

# Miller School Researchers Explore Limb-Saving Treatments for Peripheral Artery Disease

Vascular surgeons at the University of Miami Miller School of Medicine are saving the limbs of even complex peripheral artery disease (PAD) patients by using advanced minimally invasive and hybrid surgical approaches, as well as traditional open surgery methods.



Dr. Jorge Rey leads a vascular surgery team at UHealth Tower.

Yet despite technological advances and improved surgical success, many patients with end-stage PAD, or critical limb ischemia, still lose their limbs to the disease. Miller School researchers are working to close the gap with studies, including trials focused on a Miller School discovery that involves using a cell adhesion molecule called *E-selectin* to heal tissue damaged by vascular disease.

“Treatments that would eradicate most if not all vascular disease limb amputations would be a transformative leap forward in peripheral artery disease and critical limb

ischemia. These are diseases that still result in over 100,000 major amputations in the United States alone and carry not only the morbidity of a major limb loss but significant mortality,” said Omaida C. Velazquez, M.D., professor and chair of the DeWitt Daughtry Family Department of Surgery, and the David Kimmelman Endowed Chair in Vascular Surgery at the Miller School.

## **Preclinical and promising**

An important area of discovery and research at the Miller School focuses on enlisting the body’s own mechanisms to grow new vasculature to the vessels. The aim is to bring nutrients to those wounds or areas of gangrene that are not healing efficiently with standard procedures.

Based on a decade of investigation into the nature of how the body activates certain signal cascades to achieve blood vessel healing and regeneration, Dr. Velazquez and Zhao-Jun Liu, M.D., Ph.D., associate professor of surgery, discovered a way to deliver *E-selectin* to repair damaged tissue.

*E-selectin* is known to participate in different physiology cascades – some inflammatory, others thrombotic. The doctors discovered in animal studies that some of those cascades regenerate blood vessels, resulting in vasculogenesis, and preserve vessel integrity.

“Those findings led us to propose a new treatment – a gene-modified cell therapy approach using a viral vector to deliver *E-selectin* to the surface of cells in order to potentiate the pro-regenerative, pro-healing vasculogenesis effect needed to save a limb for these critical limb ischemia patients,” Dr.

Velazquez said.

University of Miami patented and licensed the technology and launched the spinoff company [Ambulero](#) to potentially bring its therapeutic candidate AMB-202 to the clinic.

“An abstract of this work was submitted to the Society of University Surgeons and the last annual academic surgery meeting, which was cancelled due to the pandemic. But it was reviewed by peers and received the top prize in terms of innovation. Part of the award includes presenting the work at an international forum in Poland next year,” said Dr. Velazquez, who is Ambulero’s chief medical officer. “What we’re doing is unique. No one has tried modifying the surface of the cells with an adhesion molecule and tried gene therapy using an adhesion molecule.”

Miller School researchers are also taking part in other studies looking at using cell-based technologies to heal wounds and save limbs in PAD patients. Dr. Velazquez and Arash Bornak, M.D., associate professor of surgery and program director of the Vascular Surgery Fellowship and Integrated Residency in the Division of Vascular and Endovascular Surgery at the Miller School, are principal investigators in studies looking at using unmodified cell-based technologies to heal wounds in PAD patients.

“The University of Miami has been leading the way in the region for opening and enrolling for those trials. We see modest but real effects from those cells,” Dr. Velazquez said.

Basically, the research is looking at next-generation treatment modalities involving cellular and molecular means.

It offers patients facing limb amputation another potential option as a study participant, according to Dr. Bornak.

“Currently, we’re enrolling for the Pluristem Therapeutics trial. It’s an international trial that involves intramuscular injection of mesenchymal-like adherent stromal cells derived from human placenta. When injected into the leg muscles, these cells release different proteins, including cytokines and growth factors. The idea is to promote tissue healing through cellular and molecular means, rather than surgical technique,” Dr. Bornak said.

### **Advanced limb-saving options in practice**

Surgical options remain the standard of care. The Miller School has been at the forefront of all types of surgery to treat PAD, from minimally invasive endovascular to hybrid to purely open revascularization, according to Dr. Bornak.

Dr. Bornak said: “In terms of limb preservation or limb salvage, whether they be legs or arms, our division at the University of Miami Hospital Center of Excellence stands out in the region. We have a high volume of cases and extensive expertise in both endovascular and open surgery.”

Miller School surgeons have performed a hybrid approach combining endovascular and open approaches for the last decade. Hybrid surgery minimizes the skin incision and shortens the hospital stay and recovery, compared to the open approach.

“We have published several papers reporting on our experience with hybrid and endovascular treatments,” Dr. Bornak said. “Very early on we implemented the use of stent grafts for treatment of aortoiliac occlusive disease and have had

excellent long-term results.”

For revascularization below the knee and the upper extremities, Miller School vascular surgeons perform advanced distal bypasses.

“There are extreme cases where we bypass all the way to the plantar artery, within the foot, or to the palmar arteries in the hand, bringing blood flow directly into the affected extremity,” Dr. Bornak said.

Achieving the best outcomes for patients with vascular diseases requires having access to multiple tools and interventions, according to Jorge Rey, M.D., associate professor of surgery and chief of the Division of Vascular and Endovascular Surgery at the Miller School.

Some patients require only stenting or a balloon angioplasty to address their vascular disease. Others need complex open reconstructions to address leg disease that is so advanced that vascular surgeons have to use an open approach to reconstruct the entire vascular system from the abdomen down, or of the leg.

“What sets us apart is that we also have access to the latest clinical trials that involve new devices or investigational cellular treatments. Sometimes, we have therapies or devices that are not yet available on the market but are here in the context of our partnering with industry for clinical trials,” Dr. Rey said. “If I were a patient, I would choose to come to a place where my doctor sees multiple ways to approach my problem, as opposed to one single therapy or a one-size-fits-all approach. This disease is complex enough that it requires

access to many approaches and tools.”