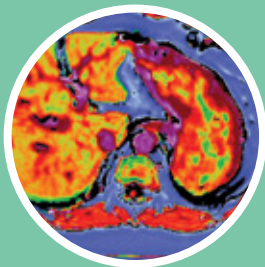


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A publication of
National Heart Centre
Singapore (NHCS)



NEW FRONTIER
IN PCI WITH
'SLENDER'
TECHNIQUES



'SWITCHING OFF'
FATTY LIVER
DISEASE



CLEARING
UP MYTHS ON
STATINS



Left: Assoc Prof Lim Soo Teik, Senior Consultant
Right: Assoc Prof Chin Chee Tang, Senior Consultant

INSIGHTS INTO CORONARY INTERVENTIONS



National Heart
Centre Singapore
SingHealth

SPOTLIGHT ON INTERVENTIONAL CARDIOLOGY



INSIGHTS INTO CORONARY INTERVENTIONS

- a subspecialty that involves using non-surgical approach to treat narrowing of arteries of the heart found in coronary artery disease.

By Dr Muhammad Bin Idu Jion, Associate Consultant,
Department of Cardiology

▲ A close-up on narrowed artery.

Cardiovascular disease encompasses ischaemic heart disease and cerebrovascular disease (stroke) and is a leading cause of mortality globally which accounts for up to 32% of all deaths. In Singapore, ischaemic heart disease is the third most common cause of death and hospitalisation. Ischaemic heart disease occurs due to a build-up of plaque in the heart arteries (coronary artery disease), and the risk increases with age and presence of other chronic diseases such as diabetes, hypertension and dyslipidaemia (abnormal levels of lipids in blood), or other risk factors such as smoking, a sedentary lifestyle and a family history of myocardial infarction (heart attack).

Symptoms of ischaemic heart disease can present in several ways. Patients may present with an insidious onset of chest pain or breathlessness which occurs on exertion, termed stable

While many people with coronary artery disease can manage the disease with lifestyle changes and medications, others with severe conditions may need interventions such as coronary angioplasty to improve the health of the heart and blood vessels.

angina, or they may present with heart failure signs and symptoms such as breathlessness on exertion or on lying flat, and water retention in the lungs and the lower limbs. Ischaemic heart disease can also present suddenly as an acute coronary syndrome, which range from unstable angina, non-ST elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI). Acute coronary syndrome carries an average three-month mortality rate of 5%. Patients with acute coronary syndrome may present with sudden or worsening chest

pains and need to be hospitalised for treatment with medications such as antiplatelets, anticoagulants and statins, and undergo coronary evaluation and revascularisation if suitable. NHCS sees about 1,000 hospitalisations for acute coronary syndrome in a year that require coronary angiography for detecting narrowing in the arteries in the heart or angioplasty (minimally invasive, non-surgical procedure for opening narrowed arteries).

Cases and Figures

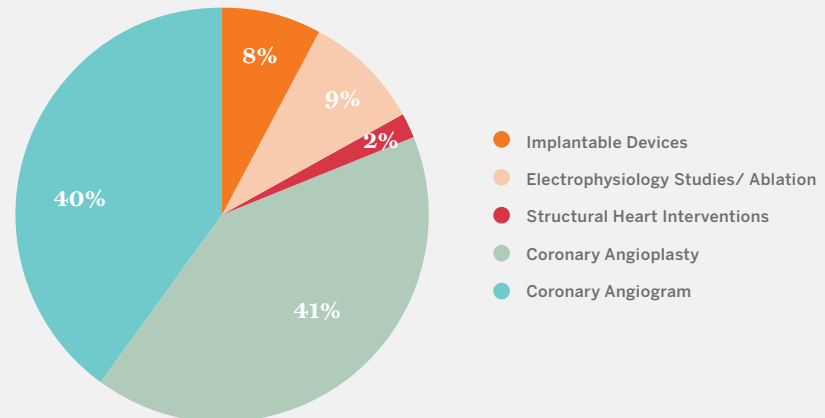
On average, NHCS performs over 6,000 invasive cardiology procedures a year; of which majority of cases involve coronary intervention procedures. In 2018, 80% of the procedures were cases of coronary angioplasty and diagnostic coronary angiography (including left and right heart studies). Twenty percent were mainly non-coronary related procedures which included device-related procedures like permanent pacemaker insertions or implantable cardioverter defibrillators, electrophysiology studies and ablation cases, and structural heart (e.g. valvular or adult congenital) interventions.

Diagnostics and Treatment

With the advances in health screening and medical imaging technologies, coronary artery diseases can now be detected earlier through non-invasive imaging tests such as cardiac computed tomography (CT) calcium score and CT coronary angiogram, and non-invasive functional tests such as stress 2D echocardiogram, myocardial perfusion imaging and treadmill exercise stress. Newer non-invasive diagnostic tests like the stress cardiac magnetic resonance imaging (MRI) are also available in NHCS.

The mainstay of treatment for coronary artery disease is medical therapy with antiplatelets, statins, antianginals and risk factors control. However, invasive coronary assessment and therapies are usually required for acute coronary syndrome, symptomatic coronary artery disease and patients with severely abnormal non-invasive stress test results.

Cardiac Lab Procedures 2018



▲ An overview of the cardiac lab procedures done in NHCS for 2018.

Advances in Coronary Interventions

The median age of patients seen at NHCS outpatient clinics is approximately 60 years old. With an increasing older patient profile, challenging coronary anatomies with calcifications are frequently encountered during angioplasty. The prevalence of coronary calcification increases procedural complexity, duration and risks. Hence, NHCS continually improves coronary intervention technologies to better treat calcified and challenging coronary lesions. This includes bringing in the latest generation of drug eluting stents and maintaining a wide variety of coronary wires, balloons and micro-catheters.

For example, in addition to current cutting/ scoring balloons, which are used to pre-dilate calcified lesion, NHCS

introduced the Non-Slip Element (NSE) lacrosse cutting balloon with nylon triangular cutting edges. This replaces the traditional wire cutting surface and helps reduce the risk of perforations.

Another example is the procedure of atherectomy to debulk extensively calcified lesions prior to coronary stenting. In addition to the rotablator, which is a revolving instrument used to break up calcified plaque in a clogged coronary artery, NHCS acquired directional coronary atherectomy devices to facilitate the debulking of eccentric calcified lesions. There is also the addition of the coronary intravascular lithotripsy balloon catheter, where lithotripsy is a medical procedure that uses shock waves to break up hardened masses in the kidney, bladder, or ureter. Coronary lithotripsy is one of the latest procedures introduced in NHCS to deal with complex calcified coronary lesions.

While medical technology plays an important role in the diagnosis and treatment of coronary artery disease and ischaemic heart disease, it is vital to recognise that preventive measures such as lifestyle modifications and managing aggressive risk factors are essential and would definitely help improve patient outcomes.

Read the next section as we share on one of the frontier procedures for percutaneous coronary intervention (PCI) - Transradial PCI.



▲ A coronary angiography in progress.



NEW FRONTIER IN PCI WITH 'SLENDER' TECHNIQUES

By Assoc Prof Chin Chee Tang, Senior Consultant,
Department of Cardiology

Over the past few decades, percutaneous coronary intervention (PCI) has had significant advancements in techniques and devices. Transradial PCI (TRI) - the recommended default approach to PCI, now comes with 'slender' techniques for patients with smaller radial arteries.

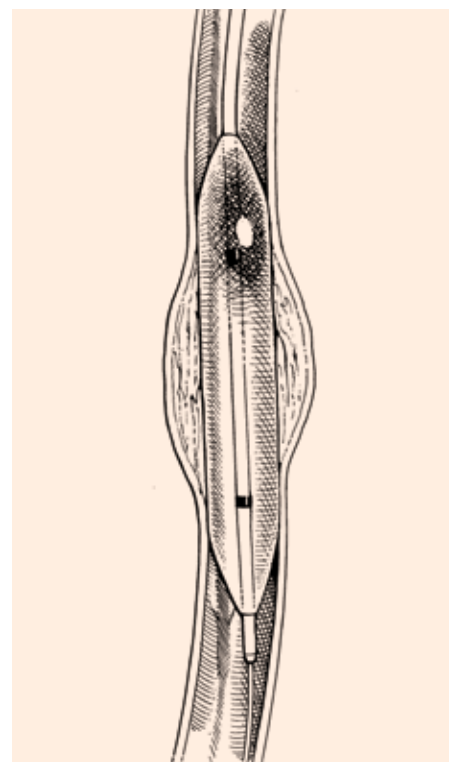
Percutaneous coronary intervention (PCI) is now one of the most common medical procedures in the world. The 'usual' set up for PCI is simple. First, a short plastic tube called a sheath is placed in one of the arteries. Second, a longer plastic tube (called a guide catheter or guider) is placed through the sheath and reaches the coronary arteries of the heart via the body's arterial system. After this, a thin wire (typically with a diameter of 0.014") is placed in the coronary artery, through the narrowing or stenosis that is to be the target of the PCI. Finally, balloons, stents, and other equipment are pushed along this wire so as to dilate and treat this stenosis.

Currently, the majority of PCI is performed with a sheath in the artery that runs along the patient's wrist. This artery is called the radial artery, and

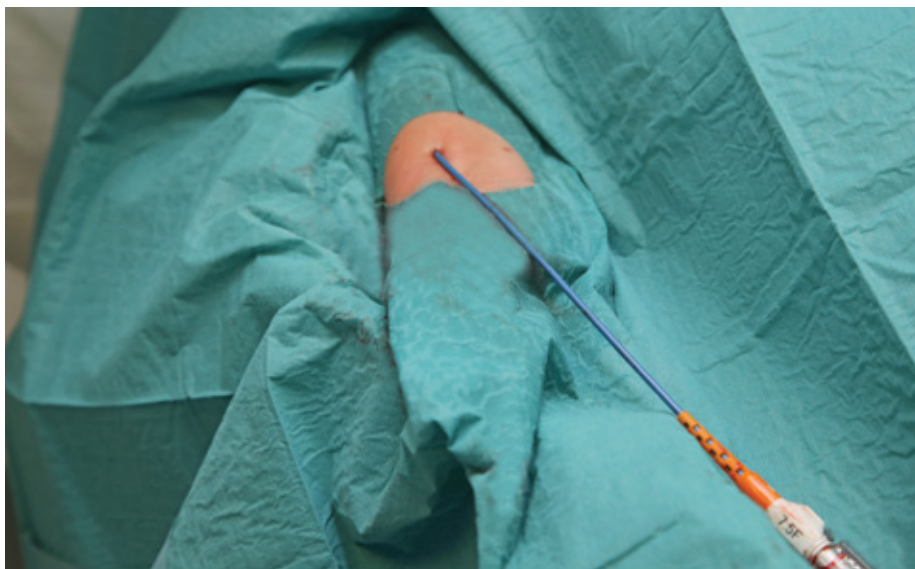
PCI performed in this fashion is termed transradial PCI (TRI). Transradial PCI has been shown to be safer, and have better outcomes than PCI performed through a sheath placed in the groin, and therefore is currently recommended by international guidelines as the default approach to PCI.

However, we know that the radial artery varies in size between individuals. In some individuals, the radial artery is of small calibre, and hence placing a sheath in the artery can be uncomfortable, and may even lead to long term problems like damage to the artery. Because of this, there was a drive to 'downsize' the equipment used in TRI so as to make the technique applicable to more people, and reduce the risk of complications.

The Japanese have been at the forefront of this movement, and have pioneered many of the techniques and



▲ An illustration of a balloon catheter in the coronary artery.



▲ The 'sheathless' guide catheter.

technological innovations for 'Slender' TRI. Many of these innovations have now spread around the world and are used more commonly in daily practice. Every component of the 'usual' PCI set up has been targeted so as to achieve the overarching aim of a more 'elegant' and safe procedure.

There are now sheaths that have thinner walls than before, yet still provide the necessary support for the guide catheters to be inserted into the artery. Because the wall is thinner, the overall diameter of these sheaths is less, hence they are easier to insert in patients who have smaller radial arteries.

Most PCI are currently performed with a guide catheter that has an inner diameter of 2mm (termed a 6 French guider). However, for most cases, a smaller guider sized guider (typically

5 French) can actually be used to perform TRI safely. As a 5 French guider is smaller, the sheath required is also smaller, hence the overall size of the system is smaller than when a conventional 6 French guider is used.

Additionally, there are now guide catheters that can be used without a sheath. These catheters have a special design and coating so that they are less likely to cause damage to the artery. These 'sheathless' guiders are inserted directly into the radial artery and because a sheath is not required, the overall size of the system is significantly less than when a sheath is used.

In Japan, companies have also developed special wires that are of smaller diameter than conventional guidewires, as well as the corresponding equipment (such as balloons) to be used

with them. Because of this innovation, TRI can be performed through smaller size guide catheters such as 4 French guiders.

The main issue with downsizing is that smaller equipment leads to less force and support during TRI. This can be an issue when dealing with more complex cases. Because of this, techniques were developed such as the use of anchor wires and anchor balloons, special guider manipulation and configuration, and other novel modifications. These techniques are now used routinely in all PCI, demonstrating how good ideas will quickly be adopted by all.

However, there are limitations to the 'slender' philosophy and there are times when 'bigger is better'. Some PCI cases are highly complex and require special techniques and equipment that cannot fit into current 'slender' technology. For instance, there are times when a balloon catheter and an ultrasound catheter need to be used simultaneously – these catheters cannot both fit into most 6 French guide catheters currently. Similarly, rotational atherectomy where a special drill is used to modify a very hard and calcified stenosis usually requires at least a 6 French guider system.

In NHCS, many of these technologies are available for carrying out 'slender' PCI. For example, 'slender' sheath are now the default sheath in daily practice in NHCS, and 5 French systems as well as 'sheathless' guide catheters are used in more cases. While there is access to many technologies, it is crucial to assess the appropriateness of methods for each case – whether be it conventional or "slender" technology.

Catch live demonstrations covering lithotripsy and orbital atherectomy cases, and specific sessions featuring key techniques such as TRI, and also the 'slender' techniques. The 'slender' techniques session is a joint session with the Slender Club Japan (SCJ), who are universally acknowledged to be the pioneers of the 'slender' movement.

Singapore LIVE (SingLIVE) is Asia's pre-eminent annual live course in cardiac interventions, and has expanded its reach and influence over the last 28 years to include many Asian key opinion leaders and experts, disseminating key opinions and practices which made the course highly relevant for many cardiologists in the region.

SingLIVE 2020 will be held from 15-17 January 2020 at Raffles City Convention Centre.

More information can be found on www.singlivecourse.com.

Register before 29 Nov 2019 to enjoy the early bird registration fees!

Singapore **LIVE** 2020
29th Annual Live Interventions in Vascular Endotherapy

‘SWITCHING OFF’ FATTY LIVER DISEASE

Breakthrough translational research paves way for the development of world’s first thorough drug target.

Researchers from the NHCS and Duke-NUS Medical School have found that deactivating a specific protein – interleukin 11 (IL11) – with drugs called therapeutic antibodies, helps reverse inflammation and scarring of the liver in patients suffering from an untreatable type of fatty liver disease, called Non-Alcoholic Steatohepatitis (NASH).

The liver plays a key role in breaking down and storing glucose and fat. In conditions such as Non-alcoholic Fatty Liver Disease (NAFLD), too much fat is stored in the liver. NAFLD, also commonly known as ‘fatty liver’, is a liver disorder and refers to a group of conditions where there is accumulation of excess fats in the livers of people who drink little or no alcohol.

The disease can progress to liver inflammation, fibrosis and NASH. NASH refers to liver inflammation and damage caused by a build-up of fat in the liver. It causes fatigue, abdominal pain, itchy skin, nausea, and can lead to liver cirrhosis. Those with diabetes and obesity are particularly at risk, and people who are slim may still be predisposed to having fatty liver disease, particularly for Asians. There is currently no treatment available for both NAFLD and NASH, whereby drugs tested previously have failed to work.

Fatty liver disease is fast becoming a global pandemic, affecting approximately one in four around the world. In Singapore, it is even more common, affecting up to one in three – even found in patients who are slim.

While fatty liver disease can be tolerated if it is not severe, it may worsen over time, resulting in the fatty liver becoming

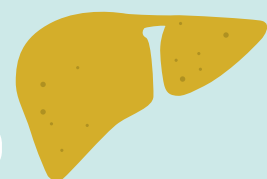
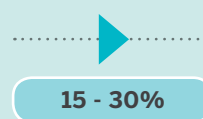


▲ The research was led by Prof Stuart Cook (right), Tanoto Foundation Professor of Cardiovascular Medicine and Director of National Heart Research Institute of Singapore, NHCS, together with Asst Prof Sebastian Schäfer (left), Senior Research Fellow from NHCS.

THE PROGRESSION OF FATTY LIVER DISEASE



Healthy Liver



Non-alcoholic Fatty Liver Disease (NAFLD)

inflamed, fibrotic and scarred, and even leading to liver failure and cancers.

The condition is also linked to insulin resistance which can cause raised blood sugars, as well as high blood cholesterol and triglycerides. Insulin resistance, obesity, high cholesterol and triglycerides are categorised as cardiometabolic disorders that are inter-related and can increase the risk of cardiovascular disease and Type 2 diabetes.

Root of the problem

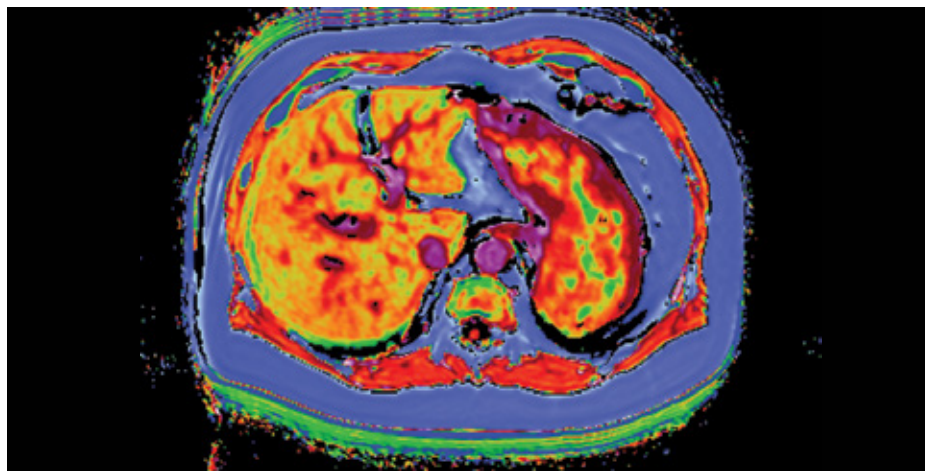
What causes fatty liver disease? A main attribution is over nutrition from the food eaten, which boils down to not just what one consumes, but also the type of food eaten, such as fatty food and high sugar drinks. With a growing 'fast food' trend, fatty liver disease has become a major health concern, as even children are now diagnosed with fatty liver and NASH.

More significantly, the research team discovered that the IL11 gene triggers the development of NASH and fat accumulates in the livers of people with the condition. IL11 is a critical protein that causes fibrosis and organ damage, which was initially thought to be anti-fibrotic until the same team of researchers overturned this misconception in 2017.

The team found that this protein is very important for fat accumulation, scarring and inflammation of the liver processes, and inhibiting IL11 not only can prevent fatty liver disease, but also reverse the condition after it has taken hold of the liver.

Hope for new treatment modality

The therapeutic antibodies developed by NHCS and Duke-NUS researchers has shown to inhibit IL11 in a pre-clinical



▲ An MRI scan of liver fat, inflammation and fibrosis.

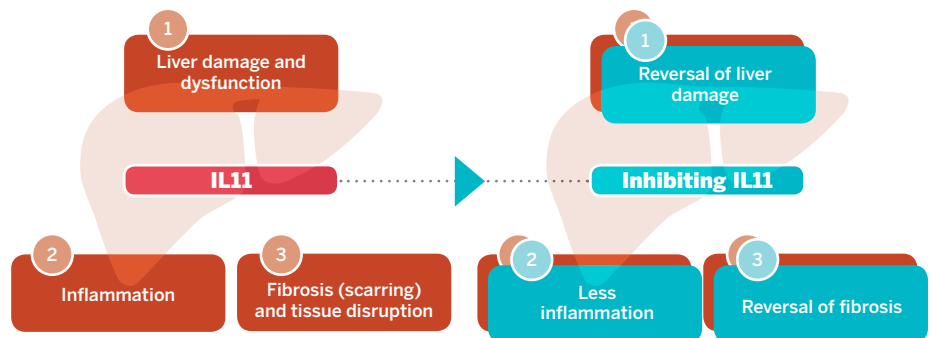
model that mimicked the human form of NASH, preventing and reversing liver inflammation, and even lowering blood levels of cholesterol and glucose.

“We identified a new approach to treat these patients and restore their liver function, while lowering the dangerous fats and glucose in their blood,” added Prof Stuart Cook, corresponding author of the research study, who is the Tanoto Foundation Professor of Cardiovascular Medicine and the Director of National Heart Research Institute of Singapore

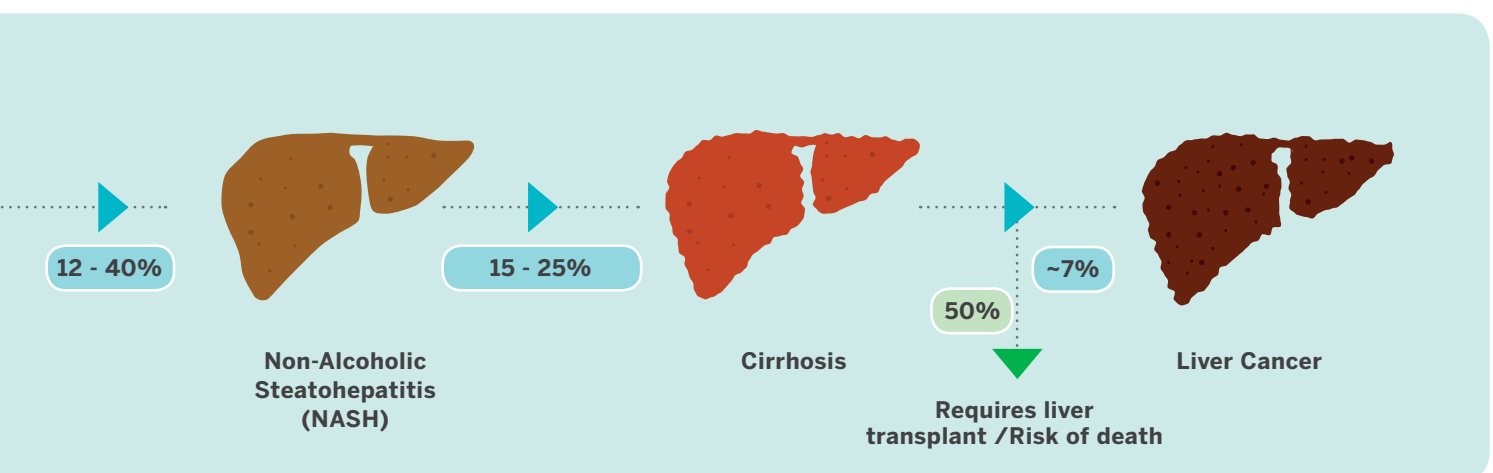
and Senior Consultant from Department of Cardiology at NHCS.

Prof Cook is also the Director and Co-Founder of Enleofen Bio, a biotechnology company established in Singapore that is now developing the antibody therapeutics for clinical trials. The drugs are aimed to be ready for clinical trials by the end of 2020.

The findings¹ were published in the top journal for liver and gut diseases, Gastroenterology.



¹ Inhibiting Interleukin 11 Signaling Reduces Hepatocyte Death and Liver Fibrosis, Inflammation, and Steatosis in Mouse Models of Non-Alcoholic Steatohepatitis. Gastroenterology. DOI: 10.1053/j.gastro.2019.05.002



CLEARING UP

MYTHS ON STATINS



Statins are commonly prescribed to help lower low-density lipoprotein (LDL) cholesterol, and reduce the risk of heart attack or stroke. While statin therapy is proven to be effective in reducing the risk, there are still misconceptions on its use and the side effects.

Too much cholesterol in the blood can lead to a build-up of plaque in the arteries and significantly increase the risk of cardiovascular disease. Statins are used primarily to reduce LDL (or known as the 'bad' cholesterol) and studies have proven that statin therapy reduces risk of major vascular events by 25% for 1 mmol/L reduction in LDL cholesterol¹. Although adverse events have been shown to be related to statin use, the occurrences are relatively rare. Let us now look at some common myths on statins.

MYTH 1

Statins frequently cause muscle ache



Truth: Statins rarely cause muscle ache.

Much of the reported symptoms are likely to be due to misattribution. Researchers found a "nocebo" effect to perceived muscle ache and statins, where patients who were given statins were more likely to think they were experiencing side effects as they expected them². When the patients were unaware they were given statins, there was no reported increase in muscle-related symptoms. But, when the patients knew they were given statins, they were more likely to report symptoms, a finding consistent with the "nocebo" effect.

MYTH 2

Statins can lead to liver and kidney damage



Truth: It is rare that statins will cause a serious liver problem, and there is no evidence that proves statins can cause an adverse effect on kidney.

Statin therapy can lead to mild increase in liver enzymes but this can be managed by lowering the dose or changing to another brand.

Randomised controlled trials have shown that there was no support for an adverse effect of statin therapy on the kidney; instead, results indicated that statin therapy might slow the progression of renal impairment³

MYTH 3

Natural supplements are safer than taking statins



Truth: There are no controlled or reliable studies to prove that supplements are safe and can prevent heart disease.

Health supplements are currently not subject to pharmaceutical regulations. Unlike medicines prescribed by the doctors, health supplements generally do not require to go through stringent clinical trial requirements and approval. They may vary in dose strength and contain ingredients that may not necessarily be identified. "Natural" supplements may not necessarily mean that they are safe for every individual, as some supplements may cause harm instead, depending on the person's health condition and whether the supplements are taken with any other medicines.

MYTH 4

Statins cause diabetes



Truth: Statins are associated with a small increase in risk of diabetes, mainly in those who are at risk of diabetes.

It is important to note that the benefits of reducing cardiovascular risk with statins outweigh the increased risk of diabetes. In addition, patients with diabetes also benefit greatly from statins, which reduce their risk of heart attack, stroke and death.

MYTH 5**Statins cause memory loss and confusion****Truth: Evidence has shown that statins are neither associated with memory loss nor have adverse effects on cognitive function^{4,5}.**

There were studies that found that statins may have a protective and symptomatic benefit in dementia and cognitive changes, and can prevent dementia, especially with long-term use⁶.

MYTH 6**Being intolerant to statins means I will never be able to take statins****Truth: Most people can tolerate statins either by changing the type of statins or by staggering their doses.**

Patients should consult their doctors on the treatment options available.

MYTH 7**I have never been told I have high cholesterol, so I will not need statins****Truth: Studies have shown that patients who took statins have lowered their LDL cholesterol and reduced their overall risk of cardiovascular events, regardless of their cholesterol concentrations¹.**

High-intensity statins regimen is warranted in patients with elevated risk of cardiovascular events even if they are presented with average or below average LDL cholesterol.

MYTH 8**Does changing my diet work as well as taking statins?****Truth: A healthy diet is very important in helping to prevent a heart attack and stroke. With both statins and diet modification⁷, the risk of heart attack/ stroke and cholesterol can be reduced.**

Statins do not just lower cholesterol level. They reduce the risk of plaques breaking off in the blood vessels, thereby reducing risk of causing a heart attack or stroke.

The claims on the side effects of statins might have resulted in the under-utilisation among those who are at increased risk of cardiovascular events. It is therefore important to always seek medical advice from doctors or reliable sources to address any concerns.

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- Exercise Prescription
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- Psychological Counselling
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Dr Ho Jien Sze	Consultant
Dr Chee Fang Yee	Associate Consultant
Dr Huang Zijuan (Sengkang General Hospital)	Associate Consultant
Dr Koh Choong Hou	Associate Consultant

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

¹ Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376(9753):1670-1681. doi:10.1016/S0140-6736(10)61350-5.

² Adverse events associated with unblinded, but not with blinded, statin therapy in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid-Lowering Arm (ASCOT-LLA): a randomised double-blind placebo-controlled trial and its non-randomised non-blind extension phase. *Lancet*. 2017 Jun 24;389(10088):2473-2481. doi: 10.1016/S0140-6736(17)31075-9.

³ Effect of statins on kidney disease outcomes: a systematic review and meta-analysis. *Am J Kidney Dis* 2016; 67: 881-92.

⁴ Testing cognitive function in elderly populations: the PROSPER study. PROspective Study of Pravastatin in the Elderly at Risk. *J Neurol Neurosurg Psychiatry* 2002; 73: 385-89.

⁵ Pravastatin and cognitive function in the elderly. Results of the PROSPER study. *J Neurol* 2010; 257: 85-90.

⁶ Randomized controlled trial of atorvastatin in mild to moderate Alzheimer disease: LEADe. *Neurology* 2010; 74: 956-64.

⁷ Effect of a Dietary Portfolio of Cholesterol-Lowering Foods Given at 2 Levels of Intensity of Dietary Advice on Serum Lipids in Hyperlipidemia: A Randomized Controlled Trial. *JAMA*. 2011;306(8):831-839. doi:10.1001/jama.2011.1202.

TAKING THE GUESSWORK OUT OF LIVING WELL

WHAT DOES LIVING WELL MEAN TO YOU?



It could mean spending quality time with family to one, and exploring the world to another. In the same vein, Advance Care Planning (ACP) helps you think about what living well means to you and in particular, how you can define for yourself, a life well lived till the very end.

"If you meet with a medical emergency and lose the ability to speak, you might think that your family will surely know what you want. But is that really the case?" asked Cindy Lau, Principal Clinical Coordinator from the ACP programme at NHCS.

Alarmingly, Cindy added that most patients do not have an answer to who can speak on their behalf if they can no longer do so. It is usually at critical

moments that patients and their loved ones realise how little they know about each other's care preferences and wish that they had tried to understand more when they had the chance.

ACP is for everyone

Disease does not discriminate – there is no preempting of medical emergencies. When it happens, it is crucial there is someone whom you trust to convey on how you wish to be cared for to the medical team.

Simply put, ACP is:

- the process of planning for your future health and personal care
- about having a conversation with your

loved ones on your personal values and beliefs, how these affect your healthcare preferences in difficult medical situations, and deciding who can be your voice when you become very ill

- a non-legally binding plan which should be updated as and when your preferences change
- applicable to everyone of all ages and health conditions, and anyone who is mentally sound

More importantly, ACP allows you to make your personal wishes known early so that in a medical emergency, your loved ones and caregivers do not have to guess what you want or do not want.

How is ACP different from AMD and LPA?

If you are confused by the above abbreviations, you are not alone.

Jane Wong, Senior Clinical Coordinator said, "There is a misconception that ACP, Lasting Power of Attorney (LPA) and Advance Medical Directive (AMD) mean the same thing or that ACP is about after-life planning."

The key differentiating factor is that ACP allows you to explore your treatment and care preferences, while involving loved ones in the decision making. It is a non-legally binding plan that helps your doctor understand what matters to you when you can no longer tell them yourself.

In a nutshell, ACP empowers you to live your life the way you want, no matter how long you live.

For instance, 45-year-old Alvin Tan met with a car accident which left him seriously injured. His doctor said he was unlikely to regain consciousness and asked if there is someone whom Alvin trusts to make his care decisions.

Scenario A –

Alvin does not have an ACP

"Does Alvin wish to continue with life-sustaining treatment, or would he prefer not to have any medical interventions to keep him breathing?" - This is a difficult and potentially conflicting decision that Alvin's loved ones have to make, as they do not know his wishes.

Scenario B –

Alvin has an ACP

Prior to the accident, Alvin had indicated clearly in his ACP how he wished to be cared for in medical emergencies. His doctor can proceed to care for him according to his preferences. His family and loved ones will have assurance and peace of mind that they are fulfilling his wishes.

i **Advance Medical Directive (AMD)** is a legal advance directive stating your preference not to have extraordinary life-sustaining treatment. It is a legally-binding document and must be signed in the joint presence of a doctor and a witness who must not stand to gain from your death.

i **Lasting Power of Attorney (LPA)** appoints donee(s) to make financial or personal welfare decisions for you if you lose your mental capacity. It is a legally-binding document that needs to be certified by a Certificate Issuer after you have completed it.



RESEARCH PUBLICATIONS

April 2019 – August 2019

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Translating Cardioprotection for Patient Benefit: The EU-CARDIOPROTECTION COST Action *J Am Coll Cardiol.* 2019 Apr 23;73(15):2001-2003. doi: 10.1016/j.jacc.2019.03.020

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Left Ventricular Fibrosis in Patients with Aortic Stenosis *Surgical Management of Aortic Pathology* pp 127-139. DOI: https://doi.org/10.1007/978-3-7091-4874-7_8

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MAY 2019

Echocardiographic reference ranges for normal non-invasive myocardial work indices: results from the EACVI NORRE study *Eur Heart J Cardiovasc Imaging.* 2019 May 1;20(5):582-590. doi: 10.1093/ehjci/ey188

A Population-wide study of electrocardiographic (ECG) norms and the effect of demographic and anthropometric factors on selected ECG characteristics in young, Southeast Asian males—results from the Singapore Armed Forces FA Population-wide study of electrocardiographic (ECG) norms and the effect of demographic and anthropometric factors on selected ECG characteristics in young, Southeast Asian males—results from the Singapore Armed Forces ECG (SAFE) study *Noninvasive Electrocardiol.* 2019 May;24(3):e12634. doi: 10.1111/anec.1263

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