



THE CAROTID PLAQUE – UNDERSTANDING THE UNSTABLE PLAQUE ON CAROTID DUPLEX-ULTRASOUND

Stroke is one of the major health care problems in the world today. It is the third leading cause of mortality in the western countries and the most common cause of mortality of any neurological disorder. A significant proportion of strokes are ischemic in nature, and it is estimated that 20-25 percent of all strokes can be attributed directly to internal carotid artery (ICA) atherosclerosis. As many of these strokes occur without any prior symptoms, it would be advantageous if patients who are at the highest risk of stroke from ICA stenosis could be identified and treated in advance of any ischaemic neurological events.

Over the last 20 years a lot has been learned about the morphological characteristics of an atherosclerotic plaque responsible for plaque progression and instability. The raised lesion or fibro-lipid plaque is the archetypal lesion of atherosclerosis and complications of this lesion (fissure and ulceration) form the basis of most cases of occlusive arterial disease. All atherosclerotic plaques share two basic morphological components:

Fibrous cap: a thick layer of fibrous connective tissue, which is significantly thicker and much less cellular than the normal intima and contains lipid-filled macrophages, collagen and smooth muscle cells.

Atheroma: A necrotic mass of lipid that forms the core of the lesion. Loss of continuity of the endothelium is the main step in the progression of a plaque and increases the permeability of the intima to lipoproteins, permits platelet-vessel wall interaction and release of growth factors leading to formation of thrombus on the vessel wall.

There is ample clinical and histological evidence that carotid atherosclerotic plaques with large necrotic lipid core, thin plaque cap or ulceration, dense inflammatory infiltrate, intra-plaque haemorrhage and angiogenesis are vulnerable to rupture and development of ischaemic neurological and ocular events. Duplex ultrasound identification of these changes within carotid atherosclerotic plaques identifies patients with carotid atherosclerotic stenosis at significant risk of neurological events.

Carotid Duplex ultrasound is arguably the most important imaging modality for preoperative assessment of patients with carotid atherosclerotic disease. It is non-invasive, relatively inexpensive and very accurate at identification of significant ICA stenosis. In measuring the degree of stenosis, the flow and velocity characteristics assessed by colour flow Doppler are utilized. Duplex devices also generate high resolution B-mode ultrasound images of the atherosclerotic lesion. These images do not contribute significantly to the assessment of carotid artery stenosis. However, the B-mode ultrasound image can be used to assess morphologic characteristics of an atherosclerotic lesion. Plaques that are echolucent (appear dark on Duplex ultrasound) with irregular or ulcerated surfaces and intra-plaque haemorrhage are associated with histologic characteristics of plaque instability, ipsilateral neurological or ocular events, CT evidence of carotid territory cerebral infarction or evidence of embolization on trans-cranial ultrasound. Echogenic (white on ultrasound) plaques with smooth surfaces on the other hand have a lower embolic risk.

With major advances in best medical therapy in the form of options for aggressive lipid control, single or dual anti-platelet therapy and anti-platelet with low dose oral anti-coagulation with direct oral anti-coagulants like Dabigatran or Rivaroxaban, fewer patients are now considered suitable for carotid endarterectomy or stenting – procedures that carry a stroke risk of their own. An of carotid plaque morphology as seen on a thorough Carotid Duplex Ultrasound helps physicians make these decisions to reduce stroke risk and prevent unnecessary carotid interventions.



Fig 1. A carotid endarterectomy specimen of an ulcerated carotid plaque with intra-plaque haemorrhage

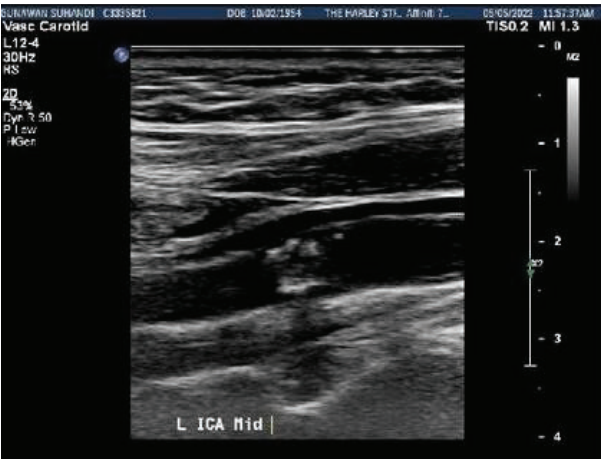


Fig 2. B-Mode Duplex of an echolucent ulcerated (high risk unstable) ICA plaque causing over 90% stenosis (Image courtesy the Harley Street Vascular Diagnostic Laboratory)

WHAT IS THE ROLE OF PRIMARY CARE PHYSICIANS IN STROKE PREVENTION IN HIGH RISK PATIENTS?

The incidence rate of stroke in Singapore and around the world has been steadily increasing over the past decade (Figure 1), in part due to people adopting more unhealthy lifestyles and worsening cardiovascular risk factors over time. Cerebrovascular disease was the fourth most common cause of death in 2019, accounting for close to 6% of all deaths in Singapore. Although overall mortality from stroke appears to be decreasing (likely due to earlier acute intervention and better post-stroke care), it is important to take preventative measures to decrease stroke rates and reduce the considerable morbidity and strain on social and healthcare services that result from this disease.

Primary care physicians/ general practitioners are instrumental in assessing patients' general medical conditions and cardiac risk factors as well as determining whether the patient needs to undergo further specialist tests or investigations. Their role is therefore very important in identifying the patients at higher risk of getting a stroke based on their risk profile or symptoms. Patients who have already suffered a stroke or deemed to be high risk, often require a co-ordinated care approach involving multiple disciplines, which may include cardiologists, neurologists, endocrinologists, rehab doctors and dietitians.

Important risk factors for stroke which the primary care physician should help diagnose and treat include:

- Hypertension
- Hyperlipidaemia
- Diabetes
- Atrial fibrillation
- Obstructive sleep apnoea
- Lifestyle issues - smoking, obesity/ lack of exercise, excessive alcohol consumption, high salt intake

Practical measures that can be taken in primary care in stroke prevention:

- 1) Identify the higher risk patient** – Diabetics, hypertensives, elderly, renal impairment, atrial fibrillation, prior transient ischaemic attack (TIA)/ stroke
- 2) Give appropriate lifestyle and risk factor modification advice** – e.g. diet, exercise, weight loss, smoking cessation
- 3) Refer to specialist for appropriate evaluation if appropriate**
 - Cardiac assessment (echocardiogram, Holter monitor, assess for coronary artery disease)
 - Vascular assessment for carotid or peripheral vascular disease
 - Neurological assessment – for patients with prior TIA/ stroke
- 4) Decide on appropriate antithrombotic/ antiplatelet therapy (with specialist involvement if required)**
 - Decide on need for oral anticoagulation in patients with AF and most appropriate choice. Figure 2 shows the latest international recommendation for starting oral anticoagulation in patients with AF. Generally, in patients with AF who are below the age of 65 and have no other risk factors, they do not need to be started on oral anticoagulation (there is no indication for aspirin alone in stroke prevention)
 - Combination of antiplatelets/anticoagulation is not usually indicated for secondary stroke prevention
 - Dual antiplatelet therapy is not usually recommended long term
- 5) Co- manage high risk patients with specialist**
 - Patients will often require specialist input in case of events or complications
 - Annual cardiac assessment for patients with cardiovascular disease
 - Annual diabetic eye-check, foot screen and neurological assessment

Conclusion:

A co-ordinated approach between the primary care physician/ GP and specialists is essential in reducing the burden of stroke in the community and improving overall patient care and quality of life. Primary care physicians should work closely with appropriate specialists to decide on the most suitable tests and treatments for high risk patients and continually reassess patients' stroke risk over time as their risk profile can change.

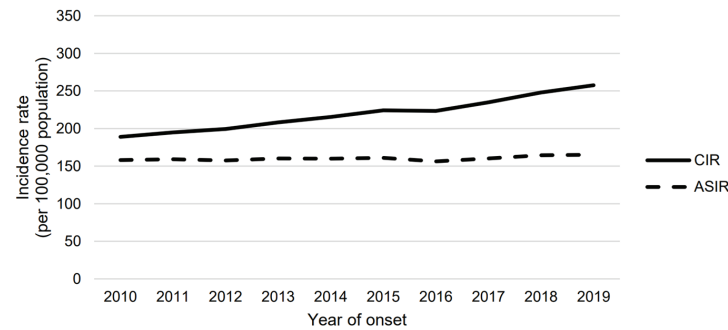


Figure 1. Incidence rate of stroke in Singapore (per 100,000). (From Singapore stroke registry annual report 2019; CIR= Crude Incidence Rate; ASIR= Age Standardized Incidence Rate)

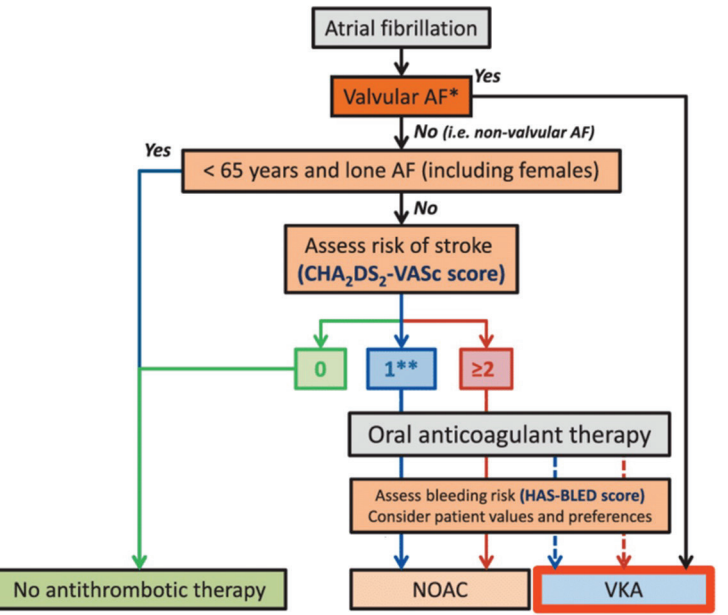


Figure 2. Which patients with atrial fibrillation to start oral anticoagulation. (Adapted from the European Society of Cardiology AF guidelines 2020)

PRE-AEROBIC EXERCISE CARDIAC SCREENING IN ASYMPTOMATIC ADULTS

In Dec 2022, Singapore will host it's annual mass participation endurance event, the Standard Chartered marathon. The increasing interest in running marathons is, in part, due to public health initiatives stressing the benefits of regular aerobic exercise. Aerobic exercise refers to activity that allows the metabolism of stored energy through aerobic glycolysis and fat metabolism through β -oxidation. Large muscle groups are recruited to dynamic activity resulting in substantial increased in heart rate and energy expenditure.

Pre-exercise screening, which is endorsed by the 2020 ESC Guidelines, is used to identify people who may have medical conditions which put them at a higher risk of an adverse event during physical activity/exercise. The transient risk of physical activity should be put into perspective. The probability of an adverse event of a significant nature is extremely low but when they occur, invariably there is a news headline and attracts attention to the health risks of regular exercise, endurance and recreational. <https://www.straitstimes.com/sport/standard-chartered-marathon-singapore-29-year-old-man-dies-after-collapsing-during-half>

It is recognized that most of the exercising aging population engage in team sports or solo recreational exercise for leisure and these individuals have a higher prevalence of risk factors for ischaemic heart disease (IHD) or established disease. In parallel with the physician-led drive to promote regular exercise, our clinic is regularly confronted with consultations on the safety of participation in regular moderate intensity exercise, with a surge of interest in the prelude to the marathon. A balance needs to be achieved on the multiple benefits of exercise, the patient's aspirations for improved cardio-respiratory fitness, their desire to fulfill a personal accomplishment and the small risk of sudden cardiac death.

Screening strategies must be tailored to the target population. Sudden cardiac death (SCD) in young athletes predominantly results from structural and electrical disorders of the heart, including cardiomyopathies, ion channel disorders, and coronary anomalies. Atherosclerotic plaque disruption is the leading condition leading to major adverse cardiovascular events in more senior athletes enjoying recreational exercise. In longer term endurance athletes, myocardial ischaemia can arise from "demand" ischaemia resulting from the imbalance between oxygen supply and the obstruction from a severe stable plaque stenosis.

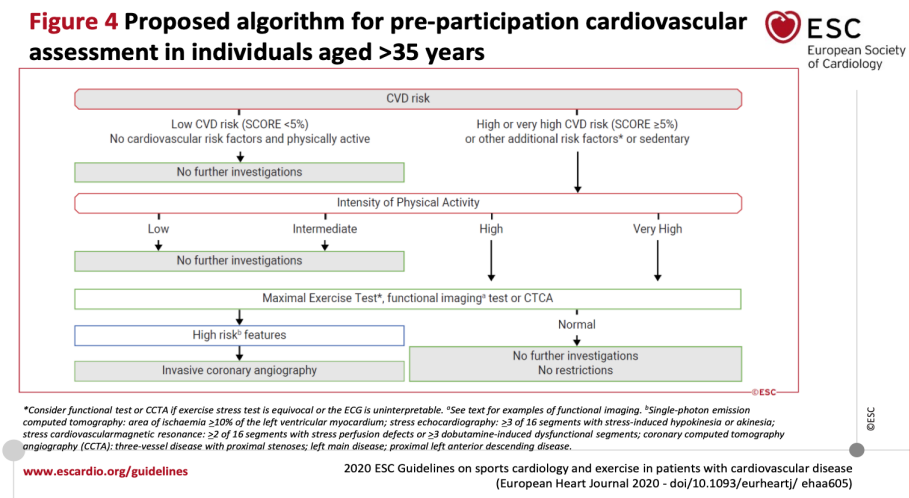
Screening Protocols

Younger athletes - Pre-participation screening questionnaires have a low sensitivity and high positive response rate, rendering them less useful and so not recommended. Physical examination, ECG and an echocardiogram will detect the majority of disorders.

Older (>35 years old) athletes – Recommendations and the evidence base for precision testing is limited. Routine screening for ischaemia with traditional exercise treadmill testing is asymptomatic individuals has a very low positive predictive value and a high number of false positive tests. The latter limitation can be mitigated by the use of exercise stress imaging, which our clinic routinely offers. Exercise testing may also provide additional information on the blood pressure response to exercise, the occurrence of exercise-induced arrhythmias and to assess symptoms of physical performance and it's relation to exercise training. Cardiopulmonary exercise (CPEx) testing is another useful modality in those adults just about to embark on a moderate to vigorous schedule to assess overall performance, facilitating individualized recommendations regarding exercise type, intensity and training zones.

Following normal investigations, there need be no restrictions to sports participation. Although normal testing results which confirm a high exercise capacity is associated with a good prognosis, it has limited sensitivity in diagnosing non-obstructive coronary plaque disease. The subsequent development of symptoms during exercise should always prompt reassessment. In asymptomatic adults stratified to be at high risk or very high risk (diabetes, strong family history of ischaemic heart disease), CT coronary angiography (CCTA) should be considered in the pre-participation risk assessment. Identification of plaque presence should mandate aggressive management of risk factors. In those where obstructive disease is reported, further assessment and treatment is indicated.

A proposed algorithm for CV risk assessment in asymptomatic adults aged > 35 years old with risk factors and/or a possible sub-clinical coronary coronary syndrome before engaging in recreational or endurance sports is summarized in the Figure (from ESC Guidelines 2020).



By **Dr. Sriram Narayanan**

Senior Consultant Vascular & Endovascular Surgeon
The Harley Street Heart & Vascular Centre

By **Dr. Reginald Liew**

Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

By **Dr. Rohit Khurana**

Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre



THE ASSESSMENT OF DYSPNEA IN PATIENTS WITH DIABETES

Diabetes comes with a host of microvascular and macrovascular diseases. Despite treatment, almost 50% of patients with diabetes will die of cardiovascular disease. Patients with diabetes commonly get earlier and more diffuse coronary artery disease, in addition, they are 2-5x more likely to get heart failure than non-diabetics. In one screening study of well-controlled asymptomatic diabetic patients 5% had undiagnosed heart failure with reduced ejection fraction (HFrEF) and 22% had undiagnosed heart failure with preserved ejection fraction (HFpEF).¹

Dyspnea is a common complaint seen in primary care. In patients with diabetes, the two main differential diagnoses to exclude are **ischemic heart disease and heart failure**.

What are the most important initial investigations in a patient with diabetes and dyspnea?

- ECG
- Chest xray
- Haemoglobin
- NTproBNP
- Echocardiogram
- Stress test / CT coronary angiogram

NTproBNP

NTproBNP is an excellent test for excluding heart failure in a breathless patient. If NTproBNP < 125pg/ml or the BNP <35pg/ml in a dyspneic patient then heart failure is very unlikely. If the test is positive then the patient should go on to have an echocardiogram (see flowchart)².

Echocardiogram

If NTproBNP is positive or not available, then the patient should have an echocardiogram to assess for LV dysfunction. This will also allow confirmation of the heart failure phenotype.

Stress Testing/ CT Coronary Angiogram

Diabetic patients can often have silent ischemia. The majority of patients with diabetes have elevated cardiac risk. Dyspnea in a diabetic patient warrants an assessment for ischemia or anatomical imaging with a CT coronary angiogram.

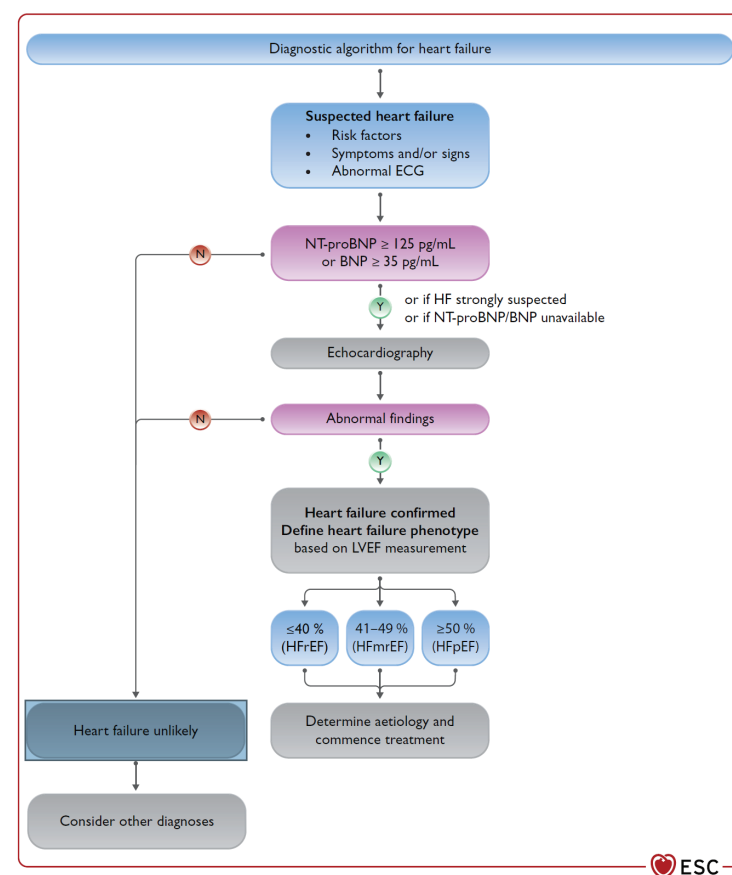
Treatment of Heart Failure

The standard of care in HFrEF is now 4 drug classes in all patients. ACE-I/ARNI, beta-blocker, MRA and SGLT2 inhibitor. In 2021 we finally saw a positive HF trial in patients with LVEF > 40%. SGLT2 inhibitors like empagliflozin (EMPEROR-HF) reduce HF hospitalization and CV death in patients with HFmEF and HFpEF. SGLT2 inhibitors are now the only drug type with a class IIa recommendation in all types of heart failure regardless of ejection fraction and regardless of diabetic status.

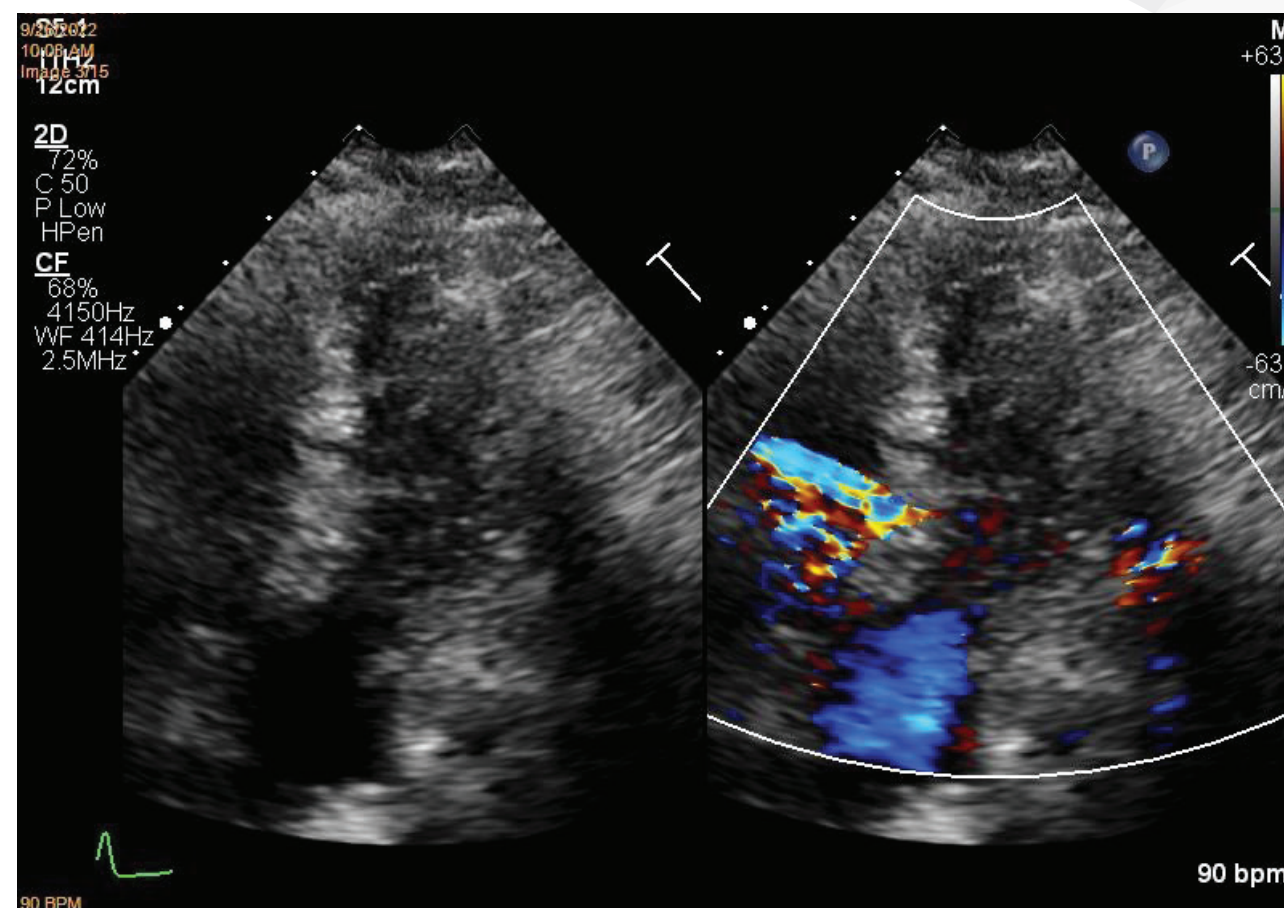
Conclusion

Dyspnea is common in patients with diabetes. The two most important cardiovascular causes are ischemic heart disease and heart failure. NTproBNP, echocardiography and a stress test are simple tools that can provide valuable diagnostic information in these patients.

- 1 - Boonman-de Winter LJ et al. Diabetologia. 2012;55:2154-2162.
- 2 - ESC Heart Failure Guidelines 2021o



QUIZ



A 33 year old gentleman was diagnosed with a cardiac murmur soon after birth. He was lost to follow up. A recent physical examination as part of a pre-immigration medical clearance detected a murmur which led to his referral to our clinic. He was asymptomatic, NHYA -I, and had no clinical signs of congenital heart disease. The murmur was very loud, pan-radiating and heard most at the lower left sternal edge with a palpable thrill. Refer to the apical 5-chamber view on the transthoracic echocardiogram.

What is the diagnosis?

Answer is available on our website:

<http://www.harleystreet.sg/quiz - answers/medbulletin-nov-2022/>

MEDBULLETIN
NOV2022

THE HARLEY STREET
HEART & VASCULAR CENTRE

INTRODUCTION

For our second issue of this newsletter 2002, we will touch on cardiovascular risk stratification focusing on patients with diabetes. Dr Michael MacDonald will share on assessment of dyspnea in patients with diabetes. Primary care physicians play a pivotal role in stroke prevention, particularly in the high-risk group of patients and Dr Reginald Liew will take you through your role. Dr Rohit Khurana will share the ESC guideline-based approach to cardiac screening in asymptomatic adults wishing to participate in high intensity recreational sports and endurance events.

We hope you enjoy the articles and find them relevant to your practice setting. We would like to take this chance to wish all primary care partners a happy holiday season ahead.

From The Harley Street Heart and Vascular Centre

From left to right:
**Dr. Rohit Khurana, Dr. Michael MacDonald,
Dr. Reginald Liew, Dr. Sriram Narayanan**



<http://www.harleystreet.sg/heart>
Email enquiries@harleystreet.sg

LICENSE: MCI (P) 047/02/2022

By **Dr. Michael MacDonald**

Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

By **Dr. Rohit Khurana**

Senior Consultant Cardiologist
The Harley Street Heart & Vascular Centre

Mount Elizabeth Novena
Specialist Centre
#05-30, 38 Irrawaddy Road
Singapore 329563

Gleneagles Hospital
#02-38/41 (Annexe Block)
6A Napier Road
Singapore 258500

Mount Elizabeth
Medical Centre
#11-07, 3 Mount Elizabeth
Singapore 228510