

Peter Munk Cardiac Centre

CLINICAL AND RESEARCH REPORT



VOL. 10 NO.1 / SUMMER 2014

CARDIAC ONCOLOGY

Making a difficult journey a bit easier

PMCC PROGRAM AIMS TO REDUCE CARDIOVASCULAR
RISKS OF CANCER TREATMENT

Fighting cancer is difficult enough without having to worry about an increased risk of heart disease. Yet many patients must face the added concern that treatments used to fight their cancer may actually be contributing to heart problems. Helping to diffuse this dangerous double threat is one of the prime objectives for cardiologist, Dr. Dinesh Thavendiranathan, who heads the Peter Munk Cardiac Centre's cardiac oncology program.

While oncologists have long been aware that some forms of chemotherapy can cause damage to

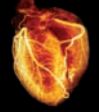


Dr. Dinesh Thavendiranathan believes earlier detection and better treatments are the keys to fighting heart disease in cancer patients.

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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



...Making a difficult journey a bit easier continued.

the heart, the problem has received much more attention in recent years as new methods have become available to detect early heart injury and cardiologists have become more interested in the problem. "We have been more successful in treating cancer over the last two decades," explains Dr. Thavendiranathan.

"Survival rates have increased dramatically, and we have people living longer with cancer, which gives potential heart problems more time to develop. Breast cancer is perhaps one of the best examples of this. Unfortunately, there is a subgroup of cancer patients who, partially due to their treatment, are at risk of cardiac dysfunction."

Among the cancer-fighting drugs linked to heart problems are anthracyclines (used to fight a wide range of cancers, including, leukemia and lymphomas) and trastuzumab, a medication that has dramatically improved outcomes and survival in the treatment of breast cancer.

In addition, an ever-increasing range of advanced cancer-fighting drugs, newly introduced or in development, have been linked to potential cardiac side effects, such as arrhythmia, hypertension, blood clots and heart failure.

These and other factors are contributing to a growing number of individuals at risk.

A range of potential problems

Heart problems linked to chemotherapy can range from mild abnormalities of heart function to heart failure and death. In many cases, cardiologists need to become involved. "In some cases, we may need to suspend the chemotherapy at least transiently, which is obviously not optimal for the patient," says Dr. Thavendiranathan.

The Cardiac Conditions in Oncology program was started in 2012 to help bring a cardiology perspective and expertise to the problem. As Dr. Thavendiranathan explains, there is still much to learn. "The field is very young," he says. "There are so many things we still don't know. For example, can we prevent drug toxicity by treating the heart early in the cancer treatment process? Or are certain patient populations at greater risk than others? There are lots of aspects to be studied."

Two of the main areas of focus are treatment and detection. "On the surface, one obvious option is to consider treating all cancer patients with heart medications to prevent the development of problems," Dr. Thavendiranathan comments. "But this raises questions of drug tolerability and potential interactions and side effects."

Focus on detection

"Another focus is on better and earlier detection of potential problems," he continues. "We need to find ways of identifying patients at risk and detecting the problem before symptoms appear. We want to prevent the heart from getting to the failure stage."

The two main methods of detection being investigated are biomarkers – molecules in the blood that provide some measurable indicator of a specific biological state or condition (in this case, heart disease) – and medical imaging. It is in the latter area where Dr. Thavendiranathan and his colleagues really come into play.

The most commonly used imaging procedure currently used to detect the potential of heart problems in these

cases is the multigated acquisition, or MUGA, scan. The MUGA scan uses a radioactive tracing material, a gamma camera and a computer to create images of the blood flowing through the heart. It measures an individual's ejection fraction, which is the amount of blood pumped out of the heart during each contraction. A normal ejection fraction is between 55 and 75 per cent.

If the ejection fraction falls below normal levels, it can be a sign of heart disorders.

"The problem is that by the time the ejection fraction falls it is often late," says Dr. Thavendiranathan. "These patients may progress to heart failure despite intervention."

"We have been using echocardiography to measure myocardial strain [the rate of change in the length of the myocardial muscle] and have found that this rate falls before the ejection factor does. Myocardial strain falls and then ejection factor drops, indicating a potential for heart problems. So, measuring myocardial strain could provide an earlier warning sign. If we can identify patients earlier, we may be able to initiate preventative treatment."

Questions to answers

However, Dr. Thavendiranathan admits there are still questions about exactly what to do when the problem is detected. As such, the PMCC is involved in ongoing research in this area, including participating in the SUCCOUR study, a Tasmania-based 25-centre international study, for which Dr. Thavendiranathan is the principal investigator for North America.



CARDIAC REHABILITATION

Sharing expertise with the world

PMCC EXPERT INVOLVED IN GLOBAL INITIATIVE

Cardiovascular disease is the leading cause of mortality worldwide, and one of the Peter Munk Cardiac Centre's experts in cardiac rehabilitation is involved in an international initiative to find solutions on a global scale.

The Centre's, Dr. Sherry Grace, played a key role in the first biennial meeting of the International Council of Cardiovascular Prevention and Rehabilitation (ICCP) at the World Congress of Cardiology, held recently in Melbourne, Australia. Dr. Sherry Grace sits on the ICCPR's Executive Committee and was involved in a special World Heart Federation strategy development workshop on solutions for reducing the burden of CVD through secondary prevention and risk reduction.

Among her other ICCPR responsibilities, Dr. Sherry Grace is also co-chairing a writing panel for a consensus statement on cardiac rehabilitation delivery in low-resource settings. The panel will produce a publication, invited by the high-impact journal *Nature Reviews: Cardiology*. This publication will summarize available evidence on how to adapt cardiac rehabilitation, as practiced at PMCC for example,

for low-resource settings. The World Health Organization is engaged in the project, which will support implementation.

Not only will this be of value for assisting low- and middle-income countries to develop cardiac rehabilitation services, but it will be helpful for many low-resource settings in higher-income countries, like remote northern regions of Canada. Dr. Sherry Grace is eager to start field testing the model of care.

According to the World Health Organization, cardiovascular disease accounts for over 17 million deaths per year worldwide. Cardiac rehabilitation has been shown to reduce both morbidity and mortality by 25%. Although a fully comprehensive cardiac rehabilitation model may not be feasible in many low and



Dr. Sherry Grace of the PMCC (third from right) and colleagues from the International Council of Cardiovascular Prevention and Rehabilitation at the World Congress of Cardiology.

some middle-income countries, mainly because of shortages of healthcare professionals and resources, alternative service delivery models have been shown to be effective.

Dr. Sherry Grace has already co-authored a paper in this area in *Nature Reviews: Cardiology*, describing the availability of cardiac rehabilitation around the world.

To learn more about the ICCPR: www.globalcardiacrehab.com.

...Making a difficult journey a bit easier continued.

"We can spot the danger earlier, but 'so what?'" he asks. "It's not just a case of early detection. It's knowing what the most effective intervention is. It's knowing how to prevent undesirable outcomes."

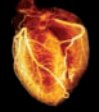
Dr. Thavendiranathan is also the principal investigator in a Toronto-

based study involving the PMCC, Sunnybrook and St. Michael's Hospital that is looking at ways to improve imaging and detection via echocardiography and MRI scanning.

"We want to find ways to add to the knowledge gained from these tests," he says. "For example, is there more

to be detected from measurements such as cellular edema [swelling], cell inflammation or heart scarring? This kind of knowledge may be able to help us prevent heart problems in people undergoing cancer therapy."

And that could help make an already challenging journey that much easier.



CARDIOVASCULAR SURGERY

Welcome to the future of surgery

A LOOK AT THE MULTI-PURPOSE OPERATING ROOM AT THE PETER MUNK CARDIAC CENTRE

“I’m sorry. There are no treatment options available for you.” These are words no surgeon ever wants to tell a patient and their family while they await treatment.

Thanks to the Multi-Purpose Operating Room (MPOR) at the Peter Munk Cardiac Centre (PMCC), cardiovascular surgeons rarely have to deliver such a message. The MPOR is transforming the way heart disease is treated in Canada and around the globe, allowing for innovative and minimally invasive surgical procedures – operations that require smaller incisions, or no incisions at all – thereby allowing the most high-risk individuals to be treated.

The MPOR is being recognized across Canada for its innovative approach to patient-centred care. Most recently it was featured on CTV’s *Canada AM*, where Dr. Barry Rubin, Program Medical Director of the PMCC, gave Dr. Marla Shapiro a personalized tour, explaining why this state-of-the-art operating room makes such a difference on patient outcomes.

“Among the innovations in cardiac care that the MPOR pioneers are complex procedures that enable faster recovery after surgery,” says Dr. Rubin. “An integrated approach to surgery that brings together highly specialized surgeons, cardiologists, and radiologists to carry out advanced image-guided procedures results in shorter time between diagnosis and treatment. It also shortens the time from treatment to discharge and full recovery.”



Dr. Barry Rubin, Medical Director of the Peter Munk Cardiac Centre, in the state-of-the-art Multi-Purpose Operating Room (MPOR). Opening its doors in 2010, the MPOR is double the size of the standard OR at UHN, and designed to maximize the benefits of the up-to-the-minute imaging equipment.

More than twice the size of a traditional operating room, the MPOR is outfitted with equipment that facilitates diagnosis and treatment. Prior to its inception, individuals admitted to the PMCC experiencing chest pain were administered multiple tests in various locations to pinpoint the nature of their pain – whether it was caused by a heart attack, a torn blood vessel in the chest, or a blood clot in the lungs, for example.



Dr. Rubin tours Canada AM Medical Expert Dr. Marla Shapiro around the MPOR, explaining why it makes such a difference on patient outcomes.



Employing a multi-disciplinary paradigm to treatment, PMCC physicians deliver care through a team-based approach. Designed around patient-centred care, PMCC physicians have all the necessary technology and equipment at their disposal in the MPOR to better diagnose and treat patients in a timely and effective manner.

Whether they require a trip to the cath lab for an angiogram, or to the Radiology Department to undergo testing for a suspected ruptured aorta, each test takes valuable time away from a surgeon's ability to effectively treat a patient.

"Time is of paramount importance in these instances," explains Dr. Rubin. "With new technology, patients can come directly from the ER into the MPOR and their chest pain can be more readily diagnosed with all the necessary equipment in one facility. This hybrid operating room employs the most advanced technology to deliver optimal patient outcomes."

When it opened in 2010, the MPOR was the only operating room in Canada with an integrated CT scan and digital angiography unit. This allows surgeons and medical imaging physicians, working together, to precisely identify the cardiac or vascular problems a patient may be experiencing. "We now have a second, even more advanced hybrid operating room, the Guided Therapeutics OR,

that has two CT scanners, one of which is mounted on an 8-ft robot arm that can move in and out of the operating field during surgery," says Dr. Rubin.

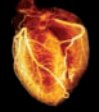
A state-of-the-art, flat panel digital angiography unit allows precise visualization of blood vessels during surgery and mobile monitors provide all team members with unobstructed views of x-ray images and vital clinical signs in real time. Endovascular stent grafts, tubes composed of fabric supported by a metal mesh commonly used to reinforce a weak spot in an artery (aneurysm), are now implanted into patients with x-ray guidance. Now there is no patient too small that surgeons cannot place stent grafts into due to the availability of enhanced image quality and display.

The PMCC not only uses the most advanced equipment, it also employs a multidisciplinary approach to treatment, where care is delivered through a team-based approach, a novel paradigm that does not adhere to the traditional boundaries

associated with individual specialties.

"One of our main operating principles is the belief in multidisciplinary care," explains Dr. Rubin. "For example, when we fix an aortic valve, the main valve that controls blood flow going out of the heart, x-ray guidance in the MPOR allows a team of cardiovascular surgeons, interventional cardiologists, vascular surgeons and cardiac anaesthesiologists to make a small incision in the groin, or even no incision at all (instead, placing a needle into the artery) and feed a tube up and inside a patient. This is a much less invasive procedure compared to the traditional approach, whereby one would have to make an incision through the chest to cut the valve out and sew in a new valve."

"With the excellence of this technology and the team-based approach to care, we say no to almost nobody. People who we would have no doubt turned down previously, we routinely operate on now. And they do well – this is remarkably gratifying for the whole team."



FOCUS ON RESEARCH

Sleep vital to heart attack recovery

STUDY SHOWS VALUE OF A GOOD NIGHT'S SLEEP

To improve heart attack recovery, hospitals should make sure natural sleep cycles are not disturbed in the first few days after a heart attack. That's the main finding of an important new study on cardiac healing and recovery recently published in the respected medical journal, *Circulation Research*.

Dr. Michael Sole, a cardiologist at the Peter Munk Cardiac Centre, is the lead author of the study; *Short-Term Disruption of Diurnal Rhythms After Murine Myocardial Infarction Adversely Affects Long-Term Myocardial Structure and Function*.

Dr. Sole defines a natural sleep cycle as approximately seven to eight hours of sleep when it's dark outside and being awake during daytime. He has witnessed the impact of interrupted sleep patterns on patients who are recovering in hospital after a heart attack during his 40 years as a cardiologist. His observations were, in part, the impetus for the study.

Disrupting sleep cycles

For the study, Dr. Sole's team induced heart attacks in mice and then monitored their recovery. By altering light and dark cycles, the natural sleep patterns of the mice were disturbed for only a few days after the heart attack. This was done to mimic a stay in the Coronary Intensive Care Unit (CICU) of a hospital. The mice were then returned to a normal day and night environment.

The outcomes of the disturbed mice were compared to those that followed a natural sleep cycle after a heart attack. The mice exposed to rhythm disruption showed impaired healing with permanent heart enlargement and worse heart function compared to the mice who



Dr. Michael Sole has seen the negative effects of interrupted sleep on heart attack patients.

maintained a normal, undisturbed day and night schedule.

The healing of a damaged heart requires a specific, orderly sequence of events. Dr. Sole likens it to renovating a house.

"If you disrupt day/night rhythms during those critical first few days after your heart attack, then the clearing of debris, the putting up of scaffolding and then rebuilding the walls becomes disordered and you never achieve a tight scar [a proper wound repair]," he says. "Like a house renovation - events must happen in a precise order, or it won't be done well."

"The findings from this study demand similar testing on hospital patients," says Dr. Sole.

It also suggests that hospitals need to pay more attention to ensuring patients recovering from heart attacks are able to get a good night's sleep.

Among potential solutions to make hospitals more sleep-friendly, he suggests simple additions, like the use of blue light-blocking glasses, earplugs, low-volume ringtones and greater attention to hospital noise at night. Multi-bedded rooms could yield short-term savings but may come with long-term costs.

"The first thing is awareness," said Dr. Sole. "Awareness that what we do in the short-term may have profound adverse effects in the long-term. And that's contrary to what we're trying to accomplish when we treat a patient in hospital."



EXPLORING THE LINK BETWEEN ESTROGEN AND HEART DISEASE

Cardiovascular risk in postmenopausal women is being investigated in the Peter Munk Cardiac Centre's Clinical Cardiovascular Physiology Laboratory Centre by Dr. Emma O'Donnell, a Postdoctoral Fellow at the PMCC.

Working with Dr. Paula Harvey, Director of Cardiovascular Research at Women's College Hospital, and Dr. John Floras, Director, Cardiology Research at PMCC, Dr. O'Donnell is examining how and why estrogen deficiency influences cardiac risk.

"We know that estrogen deficiency in postmenopausal women is associated with increased cardiovascular risk, including impaired brachial artery endothelial function and hypertension," Dr. O'Donnell explains. "But we also know that CV risk is also associated with aging. And we know that many premenopausal women also experience estrogen deficiency. Part of our work is trying to 'tease out' the effects of estrogen deficiency independent of aging."

In premenopausal women, a common and reversible cause of estrogen deficiency is functional hypothalamic amenorrhea (FHA). FHA is more commonly observed among active women than sedentary women in association with 'energy deficiency' in active women due to high energy expenditure (i.e., exercise) combined with insufficient caloric intake.

The research currently being undertaken is studying active women with, and without, estrogen deficiency as well as sedentary women. All have been matched for age, Body Mass Index, etc. to provide comparable data.

"Our lab has shown that despite being young - 18-35 years old - and otherwise healthy with normal body weight and no chronic diseases, recreationally active women with FHA demonstrate impaired brachial artery endothelial function, similar to that observed in older postmenopausal women," says Dr. O'Donnell. "An acute bout of exercise, a known potent stimulus to increased nitric oxide

- a key dilating factor in the blood vessels - improves endothelial function in FHA women, but does not fully restore it. These findings suggest estrogen deficiency not only impairs endothelial function but may also elicit vascular remodeling. Previous studies have identified that impaired endothelial function is a permissive factor in the development and progression of atherosclerosis. However, it currently remains unknown whether these young women are at increased risk of accelerated coronary artery disease."

"In light of the growing number of women participating in recreational and competitive athletic activities, it is likely that the number of active women reporting FHA will also increase. As such, future studies to examine the long term cardiovascular consequences of these perturbations will be of importance."

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In the news

Dr. Viv Rao joins CBC's *Health Check Up*

Dr. Viv Rao, cardiovascular surgeon at the Peter Munk Cardiac Centre, was among a panel of three noted physicians and a representative of a patients' association who took part in CBC The National's *Health Check Up* panel, discussing various health issues ranging from wait times to the value of a second opinion, and whether or not the Internet is a good source of health information.

Hosted by Peter Mansbridge, the *Health Check Up* panel was launched in March of this year and has proven very popular with viewers. Joining Dr. Rao on the most recent panel were Dr. Danielle Martin from the Women's College Hospital, Dr. Samir Sinha from Mount Sinai Hospital and Sholom Glouberman from Patients Canada. Dr. Rao has been selected to be a regular contributor to the panel.

In discussing the role of the Internet and other educational sources, including television, Dr. Rao emphasized that it was important to ensure the validity of the source of the information and noted that "the well-informed patient is better equipped to take charge of their own healthcare."



The PMCC's Dr. Viv Rao (left) can be seen on CBC's popular *Health Check Up*.

Teddy Bear Picnic teaches heart health

Teaching kids about the importance of a healthy heart took centre stage for a full week at Toronto's Centre Island this summer, with the help from experts from the Peter Munk Cardiac Centre.

The *Beasley Bear's Teddy Bear Picnic* brought medical professionals from the PMCC to the Island to interact with school-age children. Bear (and people) checkups, healthy food challenges and more were on the menu at the successful fundraiser.

Bill Beasley, President of William Beasley Enterprises, Ltd., has had personal experience with heart issues. His father underwent surgery at the PMCC, and he believes in the Centre's mission to offer education as well as heart expertise. The *Teddy Bear Picnic* will help to provide education and raise funds for the PMCC for the next 10 years.



Beasley Bear's Teddy Bear Picnic on Toronto's Centre Island teaches kids the importance of healthy hearts.

For more information, please visit

www.petermunkcardiaccentre.ca

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