院訊
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聖保祿醫院
St. Paul's Hospital

MESSAGE
FROM THE CHIEF MEDICAL EXECUTIVE

Dr. William Ho
Chief Medical Executive

Post Pandemic Era

It's been a lot of turmoil during the past five years in Hong Kong. Never have we been worried about our personal security living in this city until 2018. And apart from a brief few months in 2003, never have we experienced such a prolonged, major epidemic that took away so many lives, caused so much disruption in our social wellbeing, and even fundamentally changing the way some people work. Running a hospital during this period is also like riding a roller coaster when we look at the huge swings in patient numbers, and the multiple unexpected challenges including manpower shortage either due to sickness or emigration. Now that the dust seems settled, what is the outlook?

By the time this Newsletter issue is released, our Hospital will be well underway in another round of Organization Wide Assessment by ACHS, which I predict should be smooth sailing. Despite the HA's withdrawal a few years ago and even suspension of the Government's Steering Committee on Hospital Accreditation, private hospitals have nevertheless pressed on with this international accreditation scheme voluntarily, with the sole purpose of assuring continuous quality improvement and external benchmarking. Whatever the environmental changes, we hold dear to our mission and values on professionalism and service excellence.

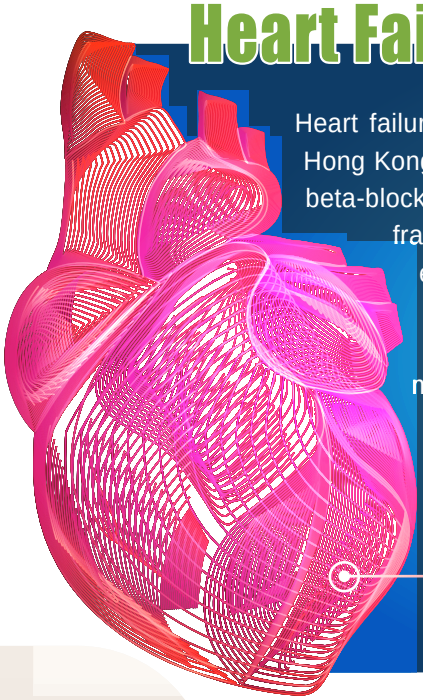
Changes in St. Paul's Hospital are most visible as our Hospital Redevelopment Project that spanned over a decade is finally closing in towards substantial completion within the year. The vision of creating a haven for healing and spirituality, with two modern hospital blocks flanking a beautiful garden that leads up to the magnificent Christ the King Chapel is rapidly taking shape. A fully renovated Oncology Day Centre on the 3/F of our Main Block has commenced service. Construction of a Radiotherapy Centre in the basement is well underway, with service commencement expected by the end of next year. Meanwhile, the addition of the second Cardiac Catheterization Laboratory and more ICU beds have equipped us with better capacity to handle the increasing demand. Other projects in the pipeline include new Specialist Centres in Block A, and expansion of the Renal Dialysis Centre in view that the current capacity is completely filled. Our Elderly Day Care Centre on 7/F of Block A, the first of its kind being run by private hospitals in Hong Kong, is back on track following subsidence of COVID-19, with increasing enrolment, to the extent that we may be planning for expansion in due course.

In hospital management, we have dedicated continuous effort in strengthening the functions of various corporate and clinical governing bodies. New members with non-healthcare backgrounds have added community perspectives and diversity in the Hospital Governing Committee. High caliber clinical experts have joined as Chair-persons and new members of several Clinical Advisory Committees to guide our medical development. We continue to welcome new applicants who choose to sign on as our visiting doctors, even though the Hospital has tightened credentialing rules to ensure that only adequately trained Specialists are granted relevant privileges. Quality assurance activities, clinical audits and monitoring of clinical indicators remain vibrant, to live out our mission of assuring patient safety and high quality care. While nursing and support staff shortage remains a territory-wide issue, every effort is spent to optimize the use of existing manpower, including encouraging more day admissions.

We have come a long way from the turmoil and disruptions; it's time to refocus, refine and rebuild.

Dr. Chan Chi Pan
Resident Consultant Cardiologist

An Update on Medical Treatment for Heart Failure with Reduced Ejection Fraction



Heart failure causes significant morbidity and mortality in the aging population worldwide, and Hong Kong is no exception. Traditionally, angiotensin-converting enzyme inhibitors (ACEIs) and beta-blockers (BBs) have been the mainstay of treatment for heart failure with reduced ejection fraction (HFrEF). Mineralocorticoid receptor antagonists (MRAs) are also used, based on evidence from clinical trials. Ivabradine is another treatment of choice for selected patients. Non-pharmacological treatment options include the use of devices like an implantable cardioverter defibrillator (ICD) or a cardiac resynchronisation therapy pacemaker (CRT-P).[1]

In recent years, newer drug treatments for HFrEF have emerged such as angiotensin–neprilysin inhibitors (ARNIs), sodium–glucose co-transporter inhibitors (SGLT2is) and soluble guanylate cyclase (sGC) stimulators. International guidelines have also been updated based on results of different clinical trials.

Angiotensin–neprilysin inhibitors

Neprilysin degrades multiple endogenous vasoactive peptides, thus its inhibition increases the levels of these peptides, counteracting the neurohormonal overactivation that contributes to vasoconstriction and sodium retention in patient with HFrEF. When combined with renin– angiotensin axis inhibition, the clinical benefits increase as proven in the PARADIGM-HF study.

Since publication of the PARADIGM-HF trial in 2014, ARNIs have become a class I treatment for HFrEF in multiple clinical guidelines.[2] The trial was stopped early because of the overwhelming benefit observed. In the study, compared with enalapril, use of an ARNI caused an absolute risk reduction of 4.7% in the primary endpoint of death from cardiovascular causes or hospitalisation for heart failure. Death occurred in 17% of patients in the ARNI group and 19.8% of patients in the enalapril group ($p<0.001$). Furthermore, the risk of hospitalisation for heart failure was reduced by 21% in the ARNI group relative to the enalapril-treated patients ($p<0.001$).[3]

The risk of angioedema is high when neprilysin is used with an ACEI. To ameliorate this risk, when switching from ACEI therapy, a 36-hour washout period is required before starting the ARNI.

Sodium–glucose co-transporter inhibitors

As oral hypoglycaemic agents, SGLT2is were initially used to treat type 2 diabetes mellitus (T2DM). Yet three landmark trials (EMPA-REG OUTCOME, CANVAS and DECLARE–TIMI 58) have consistently demonstrated a cardiovascular benefit with SGLT2i therapy. Subsequent studies (EMPEROR-Reduced and DAPA-HF) have confirmed the clinical benefit of using SGLT2is for patients with HFrEF, regardless of their diabetes status.

The DAPA-HF trial enrolled 4,744 patients with symptomatic HFrEF regardless of their diabetes status. The composite primary outcome of worsening of heart failure or cardiovascular death occurred in 16.3% of patients in the dapagliflozin group and 21.2% patients in the placebo group ($p<0.001$). Findings were similar for the diabetic and non-diabetic patient subgroups.[4]

In the EMPEROR-Reduced trial, 3,730 patients with left ventricular ejection fraction less than 40% were randomised to receive empagliflozin or placebo. At a median follow up of 16 months, the primary outcome (hospitalization for worsening heart failure or cardiovascular death) had occurred in 19.4% of patients receiving empagliflozin and 24.7% of patients receiving placebo

(p<0.001). Again, the results for the primary outcome were consistent in the diabetic and non-diabetic patient subgroups.[5]

Given the evidence from these trials, SGLT2is have been incorporated into guidelines as the standard treatment for patients with HFrEF with or without T2DM. The most concerning side effects of these agents include an increased incidence of urinary tract infection and the risk of euglycaemic diabetic ketoacidosis. Patients should be taught to withhold their dose if their appetite is poor or during prolong fasting, for whatever reason.

Soluble guanylate cyclase stimulators

Vericiguat is an oral sGC stimulator. Stimulating sGC enhances the cyclic guanosine monophosphate pathway and thus causes vascular smooth muscle relaxation and vasodilation.

Vericiguat was studied in the VICTORIA trial, where it was assessed in patients with left ventricular ejection fraction of 45% or less and recent decompensated heart failure status. The primary outcome (cardiovascular death or first hospitalisation for heart failure) occurred in 35.5% of patients in the vericiguat group compared with 38.5% of patients in the placebo group (p=0.02) (Figure 1).[6]

The most common side effects observed with vericiguat are hypotension, syncope and anaemia. One should note that patients using phosphodiesterase type 5 inhibitors or long-acting nitrates were excluded from the VICTORIA trial. Coadministration of these drugs with vericiguat is not recommended because of the potential risk of extreme hypotension.

Summary

New classes of drugs are emerging for use in heart failure, including the ARNIs, SGLT2is and sGC stimulators. Together with already established treatments, these agents improve morbidity and mortality outcomes for patients with HFrEF (Figure 2). We should not overlook these important new treatment classes when we encounter HFrEF patients in the future.

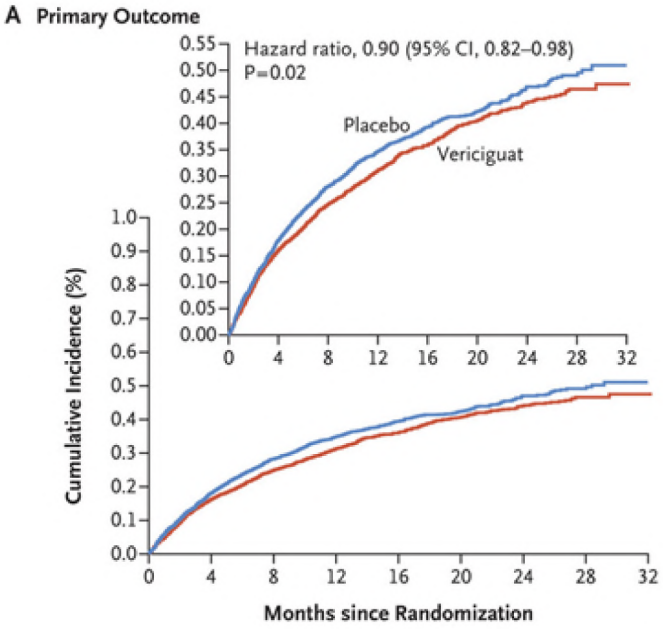


Figure 1. Effect of vericiguat on the primary outcome of cardiovascular death or first hospitalisation for heart failure in the VICTORIA trial.[6]

CI, confidence interval

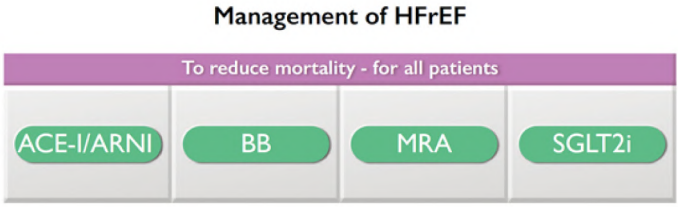


Figure 2. The 'four pillars' of HFrEF treatment, according to the European Society of Cardiology.[1]

ACE-I, angiotensin-converting enzyme inhibitor; ARNI, angiotensin–neprilysin inhibitor; BB, beta-blocker; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium–glucose co-transporter inhibitor

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LAU, Jeffrey Ka Chun

Glucagon-Like Peptide-1 (GLP-1) Agonists for Weight Management

According to the Population Health Survey 2020-22 conducted by the Department of Health, 22% of people aged 15-84 were overweight in Hong Kong, and 32.6% were obese.[1] Overweight and obesity were the most common among females aged 65-84 and males aged 45-54. Adults with a body mass index (BMI) greater than or equal to 25kg/m^2 are classified as overweight and obese if their BMI is greater than or equal to 30kg/m^2.[2] In recent years, there has been a surge in the development of new and innovative weight loss treatments. One such development is using GLP-1 agonists for weight loss. GLP-1 agonists are a class of medications originally developed for treating type 2 diabetes. They work by mimicking the effects of the hormone GLP-1, produced in the gut, to regulate blood sugar levels. This new approach has shown promising results in clinical trials and is a potential game-changer for those struggling to shed excess pounds. This article will provide an overview of GLP-1 agonists and their role in weight management.

Understanding GLP-1: Unveiling the Hormonal Mechanism for Weight Management

Studies have shown that individuals with obesity often have lower levels of GLP-1, which may contribute to their difficulty in losing weight.[3] Exogenous administration of GLP-1 has been found to result in significant weight loss in animals and humans,[4] and effects are through its actions on the central nervous system.[5] Specifically, GLP-1 receptors are present in areas of the brain involved in appetite regulation, such as the hypothalamus. Activation of these receptors by GLP-1 can result in decreased appetite and increased satiety, leading to reduced food intake and weight loss. In addition to their effects on appetite, these medications have increased energy expenditure and promote weight loss through other mechanisms, such as reducing fat storage and increasing fat oxidation.[6]

Benefits of GLP-1 agonists for weight loss

There are several benefits associated with using GLP-1 agonists for weight loss, including:

Effective weight loss: Several clinical trials have demonstrated the effectiveness of GLP-1 agonists in promoting weight loss in individuals with obesity. In many cases, the weight loss achieved with these medications was more significant than

other methods to reduce weight, such as lifestyle interventions. In the STEP 1 clinical trial, the mean body weight reduction for patients who used Wegovy (semaglutide) was 15% (~15.8kg) at 68 weeks compared to 2% from the placebo group who had reduced calorie diet and increased physical activity.[7] Based on the SCALE trial, Saxenda (liraglutide) could achieve a mean body weight reduction of 7.4% (~9.5kg) at 52 weeks.[8]

Long-term weight maintenance: Some studies have suggested that the weight loss achieved with GLP-1 agonists may be more sustainable over the long term. The mean body weight reduction of patients who received Wegovy (semaglutide) in the STEP 5 clinical trial could be sustained at 15% (~15.8kg) at 104 weeks.[9] More than 50% of patients who received Saxenda (liraglutide) could maintain 5% weight loss at 3 years, and weight gain was observed after treatment discontinuation.[10]

Reduced appetite and increased satiety: The appetite-suppressing effects of GLP-1 agonists can help to reduce food intake and make it easier for individuals to adhere to a calorie-restricted diet.[11]

Improved metabolic health: Besides their weight loss effects, GLP-1 agonists improve various aspects of metabolic health, such as blood sugar control, blood pressure, and lipid levels, which can be particularly beneficial for individuals with obesity-related comorbidities, such as type 2 diabetes or cardiovascular disease.[12] Trulicity (dulaglutide) was found to have a mean HbA_{1c} reduction of 1.5% to 1.8% at 36 weeks,[13] with a mean HbA_{1c} of 6.8% to 7% at 52 weeks. [14]

Comparison of GLP-1 agonists available in the market[14-23]

Wegovy (semaglutide) and Saxenda (liraglutide) are the only two GLP-1 agonists licensed for weight loss alongside a reduced-calorie diet and sustained physical activity. In contrast, other GLP-1 agonists are approved by the FDA for managing type 2 diabetes, and clinical studies have consistently demonstrated their ability to induce weight loss compared to control groups.[23]

Brand name	Dose, route, and frequency	Efficacy for weight loss	Licensed indication
Saxenda® (liraglutide)	0.6mg gradually increase to 3mg once daily (subcutaneous injection)	50% of patients achieved 5% weight loss at 56 weeks	Patients with a BMI ≥30 kg/m², or ≥27 kg/m² with one or more weight-related comorbidities (e.g., high blood pressure, high cholesterol), and patients aged 12-17 years with body weight above 60 kg.
Wegovy®* (semaglutide)	0.25mg gradually increased to 2.4mg once weekly (subcutaneous injection)	30% of patients achieved 15% weight loss at 68 weeks and up to 20% at 104 weeks	Patients with a BMI ≥30 kg/m², or ≥27 kg/m² in the presence of weight-related comorbidity (e.g.,s high blood pressure, high cholesterol) and patients aged 12 years and older with an initial BMI at ≥95th percentile standardized for age and sex.
Bydureon BCise® (exenatide extended-release)	2mg once weekly (subcutaneous injection)	Mean weight reduction by 1.4kg over 28 weeks	Type 2 diabetes mellitus
Byetta®* (exenatide)	5mcg gradually increase to 10mcg twice daily (subcutaneous injection)	Mean weight reduction by 2.7kg to 2.9kg over 24 weeks	Type 2 diabetes mellitus
Mounjaro®* (tirzepatide)	2.5mg gradually increase to 5-15mg once weekly (subcutaneous injection)	Mean weight reduction by 6.3kg to 7.8kg over 40 weeks	Type 2 diabetes mellitus
Ozempic® (semaglutide)	0.25mg to 2 mg once weekly (subcutaneous injection)	Mean weight reduction by 2.75kg to 3.56 over 30 weeks	Type 2 diabetes mellitus
Rybelsus® (semaglutide)	3mg gradually increase to 7-14mg once daily (oral)	Mean weight reduction by 2.3kg to 3.7kg over 24 weeks	Type 2 diabetes mellitus
Trulicity® (dulaglutide)	0.75mg gradually increase to 4.5mg once weekly (subcutaneous injection)	Mean weight reduction by 3kg to 4.6kg over 36 weeks	Type 2 diabetes mellitus
Victoza® (liraglutide)	0.6 mg gradually increase to 1.8mg once daily (subcutaneous injection)	Mean weight reduction by 2.1kg to 2.5kg over 52 weeks	Type 2 diabetes mellitus

*Not available in Hong Kong

Potential side effects and safety concerns of GLP-1 agonists

The most commonly reported side effects of GLP-1 agonists include nausea, vomiting, diarrhea, and constipation.[15-23] These side effects are typically mild and transient and may improve with continued use. However, hypoglycaemia could be a common side effect, especially for patients who are concurrently on other anti-diabetic medications (e.g., metformin, sulfonylureas); patients should be informed of the risk of hypoglycaemia and educated on the signs and symptoms, as well as proper management of hypoglycaemia.

More severe side effects are rare but can occur. For example, GLP-1 agonists have been associated with an increased risk of pancreatitis.[15-23] Although this risk appears relatively low, patients should be observed for any signs and symptoms of pancreatitis (e.g., persistent severe abdominal pain, sometimes radiating to the back with or without vomiting). Furthermore, GLP-1 agonists should be used cautiously in patients with renal impairment, as acute kidney injury has been reported. Dose reduction is unnecessary for most GLP-1 agonists in renal-impaired patients. Only Byetta and Bydureon BCise are not recommended for severe renal impairment, and Byetta requires dose modification for moderate renal impairment.[21-22] GLP-1 agonists carry a black box warning from the Food and Drug Administration (FDA) for the risk of Thyroid C-Cell Tumours. Patients with a personal or family history of Medullary Thyroid Carcinoma (MTC) or Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) are contraindicated from using GLP-1 agonists. Patients should be further evaluated if their serum calcitonin is elevated or if thyroid nodules are noted on physical examination or neck imaging. Routine monitoring is required for early detection of MTC.

Conclusion: The future of weight loss with GLP-1 agonists

GLP-1 agonists represent an exciting new approach to weight loss. These medications not only promote weight loss but also improves the overall metabolic health. While GLP-1 agonists are not a one-size-fits-all solution for weight loss, they may be a valuable tool for individuals struggling with obesity and related comorbidities. With continued research and development, GLP-1 agonists could play an increasingly crucial role in the fight against obesity in the years to come and revolutionize our approach to weight loss.

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PHARMACEUTICAL
UPDATES

NEW DRUG APPROVAL

At the Drug and Therapeutics Committee (DTC) meeting in April 2023, the following drug has been approved and added to the formulary at SPH:

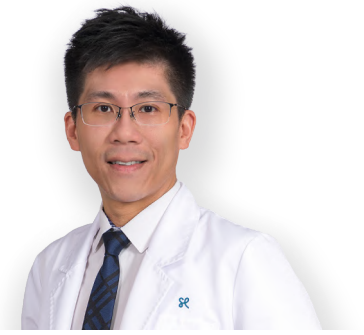
Drugs	Indication(s)	Remarks
TRUXIMA (RITUXIMAB) INFUSION 500MG/50ML	• Non-Hodgkin's Lymphoma • Chronic Lymphocytic Leukemia	On request only

INTRODUCTION
OF NEW FACES

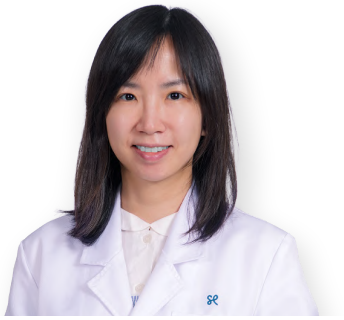
Dr. Au Shek Yin
Resident Consultant Cardiologist

I am Stanley Au Shek Yin. I graduated from HKU in 2006. I am dual- trained in ICU and cardiology, and I spent most of my time in Queen Elizabeth Hospital during my training. I like medical education and research and my research interests include critical care cardiology, echocardiography, mechanical ventilation and medical-legal issues. I am proud to be part of St Paul's family since February 2023. I have a strong vision to develop quality ICU care in the private setting. Adjustment with transition from Hospital Authority was tremendous but luckily support from colleagues here has been unlimited. I am looking forward to working with all of you to give healing hands to all those in need.

Hello everyone, I am Kevin. The newly joined cardiologist. I graduated from the Chinese University of Hong Kong and completed my cardiology training in PYNEH. I underwent one year overseas training in interventional cardiology in the Lausanne University Hospital in Switzerland. I enjoy being an interventional cardiologist and hopefully I can use what I have learnt to treat patients well. I look forward to working with all of you!



Dr. Chan Chi Pan
Resident Consultant Cardiologist



Dr. To Ming Chun
Resident Consultant Pathologist

I am delighted to be a member of this St. Paul's family this year. I graduated from The Chinese University of Hong Kong and completed my residency at Princess Margaret Hospital. My subspecialty interest is in renal pathology, and I underwent overseas training at Vanderbilt University under Professor Agnes Fogo. I look forward to working with all of you and contributing to the team.