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Caution should be exercised when treating these patients with Ozempic®. **Paediatric population:** No data are available **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Special warnings and precautions for use:** Ozempic® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Ozempic® is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients after rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started. There is no experience in patients with congestive heart failure NYHA class IV and Ozempic® is therefore not recommended in these patients. Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions. This should be considered when treating patients with impaired renal function as nausea, vomiting, and diarrhoea may cause dehydration, which could cause a deterioration of renal function. Acute pancreatitis has been observed with the use of GLP-1 receptor agonists. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, Ozempic® should be discontinued; if confirmed, Ozempic® should not be restarted. Caution should be exercised in patients with a history of pancreatitis. Patients treated with Ozempic® in combination with a SU or insulin may have an increased risk of hypoglycaemia. Consider reducing the dose of SU or insulin when initiating treatment with Ozempic®. In patients with diabetic retinopathy treated with insulin and Ozempic®, an increased risk of developing diabetic retinopathy complications has been observed. Caution should be exercised when using Ozempic® in patients with diabetic retinopathy treated with insulin. 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Discontinue at least 2 months before a planned pregnancy. **Undesirable Effects:** Very common (≥1/10): Hypoglycaemia when used with insulin or sulfonylurea, nausea, diarrhoea; Common (≥1/100 to <1/10): Hypoglycaemia when used with other oral antidiabetics, decreased appetite, dizziness, diabetic retinopathy complications, vomiting, abdominal pain, abdominal distension, constipation, dyspepsia, gastritis, gastro-oesophageal reflux disease, eructation, flatulence, cholelithiasis, fatigue, increased lipase, increased amylase, weight decreased; Uncommon (≥1/1,000 to <1/100): Hypersensitivity, dysgeusia, increased heart rate, acute pancreatitis, injection site reactions; Rare (≥1/10,000 to <1/1,000): Anaphylactic reaction; Not known (cannot be estimated from available data): Angioedema Date of review: Jun 2023

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Message From the President

Dr Lam Tat Chung, Paul
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FRCP, FRCPsych, FHKAM (Medicine), FHKAM (Psychiatry)
Specialist in Psychiatry (Private Practice)
President

Dear Members and Doctors,

After having been the President of the Society for over 20 years, I have to announce my exit from the position. The Society needs new talents, new energy and new ideas to continue its growth. After all, we are now in the age of AI.

Over the last 20 years, we have seen the progress of the work of the Society. There is now a Journal published every month, and regular CME activities. We have seen the increase of members, and have overall delivered a useful function to the local medical community in providing educational and social activities.

I have to thank the many people who have contributed to the success of the Society.

First to my dear wife, Annie, who has always given enlightenment and great advice. I have to thank all the Executive Committee members who have worked hard in leading the Society. My thanks also go to all the speakers at our meetings, and to the editors and authors who have contributed their excellent articles to the Journal. I am also most grateful to the doctors who have attended our meetings and read our Journal.

May I wish the new Committee every success in the years to come.

Dr Lam Tat Chung, Paul
President
March 2025

Editorial

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Chief Editor

Glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) have demonstrated benefits in patients with diabetes and in non-diabetic obese patients, improving cardiovascular outcomes beyond weight loss. These benefits can also be seen in patients with heart failure, regardless of ejection fraction, with or without atrial fibrillation, as Dr Myles Chan explains. Another class of drugs with dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) RAs might have even greater efficacy in weight reduction, with a similar safety profile, adds Dr Canice Ng.

The traditional use of aspirin as primary prevention to reduce atherothrombotic events has been challenged, Dr Andrew Ng warns, as it has shown an excess of bleeding and mortality. Instead, cholesterol control is a better target, especially for those with less than 50% stenosis in the coronary or cerebral arteries. In patients with atrial fibrillation and stable coronary artery disease, they can take anticoagulation therapy and forgo antiplatelet therapy.

Surgical aortic valve replacement remains the mainstay treatment for symptomatic patients with severe aortic regurgitation. For patients with a high surgical risk profile, dedicated transcatheter aortic valve implantation (TAVI) might be considered, as addressed by Dr Ivan Wong.

GLP-1 in Obesity and Heart failure

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Key words:
Cardiovascular disease (心血管疾病);
Glucagon-like peptide-1 receptor agonists (胰高血糖素樣肽-1受體促效劑);
Heart failure (心臟衰竭); Obesity (肥胖);
Semaglutide (司美格魯肽)

Glucagon-like peptide-1 (GLP-1) receptor agonists (RAs) are a well-established treatment option in the armamentarium to treat diabetes. Their benefits have been shown to go well beyond glycaemic control. Cardiovascular outcome trials assessing GLP-1 RAs have consistently shown a reduction in major adverse cardiovascular event (MACE) rates, with the positive effect achieved through several mechanisms.[1] GLP-1 RAs are associated with reduction in blood pressure, weight loss, lipid level reduction, and endothelial function improvement.[2-5]

GLP-1 RAs augment insulin secretion after meals and inhibit glucagon production from pancreatic alpha cells at hyperglycaemia. As well as endogenous GLP-1, GLP-1 RAs also have a number of other effects such as promoting weight loss, delaying gastric emptying, lowering blood pressure (both systolic and diastolic) and lowering total cholesterol.[6] They also have been shown to reduce atherothrombotic events and have positive effects on kidney function in type 2 diabetic patients.[7]

Originally designed as a treatment for diabetes, the appeal of GLP-1 RAs has markedly broadened as a treatment option for obesity. Most cardiovascular outcome trials showing the benefits of GLP-1 RA in the past were in patients with type 2 diabetes. More evidence has surfaced to promote the use of GLP-1 RAs in non-diabetic patients, with improved cardiovascular outcomes beyond weight loss.

Semaglutide, a GLP-1 RA commonly used to treat diabetes and used as an antiobesity medication, is showing many cardiovascular benefits beyond weight loss, including reducing the risk of death, reducing serious COVID-19–related events and improving heart failure symptoms.

The SELECT trial

The SELECT trial showed that in patients with obesity and established cardiovascular disease (CVD) without diabetes, once-weekly semaglutide was associated with a decreased risk of MACE comprised of cardiovascular (CV) death, non-fatal myocardial infarction (MI), and stroke, compared with placebo. Patients aged ≥45 years with body mass index (BMI) ≥27 kg/m^2 and established CVD were randomised to receive once-weekly subcutaneous semaglutide (n=8,803) versus placebo (n=8,801). Semaglutide was initiated at 0.24 mg once weekly and increased every 4 weeks as tolerated until the target (2.4 mg weekly) or maximally tolerated dose was reached. There was a total of 17,604 enrolees, with a mean duration of follow-up of 40 months.

The primary outcome, MACE (composite of CV death, non-fatal MI and non-fatal stroke), for semaglutide versus placebo, was 6.5% versus 8.0% (hazard ratio [HR], 0.80; 95% confidence interval [CI], 0.72–0.90, p<0.001).

Heart failure (HF) composite outcome, CV death or HF hospitalisation for semaglutide versus placebo was 3.4% versus 4.1% (HR, 0.82; 95% CI, 0.71–0.96).

In patients with overweight or obesity and established CVD without diabetes mellitus, once-weekly subcutaneous semaglutide was associated with a 20% reduction in MACEs during a mean exposure period of 33 months.

In the mortality substudy, among participants who developed COVID-19, those who were treated with semaglutide had fewer COVID-19–related adverse events or deaths from COVID-19.

In patients with heart failure, semaglutide was associated with decreased MACE, HF hospitalisation, and CV death compared with placebo. There was no interaction with HF subtype, and adverse event profiles were similar to the overall cohort. These findings support the safety and clinical use of semaglutide in patients with obesity, atherosclerotic CVD, and HF with reduced ejection fraction (HFrEF) or HF with preserved ejection fraction (HFpEF) with New York Heart Association (NYHA) class I–II symptoms.[8]

The STEP-HFpEF trial

Semaglutide can also improve HF outcomes by impacting the pathophysiology of HFpEF patients based on three new substudies from the STEP-HFpEF program. The goal of the trial was to compare the safety and efficacy of semaglutide among patients with HFpEF and obesity. A total of 52 participants[9] with a BMI ≥30 kg/m^2, left ventricular (LV) ejection fraction ≥45%, NYHA functional class II, III or IV symptoms, with at least one of the following findings – elevated LV filling pressures, elevated natriuretic peptide levels plus echocardiographic

abnormalities, or hospitalisation for HF in the 12 months before screening plus ongoing treatment with diuretics or echocardiographic abnormalities – were randomised to once-weekly semaglutide or matching placebo.

The results found that among obese patients with HFpEF, once-weekly subcutaneous semaglutide was superior to placebo in improving body weight (~11% greater weight loss) and patient-oriented quality of life outcomes, including Kansas City Cardiomyopathy Questionnaire–Clinical Summary Score (KCCQ-CSS) and 6-minute walk distance at 52 weeks. Semaglutide produced improvements in HF-related symptoms, physical limitations and exercise function, regardless of baseline health status or sex.

In the atrial fibrillation (AFib) subanalysis, once-weekly semaglutide (2.4 mg) was associated with even greater improvements in HF-related symptoms and physical limitations in those with versus without AFib, though improvements were seen in both groups.

In the echocardiography substudy, once-weekly semaglutide (2.4 mg) improved multiple domains of cardiac structure and cardiac function, including improved left atrial volume, LV diastolic function and right ventricular size, compared with placebo.[9]

These promising findings provide evidence for the prescription of GLP-1 RAs as a treatment not only for weight loss but also for reducing MACE in obese non-diabetic patients. The European Society of Cardiology currently has this recommendation: The GLP-1 RA semaglutide should be considered in overweight (BMI >27 kg/m²) or obese chronic coronary syndrome patients without diabetes to reduce CV mortality, MI or stroke. (Class IIa, LoE B)

A complete list of references can be downloaded from www.SOPHYSICIANSHK.org

What Clinicians Should Know About Antiplatelet Therapy for Patients With Cardiovascular Concerns

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Key words:
Acute coronary syndrome (急性冠狀動脈綜合症); Antiplatelet therapy (抗血小板治療); Atherothrombotic events (動脈粥樣硬化血栓形成); Ischaemic stroke (缺血性中風); Myocardial infarction (心肌梗塞)

Antiplatelet therapies are widely utilised as a mechanistical prevention of atherothrombotic events, such as acute myocardial infarction or ischaemic stroke. However, they are inherently associated with substantial increase in bleeding risks. This article aims to discuss the latest evidence-based practice to antiplatelet management for a wide range of patient populations.

Perils of bleeding events

It has become evident that bleeding events can adversely impact both short-term and long-term outcomes, including survival, bleeding events and atherothrombotic events.[1] Bleeding events can result in disruption of thrombosis and haemostasis, as well as activation of proinflammatory and procoagulation cytokines, exaggerated by transfusion of blood products and interruption in antithrombotic therapy. It is undisputable that a major bleeding event is at least as atrocious as a thrombotic event.

Healthy or apparently healthy individuals

Traditionally, aspirin was given as 'primary prevention' to reduce atherothrombotic events based on overoptimistic interpretation of inconclusive data. Such precarious practice is nowadays overthrown after meta-analyses of several large randomised clinical trials concluded that aspirin can marginally reduce atherothrombotic events with a clear excess in bleeding, resulting in neutral

effect on mortality.[2,3] Conceivably, with the availability of highly efficacious therapies, cholesterol control is a better risk-free target to reduce cardiovascular risks.

Most cardiovascular-healthy individuals do not require antithrombotic therapy, regardless of age or diabetic status. This recommendation is probably applicable to most patients with less than 50% stenosis in coronary arteries or cerebral arteries, as most of such haemodynamically insignificant stenoses are findings that surfaced as a result of liberal screening or testing. As a reminder, tight cholesterol control is still imperative in such context.

Stable atherosclerotic cardiovascular disease

This category includes survivors of an atherothrombotic event such as ischaemic stroke or acute myocardial infarction, or those with significant arterial obstruction (usually >50%) with or without symptoms. Although single antiplatelet therapy, predominantly aspirin, is very commonly prescribed to this group of patients, the evidence behind this is flimsy. Only two randomised trials, both performed more than 30 years ago, have assessed the role for aspirin in this stable phase.[4,5] The benefits of aspirin were marginal and were mainly restricted to the early period after an acute atherothrombotic event.

Still, the use of single antiplatelet therapy is dogmatically the standard of care in this clinical setting. For this purpose, aspirin or clopidogrel are widely accepted as equally effective, while gastrointestinal bleeding risk is lower with the latter. Many experts have called for contemporary trials to evaluate this approach. Meanwhile, for patients with a clear contraindication to antiplatelet therapy (such as a bleeding event) and without a recent atherothrombotic event, physicians should be allowed to have a relatively low threshold to cease antiplatelet therapy.

Table 1. Calculation of CARDIAC score for prediction of major bleeding.[8]

Variables	Score	Range
Anticoagulation therapy on discharge	2	0 or 2
Age		0 to 4
<50	0	
50–59	1	
60–69	2	
70–79	3	
80 or above	4	
Renal insufficiency		0 to 4
eGFR >60 mL/min/m^2	0	
eGFR 45 to 60 mL/min/m^2	1	
eGFR 30 to <45 mL/min/m^2	2	
eGFR 15 to <30 mL/min/m^2	3	
eGFR <15 mL/min/m^2	4	
Drop in haemoglobin		
Every g/dL below baseline value, rounded to the nearest integer using the lowest haemoglobin during hospital stay for percutaneous coronary intervention	1 per g/dL drop	Lowest 0, highest 10 in our cohort
Anaemia at baseline		
Every g/dL below 12g/dL of baseline haemoglobin, rounded to the nearest integer	1 per g/dL below 12	Lowest 0, highest 8 in our cohort
Total score	0–16 in our cohort	

The optimum cut-off was ≥5, indicative of high bleeding risk.
CARDIAC, anticoagulation therapy, age, renal insufficiency, drop in haemoglobin, baseline anaemia in Chinese patients; eGFR, estimated glomerular filtration rate

Recent acute coronary syndrome

Acute coronary syndrome (ACS), ranging from ST elevation or non-ST elevation myocardial infarction to unstable angina, is most commonly a result of atherosclerotic plaque rupture and thrombosis mediated by platelet aggregation. Therefore, in patients with ACS, a combination of aspirin and a P2Y12 inhibitor (dual antiplatelet therapy [DAPT]) is clearly indicated. DAPT can reduce the risk of a second episode of atherothrombotic event and mortality.[6,7] The P2Y12 inhibitor can be either clopidogrel or its more potent counterpart, ticagrelor. Both aspirin and all of the P2Y12 inhibitors require loading doses to achieve immediate platelet inhibition. Since the excess in atherothrombotic risk remains elevated for the next 12 to 30 months, the optimal duration of DAPT should be at least 12 months. This recommendation of DAPT is irrespective of whether coronary stenting is performed. However, many patients who are too fragile to undergo coronary intervention are also concomitantly too fragile for DAPT, and hence, clinical discretion should be allowed.

After coronary stent implantation

After implantation of coronary stents, the contact between metal surface and bloodstream can trigger platelet aggregation, resulting in stent thrombosis. Hence, DAPT is mandatory after coronary stent implantation. Contemporarily, all coronary stents contain a drug elution mechanism that can vastly reduce progressive in-stent restenosis (a phenomenon distinct from the aforementioned stent thrombosis). With better material science, contemporary stents are universally thin strut (60–81 microns)

with very low thrombogenicity. This has substantially shortened the minimum period of DAPT required after stent implantation to an absolute minimum of 1 month, from the previous convention of 1 year. Still, for most patients without a clear justification to abbreviate DAPT, the contemporary duration of DAPT after coronary stent implantation is around 6 months, or even 1 year for those with ACS as discussed in the previous section. The bleeding risk score CARDIAC (anticoagulation therapy, age, renal insufficiency, drop in haemoglobin, baseline anaemia in Chinese patients; Table 1) was developed and validated by the author with more than 30,000 Hong Kong patients.[8] This simple scoring system may aid clinicians to devise the best antiplatelet strategy. Thereafter, either antiplatelet agent can be omitted while the other should be continued. In this setting, there is growing evidence that clopidogrel monotherapy may be a better option than aspirin monotherapy.[9] After approximately 1 year, such scenario becomes stable coronary artery disease as discussed in the previous section.

Concurrent anticoagulation therapy

Some patients may require anticoagulation therapy for other indications such as atrial fibrillation. In most situations, anticoagulation therapy can adequately replace the need for aspirin. For example, patients who receive coronary stent implantation can take one anticoagulant and clopidogrel without aspirin in lieu of DAPT.[10] Patients with atrial fibrillation and stable coronary artery disease can take anticoagulation therapy and forgo antiplatelet therapy.[11] It appears that omission of aspirin in patients taking anticoagulation therapy can reduce bleeding risk without any incremental thrombotic risk. This recommendation is applicable to all anticoagulation therapies, including direct oral anticoagulant or warfarin.

Table 2. Quick reference for antiplatelet strategies.

Scenario	Recommended strategy	Acceptable alternative
Healthy individuals	No antiplatelet therapy	Aspirin alone
Stable coronary or cerebral artery disease	Aspirin alone **or** Clopidogrel alone	No antiplatelet therapy
Acute coronary syndrome	DAPT with aspirin and ticagrelor for 12 months, then aspirin alone	DAPT with aspirin and clopidogrel for 12 months, then either: • Extended DAPT with aspirin and low-dose ticagrelor 60 mg BD from 12 months up to 30 months • Aspirin and rivaroxaban 2.5 mg BD for 12 months (up to 31 months)
Coronary stent implantation (drug eluting stents)	DAPT for 6 months, then either aspirin or clopidogrel	DAPT ranging from 1 to 12 months
Taking oral anticoagulant	In lieu of aspirin in DAPT **or** In lieu of single antiplatelet therapy	
Acute ischaemic stroke	DAPT with aspirin and clopidogrel for 3 weeks, then either aspirin or clopidogrel	Aspirin alone **or** Clopidogrel alone

DAPT, dual antiplatelet therapy; BD, twice daily

Acute ischaemic stroke

After acute ischaemic stroke or transient ischaemic attack (TIA), physicians are sandwiched between the opposing needs to prevent a recurrent atherothrombotic event and avoid haemorrhagic transformation. The sweet spot appears to be, for high-risk TIA and minor ischaemic stroke, DAPT for 3 weeks followed with either aspirin and clopidogrel; conversely, for patients with low-risk TIA (with lower thrombotic risk) and moderate-/high-risk ischaemic stroke (with higher haemorrhagic risk), aspirin alone is optimal.

Interruption of antiplatelet therapy for surgery

In congruence with the discussion above, for patients with stable coronary artery disease, aspirin or other antiplatelet therapy can be safely interrupted for several days before and after surgery or other invasive procedures. This strategy has been shown to reduce bleeding without excess in atherothrombotic risk.[12] For patients early (1–12 months) after ACS or coronary stenting (and, to some extent, ischaemic stroke), it may be more advisable to continue aspirin while withholding P2Y12 inhibitors (ie, clopidogrel or ticagrelor). For patients requiring urgent surgery within 1 month of ACS or coronary stenting, any interruption to DAPT will require clear justification.

Summary

In general, the protective effect from antiplatelet therapies reaches its zenith at approximately 1 month after an atherothrombotic event or coronary stent implantation. The associated bleeding risk is more homogenously spread throughout the period of therapy. Hence, physicians should navigate wisely in different clinical scenarios. A quick reference is shown in Table 2.

A complete list of references can be downloaded from www.SOPHYSICIANSHK.org

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Presentation: Clopidogrel film-coated tablets. **Indications:** Secondary prevention of atherothrombotic events in (a) adult patients suffering from myocardial infarction (from a few days until less than 35 days), ischemic stroke (from 7 days until less than 6 months) or established peripheral arterial disease (b) adult patients suffering from acute coronary syndrome: (i) Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention (PCI), in combination with acetylsalicylic acid (ASA) (ii) ST segment elevation acute myocardial infarction, in combination with ASA in patients undergoing PCI (including patients undergoing a stent placement) or medically treated patients eligible for thrombolytic/ fibrinolytic therapy. In adult patients with moderate to high-risk Transient Ischemic Attack (TIA) (ABCD2 score≧4) or minor Ischemic Stroke (IS) (NIHSS≦3) within 24 hours of either the TIA or IS event. Prevention of atherothrombotic and thromboembolic events, including stroke, in combination with ASA in adult patients with atrial fibrillation who have at least one risk factor for vascular events, are not suitable for treatment with Vitamin K antagonists (VKA) and who have a low bleeding risk. **Dosage:** Adults and elderly: 75 mg once daily. For patients with acute coronary syndrome: (a) Non-ST segment elevation acute coronary syndrome (UA/NQWMI), loading dose (LD) 300 mg or 600 mg (patients <75 years when PCI is intended), followed by 75 mg once daily (with ASA 75 mg-325 mg daily). Since higher doses of ASA were associated with higher bleeding risk, recommended dose of ASA ≤100 mg. (b) ST segment elevation acute myocardial infarction, (i) 75 mg once daily with a 300 mg LD in combination with ASA and with or without thrombolytics for medically treated patients eligible for thrombolytic/ fibrinolytic therapy. For patients ≥75 years, initiate clopidogrel without LD. (ii) 600 mg LD in patients undergoing primary PCI and in patients undergoing PCI more than 24 hours of receiving fibrinolytic therapy when PCI is intended. For patients ≥75 years, initiate 600 mg LD with caution. Initiate 300 mg LD in patients undergoing PCI within 24 hours of receiving fibrinolytic therapy. Continue with 75 mg once daily with ASA 75 mg-100 mg daily. Combined therapy should be started as early as possible after symptoms start and continued up to 12 months. For adult patients with moderate to high-risk TIA or minor IS, LD of clopidogrel 300 mg followed by clopidogrel 75 mg once daily and ASA (75 mg-100 mg once daily). For patients with atrial fibrillation, 75 mg daily with ASA (75-100 mg daily). Children and adolescents: not recommended under 18 years. **Contraindications:** Hypersensitivity to clopidogrel or excipients; severe hepatic impairment; active pathological bleeding such as peptic ulcer & intracranial hemorrhage. **Precautions:** If a patient is to undergo elective surgery and antiplatelet effect is not necessary, clopidogrel should be discontinued 7 days prior to surgery. Use of clopidogrel 600 mg LD in patients ≥75 years should be considered only after an individual assessment of the bleeding risk by the physician. Patients who may be at risk of increased bleeding from trauma, surgery or other pathological conditions; hypersensitivity to thienopyridines; patients with renal impairment; patients with moderate hepatic disease who may have bleeding diatheses. In acute minor IS or moderate to high-risk TIA patients, dual antiplatelet therapy should be started no later than 24 hours after event onset. In non-minor IS patients, clopidogrel monotherapy should be started only after first 7 days of the event and use of dual antiplatelet therapy is not recommended. Dual antiplatelet therapy is not recommended in recent minor IS or moderate to high-risk TIA patients for whom intervention is indicated or planned. Patients with genetically reduced CYP2C19 function. Patients treated concomitantly with clopidogrel and CYP2C8 substrates. **Interactions:** Not recommended with oral anticoagulants, caution with glycoprotein IIb/IIIa inhibitors, aspirin, heparin, thrombolytics or NSAIDs (including Cox-2 inhibitors), selective serotonin reuptake inhibitors (SSRIs). Drugs that induce or inhibit CYP2C19, including proton pump inhibitors. CYP2C8 substrates such as rapaglinide and paclitaxel. **Pregnancy and Lactation:** Clopidogrel should be discontinued as a precautionary measure. **Undesirable effects:** haemorrhagic disorders; haematological including bleeding such as purpura, bruising, haematoma and epistaxis; gastrointestinal system disorders such as dyspepsia, abdominal pain and diarrhea. For uncommon, rare and very rare undesirable effects, please refer to the full prescribing information. **Preparations:** 75 mg x 14's; 75 mg x 28's; 300 mg x 30's. **Legal Classification:** Part 1, First & Third Schedules Poison Full prescribing information is available upon request. API-HK-CLO-24.06

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Symptomatic Severe Aortic Valve Regurgitation: Latest Update in Transcatheter Treatment

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Key words:
Aortic valve regurgitation (主動脈瓣逆流); Aortic valve stenosis (主動脈瓣狹窄); Surgical aortic valve replacement (手術主動脈瓣膜置換); Transcatheter aortic valve implantation (經導管微創主動脈瓣植入術)

Aortic valve regurgitation (AR) is a frequently encountered, overlooked and undertreated disease associated with heart failure symptoms and substantial morbidity and mortality. It was shown in the Framingham study that AR has an estimated prevalence of 4.9%, with moderate or severe AR occurring in 0.5% of the study population.[1]

Notably, medical therapy in symptomatic severe AR patients based on angiotensin-converting enzyme inhibitors and vasodilators is only supportive and might temporarily relieve heart failure symptoms; however, the natural course of the disease does not change unless patients undergo definitive aortic valve treatment.[2] Early intervention before the onset of heart failure is also crucial for the best possible long-term outcome.

Definitive treatment for severe native pure AR patients with symptoms, left ventricular ejection fraction ≤55%, or left ventricular end-systolic diameter >50 mm, until recently, was largely surgical aortic valve replacement (SAVR). SAVR is still the mainstay treatment for patients with an acceptable surgical risk profile.

With the advent of transcatheter aortic valve implantation (TAVI), the scope of treatment has been widened to patients with high or extreme surgical risk profile. The development and current status of transcatheter treatment of symptomatic severe AR will be covered in this article.

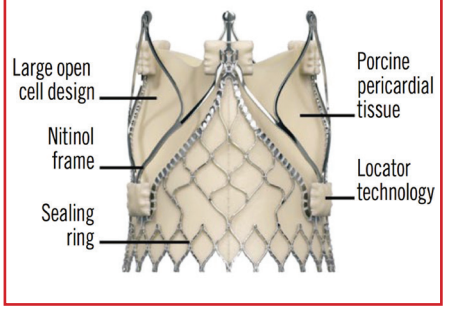
Non-dedicated TAVI devices for AR

TAVI is currently an established therapy for elderly patients with symptomatic severe aortic valve stenosis (AS) across all surgical risk categories. Before the invention and approval of dedicated TAVI devices, there were isolated registries reporting on the results of the off-label use of commercially available non-dedicated TAVI devices in treating severe native AR. Of note, use of non-dedicated TAVI devices in pure AR is hampered by unacceptable rates of embolisation and paravalvular regurgitation, predominantly because of dilated annulus and lack of calcium for valve anchoring and positioning. In a recently published meta-analysis including a total of 34 studies encompassing 2,162 patients,[3] patients undergoing TAVI with dedicated devices had a lower all-cause 30-day mortality rate (3% vs 9%; p<0.01) and higher device success (93% vs 82%; p<0.01) compared with off-label devices. The risk of at least moderate AR (2% vs 5%; p=0.03), valve embolisation/migration (2% vs 8%; p<0.01), pacemaker implantation (11% vs 20%; p<0.01), and reintervention (4% vs 10%; p<0.01) at 30 days and all-cause mortality at 1 year (6% vs 24%; p<0.01) were lower in the dedicated device group. These findings support the use of dedicated TAVI devices as a safer alternative for high-risk patients.

Dedicated TAVI device for AR

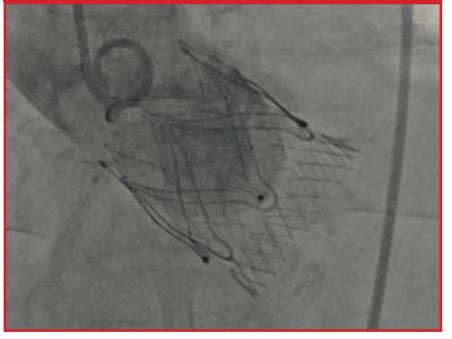
The JenaValve Trilogy system[4] received European conformity (CE) marking for the treatment of AR and AS in year 2021 (Figure 1, Figure 2). To date, it is the only approved transfemoral TAVI device for the treatment of severe AR. This device was first introduced in Hong Kong SAR, the first region in Asia to have the device commercially available, in 2023.

Figure 1. The JenaValve Trilogy transcatheter heart valve.



Source: Curio J, et al. JACC 2024,[4] reused under the terms of the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Figure 2. Final aortogram after implantation of the JenaValve Trilogy.



In the prospective, multicentre, single-arm ALIGN-AR study,[5] use of the JenaValve Trilogy system to treat symptomatic severe AR at high surgical risk was shown to have low rates of 30-day and 1-year mortality; a composite safety event rate that was non-inferior to rates in TAVI performed for AS; significant and sustained improvement in functional status and patient reported outcomes; improvements in left-ventricular remodelling; excellent valve haemodynamics with a large effective orifice area, low mean gradients, and minimal paravalvular regurgitation; and high permanent pacemaker rates that declined during the course of the trial.

The ALIGN-AR 2-year follow-up data[6] confirmed the continued safety and efficacy of the system. After 2 years, the all-cause mortality rate remained below the study's predefined performance goal of 25% at 1 year. The 2-year data also reported excellent haemodynamic outcomes, very low rates of paravalvular leak, and sustained improvements in quality of life.

In the upcoming prospective, randomised ARTIST trial,[6] outcomes between non–high-risk patients with moderate-to-severe and severe AR treated with the JenaValve Trilogy device and those undergoing SAVR will be compared. The ARTIST study aims to provide important information to clinicians on TAVI with the JenaValve Trilogy as an option for patients with AR in comparison to surgery.

Conclusion

Severe AR is a lethal disease that is underdiagnosed; under-referred and undertreated. SAVR remains as the gold standard approach in patients with severe AR and acceptable risk profile. TAVI with transfemoral dedicated device has demonstrated promising results for high surgical risk patients with pure native AR. With the evolution pathway of TAVI in symptomatic severe AS in mind, future trials are necessary before expanding TAVI indication for symptomatic severe AR patients across lower surgical risk categories.

A complete list of references can be downloaded from www.SOPHYSICIANSHK.org

Semaglutide and Tirzepatide for Heart Failure With Preserved Ejection Fraction and Obesity

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GLP-1 receptor agonist (胰高血糖素樣肽-1受體促效劑); Heart failure with preserved ejection fraction (正常收縮分率心臟衰竭); Obesity (肥胖)

Epidemiological studies indicate that many patients who have heart failure with preserved ejection fraction (HFpEF) also suffer from obesity.[1] Growing evidence suggests that adipose tissue may play a pivotal role in the development, progression and adverse outcomes of HFpEF.[1] The presence of visceral adiposity is associated with increased inflammation, left ventricular hypertrophy, insulin resistance, and diastolic and systolic left ventricular dysfunction, as well as arterial, skeletal muscle, and physical dysfunction.[1] Patients with established HFpEF who exhibit the obesity phenotype display distinct clinical and haemodynamic characteristics. These include expanded plasma and stressed blood volume, reduced venous capacitance, elevations in exercise pulmonary wedge pressures, adverse haemodynamic response to diuresis, higher inflammatory markers, and more pronounced hypertension, as well as more severe symptoms and exercise intolerance.[2] Moreover, obesity leads to a deficiency in natriuretic peptides due to decreased production and increased clearance. This deficiency results in a reduced capacity for vasodilation and natriuresis.[3]

Studies have shown that 2.4 mg once-weekly semaglutide, a long-acting glucagon-like peptide-1 (GLP-1) receptor agonist, had great efficacy in weight reduction, with acceptable safety.[4] Meanwhile, tirzepatide, a once-weekly dual agonist for the GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor, had even greater efficacy

in weight reduction, with similar safety profile.[5] Semaglutide and tirzepatide are the best-studied GLP-1 receptor agonists in patients with obesity (body mass index ≥30) and HFpEF. Their efficacy and safety had been well studied in the STEP-HFpEF and Summit trials. Other agents are unproven in this population. It is unclear if there is a class effect.

Both the STEP-HFpEF and Summit trials demonstrated positive outcomes regarding reductions in symptoms and physical limitations.[6,7] In the STEP-HFpEF trial, the primary outcomes were change in the Kansas City Cardiomyopathy Questionnaire Score (KCCQ score) and body weight. In the Summit trial, the primary endpoints were a composite of adjudicated death from cardiovascular causes or worsening heart failure event and the change in KCCQ score. Both trials showed significant reduction in KCCQ score (2.4 mg once-weekly semaglutide vs tirzepatide, 7.8% vs 6.9%, p<0.001) while other agents like sodium–glucose cotransporter 2 inhibitors, sacubitril–valsartan, and spironolactone for HFpEF only produced modest changes in KCCQ scores (ranging from 0.5 to 2.3 points).[6-10]

In STEP-HFpEF, although hospitalisation for heart failure was not the primary outcome, there was a significant reduction in adjudicated events of hospitalisation for heart failure or urgent visits (2.4 mg once-weekly semaglutide vs placebo; hazard ratio [HR], 0.08; 95% CI, 0.00–0.42). A pooled analysis of four randomised, placebo-controlled trials (SELECT, FLOW, STEP-HFpEF, and STEP-HFpEF DM) found that semaglutide reduced the risk of the combined endpoint of cardiovascular death or heart failure events (5.4% in the semaglutide group vs 7.5% in the placebo group; HR, 0.69; 95% CI, 0.53–0.89]; p=0.0045). This combined endpoint was mainly driven by reduction in risk of worsening heart failure events (2.8% vs 4.7%; HR, 0.59; 95% CI, 0.41–0.82; p=0.0019).[11] However, a subgroup analysis suggested that patients with BMI ≥35 kg/m^2 were more likely to benefit from semaglutide than patients with lower BMI (HR, 0.49; 95% CI, 0.33–0.70 vs HR, 0.96; 95% CI, 0.67–1.38 in patients with BMI <35 kg/m^2). In the Summit trial, patients randomly assigned to tirzepatide treatment experienced a lower risk of a composite endpoint of cardiovascular death or worsening heart failure (HR, 0.62; 95% CI 0.41–0.95; p=0.026). This composite endpoint was primarily influenced by a reduction in adjudicated worsening heart failure events resulting in hospitalisation (HR, 0.54; 95% CI, 0.34–0.85). The rates of cardiovascular mortality (2.2% vs 1.4% in the placebo group) and all-cause mortality (5.2% vs 4.1%) were similar between the groups.[7]

Patients in the STEP-HFpEF trial had baseline N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels that were twice those of patients in the Summit trial. However, the Summit trial had a higher percentage of patients experiencing heart failure events, as additional criteria were used to enrich the study population's risk of heart failure. The effects of tirzepatide on the two primary endpoints did not seem to diminish in patients with NT-proBNP levels below 200 pg/mL. In the STEP-HFpEF trial, the percentage change in NT-proBNP levels from baseline to week 52 was –20.9% for the semaglutide group versus –5.3% for the placebo group. In contrast, the NT-proBNP changes in the SUMMIT trial (as ratios of geometric means) were 0.93 for the tirzepatide group and 1.04 for the placebo group (HR, 0.9; 95% CI, 0.79–1.01). Therefore, even if patients showed significant symptom improvement, the absolute changes in NT-proBNP levels following treatment may not be numerically substantial. Nonetheless, previous studies showed that higher BMI correlates with lower NT-proBNP levels, and NT-proBNP levels can rise with weight loss in patients with type 2 diabetes who had normal baseline NT-proBNP levels. The reduction in NT-proBNP levels with treatment despite significant reductions in body weight, along with the lower number of adjudicated heart failure events, suggests that the decongestive and favourable haemodynamic effects of semaglutide and tirzepatide might be substantial.

In the STEP-HFpEF trial, semaglutide was administered at an initial dose of 0.5 mg subcutaneously once a week, and then titrated up to a maximum dose of 2.4 mg weekly. It is important to note that only the 2.4 mg dose of semaglutide is indicated for the treatment of patients with obesity and HFpEF. There are still insufficient data to demonstrate that lower doses of semaglutide can achieve significant reductions in heart failure symptoms for this patient group. While lower doses of semaglutide may lead to weight loss, they are only indicated for diabetes management and are not labelled as weight loss medications. On the other hand, tirzepatide is initiated at a dose of 2.5 mg weekly and then titrated up to a maximum of 15 mg weekly. The efficacy of tirzepatide for HFpEF does not appear to be dose dependent.

In summary, GLP-1 receptor agonists, including 2.4 mg weekly semaglutide and tirzepatide, should be considered as first-line treatment for patients with obesity (BMI ≥30 kg/m^2) and HFpEF.

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Protect your patients with the updated JN.1 COVID-19 vaccine

COVID-19 remains a significant health burden in Hong Kong

- In Hong Kong, the COVID-19 infection waves reportedly occur **every 4 to 6 months**.[1]
- The number of severe and fatal COVID-19 cases post-pandemic has **reached or surpassed** the past 3 influenza seasons from 2023–2024 in Hong Kong.[2*]

Who should receive the updated COVID-19 vaccination?

The Hong Kong Centre for Health Protection recommends the updated vaccine for **high-risk groups if their last vaccination or infection was >6 months**; this includes pregnant women, healthcare workers and those aged[3]:

- >50 years
- 18–49 years with underlying comorbidities†
- ≥6 months who are immunocompromised‡

Why is the updated COVID-19 vaccination important for high-risk patients?

Comorbidities are associated with an increased risk of death from COVID-19 infection[4§]

CVD	Diabetes	Hypertension
OR, 3.06; 95% CI, 1.50–6.26; p<0.01	OR, 2.15; 95% CI, 1.17–3.93; p=0.01	OR, 2.27; 95% CI, 1.13–4.56; p=0.02

Adapted from Kim W, et al. Korean J Clin Pharm 2020;30:169-176.

The updated COVID-19 vaccine confers[6]:
60% additional protection against COVID-19–related hospitalisation

A higher number of COVID-19 vaccine doses has been associated with a reduced risk of major CVD sequelae and mortality.[5‖]

As part of the government vaccination programme, the updated COVID-19 vaccine is available for free to high-risk patients at designated private clinics, GOPCs, SOPCs at major hospitals and more. Scan the QR code for more details!

Encourage Your Patients To Vaccinate Today.

*Data between weeks of 29 January 2023 to 27 July 2024.[2] †Persons with chronic CVD, lung disease, metabolic or kidney diseases, obesity, chronic neurological conditions that compromise respiratory function, persons who are unable to care for themselves, and children and adolescents on long-term aspirin therapy.[3] ‡Persons who are on active immunosuppressive treatment (past 12 months to present), organ or stem cell transplant recipients, severe primary immuno-deficiency, chronic dialysis, and advanced or untreated HIV disease.[3] §Estimated odds ratio for mortality linked to various comorbidities from a meta-analysis of seven global studies with 26,542 participants.[4] ‖Data from a retrospective population-based cohort study in Hong Kong on 1,175,277 patients with COVID-19 infection.[5]

Abbreviations: CI, confidence interval; **COVID-19,** coronavirus disease 2019; **CVD,** cardiovascular disease; **GOPCs,** general outpatient clinics; **HIV,** human immunodeficiency virus; **OR,** odds ratio; **SOPCs,** special outpatient clinics.

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GLP-1 in Obesity and Heart failure

Dr Myles Chan

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What Clinicians Should Know About Antiplatelet Therapy for Patients With Cardiovascular Concerns

Dr Ng Kei Yan, Andrew

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Symptomatic Severe Aortic Valve Regurgitation: Latest Update in Transcatheter Treatment

Dr Wong Man Ho, Ivan

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