Several studies have demonstrated up to a 50% chance of spontaneous recovery in CLI patients treated with placebo. To us, spontaneous remission seems unlikely. This is a high-risk patient with comor-



**Figure 2.** Lower extremity angiogram of the left leg demonstrates complete occlusion of the common femoral artery extending to the origins of the superficial femoral artery (SFA) and profunda femoris, complete occlusion of the distal SFA and popliteal artery extending to involve all 3 infrapopliteal arteries with single vessel runoff via a reconstituted posterior tibial artery. On the right leg, there is complete occlusion of distal SFA, P2 and P3 segments of the popliteal artery with subtotal occlusion of the tibiofibular trunk.

mortality.<sup>6</sup> Tellez-Plaza et al reported urine cadmium to be associated with PAD.<sup>7</sup> A meta-analysis by Chowdhury et al totaling approximately 300,000 patients demonstrated urine cadmium as an independent predictor of cardiovascular risk.<sup>8</sup> We have reported in patients with coronary artery disease that there may be a stepwise increase in PAD severity proportional to urine cadmium, a metric that informs on total body burden of cadmium. Patients with CLI demonstrated about a 4-fold increase in urinary cadmium levels com-

electron beam tomography were enrolled into a 4-month study and offered edetate disodium with tetracycline. It showed that in the 77 patients completing the study, 57% had significant decrease in total coronary arterial calcium ( $P=.001$ ).<sup>11</sup> In contrast to coronary arteries, peripheral artery disease symptoms are caused by obstruction not plaque rupture. Thus, a decrease in calcified lower extremity plaque volume by edetate disodium, through either mechanism, may help improve microvascular flow.

Patients with diabetes and critical limb ischemia have a decreased quality of life, and a high risk of death. They pose an increased financial burden for the healthcare system as well as to their families. Although advances in the management and technology of limb salvage have reduced amputations, focus should also be placed on creative and original adjunctive medical interventions. Toxic metals are ubiquitous, obtained through water, air, and soil, and associated with PAD. Urine cadmium level, a surrogate for total body cadmium burden, correlates with the severity of PAD. Although hazardous to extrapolate from a single case, we consider edetate disodium chelation to be worthy of larger trials to define its adjunctive role for “no-option” patients prior to amputation. TACT3a, an ongoing trial currently enrolling at our institution, will further test the effects of edetate disodium-based chelation in patients with diabetes and CLI. ■

Disclosures: None

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**“Urine cadmium level, a surrogate for total body cadmium burden, correlates with the severity of PAD. Although hazardous to extrapolate from a single case, we consider edetate disodium chelation to be worthy of larger trials to define its adjunctive role for “no-option” patients prior to amputation.”**

bid conditions such as diabetes, coronary artery disease with bypass grafting, and a previous amputation. Although more studies are needed to identify the mechanism of action, our hypothesis of edetate disodium chelation reducing the total body burden of toxic metals may explain the positive outcomes. This hypothesis is supported by several epidemiologic studies. Lanphear et al in a population-based study of NHANES demonstrated that even at a low-level, lead is an important risk factor associated with cardiovascular

pared to those without PAD.<sup>9</sup>

An alternative hypothesis is that edetate disodium, a known calcium chelator, may reduce intravascular calcium resulting in arterial decalcification, and better flow, possibly because of improved microvascular compliance. Lei et al demonstrated, in an *in vitro* study, that edetate disodium could effectively remove calcium from calcified aortic elastin and human aorta.<sup>10</sup> Similarly, a study totaling 100 patients with stable coronary artery disease and positive coronary artery calcium measured with



# CLI GLOBAL SOCIETY

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## FINDINGS FROM RECENT STUDY:

- CLI is a serious problem that threatens both life and limb. Patients with CLI suffer poor long-term prognosis and generate high healthcare costs.
- Revascularization and attempts to salvage the limb are effective in saving both limbs and reducing mortality.
- Considerable efforts are needed to raise disease awareness and implement coding to better define and identify the disease.

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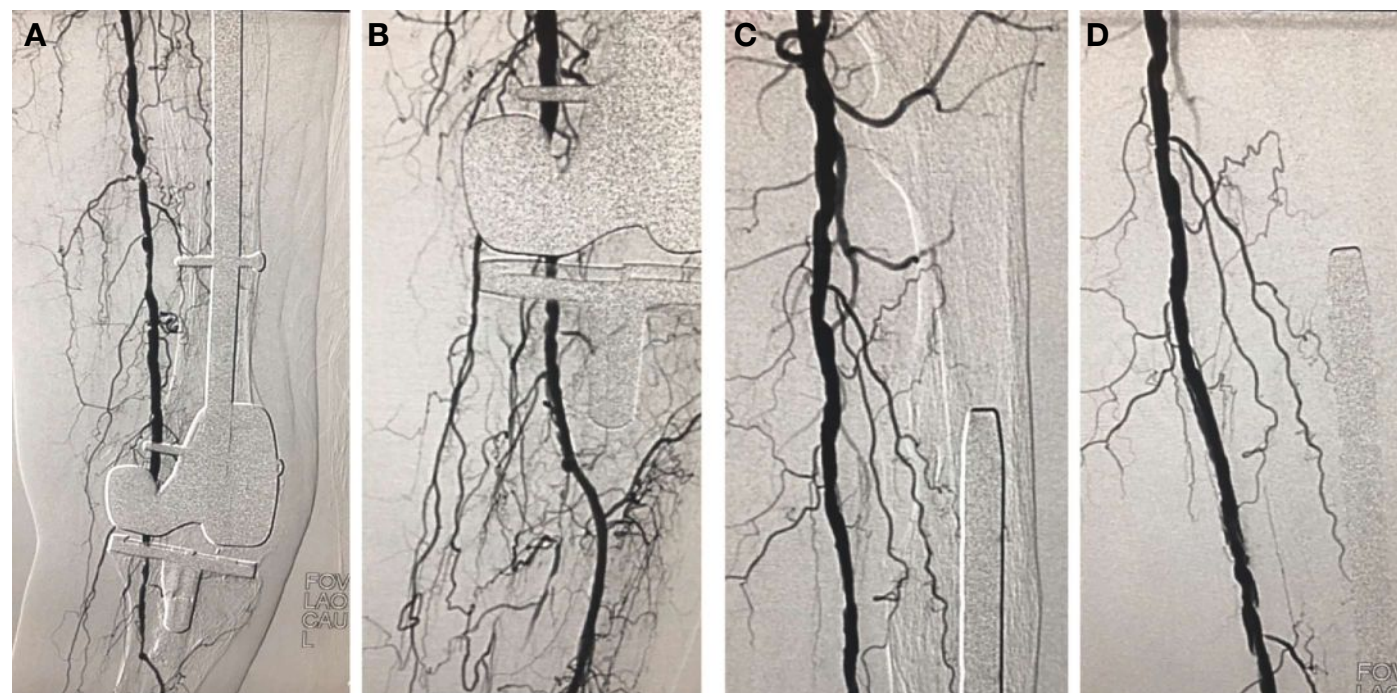


## ANSAARIE from page 6

his right foot had a wound in the plantar aspect including the right heel.

An initial angiogram was performed using the left ulnar artery (The left radial artery was used for arterial bypass). The artery was visualized under ultrasound guidance. The size of the vessel, the flow in the proximal and distal segment, as well as the site of the intended access, was visualized in detail with color, and the vessel was confirmed as a suitable access site. The vessel was accessed using the modified Seldinger technique under ultrasound guidance. Once the needle was visualized entering the anterior wall of the left ulnar artery, a microwire was passed, and then a 5-Fr Glidesheath Slender (Terumo) was placed in the left ulnar artery without any complication. An angiogram of the right lower extremity revealed a non-obstructive disease of the right SFA, high-grade lesion in the right popliteal artery, multiple high-grade lesions in the anterior, and posterior tibial artery with chronic total occlusion (CTO) of the right peroneal artery. In the right foot, the right posterior tibial artery was 100% occluded at the level of the ankle.

Due to the concern with radiation and the total length of procedure, we planned to proceed with staged intervention. Over the stiff 0.035-inch, 1.5-mm J-tip 400-cm Glidewire, the 5-Fr Glidesheath Slender was exchanged for a R2P Destination Slender guiding sheath 6 Fr, 119 cm. After the sheath was placed from the left ulnar artery into the right common iliac artery under radiographic guidance, the patient was given 70 units/kg of heparin. All the lesions in the right lower extremity were crossed using a 5-Fr, 200-cm ViperCath and a 0.014-inch ViperWire. This wire was successfully placed in the distal segment of the right posterior tibial artery. Then, a 1.75 diameter Solid Diamondback 360 Extended Length Peripheral OAD, with exchangeable handle, was used to perform the atherectomy of the right popliteal artery. After the atherectomy procedure,

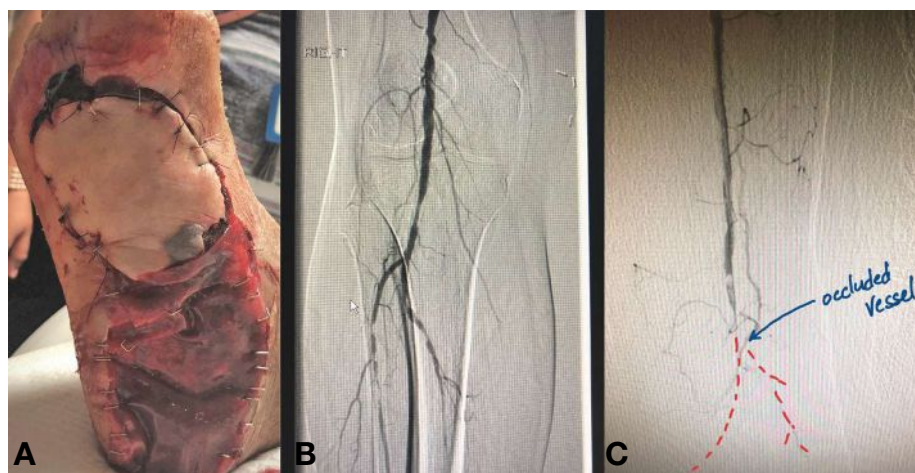


**Figure 3.** (A) Initial angiogram via (L) Radial artery showing severe multiple high-grade lesion in the mid-left SFA. (B) Final angiogram after atherectomy and angioplasty via (L) Radial artery showing successful revascularization of the mid-left SFA & popliteal artery. (C) Initial angiogram via (L) Radial artery showing a lesion in the mid-left SFA. (D) Final angiogram after atherectomy and angioplasty via (L) Radial artery showing successful revascularization of the mid-left SFA.

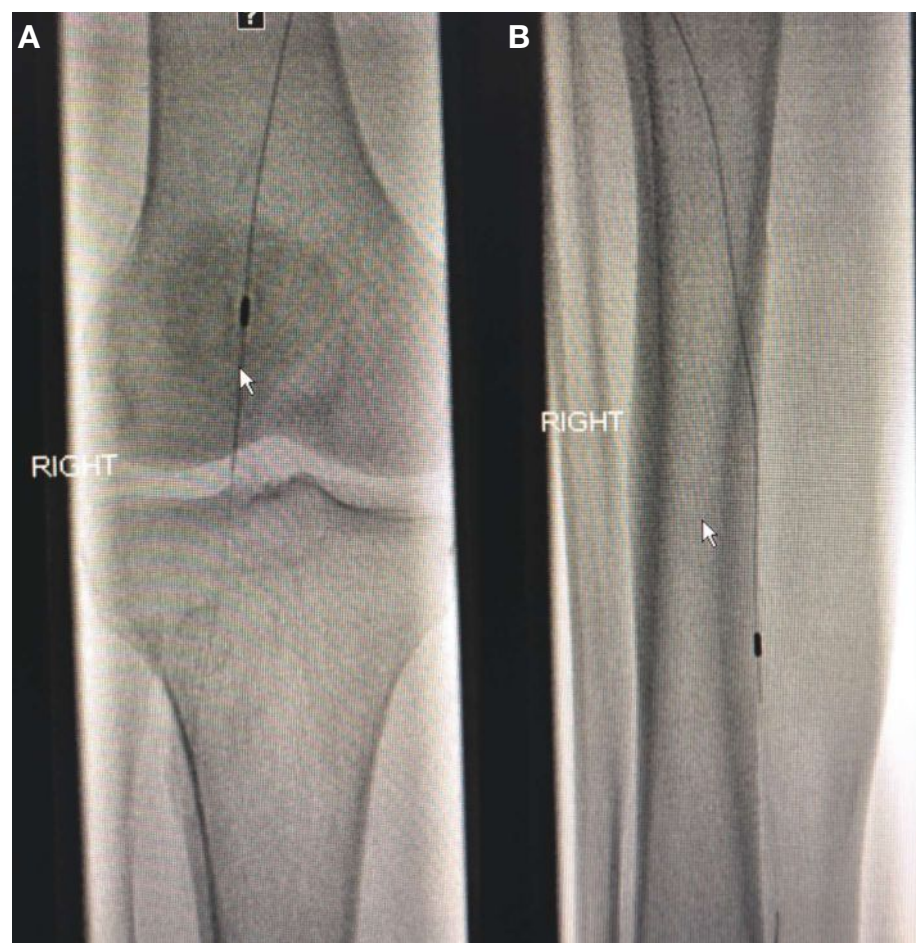
we moved forward and exchanged the crown size for the 1.50 diameter Solid Diamondback 360 Extended Length Peripheral OAD. This burr was then used to perform the atherectomy of the right posterior tibial artery.

Next, we used a 5.0 x 100 mm Ultraverse Rx balloon and performed balloon angioplasty of the right popliteal artery using maximum inflation pressure of 10 atmospheres for 2 minutes. Following this, a 3.0 x 200 mm Ultraverse Rx balloon was used and angioplasty of the right posterior tibial artery was performed using a maximum pressure of 8 atmospheres for 2 minutes. After this, the 0.014-inch Viper wire was directed out of the right posterior tibial artery and placed in the right anterior tibial artery using the 3.0 x 200 mm Ultraverse balloon. After the successful placement of the wire in the right anterior tibial artery, balloon angioplasty of the proximal and mid-right anterior tibial artery was performed using a similar technique. After

**“These complications are not as benign as once thought, and as the patient population is aging, with additional comorbidities, access site complications are increasingly taxing for patients and add significantly to the associated healthcare cost.”**



**Figure 4.** (A) Wound of the right foot on the plantar surface. (B) Initial angiogram via (L) ulnar artery showing a high-grade lesion in the right distal popliteal artery, right anterior tibial artery, and CTO of the right posterior tibial artery. (C) Initial angiogram with annotation showing occluded vessels in the right foot.



**Figure 5.** (A) Orbital atherectomy via (L) ulnar artery access using an extended length 1.75 mm OAD device in the right popliteal artery. (B) Orbital atherectomy via (L) ulnar artery access using an extended length 1.5 mm OAD device in the right posterior tibial artery.



the balloon catheter was removed, the final angiography showed an excellent angiographic result, with no side branch compromise, no flow limiting dissection, and no distal embolization.

At this time, we deemed the first stage of the procedure complete, and the R2P Destination Slender Guiding Sheath 6 Fr, 119 cm was removed over the stiff 0.035-inch, 1.5-mm J-tip 400-cm Glidewire under radiographic guidance with no complications. Homeostasis was achieved using the TR Band at the ulnar site access. The patient was brought back in 72 hours after confirming his renal function was stable. This time, the access point was the right posterior tibial artery. The vessel was accessed in an antegrade fashion under ultrasound guidance. The entry

site was infiltrated with a local anesthetic, lidocaine 2% solution. The vessel was accessed using the modified Seldinger technique under ultrasound guidance. Once the needle was visualized entering the anterior wall of the right posterior tibial artery, a microwire was then passed in an antegrade fashion under radiographic guidance, and then a 4-Fr Pinnacle Precision (Terumo) was placed in the right posterior tibial artery without any complication. Next, a 0.018-inch V-18 wire was used to cross the right posterior tibial artery CTO, and the wire was placed successfully into the right medial plantar branch of the right posterior tibial artery. After crossing all the CTOs, balloon angioplasty of the right medial plantar artery, right common plantar artery, and

the distal segment of the right posterior tibial artery, was performed using a 2.0 x 100 mm Ultraverse balloon. Following the first angioplasty, the 0.018-inch V-18 wire was then redirected with a 0.018-inch crossing catheter and placed in the lateral plantar branch of the right common plantar artery. Balloon angioplasty of the lateral plantar branch was performed using a 2.0 x 100 mm Ultraverse balloon. After the balloon catheter was removed, the final angiography showed an excellent angiographic result, with no side branch compromise, no flow limiting dissection and no distal embolization. The 4-Fr Pinnacle Precision was removed and hemostasis was achieved using manual pressure.

## CONCLUSIONS

In conclusion, there has been an increased awareness of the femoral, brachial and popliteal access site complications and the morbidity and mortality associated with them. These complications are not as benign as once thought, and as the patient population is aging, with additional comorbidities, access

site complications are increasingly taxing for patients and add significantly to the associated healthcare cost. Here, we provided two of our cases, which at one time were done solely via femoral artery access. We believe that as we gain mastery in alternative access technique, M<sub>4</sub>LEI will be a valid and preferred option for our patients. M<sub>4</sub>LEI is the umbrella under which alternative access like transradial, transulnar, and transpedal reside. Its success is dependent upon avoiding large vessel access and, therefore, associated complications. We hope to ignite a meaningful discussion with this presentation and encourage our colleagues to give M<sub>4</sub>LEI a try. ■

*Disclosure: Dr Ansaarie is a faculty member for Terumo and CSI.*

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**Figure 6.** (A) Final angiogram via (L) ulnar artery post atherectomy and angioplasty showing successful revascularization of the right popliteal artery. (B) Final angiogram via (L) ulnar artery post atherectomy and angioplasty showing successful revascularization of the right anterior and posterior tibial artery.



**Figure 7.** (A) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the left SFA. (B) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the mid left anterior tibial artery. (C) Orbital atherectomy via (L) Radial artery access using an extended length 1.5 mm OAD device in the left dorsalis pedis artery.

## MUSTAPHA from page 11

President Barack Obama to develop nationwide strategic plans to address the nation's deadliest cancers. This is defined as those with a 5-year mortality rate > 50%, which includes cancers of the pancreas, lung, brain, esophagus, liver, ovary, and stomach. This legislation authorized governmental research agencies to develop a comprehensive plan of action to coordinate prevention, early detection, and treatment research to lower mortality rates associated with these cancers. Unfortunately, no such legislation is pending for CLI, even though the 5-year mortality of CLI is >50%. The annual incidence of CLI is greater than that of esophageal cancer, stomach cancer, brain cancer, and ovarian cancer combined.<sup>1</sup> Considerable efforts are needed to raise disease awareness, implement coding to better define and identify

the disease, refine diagnostic algorithms, establish evidence-based treatment pathways, and address the high mortality rates associated with this diagnosis.<sup>10</sup> Overall, the high incidence of CLI in combination with its highly fatal course make this disease an underrecognized major threat to public health.<sup>1</sup> ■

*Disclosures: The authors report no conflicts of interest regarding the content herein.*

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## A CALL TO ACTION:

The CLI Global Society encourages collaboration among the major vascular, interventional, medical, and podiatric societies to continue raising public and health professional awareness. Further, the Society advocates for the formation of Alliances composed of multidisciplinary health care providers who will petition lawmakers in a focused, concerted effort to designate CLI as a national public health priority in the same way as the deadliest cancers.



## INGRASSIA from page 3

microns compared to 38 microns for a 60 MHz catheter).<sup>9,10</sup> The use of IVUS for evaluating lesion length in the peripheral vessels may be challenging due to long image acquisition times with mechanical pullback (0.5–1 mm/s) or because a manual pullback is employed.

**OCT.** The use of OCT outside of the coronaries is currently an off-label application. OCT utilizes near infrared light as an imaging source. Due to the faster speed of light compared with sound, OCT offers superior spatial resolution with an axial resolution of 10 to 20 microns. Additionally, a faster frame rate (100 fps compared with 30 fps for IVUS) and a faster pullback (20 mm/s) allow for faster image acquisition. OCT utilization in the periphery, however, is also not without its drawbacks. As OCT tissue penetration is less than IVUS (2 mm), there is less visualization deeper into the arterial wall. Additionally, the use of OCT requires removal of red blood cells from the imaging field. Conventionally this is achieved with flush injection of iodinated contrast so that a simultaneous angiogram can be performed. The requirement of additional contrast injections for imaging

over-sizing which can impact long-term patency.<sup>13–15</sup> The VIPER (Viabahn Endoprosthesis with Heparin Bioactive Surface in the Treatment of Superficial Femoral Artery Obstructive Disease) was designed to evaluate the Viabahn stent graft (Gore Medical) in superficial femoral artery lesions longer than 5 cm. At 12-months follow-up, the study showed that stent grafts that were not aggressively oversized (< 20% of the proximal reference vessel) had a primary patency rate when compared with aggressively oversized (> 20% of the proximal reference vessel) stent grafts (respective patency rates, 88% vs 70%;  $P=.047$ ).<sup>16</sup>

Determining plaque type and composition can direct the use and type of atherectomy device. In a comparison of angiography versus IVUS for atherosclerosis evaluation in the lower extremities, IVUS more readily identified concentric plaques which may masquerade as angiographically normal vessels. Conversely, angiographically guided analysis of calcium burden more frequently assigned moderate to severe calcification grades when compared to IVUS.<sup>17</sup> In patients being considered for intravascular lithotripsy with a balloon catheter that is single use and with limited treatment length, identification of the most calcified areas for

**“In patients being considered for intravascular lithotripsy with a balloon catheter that is single-use and with limited treatment length, identification of the most calcified areas for treatment could generate the highest return on procedural investment (Figure 2).”**

may, therefore, limit the use of OCT in patients with renal dysfunction. Various alternative flush media have been evaluated in peripheral OCT including heparinized saline, iodinated contrast, dextran, and CO<sub>2</sub>.<sup>11</sup> Possibly due to the retention of gas bubbles, CO<sub>2</sub> was found to produce inferior images and is currently not considered suitable for use as a flush media in OCT imaging.<sup>12</sup>

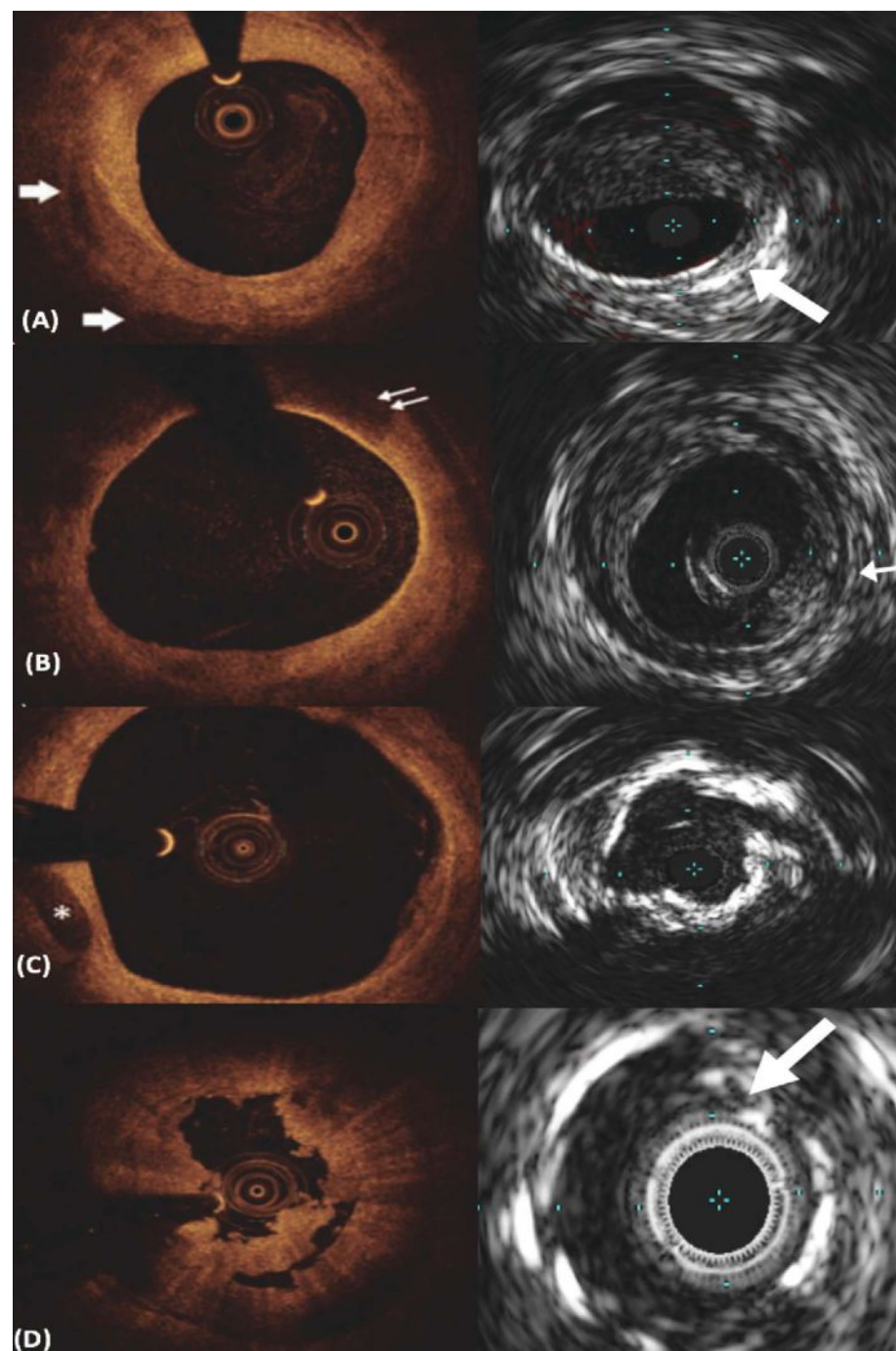
#### ROLE OF IV IMAGING IN ENDOVASCULAR INTERVENTIONS

**Pre-Intervention Imaging.** IV imaging is not only useful in establishing a diagnosis, but also aids in determining the most effective treatment strategy (Figure 1). Pre-intervention IV imaging determines vessel size enabling precise sizing of treatment devices. Self-expanding stents frequently have less radial force than balloon expandable scaffolds, and thus in vessels with severe calcification, better vessel prep may be indicated. Moreover, stent sizing, especially with self-expanding stents, can be more accurately assessed in order to avoid both under- and

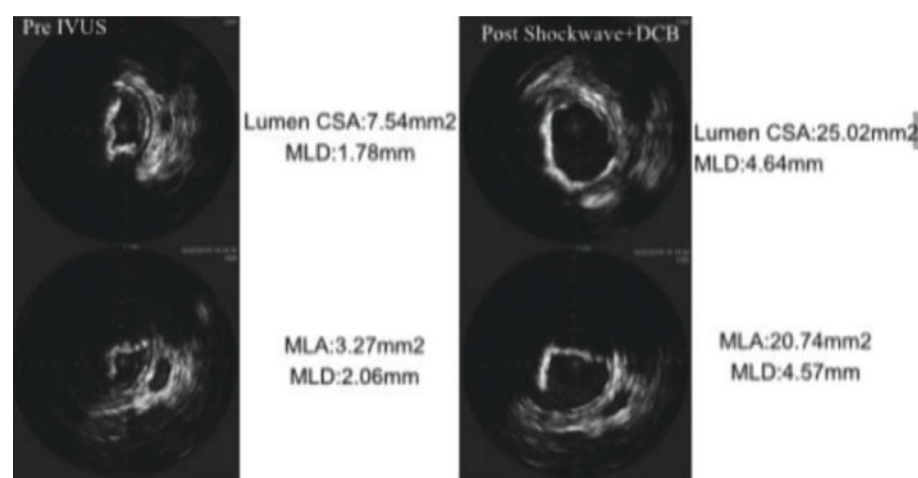
treatment could generate the highest return on procedural investment (Figure 2).

Directional atherectomy prior to DCB allows for adequate vessel preparation and more complete delivery of paclitaxel to the vessel wall. After the encouraging results of the DEFINITIVE AR study<sup>18</sup> which suggested that directional atherectomy before the use of DCB resulted in lower rates of dissection and bail-out stenting, the routine use of adjunctive atherectomy was expected to increase significantly. Particularly with directional atherectomy, IV imaging may be useful for targeting debulking therapies to areas of the vessel that are appropriate for atherectomy while avoiding areas that do not show significant calcification.

**Post-Intervention Imaging.** IV imaging post-intervention can aid in assessing the adequacy of the intervention, and it can be a useful tool for use in screening for complications (Figure 3). For example, IV imaging may demonstrate arterial dissection that is not appreciated angiographically and require treatment. OCT may be more sensitive



**Figure 1.** Histopathology of coronary disease on OCT and IVUS. (A) Fibrous plaque with discrete areas of calcification (arrows). (B) Lipid rich plaque which absorbs light on OCT and appears brighter on IVUS (arrows). (C) Examples of coronary calcification. The depth and extent of calcium are more clearly delineated with OCT (asterisk) than with IVUS. (D) An example of white thrombus on OCT and IVUS. White thrombus (platelet rich) vs. red thrombus (fibrin rich) can be easily distinguished on OCT but not on IVUS. IVUS = intravascular ultrasound; OCT = optical coherence tomography.



**Figure 2.** IVUS example showing improvement in luminal size from pre intervention IVUS (left panels) compared to post-shockwave with DCB (right panels). CSA = cross sectional area; MLD = minimal lumen diameter; MLA = minimal lumen area; DCB = drug coated balloon. IVUS = intravascular ultrasound.



at identifying dissections than IVUS, though the clinical utility of this difference has not been evaluated with rigorous clinical trials.

## CONCLUSION

The use of adjuvant IV imaging in the periphery holds great promise by tailoring interventional therapies to lesion subsets and providing more durable results. Given promising early studies, IV imaging in the periphery is expected to be an area of considerable growth in the endovascular field. ■

**Disclosures:** SP: Advisory board for Abbott Vascular, Boston Scientific, Medtronic, Philips/Spectranetics; JI, MTF, no disclosures.

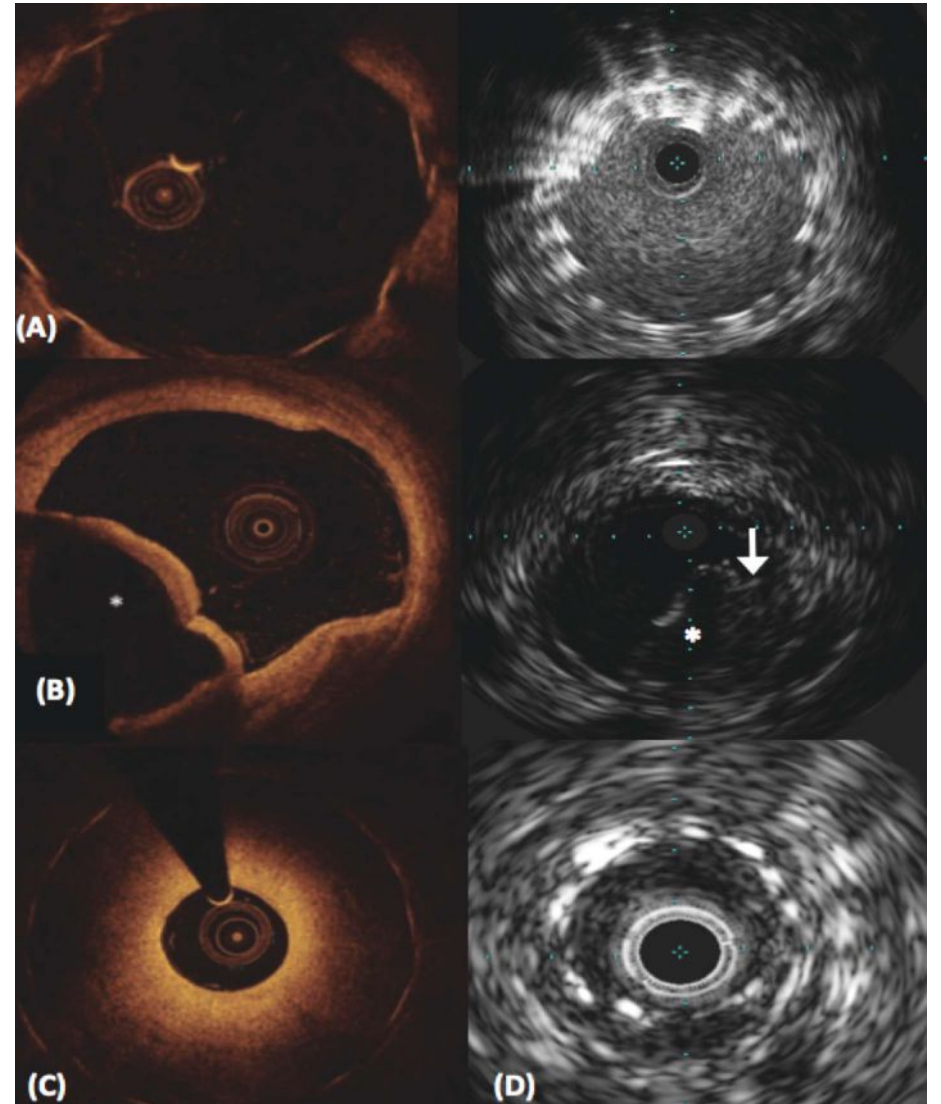
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**Figure 3.** Post-intervention IVUS and OCT assessments (A, right and left panels). A well-expanded SFA stent on OCT and IVUS. (B, right and left panels) Significant dissection delineated on OCT and IVUS with the asterisk denoting the false lumen. The arrow on IVUS marks the dissection flap. (C) OCT imaging demonstrating severe neo-intimal hyperplasia. (D) IVUS image of a severely under-expanded peripheral stent. SFA = superficial femoral artery; IVUS = intravascular ultrasound; OCT = optical coherence tomography.

## STAR from page 8

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# Selected Abstracts from the Amputation Prevention Symposium (AMP) 2019

August 14-17, 2019, Chicago, Illinois

*Driven by a team of renowned multidisciplinary course directors, and led by Jihad A. Mustapha, MD, a pioneer in the field of interventional cardiology, AMP has served as an excellent forum to connect clinicians—interventional cardiologists and radiologists, vascular surgeons, and the entire limb salvage team—with the foremost experts in CLI to gain knowledge on the latest advances in revascularization and learn from one another to save limbs and save lives.*

## 003 National Medical Center “20 de Noviembre” Experience With Drug-Coated Balloons in Peripheral Arterial Disease.

*N.E. Santana; I.E. Sánchez*

### Purpose

The main downside to percutaneous transluminal angioplasty (PTA) continues to be the high rates of in-stent restenosis. Restenosis occurs in more than 60% of patients treated with PTA, usually due to neointimal proliferation. In the recent years, paclitaxel has been used as the drug of choice on drug-coated balloons (DCB). Thus, it is now possible to deliver an antiproliferative drug to a diseased artery segment, “leaving nothing behind.” We conducted a retrospective analysis of the cases treated by DCB for PAD in the National Medical Center “20 de Noviembre” in Mexico City.

### Materials and Methods

We analyzed all patients treated by DCB from January 2017 through September 2018. The variables studied were anatomical segment treated (above-the-knee vs below-the-knee), Rutherford class, technical success rate, postoperative thrombosis, minor amputation rate, major amputation rate, and limb salvage rate at 6 months.

### Results

A total of 25 patients were treated using DCB. Eighteen patients (72%) had below-the-knee disease and 7 (28%) had above-the-knee disease. Twenty-four patients (96%) were Rutherford Class 4 through 6, and 1 patient (4%) was Rutherford Class 3. Technical success was achieved in 22 patients (85%), and 3 patients (12%) presented with acute ischemia after surgery. Twenty-one patients (84%) underwent minor amputation, 3 patients (12%) underwent major amputation, and 1 patient (4%) did not require any amputation. The limb salvage rate was 88%.

### Conclusions

This report shows promising results of the use of DCB for patients with PAD. The results of this study are consistent with a number of previous publications. The limb salvage rate at 6 months in this cohort was high (88%), even considering that the vast majority of patients had critical limb ischemia.

## 004 National Assessment of Availability and Utilization of SET for PAD in Patients With Intermittent Claudication

*A. Dua; S. Sharma; O. Aalami*

### Purpose

Supervised exercise therapy (SET) is an inexpensive, low-risk, and effective option when compared with invasive therapies for treatment of patients with peripheral artery disease (PAD) and intermittent claudication (IC). Randomized controlled trials have demonstrated the benefits of SET in improving maximum walking

distance in IC patients, and society guidelines recommend SET as first-line therapy. In 2017, the Centers for Medicare & Medicaid Services (CMS) added coverage of SET. We aimed to evaluate the availability and utilization of SET programs, determine the awareness of SET CMS coverage in the United States (US), and gauge the academic interest in SET in the vascular community.

### Materials and Methods

An eight-question online survey was sent to 900 vascular surgeons, cardiologists, and vascular medicine physicians across the US. The most recent 2-year programs for the Vascular Annual Meeting (VAM), Midwestern Vascular Surgical Society (MVSS), Eastern Vascular Society (EVS), and Western Vascular Society (WVS) were reviewed to identify SET-related abstracts and gauge academic interest and awareness for SET within the vascular surgery community.

### Results

We received 131 (14.6%) physician responses to the survey. All 50 states were represented. The majority (54.2%) of responders stated that there was no SET program at their facility, and 5.4% did not know if there was a program at their facility. Of those who did have a SET program available, 81.1% had programs associated with cardiac rehab, and 18.8% had a PAD-specific program. A significant number of physicians (48.9%) had never referred a patient for SET, and 26% were not aware that CMS covered SET sessions. Of the physicians who were aware of CMS reimbursement, 36% had never referred a patient to a SET program. Of all surveyed physicians, 97.7% indicated that they would refer patients to a SET program if one was available. Top barriers to utilization of a SET program included that there were no SET centers available and that the nearest SET program was not accessible without significant cost or travel expense to the patient. A review of major vascular meeting programs for the last 2 years yielded no identification of a SET-related abstract.

### Conclusions

There is a lack of availability and utilization of SET for PAD patients with claudication, despite guideline recommendations. When SET is offered, it is typically through cardiac rehabilitation programs. Travel distance, lack of SET program availability, and low reimbursement rates are the primary areas that could be addressed to improve utilization of SET.

## 006 Single-Center Study of Chocolate Balloon Angioplasty as an Adjunctive Therapy in Critical Limb Ischemia Patients

*S. Vijaykumar; M. Thawabi; G. Chennu; S. Waxman; M. Cohen; J. Shao*

### Purpose

Severe symptomatic peripheral artery disease (PAD), especially critical limb ischemia (CLI), is associated with a high amputation rate and poor functional status, which

increases morbidity and mortality in this population. This study analyzed the safety and efficacy outcomes of Chocolate percutaneous transluminal angioplasty (PTA) balloon (Medtronic) as an adjunctive therapy in both above-the-knee (ATK) and below-the-knee (BTK) interventions in CLI patients.

### Materials and Methods

From October 2017 to November 2018, CLI patients who underwent Chocolate balloon PTA as an adjunctive therapy were enrolled from a single center. Data relating to patient characteristics included Rutherford classification and ATK/BTK lesion status. Procedure details, including procedure time, fluoroscopy time, and contrast used, were collected prospectively. The primary outcome was all-cause mortality. Secondary outcomes included target vessel revascularization, ipsilateral major amputation, and bailout stenting rate.

### Results

Fifty patients and a total of 59 limbs underwent Chocolate balloon PTA. The baseline characteristics included a mean patient age of 71.8 years. Fifty percent of patients were males. Patients had a mean BMI of 27.8, and 64% of patients had diabetes mellitus, 96% had hypertension, 78% had hyperlipidemia, and 38% had chronic kidney disease. Fifty percent of patients were smokers. Rutherford classification (RC) of limbs included RC 4: 29; RC 5: 24; and RC 6: 6. Forty-five percent of lesions were ATK lesions, and 77% were complex BTK lesions. Adjunctive atherectomy (orbital) was performed on 98.4% of lesions. Average procedure time approximately 149 minutes, while fluoroscopy time was approximately 40 minutes and contrast used was 123 mL. Average follow-up was 3.2 months from index procedure. The all-cause mortality rate was 3 patients (6%), target vessel revascularization occurred in 8 limbs (13.5%), ipsilateral major amputation occurred in 1 limb (1.7%), and bailout stenting occurred in 0 limbs.

### Conclusions

Balloon angioplasty, either as a primary or adjunctive therapy, remains the core of lower extremity endovascular intervention. The Chocolate PTA Balloon is proven to be safe, with a low bailout stenting rate, as well as efficacious, with a low target-vessel revascularization and high amputation-free survival rate in both ATK and complex BTK interventions in CLI patients.

## 007 Treatment of Severe Claudication Using Crosser, Diamondback, Balloon PTA in a Patient With Aorta-Bifemoral Grafts

*T. Bob-Manuel; R. Patel*

### Purpose

Revascularization of chronic total occlusions in the peripheral vessels is particularly challenging due to anatomy, lesion length, and calcification. In patients who have had aorto-bifemoral bypass grafts, there is an additional



challenge of gaining access to the infra-inguinal lower extremity vasculature. Alternative access sites and newer technologies can facilitate these cases.

## Materials and Methods

A 76-year-old man with a history of tobacco abuse and coronary artery disease was referred for worsening Fontaine Stage IIb claudication (left leg worse than right leg) on ambulation for the past 2 years after 2 failed percutaneous transluminal angioplasty attempts at an outside hospital. He denied signs or symptoms of critical limb ischemia (CLI). Computed tomography angiography of his abdomen with run-off showed bilateral mid superficial femoral artery (SFA) chronic total occlusions (CTOs) with collaterals to the distal SFAs. During his initial consultation with our group, the patient was placed on cilostazol and a structured walking program. He showed improvement in his time to claudication, but the claudication still significantly impaired his quality of life. Via ipsilateral, antegrade access, the left CFA CTO was crossed with a Crosser CTO Recanalization Device 6S 154cm. (Bard Peripheral Vascular). Orbital atherectomy was performed using a Diamondback 360 Peripheral Classic Crown 2mm x 30mm x 145cm (Cardiovascular Systems). Angioplasty was performed with the scoring Ultrascore balloon 035 6mm balloon (Bard Peripheral Vascular) at 6 atmospheres for 120 seconds. An angioplasty was performed with a Lutonix drug-coated balloon 6 mm (DCB) (Bard Peripheral Vascular) at 6 atmospheres for 180 seconds. There were no complications.

## Results

Post procedure, the patient no longer experienced left lower extremity claudication. Four weeks later, he returned for the same procedure on the right SFA CTO. He no longer experiences claudication.

## Conclusions

Patients with prior failed peripheral CTOs should be transferred or referred to tertiary centers that have experience in treating these lesions. Ipsilateral, antegrade CFA access can be useful in patients with SFA CTOs who have undergone aorto-bifemoral bypass grafting. Crosser, Diamondback, and DCBs can be safely used to treat long calcified SFA CTOs.

## 008

### Amputation Rates for Patients with Diabetic Foot Ulcers at the Community Level: An Income-Based Analysis

Dr. Erjia Ge and Donna Krawczyk (Pietraszek)

Using longitudinal accrual data from amputation rates of the high-risk population with a diabetic foot ulcer (DFU), standardized income and gender, we evaluated outcomes of lower limb amputation (LLA) in London, Ontario. Previous studies using a population-based cohort nationally showed the lowest income quintile at a significantly higher association of LLA. By contrast, using the high-risk population strategy, we show that a community-level analysis indicates the highest income quintile as encountering a significantly higher risk of LLA. Using community level data based on admission to hospitals for an LLA due to a DFU as the amputation rate denominator helps pin-point at-risk groups that are not found in general diabetic datasets and large population-based studies.

The study population consisted of all patients with a diabetic foot ulcer (DFU) from 2006-2009 (N= 251, 69.93% male) and all patients with a non-traumatic lower limb amputation from 2006-2009 (N=111, 71.17% male). And all patients with a DFU from 2011-2014 (N=306, 69.93% male) and all patients with a LLA from 2011-2014 (N=108, 75% male). These accrual data were compiled by the Institute for Clinical Evaluative Sciences where

DAD Evaluative Services allowed access to the use of the Canadian Institute for Health Information's Discharge Abstract database (CIHI DADD) that houses information on hospital admissions and the Canadian Institute for Health Information's National Ambulatory Care Reporting System Metadata (CIHI NARCS) that houses data from all hospital-based, emergency and community based ambulatory care in outpatient and day surgery.

The total number of new cases of amputation was significantly lower (111 in accrual years 2006-2009 and 108 from 2011-2014, P-value <.0000001) in comparison to other studies that show an increase in the total number of new cases of amputation incidences when comparing total population of people with diabetes and a decline in the rate. Our analysis shows a decrease in amputation rate by 9% in London, Ontario comparing accrual years. Because there is a smaller denominator used, a growing population overall does not skew the outcomes nor underestimate the rate. For amputation rate among diabetic foot ulcer patients, the risk of acquiring an amputation was greater in the highest income quintile for both accrual years. Compared to amputation rates in the top quintile, the relative risk for those in the lowest (5), second-lowest (4), middle (3) and second-highest (2) were lower when compared to the highest quintile reference category 0.67, 0.72, 0.79 and 0.70 respectively from 2006-2009. And from 2011 to 2014, the relative risk for those in the lowest (5), second-lowest (4), middle (3) and second-highest (2) were 0.04, 0.10, 0.16 and 0.09; and also significantly lower than the highest income quintile reference category respectively. The lowest income quintile, although having the highest number of diabetic foot ulcers compared to the highest income quintile (96 versus 30 in accrual years 2006-2009; and 99 versus 45 in accrual years 2011-2014) had a lower rate of amputations (43% and 31% for lowest income quintile category comparatively 60% and 47% for highest income quintile category, in respective accrual years). As well, it is demonstrated in other studies that diabetes affects the poor when looking at population based data, but when looking at end-stage foot complications, in this analysis individuals of a higher income quintile have more amputations (60% versus 43% respectively from 2006-2009; and, 47% versus 31% respectively from 2011-2014). Reasons for the outcome of this paper could stem from multiple factors. A diabetic foot ulcer (DFU), by contrast to other chronic diseases that are higher at a low-income quintile, here, like a breast cancer diagnosis, are at a higher risk for treatment by amputation in the highest income quintile.

## 009

### Reducing Body Burden of Lead is Associated With Resolution of Critical Limb Ischemia

F. Ujueta; G. Lamas; I. Arenas; T. Yates; B. Olivieri; R. Beasley; A. Navas-Acien

## Purpose

Epidemiologic studies have found lead and cadmium exposure to be associated with an increased risk of atherosclerosis. We report on estimated changes in total body burden of lead and cadmium in 7 patients with diabetes and critical limb ischemia (CLI) whose treatment with edetate disodium infusions led to resolution of CLI.

## Materials and Methods

Seven patients with diabetes and CLI completed 40 intravenous infusions of edetate disodium-based chelation as part of a 10-patient pilot study. The presence of CLI was based on a Rutherford Clinical Severity Scale of 4 or 5. All patients demonstrated marked improvement and resolution of CLI following the infusions. Urine was collected before and after chelation treatment at baseline, and at infusions

20 and 40, using metal-free containers and analyzed using Inductively Coupled Plasma- Mass Spectrometry. Total body lead burden was estimated as post-chelation urine lead, and cadmium burden as baseline urine cadmium, and each was expressed per gram of creatinine (Cr). Statistical analyses were paired t-tests on log-transformed values.

## Results

The mean age of patients was  $76 \pm 8.3$  years, and 57% were male. Baseline urine creatinine was  $0.92 \pm 0.24$  mg/dL (mean  $\pm$  SD). Coronary artery disease was found in 86% (6 patients), 29% (2 patients) had a smoking history and 57% (4 patients) had a non-healing ulcer or dry gangrene. The SVS WIFI (wound, ischemia, foot infection) risk staging score was high risk in 43% (3 patients) and moderate in 57% (4 patients). Following the first infusion, urine lead increased by 3733% and urine cadmium increased by 553%, compared with baseline ( $P < .001$  for both). Over the course of 40 infusions, post-chelation urine lead decreased by 39% ( $1.28 \mu\text{g/g Cr} \pm 0.29$  to  $0.78 \mu\text{g/g Cr} \pm 0.91$ ,  $P < .001$ ). Almost half of that change (45%) was already present at 20 infusions. In contrast, there was no significant change in pre-chelation urinary levels of cadmium over the 40 infusions ( $-0.48 \mu\text{g/g Cr} \pm 0.22$  vs  $-0.34 \mu\text{g/g Cr} \pm 0.36$ ,  $P = \text{NS}$ ).

## Conclusions

This analysis of a small number of patients with diabetes and CLI suggests that edetate disodium-based chelation may reduce lead body burden in conjunction with a strongly positive clinical response to the therapy. While causality cannot be established, these data suggest future directions for investigation, which are currently being carried out in TACT2 and TACT3a.

## AMP THE CLI MEETING

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# The Amputation Prevention Symposium 2019: #BringYourSpecialtyToTheTeam

Carmen Heaney and Mia Defino

The 9th annual Amputation Prevention Symposium (AMP), kicked off August 14, 2019 at the Hilton Chicago. Founder and Course Director Jihad Mustapha, MD, of Advanced Cardiac & Vascular Centers for Amputation Prevention welcomed attendees to the conference and urged each individual to share what they learn these next few days with their colleagues. Dr. Mustapha emphasized the severity of CLI mortality as there are more individuals that die over 5 years after a CLI diagnosis than with any type of cancer, except for lung cancer. While there have been national initiatives to target pancreatic and colorectal cancer to reduce mortality rates, there remains a lack of awareness of CLI mortality<sup>1</sup> (see graph below).

## KEYNOTE ADDRESS

Professor Richard Neville, Associate Director, INOVA Heart and Vascular Institute, focused on how innovation and multidisciplinary teams can advance the treatment for CLI patients during the Alan T. Hirsch Memorial Keynote Address. He encouraged attendees to “bring the talents your specialty can offer to the team rather than leaving it at the door” suggesting that finding ways to share expertise can lead to better patient outcomes and increased satisfaction with treatment. This focus translated directly into how specialists will be evaluated in the future, where physicians and healthcare providers will need to optimize patient quality of life while minimizing

costs. He also discussed a recent study by the CLI Global Society that has helped gather more statistics about the burden and unmet needs of CLI patients, with less than one-third of patients with CLI being prescribed optimal medical therapy. The population-based study evaluated the outcomes following an initial diagnosis of CLI. Of 36.5 million Medicare beneficiaries considered, there were 116,031 with CLI diagnosis and 72,199 incident cases of primary CLI. After initial diagnosis, there was a 46% survival rate at a median of 3.5 years, with 87% freedom from amputation. Revascularization led to increased survival compared with amputation over 4 years. Costs per patient per year after CLI diagnosis increased by 30% with the majority of cost attributed to inpatient hospital stay (62%) and the average per patient cost the highest when patients presented with gangrene. Overall, there were extremely high healthcare costs, poor prognosis, and major amputation led to decreased survival, higher rate of subsequent amputation, and higher annual healthcare cost in CLI patients.<sup>2</sup>

Dr. Mustapha presented more findings from the CLI Global Society, regarding the determinants of long-term outcomes and costs in the management of CLI, to encourage attendees to be part of the considerable effort needed to raise disease awareness and implement coding to better define and identify CLI disease. “Without awareness we are not going to be able to achieve the goal that we want,” he said. Currently, CLI prevalence is estimated



Jihad Mustapha, course director (left) and Richard Neville, Keynote (right)

from administrative claims databases using ICD clinical diagnosis codes that yield high sensitivity when patients with a CLI diagnosis code likely have the disease, but there is a loss of specificity when patients without a CLI diagnosis code may actually have the disease—leading to underdiagnosis. To address underdiagnosis and undertreatment of CLI, proper imaging and increased awareness is needed.<sup>1</sup> The CLI Global Society has brought together representatives from SCAI, SVS, SVM and SIR to form a coalition that has developed a proposal to differentiate CLI from PAD in medical coding and billing nomenclature beginning with the ICD-10 diagnosis codes. This proposal is currently under review by the CDC and the Prevention ICD-10 CM Coordination & Management Committee for the 2021 update.

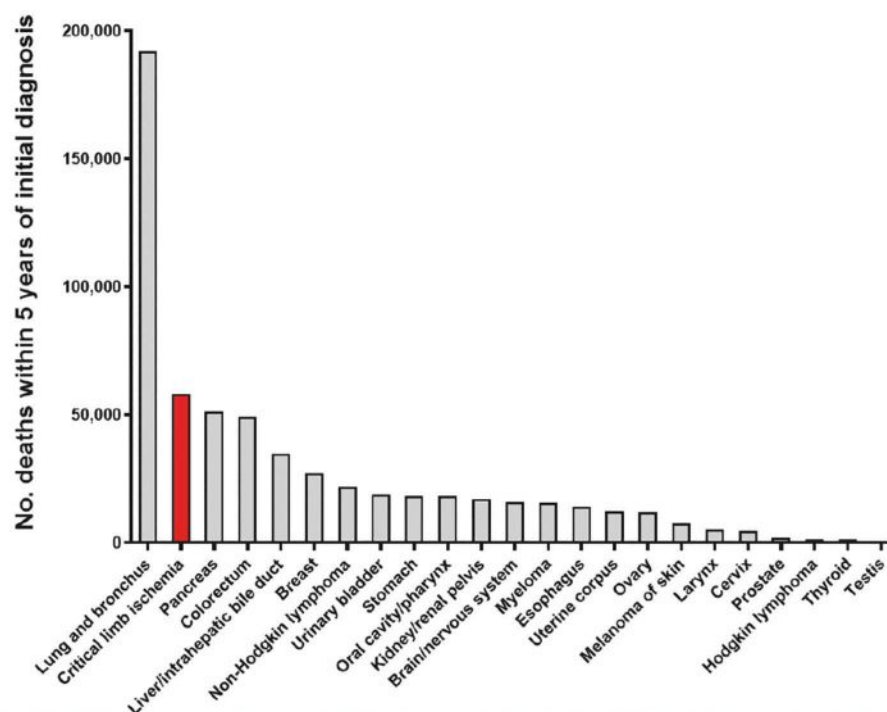
R. Kevin Rogers, MD, from University of Colorado Denver provided an update on the COMPASS trial that was stopped early because of robust results in improvements in limb outcomes in the low-dose rivaroxaban (2.5 mg twice daily) plus aspirin (100 mg) daily group compared with aspirin alone and rivaroxaban 5 mg twice daily alone. This is encouraging as the study was done specifically in PAD patients. Other pharmacological therapies, such as aspirin, statins, and PSK-9 inhibitors were discussed by Drs. Mahmood Razavi and Lawrence Garcia, but much of the existing research needs to be extrapolated from other cardiovascular disease populations. Dr. Ido Weinberg from Harvard urged for more dedicated studies studying pharmacological agents in CLI patients.

## DRUG DELIVERY

The morning session on day 2 covered many clinical trial updates on the efficacy and safety of paclitaxel drug-eluting technology recently raised by the Food and Drug Administration (FDA) earlier this year (January, March, and August 2019).

Dr. Peter Soukas, from Brown Medical School and Cardiovascular Institute, presented on drug technology below the knee (BTK). While many randomized trials that have examined short lesions, few trials studied treatment of longer lesions and whether drug-eluting stents (DES) or drug-coated balloons (DCB) are more effective. Overall, DES has proven beneficial for BTK, but use is limited by proximal vessel location, cost, and need for prolonged dual antiplatelet therapy. DCB for BTK has failed to show superiority over percutaneous transluminal angioplasty in RCTs, possibly due to the high prevalence of diffuse, occlusive and calcified disease; dissections; recoil; impaired retention/release kinetics; and distal embolization.

Dr. Bret Wiechmann from the University of Florida shared 1-year results from the IMPERIAL Eluvia DES versus Zilver PTX DES trial. Both primary non-inferiority effectiveness and safety endpoints were met and held across subgroup analyses in diabetics and patients with chronic total occlusion. Eluvia was found to be superior to Zilver PTX for primary patency at 12 months in a post-hoc analysis and there were consistent primary patency results regardless of lesion complexity. He presented combined safety results from Eluvia with a holistic view of

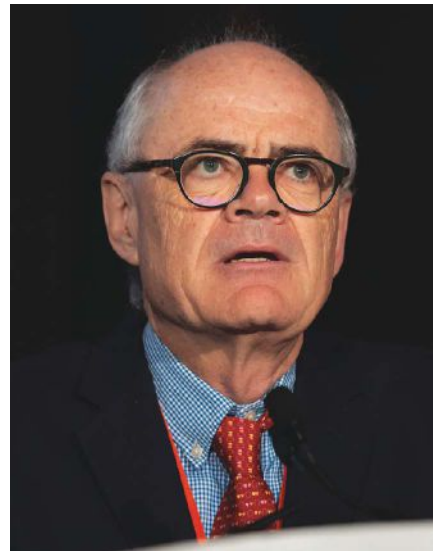


Number of deaths within 5 years of initial diagnosis show that lung cancer is the only malignancy with a higher number of deaths than critical limb ischemia. From Mustapha JA. *Vascular Disease Management*, June 2019.





Dr. Jihad Mustapha, AMP Founder and Course Director, delivering opening remarks.



Professor Thomas Zeller, Course Co-Director



Fadi Saab, MD, Course Co-Director and Live Case Operator



George Adams, MD, Course Co-Director

Boston Scientific's long-term clinical data on paclitaxel eluting devices that showed no difference in all-cause mortality when compared to non-coated devices.

"The IN.PACT Clinical Program is the largest, independently adjudicated cohort treated with DCB for femoropopliteal disease with data through 5 years," said Dr. Marianne Brodmann from the Medical University Graz. The results from this independent patient-level meta-analysis demonstrate no correlation between exposure to paclitaxel and mortality through 5 years and paclitaxel dose was not identified as a predictor of mortality by a multivariable cox regression model. It was observed that DCB patients who died were older and had more comorbidities. Dr. Brodmann encouraged real-world comparative studies to understand the role of follow-up visit compliance with lower mortality risk and to better understand long-term safety of paclitaxel products. Dr. Brodmann also presented on the Ranger DCB clinical study, a series of randomized studies generating Level 1 evidence, and commented on the excitement relating to the results from COMPARE 1 and Ranger II SFA.

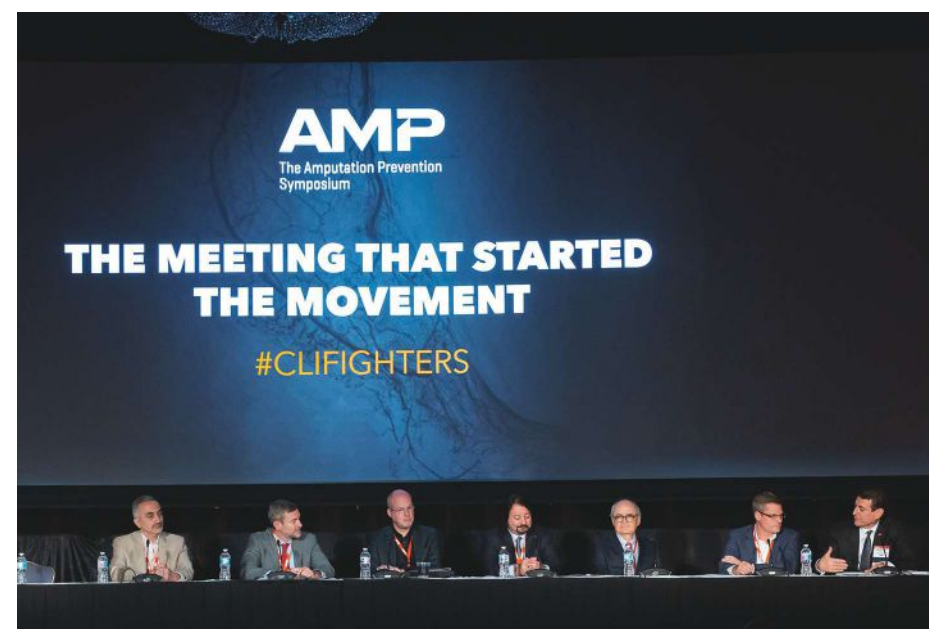
"The Lutonix Long SFA Global Registry demonstrated durable benefits at 24 months for the Lutonix DCB in real-world patients," said Michael Lichtenberg, MD from the Arnsberg Vascular Clinic. The registry captured data from patients with claudication or ischemic rest pain in Europe for two years after being treated with the Lutonix drug-coated PTA dilation catheter. He also presented data from the Lutonix Global SFA registry that showed favorable and sustainable freedom from TLR at 24 months in complex lesions and diabetics.

The ILLUMENATE Trial evaluated the CVI paclitaxel-coated PTA Catheter compared to the bare PTA balloon catheter for the treatment of de-novo or post-PTA occluded/stenotic or reoccluded/restenotic (except for in-stent) SFA and/or popliteal arteries. Dr. Sean Lyden from the Cleveland Clinic Lerner College of Medicine showed data demonstrating durable safety and patency through 3 years

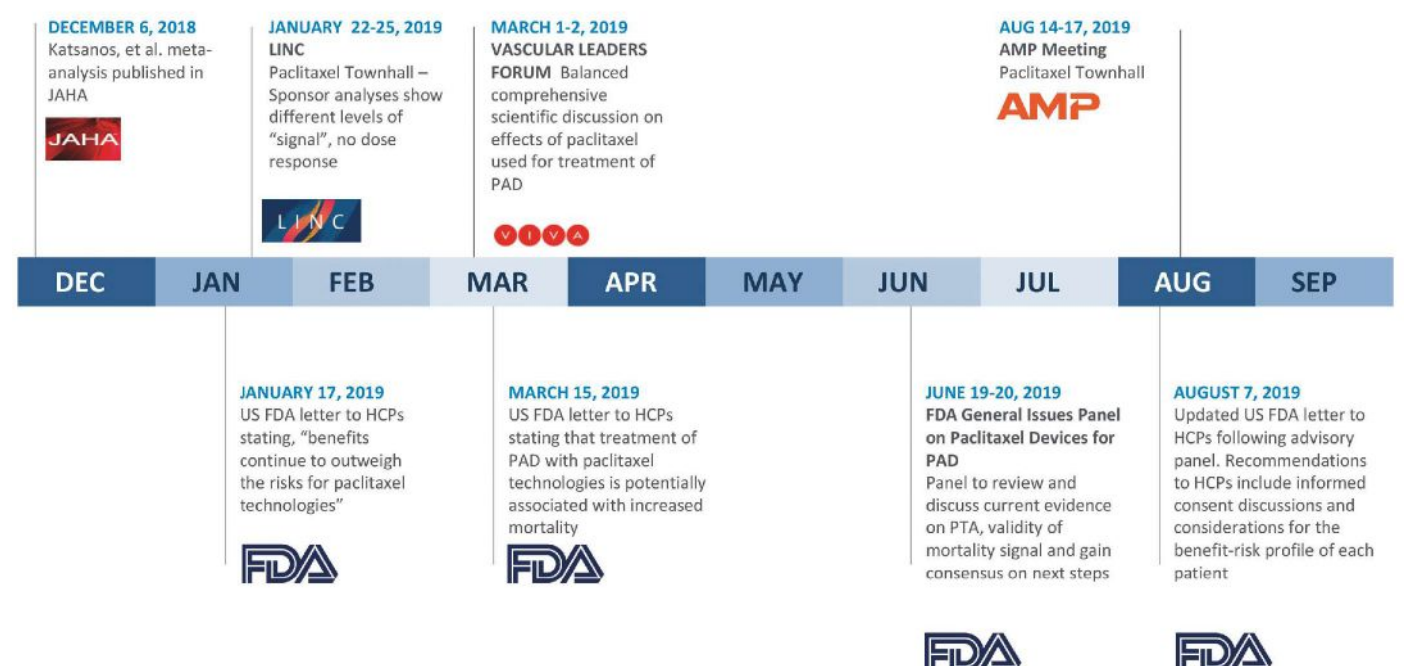
and functional and quality of life improvements observed from baseline through 3 years for the DCB cohorts. No mortality signal was observed versus PTA at 3 years.

Understanding the evidence that supports the use of certain treatments is essential for providing options to patients and optimal outcomes. Dr. Craig Walker from Tulane Medical School Cardiovascular Institute of the South discussed the evidence behind the use of atherectomy & drug technology in CLI. He uses atherectomy devices and DCBs frequently and oftentimes uses the two approaches together. Most atherectomy devices are different from each other, yet they often get lumped together in results for best practices and use guidelines. Dr. Walker called for more research and clinical studies to generate evidence for atherectomy coupled with drug delivery in CLI therapy.

Arnaud Kerzmann, MD from CHU Liège presented on a 3 Center European Experience where renal failure and



AMP: The Meeting that Started the Movement. Panelists from left to right: Drs. Mahmood Razavi, Ramon Varcoe, Michael Lichtenberg, Robert Beasley, Thomas Zeller, George Adams and Jihad Mustapha.



Timeline representation of current paclitaxel issue.





CLI Wound Summit Course Co-Directors Vickie Driver, DPM, Lee Ruotsi, MD and Dot Weir, RN.



Hands-on cadaver lab for tibial access was very well attended.



Panelists commenting during a live case demonstration: George Adams, MD, Bryan Fisher, MD, and Marianne Brodmann, MD

Rutherford classification 4–6 were only factors impacting survival. Also, results from the Zilver PASS trial comparing an endovascular versus open surgical approach were presented by Constantino Peña, MD. He mentioned that the final 12-month and preliminary 24-month results show at least a non-inferiority of Zilver PTX versus prosthetic bypass surgery above the knee, with similar patency results and less complications.

Eric Secemsky, MD, MSc, of Harvard Medical School urged the audience to find ways to use real-world data to evaluate the safety of different devices in the CLI population. He focused on three different analyses of Medicare data over different time periods and with both ICD-9 and ICD-10 diagnosis codes. All three showed no differences in survival following treatment with drug-coated versus non-drug-coated devices in unadjusted, adjusted, and subgroup analyses. He recommended continued analyses as more data continue to become available, but finds these analyses useful when discussing safety of drug-coated devices with his patients.

**Paclitaxel.** Later in the program, a paclitaxel overview and timeline was provided by Dr. George Adams (see image, page 21), and Dr. Lawrence Garcia followed with a review of patient level data. Prof. Ramon Varcoe, from University of New South Wales and Prince of Wales Hospital in Sydney, provided an overview of the safety profile of paclitaxel.

Dr. Mustapha discussed his rationale for continuing to treat CLI patients with paclitaxel. The August 7, 2019 FDA letter recommends (1) a discussion of risk and benefits of all available PAD treatment options with your patients; (2) based on current available information, alternatives to paclitaxel devices might provide more favorable risk/benefit; and (3) for individual patients judged to be at high risk for restenosis and repeat femoropopliteal interventions, clinicians may determine the benefit of paclitaxel-coated devices outweigh the risk of late mortality.

“These recommendations affirm our belief that paclitaxel-based devices provide an important therapeutic option for patients with PAD, especially those at high risk for restenosis. I for one, am very

pleased our patients will continue to have access to these devices. After reviewing the totality of the current evidence, I remain confident in the safety and efficacy of drug-coated technology.”

Dr. Joji Varghese, MD, presented a recent single center study on cause of death among CLI patients. He discussed the significant mortality of patients undergoing major amputation with 53% mortality at 5 years and 64% at 7 years. A nearly 2.5-fold increase in mortality was noted for patient with CKD and CAD undergoing major amputations. The existence of multiple co-morbid conditions (hyperlipidemia, DM, CKD, CAD) are associated with >90% mortality at 7 years for patients undergoing major amputation.

### LIVE CASES

Live cases were presented this year by Fadi Saab, MD, from Advanced Cardiac & Vascular Centers for Amputation Prevention in Grand Rapids, MI; D. Chris Metzger, MD, from Ballad Health System CVA Heart and Vascular Institute in Kingsport, TN and Steve Henao, MD, from New Mexico Heart Center in Albuquerque, NM. They shared tools, and tips for treating complex, multi-vessel, multi-lesion CLI disease.

### THE CLI WOUND SUMMIT AT AMP

This session, co-developed in partnership with the CLI Global Society, was led by course directors Vickie Driver, DPM, Lee Ruotsi, MD, and Dot Weir, RN. All aspects were relevant to treatment of CLI patients by a multi-disciplinary team were discussed. The day ended with sessions on “Beyond Revascularization: How Nurses and Mid-Level Providers Impact Care of CLI Patients” by Bailey Estes, RN and “How to Develop and Champion a Multidisciplinary CLI Team, by Paul Michael, MD.

### CALL TO COLLABORATE

On the third day, the morning session focused on how to use the knowledge and enthusiasm gained here to educate the public and other physicians and advocate for policy change. Paul Michael, MD expressed how different the AMP meeting is compared with other meetings

he attends. He especially appreciates the comradery between specialties. He discussed the history of CLI, starting with mention of the first society to recognize podiatry as a medical specialty in 1895.

Drs. Laiq Raja and Vlad Alexandrescu discussed the need to correctly identify the type of ulcer being treated and the appropriate diagnostic tools to use for differentiating different ulcers and wounds. Appropriate wound care and how to manage the CLI patient post-revascularization was emphasized by Vickie Driver, DPM, MS and Dot Weir, RN, CWON, CWS. Dr. Driver encouraged the audience to remember that no case is without hope and many pieces are required for the care of these patients. “Don’t jump to skin replacement after revascularization. Only after fully identifying the wound and the situation can one decide what is the best thing to do for the patient.” Dr. Amjad Almahameed brought up the issue of double jeopardy for patients with chronic kidney disease (CKD) and PAD. CKD is a strong and independent risk factor for PAD, CLI, and poor outcomes. These patients with CKD tend to have more amputations even after undergoing successful revascularization, more bleeding, and more wound re-infections. He warned that CKD is becoming a PAD equivalent. Lee Ruotsi, MD, focused on how to improve education for primary care and community providers as well as select specialty practices in order to accelerate recognition of PAD, CLI, and wounds so that timely and appropriate referrals can be made.

Desmond Bell, DPM described how the title of his presentation changed from “How do we improve things?” to “How we *will* defeat CLI,” since solely improving things is not adequate. He called for increased education, advocacy, and strategy in advancing care. Even though there was a decrease in lower extremity amputation rates in the US during the last two decades, there may now be a reversal in progress, particularly in young and middle-aged adults. Dr. Driver ended the session by encouraging all to help raise awareness and join the fight against CLI

by joining the CLI Global Society at [www.cliglobalsociety.org](http://www.cliglobalsociety.org).

### EARLY CAREER PROGRAM

AMP provided a record number of scholarships to Fellows and Early Career physicians who participated at all levels in the meeting. CLI Global Society members and #CLIFighters engaged heavily in a session on CLI for early career physicians and fellows, directed by Fadi Saab, MD.

### HANDS ON WORKSHOPS

George Pliagas, MD, and Gail Hadley, RN, again led the popular Hands-on Ultrasound with Live Models workshops that took place over Days 1–3 of the meeting. Dr. Pliagas directed the Hands-On Cadaver lab, Fadi Saab, MD, directed the Complex Lesion Workshop, and George Adams, MD directed the Atherectomy Workshop on Saturday. These workshops provided attendees access to multiple wires, catheters, CTO devices, and atherectomy devices. They were provided tips and tricks to overcome challenges that complex CLI cases present. They also learned decision-making for choosing the appropriate device based on lesion location, length, and morphology.

### THE CLI REVOLUTION EXPANDS TO AMP EUROPE

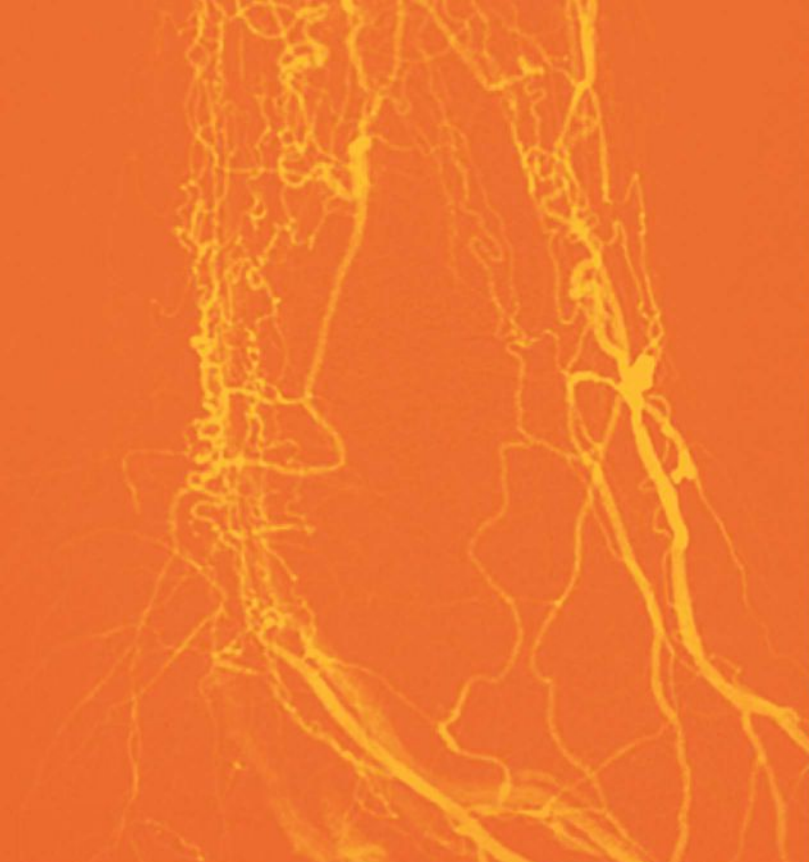
The stimulating conversations that were started at this meeting will continue as the CLI revolution expands to Europe. Join Course Co-Directors Jos C. van den Berg, MD, from Lugano, Switzerland and Jihad A. Mustapha, MD, October 2–4, 2019 in Lugano, Switzerland ([europe.amptheclimeeting.com](http://europe.amptheclimeeting.com)). ■

Disclosures: None

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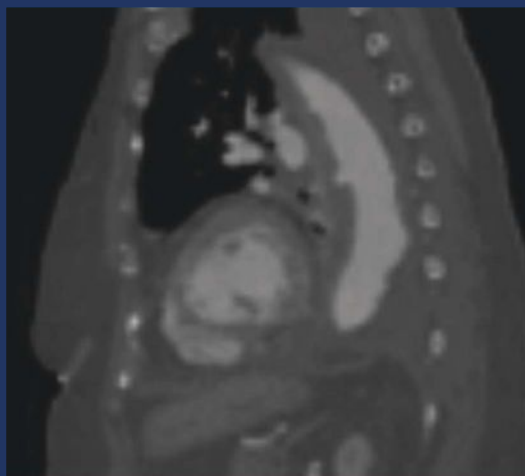
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