

# UCSF Heart & Vascular Center



UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

winter 2009

VOLUME 5 NUMBER 1

## Aggressive diagnosis and medical management best for asymptomatic PAD

Despite substantial research showing that peripheral artery disease (PAD) puts people at increased risk for heart attack, stroke, amputation and other vascular-related conditions, PAD remains significantly underdiagnosed and undertreated.

“These are very vulnerable patients,” says Michael S. Conte, MD, chief of Vascular and Endovascular Surgery at UCSF Medical Center and one of the country’s leading PAD experts. “Most are over 70. Many are diabetics or smokers or both, and have other vascular conditions – and many are

asymptomatic. Moreover, the course of the disease in individual patients is unpredictable. That’s why physicians must be especially diligent in looking for PAD in at-risk populations.”

“When patients come in with a related condition like chest pain, it is not only important to do a complete cardiac evaluation, but it is just as important to ask about things related to other vascular territories, such as neurological symptoms, claudication symptoms, erectile dysfunction and foot ulcerations,” says cardiovascular CONTINUED ON PAGE 7

### CONTENTS

<b>Perspective</b>	2
<b>Managing claudication</b>	3
<b>Claudication case study</b>	4
<b>Critical limb ischemia</b>	5
<b>Diabetes and PAD</b>	6
<b>CME</b>	8

**UCSF Medical Center**  
Heart & Vascular Center

# Peripheral artery disease

The prevalence of peripheral artery disease (PAD) is rising as the population ages and the incidence of associated risk factors skyrockets. This puts more patients at increased risk for death, myocardial infarction, stroke and limb loss, as well as for a significantly impaired quality of life.

Yet, despite efforts to increase awareness of this common condition, PAD remains underdiagnosed and is often inadequately treated. Consider that lower extremity amputations in the United States continue to increase, particularly among the growing diabetic population.

The primary treatment goals for advanced PAD should be long-term preservation of a functional limb, pain alleviation, maintenance of

quality of life and minimization of comorbid (largely cardiovascular) complications. Beyond aggressive medical management, treatment options include catheter-based and open surgical approaches to improve limb circulation.

Many centers offer a broad range of procedures, but the evidence base lags behind the technology and outcome standards are poorly defined. We believe that experienced clinical judgment – selecting the right intervention for the right patient at the right time – yields the best outcomes. Multidisciplinary collaboration improves decisionmaking, ensures thorough evaluation and management of global atherosclerosis, and optimizes short- and long-term outcomes.

The UCSF Heart and Vascular Center employs that approach through our dedicated team of talented vascular specialists and nationally recognized leadership in PAD treatment. In addition, our translational research advances the development of novel therapies for patients with limited conventional options.

We hope you'll continue to partner with us to improve PAD diagnosis and treatment. ●



*Michael S. Conte, MD  
Chief of Vascular and  
Endovascular Surgery*



## About Michael S. Conte

Before arriving at UCSF in 2008, Michael S. Conte, MD, served as associate professor of surgery at Harvard Medical School and director of vascular surgery research at Brigham and Women's Hospital, Boston. He has an active clinical practice in vascular surgery, which includes complex limb revascularization, aneurysm repair, aortic and carotid artery surgery, and hemodialysis access. His translational research focuses on control of the vascular injury response to improve the long-term results of cardiovascular grafts and interventional procedures.

# Managing claudication: Addressing the double threat of PAD and CVD

“Claudication is sometimes the first sign that an individual has cardiovascular disease [CVD], on top of their peripheral artery disease [PAD],” says Michael S. Conte, MD, chief of Vascular and Endovascular Surgery at UCSF Medical Center. “It’s as though they’re getting angina in their leg.”

Most clinicians recognize that claudication demands treatment and careful monitoring, but Conte warns that patients’ fears about limb loss can cause a fixation on addressing leg pain to the detriment of managing all cardiovascular risk factors. It’s important, therefore, to reassure patients that claudication does not mean imminent loss of limb. Nearly 70 percent of patients with claudication never progress to critical limb ischemia, much less require an amputation.

Nevertheless, because individual disease progression is unpredictable, a cardiovascular specialist should follow these patients closely. “Most research indicates that up to half of patients with PAD and claudication are not having their cardiovascular risk factors fully managed, or if they are, the targets are too modest,” says Conte.

“Global management of cardiovascular risk factors is essential for patients with claudication,” says cardiovascular specialist Yerem Yeghiazarians, MD. That type of

management begins with a comprehensive evaluation of risk factors and continues with optimized management of those factors, which includes the most effective medications, where appropriate, for cholesterol level, hypertension and diabetes, as well as lifestyle modification including smoking cessation, a healthy diet and daily exercise that features a progressive walking program.

With this type of management, most patients with claudication can slow the progression of symptoms and improve walking ability. If, however, comprehensive management fails and the patient experiences persistent and worsening disability that limits lifestyle or occupation, then it is important to refer to a center that offers the full range of options for opening the arteries and enabling these patients to walk without pain.

## Lack of guidelines complicates the treatment choice

“Though the treatment options for underlying arterial occlusion have increased, the choice – especially in the absence of any firmly established guidelines – depends on the location, length, burden of the disease and expertise of the operator,” says Yeghiazarians.

Angioplasty represents a less invasive therapeutic option and is often considered as a possible first option; open bypass surgery represents another set of options.

Lasers and atherectomies are also choices in select cases, although typically as a precursor to either angioplasty or open surgery.

“To avoid a bias for what’s available and known, a team approach is especially important,” says Conte. “The correct choice is the key to a quality outcome.”

At UCSF Medical Center, where there is access to the full range of potential treatments, an interdisciplinary conference is held monthly in which vascular specialists and cardiologists look at each individual patient’s case and decide on a treatment strategy after weighing all the applicable factors.

“We believe these conferences are very important for a systemic disease process that affects every artery from head to toe,” says Yeghiazarians.

Finally, says Conte, both before and after any procedure “these patients need to be followed closely because they’re at continued risk for the rest of their lives and because the course can be so unpredictable. But if PAD is treated correctly, we can improve quality of life and prevent morbid endpoints.” ●



Yerem Yeghiazarians, MD

# Team approach clears the way for transplant: **A case study**



Yerem Yeghiazarians, MD



J. Eduardo Rame, MD



Charles Eichler, MD

In 2006, an East Bay nephrologist referred RM, a 57-year-old man with kidney disease and claudication in both legs, to UCSF Medical Center to be evaluated for a potential kidney transplant. Cardiovascular specialist Yerem Yeghiazarians, MD, conducted a thorough evaluation that uncovered significant ischemic heart disease. Yeghiazarians then referred RM to cardiologist J. Eduardo Rame, MD, to evaluate the patient's suitability for a combined heart and kidney transplant.

Impressed by RM's desire for an active lifestyle and his willingness to work hard at rehabilitation, Rame placed the patient on an aggressive regimen of volume removal, in collaboration with his nephrologist and local dialysis team. This approach was combined with optimization of medicines for ischemic heart failure to improve the patient's capacity for physical activity. Now there was only one barrier to RM's being listed for the combined transplant: his claudication, which would limit his ability to rehabilitate appropriately.

After an angiogram revealed significant peripheral artery disease in both legs, Yeghiazarians and vascular surgeon Charles Eichler, MD, agreed that the popliteal lesion in RM's left leg was amenable to endovascular intervention. They decided on atherectomy and angioplasty, which Yeghiazarians performed successfully in March 2007.

"This improved the claudication in the left leg, but the right leg was still quite limiting," says

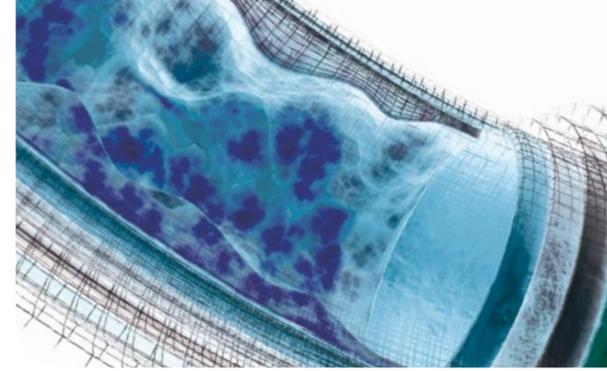
Eichler. In early April, they brought RM back to address the complete blockage of the popliteal artery in his right leg, but were unable to clear the lesion with an endovascular approach. Therefore, to relieve RM's persistent right leg symptoms, Eichler performed a successful femoral-popliteal artery bypass with a saphenous vein graft.

Today, while waiting at home for his transplant, RM – under the collaborative supervision of his community physicians and Rame – is undergoing cardiac rehabilitation three times a week, walking and enjoying a much-improved quality of life. "We believe he stands to benefit from a combined heart and kidney transplant because of his compliance, his support network and his stamina, now that he's been revascularized and can walk without symptoms of claudication," says Rame. ●

*To contact Dr. Yerem Yeghiazarians, call (415) 353-3815.*

*To contact Dr. J. Eduardo Rame, call (415) 502-4597.*

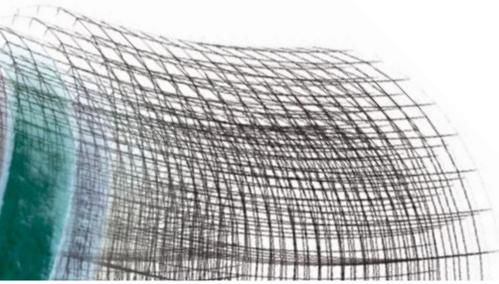
*To contact Dr. Charles Eichler, call (415) 353-4366.*



As with the other stages of peripheral artery disease (PAD), treatment of the most severe stage – critical limb ischemia – should be multifaceted and include medication and lifestyle modifications, as described in this issue's lead article. But with critical limb ischemia (CLI), clinicians can't wait to observe the effectiveness of that approach. "If these patients are not effectively revascularized, they are at severe risk for loss of limb," says cardiovascular specialist Yerem Yeghiazarians, MD.

CLI occurs when people develop severe blockages, usually at more than one location in the leg, undermining the ability of collateral arteries to at least partly accommodate the blocked flow. The clinical result is an ankle-brachial index that drops below the point where blood flow can facilitate basic activity.

"Tissue functions are impaired and there is pain, even at rest," says Michael S. Conte, MD, chief of Vascular and Endovascular Surgery at UCSF Medical Center. Wounds that fail to heal and the development of irreversible tissue damage (gangrene) are also cardinal signs of CLI.



## Critical limb ischemia is a call for revascularization

### Angioplasty, bypass or atherectomy?

Choosing the appropriate revascularization technique remains a difficult challenge because, while there are multiple options, there are no established guidelines. A multidisciplinary approach – with clinicians who possess both experience with and access to the full range of revascularization options – provides the best results, says Conte, who serves on a Society for Vascular Surgery panel that is creating guidelines for evaluating new devices.

Percutaneous therapies are less invasive than open surgery, and depending on the types of blockages, physicians often consider such therapies first, especially because recent advances have expanded the available options. “At UCSF, we offer many types of percutaneous therapies, such as balloon angioplasty, cryoplasty and stenting,” says Yeghiazarians. “Drug-eluting stents are also a possibility, but there is not much evidence on these yet for arteries in the legs.”

When the artery is completely occluded, the team may also consider atherectomy with either lasers or devices that “shave” the plaque. “These are not yet proven as stand-alone options because they tend to be limited by recurrence,” says Conte. “But as part of the armamentarium, they can offer some short-term improvement, especially when used in combination with open surgery.”

### Bypass is often the best option

In many cases – especially those who have severe disease or for whom less invasive solutions have failed – a well-done surgical bypass is the best option to preserve the limb for the long term. “Over the last 20 years, we have refined these techniques dramatically,” says Conte. “So while we always carefully consider the less invasive option, when we have excellent surgery available, we don’t dodge around it.”

The best alternative at this point is using the patient’s own vein because artificial grafts typically do not function well under low-flow conditions. Conte adds that – as

with any complicated surgery – volume, surgeon experience and technical factors strongly influence the success rate. And due to the global nature of their cardiovascular disease, getting these patients safely through leg bypass surgery requires careful attention by a team of surgeons, anesthesiologists, cardiologists and nurses.

Finally, because PAD is a chronic disease, ongoing surveillance is essential. “We follow patients closely following either surgery or angioplasty, and use ultrasound to look directly at the graft or stent,” says Conte. “This often enables us to see things before the patient even recognizes new symptoms.”

“Part of the follow-up needs to be therapy for all cardiovascular risk factors,” says Yeghiazarians. ●



Michael S. Conte, MD

### RESEARCH AND CLINICAL TRIALS PROVIDE NEW HOPE

Researchers worldwide are actively developing and testing new PAD treatments, including angiogenesis, tissue-engineered grafts, and various gene and cell therapies. “These are areas of promise, but they are not yet ready for prime time,” says Michael S. Conte, MD, who was lead investigator of the PREVENT III clinical trial, a multicenter, phase III study of an oligonucleotide therapy for the prevention of peripheral vein graft failure.

At UCSF, research efforts include drug-eluting stents, new drugs to reduce scarring in arteries and veins, gene therapy, and stem cells that may help regrow blood vessels in the leg. “In some of these areas, we are or will be doing some small-scale clinical trials for patients who have exhausted standard options,” says Conte.

# Diabetes and PAD: A dangerous, but treatable combination



An angiogram of the aorta in a patient with severe claudication shows severe aortoiliac occlusive disease with complete occlusion of the distal aorta in the abdomen.

“Diabetic patients with peripheral artery disease (PAD) can respond as well as their nondiabetic counterparts to PAD treatment, despite widespread assumptions that they do not,” says Michael S. Conte, MD, chief of Vascular and Endovascular Surgery at UCSF Medical Center. “That’s why it’s important to make the PAD diagnosis early in diabetics and to monitor their PAD aggressively.”

It’s especially important because the more than 23 million Americans who have diabetes are at substantially increased risk for PAD’s most severe complications – especially loss of limb. If a diabetic PAD patient is also a smoker, there is a markedly increased risk of amputation. “It’s like lighting matches in a gas station,” says Conte.

## Disease progression in diabetics

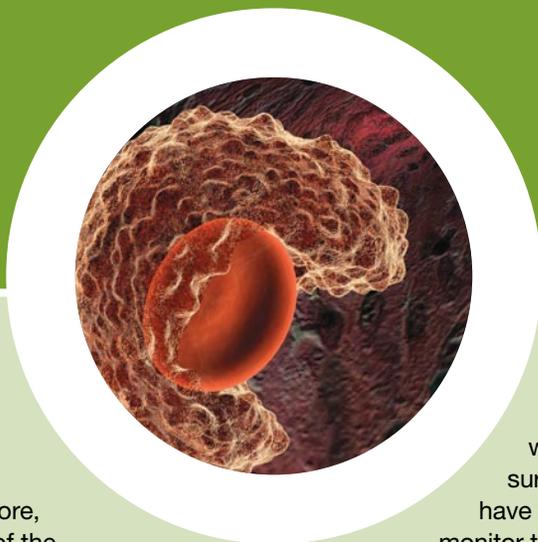
Diabetics, of course, are at risk for sores and blisters in weight-bearing areas. Because diabetes can affect blood vessels, nerves and the immune system, even a minor foot infection can be limb-threatening. PAD exacerbates these clinical

issues because of the way it hampers circulation and, therefore, the ability of the body to self-heal open wounds.

“In addition, PAD in diabetics is usually a more diffuse process that attacks the smaller blood vessels in the calf,” says Conte. “The farther down the blockage, the less effective the collateral pathways and the less reserve these people have.”

Blockages in these diffuse, smaller vessels and neuropathy from their diabetes obscure the warning signs, so diabetics rarely present with early-stage disease. Instead, they are much more likely to show up in a physician’s office with an ulcer or a black toe from advanced PAD – or in an emergency room with a heart attack or stroke.

“The downturn in diabetics can be quite rapid,” says Conte. “It’s why we argue that every visit, every diabetic should have a pulse exam and an ankle-brachial index.”



Preventive foot care with a podiatrist – who can make sure these people have the right shoes, monitor their foot status and educate them about proper foot care – is also essential. And at the first sign of an open sore that doesn’t rapidly resolve, diabetics should be referred to a vascular specialist.

“Even without a foot ulceration, if there are no pulses in the foot, diabetics should be followed by a vascular specialist because they are much more likely to progress rapidly and unpredictably, and we can’t judge their reserve,” says Conte.

This close monitoring, along with appropriately timed interventions, can salvage diabetics’ limbs. “We need to avoid therapeutic nihilism,” says Conte, who is known nationwide for his limb salvage interventions. “We can open or bypass problem vessels that are far down the leg, but surveillance is the key.” ●

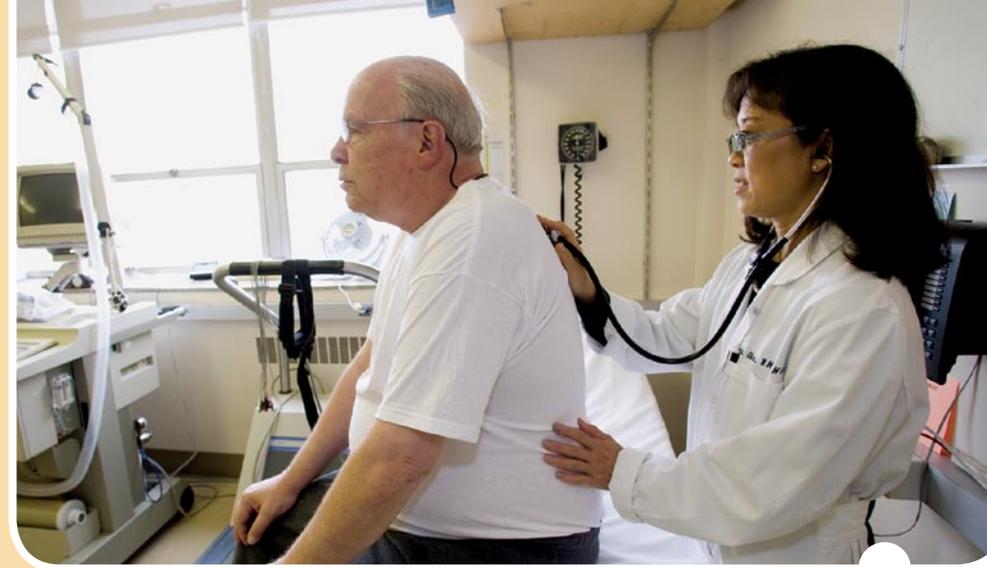
specialist Yerem Yeghiazarians, MD. “Many of these patients will often have diffuse and, at times, asymptomatic vascular problems involving organs other than the heart arteries, and these can only be diagnosed by careful history, examination and appropriate screening.”

“The key diagnostics are usually simple – typically a thorough examination of the legs and feet, a pulse exam and an ankle-brachial index,” says Conte. “And if something emerges or if there are more active symptoms, we recommend a complete diagnostic evaluation by a vascular specialist.”

### Comprehensive risk factor management

Once a patient is diagnosed, recent research indicates that PAD merits aggressive management of all cardiovascular disease (CVD) risk factors. A UCSF team is engaged in a five-year, randomized, controlled trial with PAD patients that examines how effectively reducing multiple CVD risk factors affects walking and vascular health.

“Antiplatelet therapy is the cornerstone,” says nurse-scientist Roberta Oka, RN, DNSc, who is the study’s principal investigator. But there also is strong evidence to support the use of lipid-lowering medications (statins). Hypertension and diabetes are aggressively monitored and managed. Diet and exercise are key adjunctive therapies, as are stress management and smoking cessation. Focusing on small, achievable goals set by the patient and provider – and improving self-efficacy for specific behaviors – helps patients achieve the lifestyle changes.



Roberta Oka,  
RN, DNSc, and  
patient Clinton Hallum.

“Patient education also is fundamental,” says Oka. “We focus on improving a person’s understanding of their risk factors, and the synergy between pharmacologic and adjunctive strategies to optimize self-management.”

Oka is especially concerned about the tendency to have lower expectations of what an older population can achieve. “This can lead to undermedication and a failure to lower risk factors to clinical standards,” says Oka. “We know this program is labor-intensive and not every practice can do all aspects of it, but setting goals and ongoing monitoring are extremely important. We have found patients to be very interested in improving their health and especially in improving their ability to walk, even in their late 70s and 80s, which can ease the burden on clinicians.” ●

*To contact Dr. Michael S. Conte,  
call (415) 353-4366.*

*To contact Dr. Yerem Yeghiazarians,  
call (415) 353-3815.*

*To contact Dr. Roberta Oka,  
call (415) 514-3407.*

### OPTIMAL TARGETS FOR PAD MANAGEMENT

- **Smoking:** Complete cessation
- **Antiplatelet therapy:** Aspirin (81 mg daily) or other antiplatelet therapy, as appropriate
- **Lipid management:** Treatment with lipid-lowering agents (such as statins) to achieve a target LDL of less than 100 mg/dl, or less than 70 mg/dl for patients at very high risk of events
- **Blood pressure control:** Less than 120/80 mmHg for patients without complicating conditions (JNC 7\* considers patients between 120/80 mmHg and 139/89 mmHg to be prehypertensive)
- **If diabetic:** Normal fasting plasma glucose (less than 100 mg/dl) and normal HbA1c (less than 7 percent)
- **Nutrition and weight management:** A healthy eating pattern (typically low fat and low cholesterol, leading to a BMI of 18.5 kg/m to 24.9 kg/m)
- **Exercise:** 50 minutes walking, five days per week (Inter-Society Consensus for the Management of PAD\*\*)
- **Stress management:** Improve emotional well-being

\* The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, 2003.

\*\* TransAtlantic Inter-Society Consensus (TASC) II, 2006.

## REFERRAL LIAISON SERVICE

Tel: (800) 444-2559 Fax: (415) 353-4395  
www.ucsfhealth.org

Our Referral Liaison Service provides you with improved access to our physicians and medical services. Liaisons can expedite the referral process, assist in obtaining follow-up information and are available to help resolve difficulties.

## TRANSFER CENTER

Tel: (415) 353-9166 Fax: (415) 353-9172

The UCSF Transfer Center is staffed 24/7 by a specialized team to evaluate the clinical needs of your patient to ensure the most appropriate medical care is provided and to coordinate transfer and transport from hospitals throughout the region. This centralized service provides quick access to our physicians and team members, including nurses, financial counselors, case managers and social workers. At discharge, the Transfer Center can facilitate the return transfer.

Written and designed by: UCSF Public Affairs

### Heart and Vascular Center Council:

Michael S. Conte, MD, Chief, Vascular and Endovascular Surgery  
Michael Crawford, MD, Chief, Clinical Cardiology  
Robert Kertan, MD, Chief, Interventional Radiology  
Scot Merrick, MD, Chief, Cardiothoracic Surgery  
Karen Rago, Administrative Director, Heart and Vascular Center  
Jeff Kalin, Administrator, Adult Cardiology

Photos: Elisabeth Fall, pp. 2, 3, 4, 5, 7

This publication is printed on New Leaf paper made with 100 percent recycled fibers, 50 percent post-consumer waste and processed chlorine-free.

© 2009 The Regents of the University of California PR770



University of California  
San Francisco

advancing health worldwide™

## CME COURSES

For more information, visit [www.cme.ucsf.edu](http://www.cme.ucsf.edu)

Course title	Date	City
Asian Heart and Vascular Symposium	February 7, 2009	San Francisco
UCSF Vascular Symposium	April 23-25, 2009	San Francisco

## CONTACT INFORMATION

To contact faculty members in the Division of Vascular and Endovascular Surgery, please call (415) 353-2357. To view faculty profiles or to make a direct appointment request or referral, please visit our website at [vascular.surgery.ucsf.edu](http://vascular.surgery.ucsf.edu).

To contact the Division of Cardiology about PAD-related issues, please call (415) 353-3817 or visit our website at [cardiology.ucsf.edu/clinical/interventional/faculty/Yeghiazarians.html](http://cardiology.ucsf.edu/clinical/interventional/faculty/Yeghiazarians.html).

UCSF Medical Center, San Francisco, CA 94143-0940

UCSF Heart & Vascular Center

Return Service Requested

Nonprofit Org.  
US Postage  
PAID  
San Francisco, CA  
Permit No. 8285