

Peter Munk Cardiac Centre

CLINICAL AND RESEARCH REPORT



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INTERVENTIONAL CARDIOLOGY

'High-risk' road leads to life-saving results

NEW ANGIOPLASTY TECHNIQUES PROVIDE OPTIONS FOR
COMPLEX AND CHALLENGING PATIENTS

Coronary angioplasty, or percutaneous coronary intervention (PCI), the non-surgical repair of a blood vessel, by inserting a balloon-tipped catheter and by scaffolding the blood vessel with a metallic wire mesh called a stent, has become the primary method of treating narrowed or constricted arteries, and has saved and/or improved the quality of lives of hundreds of thousands of individuals. However, for some people, this usually simple intervention can represent a high-risk procedure. Finding the best, most effective way to treat these high-risk cases, is one of the

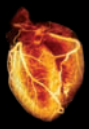


Dr. Vlad Džavík and colleagues are working at the leading edge of high-risk angioplasty.

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ABOUT THE PETER MUNK CARDIAC CENTRE

The Peter Munk Cardiac Centre is the premier cardiac centre in Canada. Since it opened in 1997, the Centre has saved and improved the lives of cardiac and vascular patients from around the world. Each year, approximately 55,000 patients receive innovative and compassionate care from multidisciplinary teams in the Centre. The Centre trains more cardiologists, cardiovascular surgeons and vascular surgeons than any other hospital in Canada. It is based at the Toronto General Hospital and the Toronto Western Hospital, members of University Health Network, which also includes the Princess Margaret Cancer Centre and Toronto Rehabilitation Institute. All four sites are research hospitals affiliated with the University of Toronto. For more information please visit www.petermunkcardiaccentre.ca



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challenges currently being tackled by Dr. Vlad Džavík and his colleagues at the Peter Munk Cardiac Centre (PMCC).

As PCI has evolved over the last 30 years, the procedure has become ever-increasingly safer and more effective. The development of highly flexible, easily deliverable coronary stents has dramatically reduced the potential of failure and life-threatening complications. It is patient complexity alone that has now become the overriding element in defining what constitutes a high-risk angioplasty.

"These high risk patients are definitely a minority, but they are a very important one," says Dr. Vlad Džavík, Interim Head of the Division of Cardiology and Director of Interventional Cardiology Research at the Peter Munk Cardiac Centre.

"They can present with serious conditions related to a severe dysfunction of the heart muscle, such as blockages in critical areas or multiple blockages. They can have extreme weakness in the left ventricular muscle or acute inflammation of the heart muscle, often with complicating comorbidities. They also sometimes present in severe cardiogenic shock, caused by a heart attack."

Damaged hearts

He also points out that these patients are often referred to University Health Network by other hospitals.

"One of the things they have in common," Dr. Džavík adds, "is that there is so much damage to the heart that its pumping function is compromised, which threatens other vital organs. If not treated quickly

and properly, these individuals can have more than a fifty per cent mortality rate."

Another important feature these patients have in common is the fact that they are not candidates for regular angioplasty, or even for open heart or bypass surgery. And this is where high-risk angioplasty plays such an important role.

Dr. Džavík and his colleagues at the Peter Munk Cardiac Centre work at the leading edge of treating these high-risk patients and perfecting the advanced specialized angioplasty techniques and devices that are needed.

Through the ongoing perfection of angioplasty techniques, Dr. Džavík says the risk of mortality for some high-risk patients is being reduced significantly. "And we can reduce the risks even more as we continue our efforts in this area," he adds.

Global recognition

The work being done at the Centre is being recognized globally. Developers of the most advanced medical devices often call on the Centre to trial and perfect their equipment. One example is the highly advanced Impella™, a break-through in Left Ventricular Assist Devices, designed to be delivered percutaneously to patients who are too high risk of surgery. Dr. Džavík was the lead Canadian investigator on an international trial of this device. The PMCC was the first centre in Canada to trial the Impella, and the first in North America to employ it in a clinical setting.

Similarly, the Centre will play the lead role in an international trial

studying the use of the state-of-the-art TandemHeart™ Percutaneous Ventricular Assist Device in cardiogenic shock. This trial is currently in the planning stage.

Pharmaceutical research is also important. Key studies underway or in the planning stage include a trial of medications to be used in cardiogenic shock to 'reduce' the size of the heart attack in individuals categorized as "very sick."

More than saving lives

Although you may be a high-risk patient, you don't have to be very sick to reap the benefits of the expertise of Dr. Džavík and his fellow cardiologists, interventionists, perfusionists, respiratory therapists, cath lab technicians, nurses and other clinicians at the PMCC.

As Dr. Džavík is quick to point out, the advances in high-risk angioplasty can also dramatically impact the lives of individuals whose conditions restrict their functionality and seriously impair their quality-of-life.

"We see patients living with coronary artery disease or experiencing some degree of heart failure," Dr. Džavík notes. "Many are older, and sometimes they are almost completely incapacitated. They experience difficulty breathing and chest pain and generally have very poor quality-of-life. The procedures we do here can change their lives. In many cases we can reduce their pain, help them to walk again and get back to enjoying life, instead of bouncing in and out of hospital every few weeks with incapacitating symptoms."



PUTTING PATRICK BACK ON HIS FEET

Shirley Longhurst characterizes her 74-year-old husband, Patrick, as a "restless individual."

"Patrick's not the type to sit around the house," says Shirley. "He's always been an active person, whether it be going for walks, shopping, or volunteering for the local Junior A hockey team." That's why, in the fall of 2012, when Patrick started to complain of shortness of breath and chest pains, Shirley became worried.

"He was finding it more difficult to undertake his regular activities," says Shirley. "His mobility and quality-of-life were significantly compromised."

On Labour Day, with his symptoms yet to subside, Patrick was taken by ambulance to the local hospital in Cobourg, Ontario, about an hour east of Toronto. Doctors there told him he had excessive fluid retention due to his heart beating irregularly. Patrick was put on blood-thinners to reduce clotting in the veins and the arteries and discharged from hospital a week later.

When symptoms did not subside, Patrick was sent to Peterborough to undergo an angiogram, a test that takes pictures of the blood-flow within the heart arteries. The test revealed significant calcium build-up in his heart arteries. This presented a high risk of heart attack. With the calcium build-up in his heart arteries, the blood-flow to Patrick's heart was significantly reduced, causing his symptoms. Without a viable solution available to Patrick at the hospital in Peterborough, he was immediately transferred that day to the Peter Munk Cardiac Centre (PMCC) to undergo further evaluation and treatment.

On September 27th, doctors at the PMCC tried unsuccessfully to perform bypass surgery on Patrick's coronary arteries. Unfortunately, the calcium build-up was too severe to allow for successful surgery. Dr. Vlad Džavík and a multidisciplinary team of cardiac specialists made the decision to perform a high-risk angioplasty procedure on Patrick the following day as the only means of saving his life. High-risk angioplasty would involve inserting the Impella™ device into his heart to help it eject blood and then mechanically dilating or widening Patrick's obstructed arteries followed by the placement of two coronary stents to keep his now widened arteries open.

The Centre's multidisciplinary approach to Patrick's cardiac care is unique to Canada and around the world. Teams of cardiologists, surgeons and imaging specialists share knowledge and consultation for best practices in patient care. In following this team-based practice, the Centre attracts the top cardiac talent from around the globe.

On September 28th, Patrick successfully underwent the procedure and was discharged from hospital on October 16th, 2012. Today, Patrick is back home, symptom-free, with no difficulty breathing, absent of any chest pains.

"Doctors at the Peter Munk Cardiac Centre gave Patrick back his quality-of-life," says Shirley. "He has now resumed many of the activities that he regularly partakes in, and is able to enjoy himself outside doing the things he is passionate about."

The treatment Patrick received was not available five years ago. Through the generous philanthropic support of donors, cardiac surgeons and cardiologists have the resources to develop procedures for treating high-risk patients such as Patrick. These resources allow doctors at the PMCC to make investments in the best equipment in the world, creating a culture that establishes a clearly defined process through which innovative procedures are born.



The high-risk procedure successfully performed at PMCC "gave Patrick back his quality-of-life", according to his wife Shirley.



CARDIOVASCULAR SURGERY

Meeting the challenges of aortic disease

DR. MARAL OUZOUNIAN BRINGS NEW KNOWLEDGE AND EXPERTISE ON COMPLEX CONDITION TO PMCC

For Dr. Maral Ouzounian, her first official day at the Peter Munk Cardiac Centre (PMCC) was very much a “trial by fire”.

“It was July 15th, and Dr. Viv Rao, Head, Division of Cardiovascular Surgery at the PMCC, had told me to just settle in and take it easy for the first few weeks,” Dr. Ouzounian recalls. “But that was not to be. My very first day of work I was faced with a patient presenting exactly the type of clinical challenge that had essentially brought me to Toronto.”

That challenge is complex aortic disease, and Dr. Ouzounian is a newly-appointed Cardiac Surgeon and Surgical Scientist at the Centre, and a Clinician Scientist with the Toronto Aortic Laboratory. She was recruited to the Peter Munk Cardiac Centre to help fill an identified need, and round out the Centre’s already impressive expertise in this important area of cardiac medicine.

Before assuming her responsibilities this summer, Dr. Ouzounian already had a history with the PMCC. After receiving her MDCM degree from Montreal’s McGill University, she completed her PhD at the University of Toronto. She subsequently completed her cardiac surgical residency at Dalhousie University in Halifax.

By then she had come to the attention of the cardiac surgery division at PMCC and Dr. Tirone David, the Melanie Munk Chair in Cardiovascular Surgery – an internationally renowned pioneer in aortic surgery, and the developer of an innovative valve-sparing aortic root replacement procedure that

bears his name (*the David Procedure*). Dr. David helped to arrange a fellowship at the prestigious Texas Heart Institute in Houston. There she worked with the noted Dr. Joseph Coselli, another pioneer and the world’s foremost specialist in thoraco-abdominal aortic surgery.

Academic and clinical focus

Naturally, Dr. Ouzounian continued her academic and clinical focus on aortic disease while in Texas. “We are seeing a rise in the number of cases of aortic diseases, particularly aneurysms and dissections,” she notes. “This may partially be due to better diagnostic techniques. In fact, now they are often being detected when they are not even being looked for. For example, a person may have a CAT scan for some other reason, and an aneurysm is detected.”

Even when detected early, aortic aneurysms can present a clinical challenge (see sidebar). “Aortic aneurysms can have a number of causes,” Dr. Ouzounian explains.

“They can be inherited, with a genetic element, or they can result from hypertension and other causes we don’t yet understand. They can present differently and require different treatment approaches.”

“If the aneurysm is uncomplicated, the basic approach is to determine if it’s stable, if it’s an appropriate size to treat and then fix it – either through open surgery or with an endovascular stent,” she continues. “Treatments are much better now, thanks to major advances over the past several years,



Dr. Ouzounian’s goal is to help PMCC provide the best possible treatment for patients with complicated aneurysms.

including the David Procedure, which was developed right here and has had a tremendous impact on the lives of patients with aortic root aneurysms.”

Unfortunately, not all aneurysms are uncomplicated. Many, particularly thoraco-abdominal aortic aneurysms – located in descending thoracic and abdominal aorta – can present a greater clinical challenge, and require a more complex surgical approach.

The chance to study this type of surgery was one of the reasons Dr. Ouzounian targeted the Texas Heart Institute and Dr. Coselli for her fellowship.

“While these may represent only a small percentage of patients, the procedure is more complicated, requiring extra precautions, such as spinal cord protection,” she notes. “At the time, many of these patients with extensive thoraco-abdominal aneurysms were being sent to Houston



for treatment.” Now, with Dr. Ouzounian’s help, this will change. “We have a strong Vascular Surgery division at PMCC with expertise in both endovascular and open repair of thoraco-abdominal aneurysms. We have a very collaborative approach and all complex cases are discussed as a team. Our goal is to be able to provide the best possible treatment of thoraco-abdominal aortic aneurysms right here at the Centre,” Dr. Ouzounian says. “University Health Network is already a *Centre of Excellence* in treating aortic aneurysms, and we want to be able to extend that to all patients, regardless of the type of treatment they require.”

New research initiatives

In addition to her clinical role, Dr. Ouzounian will also focus on research. “We want to better understand how and why the artery wall expands,” she explains. “We have formed a group of interested aortic scientists and are examining samples of aortic tissue taken from surgeries to look for clues to inflammatory changes, or for genetic indicators. We want to find ways to treat patients so surgery may not even be needed.”

As for that first day... Dr. Ouzounian found herself facing a 26-year-old man with a 10cm ruptured thoraco-abdominal aortic aneurysm. The decision had to be made to

send him to Texas or attempt a repair right away at the Centre. The choice was made – surgery on site. “When we made the incision, there was a litre of blood in his chest,” Dr. Ouzounian recalls. “He likely wouldn’t have made it to Texas.”

The patient underwent successful surgery and had his aorta replaced. “I saw him in my clinic earlier this month,” says Dr. Ouzounian. “I am happy to report that he has fully recovered.”

UNDERSTANDING AORTIC ANEURYSMS

An aortic aneurysm is a swelling, or expansion, in an artery (blood vessel), usually due to a weakness or damage in the artery wall. Blood pressure can cause the wall to bulge or balloon out at this weak point. As the aneurysm grows, there is a greater risk of rupture which, in turn, can lead to serious, and even fatal, complications. Aortic aneurysms are generally categorized based on exactly where they occur.

- **Abdominal aortic aneurysms** occur in the section of the aorta that passes through the abdomen
- **Thoracic aortic aneurysms** occur in any of the various sections of the aorta in the chest.
- **Thoraco-abdominal aortic aneurysms** span both the descending thoracic aorta and the abdominal aorta.

The complex, varying and serious nature of aortic aneurysms requires a multidisciplinary and individualized treatment approach. While medical treatment, including blood pressure control, can help slow the growth of an aneurysm, surgical intervention is usually required at some point when the bulge in the artery wall reaches a certain size. Approaches vary from the insertion of a graft via minimally invasive endovascular surgery to complex open heart surgery in the case of complex thoraco-abdominal aortic aneurysms.





FOCUS ON RESEARCH

Protection against the flu... and heart attacks

STUDY LINKS FLU VACCINE TO REDUCED RISK OF CARDIAC EVENTS

The flu vaccine may do more than ward off serious complications from influenza, it may also play a key role in reducing the risk of stroke or a further heart attack in people who have had a heart attack, according to new research conducted in collaboration with the Peter Munk Cardiac Centre.

The research, led by Dr. Jacob Udell, a clinician-scientist at the University of Toronto and cardiologist at Women's College Hospital, shows that this risk could be reduced by more than 50 per cent. In addition, the vaccine's heart protective effects may be even greater among those who receive a more potent vaccine.

"Our study provides solid evidence that the flu shot helps prevent heart disease in vulnerable patients – with the best protection in the highest risk patients," Dr. Udell said. "These findings are extraordinary given the potential for this vaccine to serve as yearly preventative therapy for patients with heart disease, the leading cause of death among men and women in North America."

The study, recently published in the prestigious *Journal of the American Medical Association*, reviewed six clinical trials on heart health in people who received the flu vaccine. The studies included more than 6,700 patients with a history of heart disease.

The researchers found that study subjects who received the flu shot showed a reduced level of risk in a number of key areas (see Table 1).

Dr. Udell carried out this research in collaboration with Dr. Michael Farkouh, senior co-author of the study and



Chair of the Peter Munk Centre of Excellence in Multinational Clinical Trials, which is within the Peter Munk Cardiac Centre at University Health Network.

"If the flu vaccine can reduce the risk of cardiac events, these shots could have considerable impact on cardiac health," said Dr. Udell. However, Drs. Udell and Farkouh caution that a large prospective clinical trial is necessary to confirm the effectiveness and safety of the influenza vaccine as a therapy that will reduce the risk of heart attack or stroke in people with heart disease. The researchers are now organizing this type of clinical trial to follow heart disease patients for up to 12 months after receiving the flu shot.

"These findings are all the ammunition we need to move forward," said Dr. Farkouh, who is also Director

of the Heart and Stroke Richard Lewar Centre at the University of Toronto. "We'll build on this research with a definitive, international trial to conclusively determine whether the flu shot prevents heart attacks."

If proven to be a safe and simple prevention method, the impact could be significant for people with or at risk of heart disease and stroke.

"Hundreds of thousands of people die each year from cardiac causes in North America," Dr. Udell said. "While preventative care involves lifestyle changes and taking your pills, now, we may also be able to tell patients by getting your flu shot, it might save your life – what a simple and significant way to reduce deaths and the burden on our healthcare system."

TABLE 1

STUDY HIGHLIGHTS

Subjects who received the flu shot:

- Had a 36 per cent lower risk of a major cardiac event (heart attack, stroke, heart failure, or death from cardiac-related causes) one year later
- Had a 55 per cent lower risk of a major cardiac event if they had a recent heart attack
- Were less likely to die from cardiac-related and other causes, and
- Were less likely to have a major cardiac event with a more potent vaccine compared with the standard seasonal vaccine



FOCUS ON RESEARCH

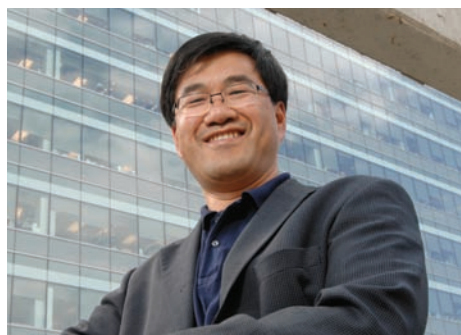
Curing hearts with stem cells

CELL SURVIVAL KEY TO MAXIMIZING DAMAGE REPAIR

Heart attacks cause irreparable damage to cardiac tissue leading to the formation of scar tissue that does not function normally.

Mesenchymal stem cells (MSCs) have been found to improve heart function when they are transplanted into patients with injured hearts. However, MSCs from older patients have limited capacity for tissue regeneration and restoration of heart function. Stem cells from young donors have a greater regenerative capacity and may be better candidates for clinical application. Unfortunately, these allogeneic stem cells – referred to as allogeneic because they come from a genetically non-identical donor – can only evade the immune system early after implantation and are eventually killed by the recipient’s immune cells.

In an attempt to improve the survival of transplanted MSCs and increase



Dr. Ren-Ke Li

their potential to repair damaged hearts, Toronto General Research Institute Senior Scientist Dr. Ren-Ke Li and his collaborators have examined which factors might help MSCs maintain their ability to not activate the recipient’s immune system. Dr. Li and his team found that a protein known as prostaglandin E₂ (PGE₂) is able to induce the expression of proteins that suppress immune responses. They were also able to show that when PGE₂ is slowly released at the site of MSC

injection, through the use of a biodegradable gel, the transplanted stem cells survive longer and improve heart function.

Preventing rejection

Explains Dr. Li, “We demonstrated that maintaining PGE₂ levels prevents the rejection of MSCs and leads to improved heart function.

Hopefully, these findings will be useful in developing allogeneic stem cell-based cardiac therapies that can improve the current standard of care for cardiovascular diseases.”

This work was supported by the Canadian Institutes of Health Research and published in the internationally respected journal *Circulation*. Dr. Li is a McEwen Centre for Regenerative Medicine scientist and Tier I Canada Research Chair in Cardiac Regeneration.

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In the news

Cardiac surgery a “family affair” for Dr. Terrence Yau

PMCC Surgeon Dr. Terrence Yau found himself in what he calls “an unusual situation” recently, performing complex cardiac surgery on a mother and her son within a few days.

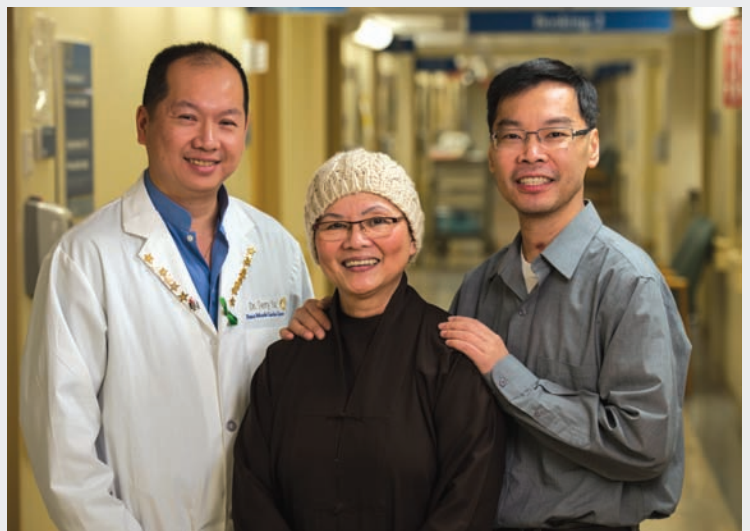
Dr. Yau’s patient Jason Truong, who had just undergone cardiac surgery, contracted a bacterial infection and his lungs failed. His last hope was a heart transplant but, due his weakened condition, he was removed from the transplant list.

Meanwhile, Jason’s mother, Lien, was in another hospital preparing for open heart surgery. She wanted to be by her son’s side, so the family made an unusual request for Lien to have her surgery at the Peter Munk Cardiac Centre. As a result, Dr. Yau found himself with two Truong patients at once.

Two days after Dr. Yau successfully performed a triple bypass on Lien, Jason’s condition improved enough to have him put back on the transplant list. Although Dr. Yau had cautioned that Jason might have to wait months for a suitable match, a heart became available the next day. Dr. Yau then assisted with Jason’s heart transplant.

“I’ve been in practice 15 years and I’ve never had two family members be operated on by me, almost simultaneously,” notes Dr. Yau, who holds the Angelo & Lorenza DeGasparis Chair in Cardiovascular Surgery Research.

In the Cardiovascular Intensive Care Unit, mother and son were placed in rooms across from each other. As Jason recovered from surgery, Lien, still recuperating herself, asked a nurse to wheel her



Jason Truong, right, and his mother Lien Truong, with Dr. Terrence Yau who performed heart surgery on both in the same week.

into his room, where she surprised her son by rising from her wheelchair and walking to his bedside.

Jason and Lien were extremely grateful to Dr. Yau and the Peter Munk Cardiac Centre for the opportunity to be close to each other during recovery.

For more information, please visit

www.petermunkcardiaccentre.ca

To support the PMCC through a donation, please visit www.inaheartbeat.ca or call 416-340-4056

Thank you – our donors – for your continued support of the Peter Munk Cardiac Centre.

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