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10 KEY TAKEAWAYS FROM THE LATEST SINGAPORE LIPID GUIDELINES

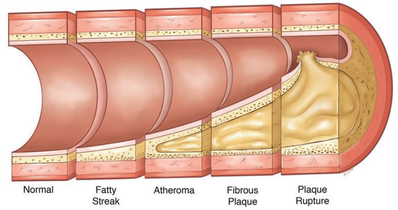
Dyslipidaemia is one of the key cardiovascular risk factors for atherosclerotic heart disease. Unlike hypertension and diabetes where there are clear cutoffs for diagnosis making, the approach to dyslipidaemia is more nuanced and labelling if the low-density lipoprotein cholesterol (LDL-C) is high for a particular patient is determined by their individual profiles.

The Ministry of Health's Agency for Care Effectiveness (MOH-ACE) Clinical Guidance (ACG) for lipid management as well as the Academy of Medicine Singapore Clinical Practice Guidelines (AMS-CPG) released in December 2023 provide a very structured approach to current day LDL-C management. They are a timely update from the 2016 local guidelines.

I am sharing my 10 Key Takeaways from guidelines.

1) Patients with the following existing comorbidities are by default high to very high risk – atherosclerotic cardiovascular disease (ASCVD), familial hypercholesterolemia, chronic kidney disease (eGFR < 60 ml/min/1.73 m2 and/or ACR ≥ 3 mg/mmol) and diabetes mellitus. They do not need further 10-year risk scoring estimates.
2) The minimum LDL-C target in the above group of patients should be < 2.6 mmol/L. Further reduction in targets to less than < 1.8 mmol/l and < 1.4 mmol/l respectively are also advised according to their risk profiles.
3) For those without any of the abovementioned comorbidities but a significantly elevated LDL-C of > 4.9 mmol/L, a moderate intensity statin should be considered.
4) The other patients who do not fall into the previously mentioned subgroups, they should have their 10-year risk estimated with reference to the Singapore modified Framingham Risk Score (SG-FRS-2023). This gives 4 risk categories (low to high risk) with ranges of LDL-C targets from < 1.8 – 3.4 mmol/L.
5) In the primary prevention cohort where the risk is deemed to be borderline to intermediate, risk enhancers are recommended to help further risk stratify. Amongst the available ones, I find the genetically determined Lipoprotein A and CT calcium score of good discerning value. There are online calculators (MESA Risk Score and Lp(a) Clinical Guidance) that incorporate these results into the calculation of risks.
6) In primary practice, Ezetimibe in an effective addition to maximally tolerated statins to achieve the LDL-C targets set out for each patient.
7) Further options in specialist care include injectables (anti PCSK9 therapy).
8) The risk of new onset diabetes from statin is low. It is estimated to be 1 new case per 1000 patients per year of statin exposure.
9) Numerous RCTS have shown that statins have no adverse effects on long term neurocognition. In addition, the incidence of neurocognitive adverse events did not increase with very low LDL-C levels (< 0.50 mmol/L).
10) The goal of lipid management is to reduce the incidence or recurrence of ASCVD through minimising accumulated exposure to LDL-C.

Atherosclerosis



By **Dr Pinakin V Parekh**
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BEYOND STATINS: EXPLORING BEMPEDOIC ACID'S ROLE IN LIPID LOWERING

Bempedoic acid, recently approved for use in Singapore, represents a significant advancement in the management of hyperlipidemia particularly for our statin intolerant patients. Bempedoic acid, is a prodrug that undergoes activation in the liver. Unlike statins, which inhibit the enzyme HMG-CoA reductase early in the cholesterol synthesis pathway, bempedoic acid targets and inhibits ATP citrate lyase (ACL). ACL is a crucial enzyme upstream of HMG-CoA reductase in the cholesterol biosynthesis pathway, converting citrate to acetyl-CoA, a precursor for cholesterol synthesis. By inhibiting ACL, bempedoic acid reduces hepatic cholesterol synthesis, which in turn stimulates the upregulation of LDL receptors and enhances the clearance of LDL cholesterol from the blood.

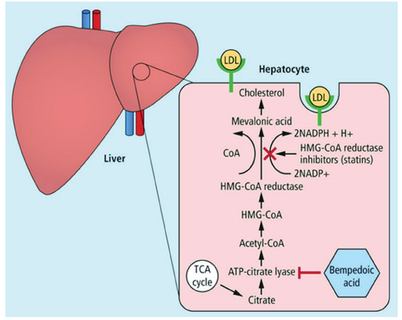
While statins are well-known for their efficacy in reducing cardiovascular risk through lowering LDL cholesterol levels, their use is sometimes limited by side effects such as muscle pain and increased liver enzymes. Bempedoic acid, by acts upstream of HMG-CoA reductase. ACL is found in the liver and not muscle cells. This pathway allows for the reduction of LDL cholesterol without the muscle-related side effects commonly associated with statins. This is particularly beneficial for patients who are intolerant to statins or those who do not achieve their lipid-lowering goals with statins alone.

Side Effect Profile
While bempedoic acid may cause less muscle pain and weakness compared to statins, it is not without its own side effects. Increased risk of tendon rupture, hyperuricemia (which can lead to gout), and elevated liver enzymes have been reported. These side effects, however, are relatively rare. The occurrence of tendon rupture was noted in about 0.5% of cases, often associated with high-dose statin co-administration. Additionally, bempedoic acid does not significantly interact with cytochrome P450 enzymes, which means it has fewer drug-drug interactions compared to statins.

Clinical Trial Evidence
The efficacy and safety of bempedoic acid have been validated in several large-scale clinical trials. For instance, the CLEAR Harmony trial demonstrated that bempedoic acid significantly reduced LDL cholesterol levels by an average of 18% when added to maximally tolerated statin therapy. Moreover, the CLEAR outcomes trial in statin-intolerant patients demonstrated a 21% reduction in LDL accompanied by a reduced incidence of cardiovascular events.

Who will it be for?
Bempedoic acid can be used alongside statins, ezetimibe and PCSK9 inhibitors. It will be a useful tool in patients that are difficult to get to target, particularly those with statin intolerance.

Conclusion
Bempedoic acid is a promising new agent in the lipid management arsenal, offering an effective alternative for patients who are intolerant to statins or require additional LDL cholesterol reduction.



By **Dr Michael MacDonald**
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THE CRUCIAL ROLE OF PRIMARY CARE IN MANAGING HEART FAILURE

Heart failure affects approximately 250,000 people in Singapore, a statistic which is on an upward trend. Primary care plays a crucial role in the management of heart failure, within all stages of the spectrum of this complex syndrome.

Early recognition of the symptoms is the first goal and extracting a detailed history and performing a comprehensive physical examination during routine check-ups is of course crucial. Patients present with symptoms such as shortness of breath, chronic cough, swelling in the legs, or unexplained weight gain and invariably fatigue. By paying particular attention to cardiovascular risk factors cardiovascular risk factors - hypertension, diabetes, obesity, smoking history, hyperlipidemia, and family history of heart disease – coupled with symptoms suggestive of heart failure should raise suspicions to trigger for **diagnostic tests**.

Diagnostic tests include:
1. **ECG:** To assess for abnormal heart rhythms or evidence of prior cardiac damage
2. **CXR:** To assess for signs of pulmonary congestion
3. **Echocardiogram:** To evaluate the cardiac structure and left ventricular function and rule out valvular heart disease and cardiomyopathy. Note that our clinics offer a rapid access echo service for our primary care colleagues. Please visit this link **https://www.harleystreet.sg/cardiac-referral/**
4. **Blood tests:** To assess for biomarkers associated with heart failure, including the renal function, N-terminal pro-B-type natriuretic peptide (NT-proBNP) and a serum iron profile.

If heart failure is suspected or confirmed, then timely referral to the cardiologist by primary care is an important role. Further evaluation and management may follow, such as a cardiac MRI and coronary angiography.

Collaboration with specialists ensures appropriate care for patients with heart failure. This is especially important when it comes to the initiation of **guideline-directed medical therapy** (GDMT), which is summarized in Figure 1. The evidence for early prescription of the "4 pillars" of medical therapy – ARB/neprilysin inhibitor, SLT2-inhibitor, beta blocker and MRA – for heart failure with reduced ejection fraction (HFrEF) is compelling with mortality benefit. Dose titration to the maximal tolerated doses should also fall under the responsibility of primary care.

Follow up of patients by primary care to assess symptoms, fluid status, and functional capacity is mandatory and can be as often as every 1-3 months. Arranging routine laboratory tests, such as electrolyte levels and renal function, to monitor for complications and medication side effects. Educating patients and their primary care-givers, who are usually other family members about daily weight monitoring, salt and fluid restriction and advising them to report significant weight fluctuations promptly. Adjustments of medication based on these parameters may be necessary. Administering the annual flu-vaccine is another primary care function.

Patients should be directed to useful government resources:
https://www.healthhub.sg/a-z/diseases-and-conditions/heart-failure-understanding-it

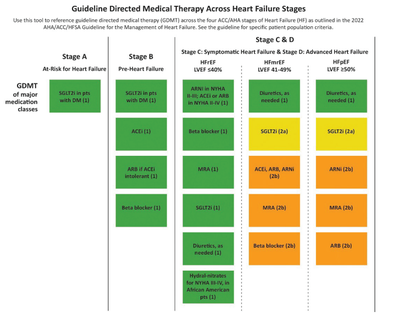
Psychosocial support and the more holistic nature that elderly patients need, arranging home-based or community rehabilitation programs, coordinating home nursing support or occupational therapy can be facilitated by primary care. Hospitalization with decompensated heart failure is a terrible set back for these patients and returning to their baseline level of independence often takes longer with more complex medical co-morbidities to consider.

For patients with advanced heart failure or significant comorbidities, primary care physicians may be asked to discuss advance care planning, palliative care, and end-of-life care preferences. They support patients and their families in making informed decisions about treatment goals and end-of-life care options.

While the direct impact of primary care on heart failure survival may vary depending on Individual patient characteristics and healthcare system factors, the evidence suggests that primary care involvement is integral to optimizing outcomes and reducing mortality in patients with heart failure.

Figure 1

CENTRAL ILLUSTRATION: 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure



By **Dr Rohit Khurana**
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UPDATES ON THE LATEST AMERICAN GUIDELINES FOR ATRIAL FIBRILLATION - AN EMPHASIS ON SCREENING AND EARLIER DETECTION

Atrial fibrillation (AF) remains the most common cardiac arrhythmia in Singapore and around the world and a major cause of disability, including stroke and thromboembolism. Some patients may present with symptoms such as palpitations, breathlessness or dizziness, although many may be asymptomatic but nonetheless be at increased risk of stroke. The updated 2023 American Guidelines for the Diagnosis and Management of Atrial Fibrillation (ACC/ AHA/ACCP/HRS Atrial Fibrillation Guideline)[1] takes into account new data since the last guidelines were written. The new guidelines highlight the need for lifestyle and risk factor modification and the benefits of earlier detection and screening in higher risk patients. It also emphasizes a rhythm control strategy, similar to what is already recommended in the latest European AF guidelines [2], since a number of large studies have shown benefit for patients being in sinus rhythm rather than remaining in AF (especially those with heart failure).

Key new points from the latest American guidelines:

1. **Stages of atrial fibrillation (AF):** AF is now recognized to be a continuum, from at-risk patients with risk factors or structural heart changes (even before developing AF) to patients with traditional paroxysmal or persistent AF types. The new proposed classification allows for earlier intervention at the pre-AF phase using lifestyle and risk factor modification to try to prevent the development of AF or earlier detection through screening of at- risk patients. Measures include more careful weight management, smoking cessation, alcohol moderation, increased exercise and control of risk factors such as hypertension, diabetes and sleep apnoea (Figure 1).
2. **Expanding beyond CHA2DS2-VASc for prediction of stroke and systemic embolism:** Patients should be regularly assessed each year for their risk of thromboembolism and stroke using a validated clinical risk score, such as CHA2DS2-VASc. Those with an intermediate annual risk score who remain uncertain about the benefit of anticoagulation can benefit from consideration of other clinical risk scores to improve prediction and facilitate shared decision making. Stroke risk modifiers include AF characteristics (e.g. AF burden), non-modifiable risk factors (sex), and other dynamic or modifiable factors (e.g. blood pressure control).
3. **Early rhythm control:** With the emergence of new and consistent evidence, the guidelines emphasize the importance of early and continued management of patients with AF that should focus on maintaining sinus rhythm and minimizing AF burden.
4. **Catheter ablation of AF receives a Class 1 indication as first-line therapy in two categories of patients:** a) Younger patients with symptomatic AF and few co-morbidities- Recent randomized studies have demonstrated the superiority of catheter ablation over drug therapy for rhythm control in appropriately selected patients. b) Patients with heart failure and AF with reduced ejection fraction- randomized studies have demonstrated the superiority of catheter ablation over drug therapy for rhythm control in this group of patients.
5. **Updated recommendations for device detected AF:** With more patients using wearables and smart watches, the detection rate of AF has improved. The latest guidelines recognize that more patients will be diagnosed earlier with such devices, allowing for earlier intervention and management.
6. **Left atrial appendage occlusion (LAAO) devices receive higher level Class of Recommendation:** With more data on the safety and efficacy of LAAO devices, the Class of Recommendation has been upgraded to 2a.

How do these updated guidelines affect practice in primary care? The recognition that earlier recognition and management of risk factors that can lead to AF (even before AF develops) is an important change that should prompt primary care physicians to more aggressively tackle these risk factors, such as hypertension, obesity and diabetes. In addition, structural heart changes, such as valvular heart disease or a dilated left atrium, can also increase the risk of AF developing- primary care physicians should have a lower threshold to look for such changes, such as requesting an echocardiogram in higher risk patients.

Primary care physicians should be aware that the detection rate for AF and other arrhythmias will increase as more patients are using smart watches and wearables that can detect their heart rhythm. Earlier detection of AF presents more opportunities for a rhythm control strategy (with catheter ablation or anti-arrhythmic medication), which can reduce the chances of AF progressing over time.

The risk of thromboembolism changes with time in patients with AF as patients get older or develop other co-morbidities, so clinicians should regularly reassess the patient's thromboembolic risk and discuss the need for anticoagulation. Ultimately, the decision for how the AF is best managed and whether patients start anticoagulation should be made jointly with the patient once all the relevant factors have been taken into consideration.

References:

1. Joglar JA, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. Published online November 30, 2023.
2. Hindricks G, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). The Task Force for the Diagnosis and Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2021;42:373–498.

Figure. Pillars for AF management *(Taken from reference 1)*

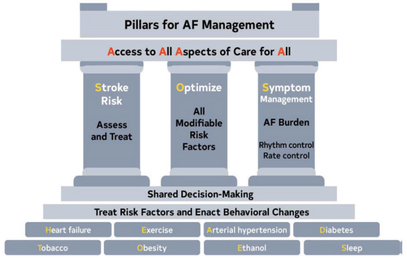

Table. Select Differences Between the 2019 and the 2023 ACC/AHA/ACCP/HRS Atrial Fibrillation Guidelines

[ACC= American College of Cardiology; AF= atrial fibrillation; AHA= American Heart Association; COR= Class of Recommendation; LV= left ventricular].

	2019	2023
Stages of AF	AF is defined in 5 terms: 1. Paroxysmal AF 2. Persistent AF 3. Long-standing persistent AF 4. Permanent AF 5. Nonvalvular AF	Atrial arrhythmia progression is split up into 4 stages: 1. At risk for AF 2. Pre-AF (evidence of structural or electrical findings predisposing a patient to AF) 3. AF (including paroxysmal, persistent, long-standing persistent, and successful AF ablation) 4. Permanent AF
Early rhythm control	A heart rate control (resting heart rate < 80 beats/min) strategy is reasonable for symptomatic management of AF (COR 2a).	In patients with reduced LV function and persistent (or high burden) AF, a trial of rhythm control should be recommended to evaluate whether AF is contributing to the reduced LV function (COR 1).
Catheter ablation of AF as first-line therapy	In patients with recurrent symptomatic paroxysmal AF, catheter ablation is a reasonable initial rhythm-control strategy before therapeutic trials of antiarrhythmic drug therapy, after weighing the risks and outcomes of drug and ablation therapy (COR 2a).	In selected patients (generally younger with few comorbidities) with symptomatic paroxysmal AF in whom rhythm control is desired, catheter ablation is useful as first-line therapy to improve symptoms and reduce progression to persistent AF (COR 1).

By **Dr. Reginald Liew**

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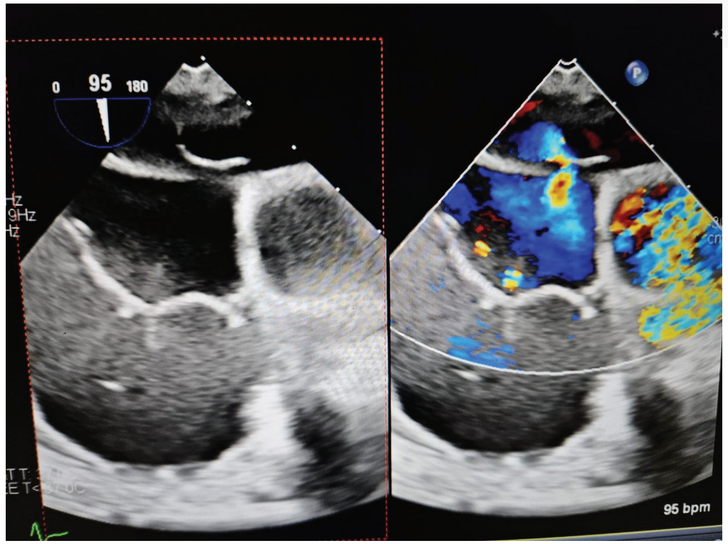
QUIZ

Question:



This 34 year old lady has a history of refractory migraines associated with aura. As part of her investigative work up, she underwent a trans-oesophageal echocardiogram revealing an important structural finding in the inter-atrial septum that is commonly associated with migraines. What does this image show?

Answer is available on our website:
http://www.harleystreet.sg/quiz - answers/medbulletin-apr-2024/

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MEDBULLETIN APR2024

THE HARLEY STREET HEART & VASCULAR CENTRE

INTRODUCTION

Warm wishes from the Harley Street Heart and Vascular Centre! We wanted to continue sharing relevant clinical topics with our primary care colleagues that will value add to your day-to-day practice. For this newsletter, our Harley Steet Cardiologists have written four interesting articles that involves the theme of early screening, detection and management of cardiovascular disease.

Dr Pinakin V Parekh starts of by reviewing the latest lipids guidelines released in Singapore (December 2023). They provide a timely update with very clear targets to strive for in different patient profiles. He emphasizes on using risk enhancers for further risk stratification in primary prevention and gives his top 10 key takeaways from the guidelines. Keeping to the subject matter, Dr Michael MacDonald describes bempedoic acid in detail. This non-statin-based lipid lowering medication has been recently approved locally and provides yet another option for our patients to meet their lipid management targets. He has also included important trial data which validates bempedoic acid's use. Shifting gears, Dr Reginald Liew provides a thorough update on atrial fibrillation. He references the newest 2023 American guidelines and provides a succinct summary of key new points. With more patients having wearable devices and smart watches, earlier detection is now achievable. Of note, catheter ablation in patients with symptomatic atrial fibrillation has a Class 1 indication. With uncontrolled atrial fibrillation being one of the many causes of heart failure, Dr Rohit Khurana provides a framework of the diagnostic workup of suspected patients. Medical therapy spanning different classes of medications from part of the core management of such patients. He reminds about timely referral to specialist care to address reversible causes such as coronary artery disease.

As usual, the newsletter ends with a short quiz aimed to test your clinical judgement and acumen. The answer to the quiz will be posted on our website (https://www.harleystreet.sg/medbulletin/).

We hope these articles will provide a quick snapshot of some cardiovascular topics that are helpful. Please feel free to contact us (at enquiries@harleystreet.sg) if you would like to provide any feedback or request a specific topic in future editions.

From The Harley Street Heart and Vascular Centre

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

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