





# MURMURS

AMERICAN COLLEGE OF CARDIOLOGY PARTNERS NHCS IN FIRST GLOBAL DIABETES REGISTRY



NHCS PERFORMS ASIA'S FIRST HEARTMATE 3 IMPLANTATION



NEW DRUG FOR PULMONARY ARTERIAL HYPERTENSION

NHCS EMBARKS ON STUDY ON HYPERTENSION AND HEART MUSCLE SCARRING DR LOUIS TEO TALKS ABOUT TEAM POWER AT CLEVELAND CLINIC

NEW APP FOR HEART FAILURE HELPS PATIENTS STAY ON TRACK **02** MURMURS OCT 2015 - MAR 2016 **03** 



# ACC PARTNERS NHCS IN FIRST GLOBAL DIABETES REGISTRY

he National Heart Centre Singapore (NHCS) has joined hands with the American College of Cardiology (ACC) in a major step towards better treatment for diabetics in Asia. The ACC is a 49,000-member medical society that leads in the formation of health policy, standards and guidelines. The ACC also operates national registries to measure and improve care, provides professional medical education, disseminates cardiovascular research and bestows credentials upon cardiovascular specialists who meet stringent qualifications.

The partnership combines data from the newly created NHCS Asian Diabetes Outcomes Registry (ADORE) with the ACC-led Diabetes Collaborative Registry to create the first global cross-specialty clinical diabetes registry. ADORE was established in 2015, a year after the Diabetes Collaborative Registry came about.

Associate Professor Carolyn Lam, Senior Consultant,
Department of Cardiology, NHCS and principal investigator
of ADORE said this partnership is "particularly important to
Singapore, which has recently announced a war on diabetes."

## Diabetes: Asia's impending health crisis

60 per cent of the world's diabetics reside in Asia, and the number is growing fast.

In Singapore alone, diabetes mellitus affects
11 per cent of the general population and
65 per cent of heart failure patients. Diabetics
often die of cardiovascular complications or
causes, and the chronic, complex condition
is also the top cause of blindness in working
adults and kidney failure.

"Diabetes is the single largest cause of disease burden in Singapore," said Assoc Prof Lam.

In 20 years, the number of people affected by diabetes worldwide will rise by 50 per cent from the current 382 million.

Adj Prof Terrance Chua, Medical Director, NHCS pointed out possible contributors to Asia's staggering diabetic statistics, including a modern lifestyle which comes with less exercise but more intake of calories, carbohydrates and sugar.

"First of all, Asia has a huge population. Secondly, there have been a lot of major changes in the lifestyles of people who were previously living in less developed countries which are now developing very fast. You see obesity and risk factors for heart disease such as diabetes, high blood pressure and high cholesterol rising very rapidly in many countries."

## Global real world evidence for better diabetic treatments

As clinical treatments for diabetes differ from country to country, both the global and Asian diabetes registries provide the much needed real world data for researchers and doctors to look into long-term treatment patterns of diabetics and their subsequent outcomes worldwide.

ADORE is a real-world, prospective, longitudinal, investigator-led registry led by an advisory board comprising endocrinologists and cardiologists from Singapore and the US. It seeks to collect comprehensive data for Type 2 diabetes treatment patterns and outcomes throughout Asia, and is aimed at creating a network of sites with patients across 12 sites: Singapore, China, South Korea, Taiwan, Indonesia, Malaysia, Thailand, the Philippines, Hong Kong, India, Vietnam and Sri Lanka.

Data collected by each of these countries is maintained by a centralised database and shared with the Diabetes Collaborative Registry. The data facilitates comparison of Asian and Western patients and it can be used in designing treatment guidelines in later stages.



"ADORE is important as we study issues like how diabetics are being treated across Asia, how complications are being managed, how often complications occur, and how treatments affect outcomes," said Assoc Prof Lam, "Partnering with ACC's Diabetes Collaborative Registry will expand the impact of ADORE as we combine our expertise and align our data collection to support transnational, comparative, and collaborative diabetes and cardiometabolic research."

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# FIRST PATIENT GETS NEW LEASE OF LIFE WITH HEARTMATE 3 DEVICE

r Rajamohan s/o Pekrisamy had to leave his job as a security guard in 2015 due to his worsening heart condition.

The 44-year-old was diagnosed in 2003 with dilated cardiomyopathy, one of the causes of heart failure, which occurs when the heart becomes weakened, enlarged and unable to pump blood efficiently.

Mr Rajamohan's symptoms included breathing difficulties, fatigue and coughs that persisted throughout the day. After a three-and-a-half-hour surgery performed by the NHCS multi-disciplinary team in November 2015, he became Singapore's first patient to be implanted with the new HeartMate 3 left ventricular assist device.

Mr Rajamohan S/O Pekrisamy (centre), Singapore's first patient to be implanted with the HeartMate 3 left ventricular assist device, with his doctors from the National Heart Centre Singapore, Adj Asst Prof David Sim (left) and Dr C Sivathasan.

"I have been suffering from heart failure symptoms for more than eight years, and I was tired and coughing most of the time and I could not walk far," said Mr Rajamohan, "Now I feel like I am almost 90 per cent of my healthy self." His heart function was at a mere 23 per cent two weeks before his surgery; normal people have a heart function of at least 50 per cent.

#### Buying time with heart assist devices

For many advanced heart failure patients like Mr Rajamohan, their hearts have weakened to a stage where the only cure is a heart transplantation. The device prolongs the lives of these patients while they wait for a suitable donor heart.

"NHCS receives more than 20 referrals for heart transplantation each year but only about three on average will eventually get transplanted due to the lack of suitable donor hearts," said Adjunct Assistant Professor David Sim, Senior Consultant, Department of Cardiology and Director of the Heart Failure Programme at NHCS.

Without such heart assist devices, less than half of these patients will survive beyond one year just on medications alone.

NHCS was the first in Singapore to establish the Mechanical Heart Device Programme in 2001 to provide advanced heart failure patients with a means to prolong their lives and improve their quality of life while waiting for a suitable donor heart. Through this programme, new technology, such as the HeartMate 3 device, are introduced as treatment options for these patients.

The HeartMate 3 is designed to improve survival, quality of life and outcomes for patients with advanced heart failure. The device is implanted next to the patient's weakened heart to help it pump oxygen-rich blood to the rest of his body.

It received the CE mark on 8 October 2015 after a one-year trial involving 50 patients from ten centres in six countries. Patients involved in the trial were followed up after the pump implantation, and results showed a survival rate of 92 per cent at the end of six months for these patients, with 83 per cent of them having a significant reduction in heart failure symptoms and no incidence of pump malfunctions during the trial period.

"Though the clinical trial results for the HeartMate
3 device are promising, we recognise that long term data
is needed for us to better understand the outcome for
patients, therefore we remain careful in assessing which
patients will be suitable for such new devices," said Dr C
Sivathasan, Director, Heart Transplant and Mechanical
Assist Device Programme, NHCS, and one of the surgeons
involved in the landmark surgery. The multi-disciplinary
team involved included cardiothoracic surgeons, a cardiac
anaesthetist, heart failure cardiologists, perfusionists, nurses,
clinical coordinators specialised in heart assist devices and
paramedical staff.

Dr Sivathasan added that not everyone is suited for such devices, such as those who are undergoing dialysis or unable to take blood thinners. Associated risks with these devices include infection of the wound site, gastro-intestinal bleeding and stroke.

#### How the HeartMate 3 works

The HeartMate 3 device runs on a magnetic levitation technology which keeps the rotor afloat in the pump even without the presence of any blood or fluid. This produces a consistent and large flow gap which lets blood flow through the pump with minimal damage to the cells and less chance of clots forming. This feature is advantageous, because ruptured blood cells can promote clotting within the device, which may lead to a stroke or problems with the pump.



The HeartMate 3 pump (right) is connected to an external controller and batteries which are located outside the patient's body.

Image courtesy of Thoratec Corporation.



The HeartMate 3 pump is implanted at the apex of the heart to help it pump sufficient oxygenated blood to meet the body's metabolic needs.

Image courtesy of Thoratec Corporation.

The HeartMate 3 is also the first heart assist device to feature an artificial pulse which mimics the natural heartbeat. Its pump is inbuilt with control electronics that enable it to store data on its parameters, speed settings and a log which records its regular operations and any anomalies. It is designed to be able to continue running even in the event of a transmission problem with the controller. Earlier devices do not have any data stored within the pumps.

The pump is connected to an external controller and batteries via a cable known as a driveline.

The HeartMate 3 separates the driveline into two segments – the pump cable and modular cable – so that doctors may easily replace the cable outside the body, if necessary, without putting patients through another surgery.

With the pump implanted in his chest, Mr Rajamohan now walks around with a controller that is powered by two lithium ion batteries. Each battery weighs 500g and a pair will last him about 17 hours as he goes about his daily business.

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# NEW TREATMENT FOR HEART FAILURE CUTS RISK OF DEATH AND HOSPITALISATION



new class of drugs has been introduced to treat heart failure.

In the PARADIGM-HF trial concluded in 2013, the angiotensin receptor blocker neprilysin inhibitor (ARNI) sacubitril/valsartan was matched against angiotensin converting enzyme (ACE) inhibitor enalapril, the long-standing gold standard treatment for heart failure, in a study to test the efficacy and safety profile of the new drug.

Results from the four-year trial involving 8,442 patients, of which 32 were from Singapore, showed more favourable cardiovascular death and hospitalisation statistics for the new drug versus enalapril. Sacubitril/valsartan reduced the risk of death from cardiovascular causes and heart failure hospitalisation by one-fifth relative to enalapril. The National Heart Centre Singapore (NHCS) is among the four centres in Singapore involved in the PARADIGM-HF study.

"Based on the trial results and when compared with enalapril, patients were seen to have better tolerance for sacubitril/valsartan and the new drug was more effective in lowering blood pressure and causes less side effects such as kidney damage and coughing," said Adjunct Assistant Professor David Sim, Senior Consultant, Department of Cardiology, and Director, Heart Failure Programme, NHCS. He was also the lead investigator of the PARADIGM-HF study at NHCS.

Taken twice a day, sacubitril/valsartan works on a dual-action mechanism, which is different from how ACE inhibitors like enalapril work, to reduce the strain on the failing heart. Sacubitril/valsartan was approved by the Health Sciences Authority for use in Singapore in February 2016.

#### Facts on heart failure

Heart failure accounts for more than 6,000 hospitalisations a year in Singapore. It is also the second most common cause for early hospital readmissions. Globally, it is estimated to cause two to three times as many deaths as some advanced cancers, and unfortunately one in three people will mistake heart failure symptoms with normal signs of ageing. Symptoms of heart failure include shortness of breath, frequent coughing which gets worse when lying down, swollen limbs and abdomen, and loss of appetite.

# STAYING ON TOP OF HEART FAILURE WITH YOUR PHONE

eart failure patients can now keep track of their medications and monitor their condition using their smart phones.

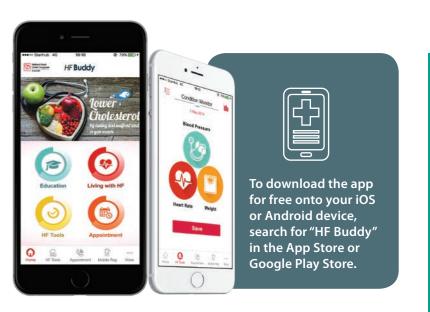
The NHCS Heart Failure team has developed the new *HF Buddy* app to help patients cope better with their heart failure condition. The app contains useful information on heart failure, as well as handy tools to help patients, even those with other medical conditions, monitor their health and stick to their medication and treatment regime.

"Being diagnosed with heart failure can be scary for patients," said Dr Lim Choon Pin, Consultant, Department of Cardiology, NHCS and one of the key members behind the HF Buddy app, "Fortunately, most patients will be able to manage their condition solely with medications and lifestyle adjustments."

He explained that the information on heart failure found in the app is useful for newly diagnosed patients, who may be worried about the risk of sudden cardiac death or whether they are still able to keep up with their daily activities, for example.

Aside from helping patients keep track of their health parameters, such as their heart rate, blood pressure, weight and daily fluid intake limit, the app also allows users to schedule reminders on when it is time for them to take their pills.

"A big determinant of how well heart failure patients do is how well they understand their own condition and medication, so we created the HF Buddy app to make it easier for patients to comply with their treatment," said Dr Lim.





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#### **NHCS HEART FAILURE PROGRAMME**

Heart failure is identified as a priority area for disease management in Singapore due to its high prevalence. Comprehensive heart failure disease management programmes have been shown to improve patient outcomes.

The NHCS Heart Failure Programme aims to improve the quality of life and survival of heart failure patients. It also strives to reduce the rate of re-hospitalisation of patients through a multi-disciplinary team-based approach comprising heart failure cardiologists, cardiothoracic surgeons, nurse clinicians, physiotherapists, dieticians and pharmacists.

#### **OUR SPECIALISTS (HEART FAILURE)**

Adj Asst Prof David Sim Senior Consultant,

Director, Heart Failure Programme

Dr Lim Choon Pin Consultant

Dr Louis Teo Associate Consultant

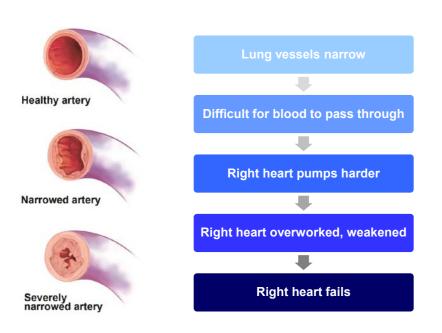
Dr Laura Chan Associate Consultant (away on HMDP)

For the full list of NHCS services and specialists, please visit **www.nhcs.com.sg.** 

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# PULMONARY ARTERIAL HYPERTENSION GETS NEW DRUG

#### Impact of pulmonary arterial hypertension on the heart



Patients with pulmonary arterial hypertension are at risk of right heart failure when their lung vessels get narrower as the disease progresses.

ulmonary arterial hypertension (PAH) is a rare, chronic and life-threatening disorder characterised by abnormally high blood pressure in the lung arteries.

Its causes include genetics, congenital heart disease and connective tissue disease. There are also people who have PAH due to unknown causes, also called idiopathic PAH.

While the actual prevalence of PAH is uncertain, the condition is estimated to affect one in 15,000 locally. Based on diagnosed cases, idiopathic PAH appears to be more common in women aged between 30 and 50.

Untreated PAH will worsen over time and may become potentially fatal when the pressure in the lungs rises to dangerously high levels. Though there is no known cure or prevention for PAH, it is still treatable.

Without treatment, only 30 per cent of PAH patients will survive up to five years, but with good medical therapy, more than 80 per cent are expected to live beyond that.

#### New trial results on PAH treatment

The SERAPHIN trial from 2009 to 2012 showed that macitentan, a new drug developed to treat PAH, reduces hospitalisation and disease progression by about half compared to placebo. At its completion, the SERAPHIN trial was the largest and longest randomised, controlled study in PAH patients to include a clearly defined morbidity/mortality primary endpoint.

The National Heart Centre Singapore (NHCS) was among the 152 centres from almost 40 countries which were involved in the trial to evaluate the efficacy and safety of macitentan in 742 patients, including 15 from Singapore. The Health Sciences Authority approved the local use of macitentan in November 2015.

"Macitentan helps to relieve symptoms in PAH patients by suppressing the harmful effects of endothelin, a hormone that controls blood flow and cell growth in blood vessels," explained Adj Assoc Prof Lim Soo Teik, Deputy Medical Director, NHCS on how the new drug works. Adj Assoc Prof Lim is also the principal investigator at NHCS for the SERAPHIN trial.



The pulmonary artery gets narrower when the endothelin is out of balance, constricting blood flow to the lungs as a consequence and forces the right side of the heart to work harder. Over time, the right heart may fail as a result.

Unfortunately, diagnosis of PAH is often delayed, by about two and a half years following its onset. This is due to under-recognition of the condition, PAH's non-specific symptoms, and confusion with other conditions.

"Symptoms of PAH are very similar to those for other more common heart and lung problems, making diagnosis of PAH challenging," said Adj Assoc Prof Lim, "These symptoms include shortness of breath during activity, fatigue and weakness, lightheadedness and fainting spells, swelling in the legs, ankles and abdomen, and chest pain."

Treatment of PAH is aimed at relieving symptoms, improving quality of life, and slowing down disease progression. Even with treatment, however, high blood pressure in the lung arteries may continue to worsen and make daily activities difficult. Lifestyle modifications, such as finding ways to ease their household chores and rearranging their living space to accommodate less physical exertion, can help PAH patients get through their daily routine.

# CONNECTING THE DOTS

# NHCS STUDIES LINK BETWEEN HIGH BLOOD PRESSURE AND HEART MUSCLE SCARRING

f you have hypertension, there is a chance that your heart muscle will thicken and develop tissue scars later on, or you might live out most of your years with minimal heart issues.

Doctors at the National Heart Centre Singapore (NHCS) have embarked on a 10-year research study to find the reasons why heart muscle scarring occurs in some hypertensive patients and not others. They are looking to recruit 500 patients with hypertension – whether newly diagnosed, well-controlled or otherwise – but have never had a heart attack, heart failure or stroke.

"Currently, only small studies of sample sizes ranging from 20 to 40 patients have been done on this topic," said Assistant Professor Calvin Chin, Consultant, Department of Cardiology, NHCS, and the principal investigator of this study, "From the 500 recruited patients, our goal is to find out how many of them have or will have heart muscle scarring, what is driving the scarring and if more extensive scarring predicts worse outcomes."

# Ten-year clinical tracking of patients

Hypertension is one of two main conditions that lead to the heart muscle thickening. High blood pressure places increased stress on the heart, and the heart muscle thickens as a result in order to continue pumping sufficient oxygenated blood to meet the body's needs. Over time, this will lead to heart failure. In Singapore, about 60 to 80 per cent of heart failure patients have hypertension.

Asst Prof Chin hopes that the findings from this study will eventually translate to effective early intervention for hypertensive patients at risk of developing heart failure.

To do that, the recruited patients will have their blood sample taken, undergo a magnetic resonance imaging (MRI) scan and have their blood pressure recorded for a continuous 24 hours as they go about their normal lives. Staff at NHCS will then follow up with a phone call to these patients each year for the next decade to find out if they experienced any major heart problems during the period.

Asst Prof Chin explained the use of MRI in this study: "The gold standard for looking at fibrosis or scarring in the heart is a cardiac biopsy, but it is invasive and may require the patient to stay in the hospital. MRI on the other hand is non-invasive and can be done within a few hours, and it allows us to look at the heart function, structure and areas of fibrosis very clearly and in great detail."

This study is part of Asst Prof Chin's Transition Award funded by the National Medical Research Council. Eligible patients who are keen to volunteer for the study may contact us at 6704 2294, 9024 2170 or remodel@nhcs.com.sq.



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# RESEARCH HIGHLIGHT

J Am Coll Cardiol. 2015 Nov 10;66(19):2092-100. doi: 10.1016/j.jacc.2015.08.882.

Importance of angina in patients with coronary disease, heart failure, and left ventricular systolic dysfunction: insights from STICH.

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**BACKGROUND:** Patients with left ventricular (LV) systolic dysfunction, coronary artery disease (CAD), and angina are often thought to have a worse prognosis and a greater prognostic benefit from coronary artery bypass graft (CABG) surgery than those without angina.

**OBJECTIVES:** This study investigated: 1) whether angina was associated with a worse prognosis; 2) whether angina identified patients who had a greater survival benefit from CABG; and 3) whether CABG improved angina in patients with LV systolic dysfunction and CAD.

METHODS: We performed an analysis of the STICH (Surgical Treatment for Ischemic Heart Failure) trial, in which 1,212 patients with an ejection fraction ≤35% and CAD were randomized to CABG or medical therapy. Multivariable Cox and logistic models were used to assess long-term clinical outcomes.

**RESULTS:** At baseline, 770 patients (64%) reported angina. Among patients assigned to medical therapy, all-cause mortality was similar in patients with and without angina (hazard ratio [HR]: 1.05; 95% confidence interval [CI]: 0.79 to 1.38). The effect of CABG was similar whether the patient had angina (HR: 0.89; 95% CI: 0.71 to 1.13) or not (HR: 0.68; 95% CI: 0.50 to 0.94; p interaction = 0.14). Patients assigned to CABG were more likely to report improvement in angina than those assigned to medical therapy alone (odds ratio: 0.70; 95% CI: 0.55 to 0.90; p < 0.01).

**CONCLUSIONS:** Angina does not predict all-cause mortality in medically treated patients with LV systolic dysfunction and CAD, nor does it identify patients who have a greater survival benefit from CABG. However, CABG does improve angina to a greater extent than medical therapy alone. (Comparison of Surgical and Medical Treatment for Congestive Heart Failure and Coronary Artery Disease [STICH]; NCT00023595).

# LEARNING TEAMWORK FROM THE BEST

r Louis Teo, Associate Consultant, Department of Cardiology, National Heart Centre Singapore (NHCS) went to world-renowned academic medical centre Cleveland Clinic on a one-year fellowship in July 2014. He recently returned from his subspecialty training in heart failure, ventricular assist devices and transplant cardiology where he learnt from many internationally recognised heart failure experts and the importance of teamwork in delivering quality healthcare.

## What was your training like?

Cleveland Clinic treats a large number of patients with advanced heart failure and performs a high volume of ventricular assist device implantations and heart transplantations annually.

My training was mainly clinical-based and consisted of five weekly rotations among the heart failure intensive care unit (ICU), inpatient and outpatient consultations, catheterisation laboratories and research. The ICU rotation was particularly "intense", where I managed very ill patients with advanced heart failure, fulminant myocarditis, mechanical hearts and heart transplants in a 10-bedded ICU. My typical ICU day there starts early in the morning at 5am and ends at around 9pm, or even later at midnight at times. Most of the ICU patients were extremely unstable with cardiogenic shock and multiple organ failure. They were on various forms of lifesupport systems such as ventilators, haemodialysis and extracorporeal membrane oxygenation.

The ICU patients required our utmost medical attention and it can get particularly challenging when a patient's condition deteriorates, and critical decisions have to be made immediately or the patient might not survive. However, it was very satisfying when we managed to save their lives and see them walk out of hospital.

## What were your most memorable moments?

Travelling on a private jet during heart transplant procurement runs was exciting and memorable. I was part of the heart transplant team, which consisted of cardiothoracic surgeons, transplant nurses and transplant coordinators. During heart procurement, we took a small Cleveland Clinic private jet and travelled for about a couple of hours to a nearby state to harvest the heart. We then secured the donor heart and brought it back to Cleveland Clinic to be transplanted into the recipient patient.

# What were your key takeaways from your stint?

During my one year with Cleveland Clinic, I have gained significant experience in the clinical management of patients who have undergone heart transplantation and ventricular assist device implantation. I have also mastered the procedural skills of right heart catheterisations and endomyocardial biopsies, especially after being exposed to many difficult and challenging cases.



Dr Louis Teo (left) with Dr Randall Starling, Medical Director of the Kaufman Center for Heart Failure, Cleveland Clinic, at his fellowship graduation ceremony.

I had the privilege of working with Cleveland Clinic's top heart failure cardiologists like Dr Randall Starling and Dr James Young, Medical Directors of the Kaufman Center for Heart Failure, Dr David Taylor, Director of the Heart Failure and Transplant Fellowship, and many others who were very willing to teach and share their wealth of knowledge and wisdom. Aside from their invaluable heart failure knowledge, I have learnt from these luminaries their bedside clinical and communication skills, as well as their dedication to the patients. Working with the nurses and transplant coordinators also allowed me to appreciate the importance of great teamwork in ensuring a successful heart failure programme.

Since my return, I have been working closely with the NHCS heart failure team to introduce new initiatives to enhance the workflow of our heart failure programme and devise local protocols for performing echocardiography scans on patients implanted with ventricular assist devices, as well as research on heart failure.



Dr Louis Teo getting ready to go on a heart procurement run on Cleveland Clinic's private jet with cardiothoracic surgeon Dr Suresh Keshavamurthy from the Lewis Katz School of Medicine, Temple University.



Local artist and heart patient KY Huang (left) with his son Andrew and their works of art at the NHCS "Life in Colour" exhibition.

# **ADDING A SPLASH** OF COLOUR TO NHCS

isitors to National Heart Centre Singapore (NHCS) might have noticed "mini galleries" popping up at parts of the 12-storey building.

A series of paintings and sculptures have been displayed at various places in NHCS since late November 2015 to inject a burst of colour into the clinical environment and bring smiles to heart patients. The art pieces are centred on the theme "Life in Colour" and range from the whimsical to the contemplative, with borrowed motifs from nature's flora and fauna.



sculpture by KY Huang.

"We wanted to brighten up our outpatient facility with splashes of colour to make the patients' experience more pleasant and interesting. The featured art pieces also complement our healing garden concept at NHCS," said Adj Prof Terrance Chua, Medical Director, NHCS.

Mr Ng Kee Yam, a heart patient of NHCS, is among the group of artists featured in

the exhibition. Better known as KY Huang in the arts circle, he held a two-week art exhibition at NHCS to showcase his series of works that capture the spirit of fun, play and graceful movements of the human body. Mr Ng's son, Andrew, 37, is also a budding artist and his sculptures were displayed as part of his father's exhibition at NHCS, alongside other colourful works of art strategically placed within the outpatient facility.

"I believe that art can be a form of therapy," said the 67-year-old father of two, "Art has given me a purpose in life, and that is to create works of art that will make people smile."

#### APPOINTMENT AND PROMOTIONS



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**DR RUAN WEN** Associate Consultant. Department of Cardiology



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