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CARDIOVASCULAR SAFETY OF SULFONYLUREAS: IT'S A LONG JOURNEY TILL CAROLINA

Dr Manish Bansal, Gurugram

- Although still more evidence is needed, it appears that modern sulfonylureas (SUs) may not be associated with cardiovascular (CV) harm.
- When affordability is not an issue, sodium-glucose co-transporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RA) are preferred in patients at high CV/heart failure risk.
- However, if the cost is an issue, modern SUs are a reasonable alternative.
- CV safety of SUs: It's a long journey till CAROLINA.

RIVAROXABAN: A NEW TREATMENT PARADIGM IN THE SETTING OF VASCULAR PROTECTION?

Dr KP Pramod Kumar, Chennai

The pathophysiology of atherosclerosis involves a diseased endothelium, lipid accumulation and low-grade inflammation. Later stages of coronary artery disease (CAD) and peripheral artery disease (PAD) are characterized by atherothrombosis induced by plaque rupture, caused by fibrin formation and platelet activation, resulting in vessel occlusion, followed by organ damage, such as myocardial infarction (MI), stroke or limb ischemia. The high disease burden associated with CAD and PAD necessitates the need for continuous vascular protection beyond the treatments available at present, including antiplatelet agents.

The factor Xa plays a key role in the etiopathogenesis of atherothrombosis. Experimental data point to the anti-inflammatory and antioxidative potential of rivaroxaban, and also suggest that the drug may improve endothelial dysfunction. The COMPASS trial revealed that in patients with stable atherosclerotic vascular disease, adding rivaroxaban 2.5 mg twice daily (vascular dose) to aspirin yielded a higher cardiovascular protection compared to aspirin alone.

The ROCKET-AF trial noted that in comparison with warfarin, rivaroxaban 20 mg once daily (15 mg if moderate renal dysfunction) (anticoagulant dose) was at least as effective as warfarin for preventing stroke or systemic embolism among patients with nonvalvular atrial fibrillation, with a trend toward a reduction in the risk of cardiovascular outcomes. Rivaroxaban, therefore, might have a vascular protective effect beyond its stroke/systemic embolism preventive activity.

Suggested Reading: [1]Barrios V, Almendro-Delia M, Facila L, et al. Rivaroxaban: Searching the integral vascular protection. Expert Rev Clin Pharmacol. 2018;11(7):719-28. [2]Bauersachs R, Zannad F. Rivaroxaban: A new treatment paradigm in the setting of vascular protection? Thromb Haemost. 2018;118(S 01):S12-S22.

CLINICAL EVALUATION IS ENOUGH TO ASSESS DECONGESTION AND DECIDE ON DISCHARGE IN HEART FAILURE

Dr Ajay Bahl, Chandigarh

- Clinical assessment based on symptoms like edema, breathlessness and orthopnea, weight records, jugular venous pressure, third heart sound on auscultation, and renal function tests should be used to guide therapy and decision on discharging patients with acute decompensated heart failure.
- Natriuretic peptides are useful in the diagnosis and prognostication of acute heart failure.
- However, guided therapy based on natriuretic peptide levels has not been shown to reduce post-discharge clinical events.

ASYMPTOMATIC TO SYMPTOMATIC HEART FAILURE – PREDICTORS OF PROGRESSION

Dr Harikrishnan S, Trivandrum

Progression from Stage A/B of heart failure to Stage C/D should be prevented or delayed to improve the outcomes. Close periodic monitoring is needed. Clinical markers are not very sensitive and specific. We need to use biomarkers like B-type natriuretic peptide (BNP)/N-terminal (NT)-proBNP.

Echocardiographic parameter ejection fraction may not be that sensitive, so parameters like GLS (global longitudinal strain) is found to be very useful. Control of risk factors is the key. BP should be controlled to the level of 130/70-80 mmHg, considering the reverse J curve phenomenon.

Diabetes should be controlled to glycated hemoglobin (HbA1c) levels of 7-8%. Early initiation of renin-angiotensin-aldosterone system (RAAS) blockers, β-blockers and aldosterone blockers may help. SGLT2 inhibitors may be useful; the data is emerging.

WHO BENEFITS FROM TAKING A STATIN, AND WHEN?

Dr BKS Sastry, Hyderabad

The beneficial effects of statins are attributed to their capacity to decrease cholesterol biosynthesis, particularly in the liver, where they are selectively distributed, and to the modulation of lipid metabolism, derived from their inhibition of HMG-CoA reductase. Statins are known to have antiatherosclerotic effects that are positively correlated with the percent reduction in low-density lipoprotein (LDL) cholesterol. Statins also exert antiatherosclerotic effects independently of their hypolipidemic action, which are referred to as their pleiotropic effects.

Guidelines from the US Preventive Services Task Force, American College of Cardiology and American Heart Association suggest four main groups of people who may obtain benefits from the use of statins:

- **Individuals who don't have heart or blood vessel disease, but have one or more cardiovascular disease (CVD) risk factors and a predicted 10-year risk of a heart attack >10%.** People with diabetes, high cholesterol or high blood pressure, or who smoke and whose 10-year risk of a heart attack is >10% constitute this group.
- **People who have CVD related to hardening of the arteries.** This group includes individuals who have had heart attacks, strokes due to blockages in a blood vessel, ministrokes (transient ischemic attacks), PAD or have undergone surgery to open or replace coronary arteries.
- **Individuals with very high LDL cholesterol.** This group includes adults with LDL cholesterol levels of 190 mg/dL (4.92 mmol/L) or higher.
- **People with diabetes.** This group includes adults aged 40-75 years who have diabetes and LDL cholesterol level of 70-189 mg/dL (1.8 and 4.9 mmol/L), particularly if there is evidence of blood vessel disease or other risk factors for heart disease, such as high blood pressure or smoking.

The US Preventive Services Task Force recommends low- to moderate-dose statins in adults 40-75 years of age, having one or more risk factors for heart and blood vessel disease and at least a 1 in 10 likelihood of having a CVD event in the ensuing 10 years.

Suggested Reading: [1]Stancu C, Sima A. Statins: mechanism of action and effects. J Cell Mol Med. 2001;5(4):378-87. [2]Available from: https://www.mayoclinic.org/diseases-conditions/high-blood-cholesterol/in-depth/statins/art-20045772.

DAPA-HF, EMPEROR-REDUCED AND DAPA-CKD: PUTTING IT ALL TOGETHER

Dr John JV McMurray, Glasgow

SGLT2 inhibitors are much more than just effective glucose-lowering therapy for T2D *(think angiotensin-converting enzyme [ACE] inhibitor or statin!).* They reduce the risk of developing heart failure in patients with T2D and chronic kidney disease (CKD) patients (even CKD patients without T2D). They reduce the risk of hospitalization and death in patients with heart failure and reduced ejection fraction, with and without diabetes – and improve symptoms/health-related quality of life. They reduce the rate of decline in estimated glomerular filtration rate (eGFR) in patients with heart failure with reduced ejection fraction (HFrEF) and the risk of end-stage kidney disease (ESKD) in patients with CKD, with and without diabetes. SGLT2 inhibitors protect the heart and kidneys and have become the new "standard of care" in HFrEF and CKD.

CORONARY ARTERY CALCIUM – WHAT LIES BENEATH?

Dr Mona Bhatia, New Delhi

Coronary artery calcium (CAC) is ready for prime time – A strong predictor of CV risk; Cost-effective, safe, widely available. Fully endorsed in the guidelines. Integrates well into our current healthcare landscape to focus on prevention and shared decision-making. CAC is recommended when the individuals' atherosclerotic cardiovascular disease (ASCVD) 10-year risk is uncertain (5-7.5% odds ratio [OR] 7.5 -20%). CAC is a companion diagnostic, helps accurately identify responders, reduce the number needed to treat, with efficient use of scarce resources. Particularly useful in patients who are statin reluctant or statin intolerant. Aids decision for nonstatin/aspirin therapy.

KETO DIET – IS IT SAFE FOR THE HEART?

Dr BRJ Kannan, Madurai

Dietary fat has been projected as a villain in the past 60 years or so. This has led to an increase in the carbohydrate intake to the tune of more than 75% of daily calories. Any diet with a carb content higher than 55-60% of daily calories would increase mortality. Keto diet, a very high-fat diet with <30% calories from carbohydrates, is unsafe for the heart. Any diet with a carbohydrate content of lesser than 40% of daily calories also would increase mortality. For the best CV outcome, we need to balance the diet by increasing the current fat intake to at least 25% of daily calories with a corresponding reduction of carbohydrates to 50-55%.

CARDIOVASCULAR IMPACT OF COVID-19: AN AMERICAN PERSPECTIVE

Dr Mark Huffman, Chicago

- COVID-19 in the US: The problems – Lack of coordination across and within states; Slow reporting of facility-based data to identify and respond to health disparities; Catastrophic health spending; Political polarization, misinformation, widespread distrust.
- The US has the largest burden of diagnosed COVID-19, accounting for 22% of global cases, and will likely have the largest burden of COVID-19 complications, including HF.
- The pandemic exposed the US's fragile and inequitable health system arrangements and under-investments in public health.
- The heart and soul of the US have been battered in 2020; a renewed spirit of cooperation, collectivism and humility are needed, as well as safe, effective and equitably-distributed vaccines.

MANAGING A CVD PATIENT – FROM PRIMARY TO SECONDARY PREVENTION

Dr Peter Lin, Canada

- JUPITER Trial – It was conducted in low-risk patients; patients with (LDL) cholesterol levels of <130 mg/dL and high-sensitivity C-reactive protein levels of 2.0 mg/L or higher were included.
- The trial was stopped after a median follow-up of 1.9 years. There was a 44% reduction in primary endpoint, 54% reduction in MI, 48% reduction in stroke, 46% reduction in revascularization and 20% reduction in death with rosuvastatin therapy.
- HOPE 3 study – It included intermediate risk patients. First co-primary endpoint: Composite of CV death/MI/stroke for rosuvastatin vs. placebo: 3.7% vs. 4.8%, hazard ratio (HR) 0.76, number needed to treat (NNT) = 91. There was no difference in incidence of diabetes in the two groups in the HOPE 3 trial (New-onset diabetes mellitus: 3.9% vs. 3.8%, p = 0.82).
- REDUCE-IT randomized patients to receive icosapent ethyl twice daily or placebo. A primary endpoint event occurred in 17.2% of the patients in the icosapent ethyl group, as compared with 22.0% of the patients in the placebo group, an absolute between-group difference of 4.8% points; the NNT to avoid one primary endpoint event was 21 (95% CI, 15-33) over a median follow-up of 4.9 years.
- Statins should form a good baseline therapy. Drugs like ezetimibe can be added later.
- Studies from the Netherlands, UK and Canada suggest that rosuvastatin is associated with lower incidence of fatal and nonfatal CVD, compared to other statins and there was no evidence of greater risk of myopathy, rhabdomyolysis, acute renal failure and acute liver injury among patients treated with rosuvastatin compared to other statins.

A GLIMPSE INTO THE 70 YEARS LEGACY OF FRAMINGHAM HEART STUDY

Dr Rakesh Yadav, New Delhi

Framingham Heart Study (FHS) has been one of the most important studies for CV health worldwide. It has firmly established various risk factors (hypertension, dyslipidemia, smoking and diabetes) for CVD, heart failure, stroke etc., and paved the path for various randomized, controlled clinical trials that led to the subsequent development and implementation of effective treatments for these conditions. With the USA's changing demographics, changing epidemiology of CV, and the formation of so-called mega-cohorts, the role of FHS has changed over the past 70 years and has maintained its importance in this regard. It remains a lodestar for epidemiological cohort studies for CVD – To understand the trends in risk factors and disease and understand what can be done to lower the risk and burden of CVD. It has also been and will continue to be an important institution to train CVD epidemiologists, biostatisticians and bioinformaticians (FHS has trained >90 fellows over the past three decades). An increasing amount of data from various cohorts is currently being made available via major data repositories, making access to data by investigators not formally affiliated with the FHS much easier. FHS has maintained its legacy even after 70 years of completion.

CARDIOVASCULAR IMPACT OF COVID-19: EUROPEAN EXPERIENCE

Dr Barbara Cassedei, England

- The European response to COVID-19 has been slow and inhomogeneous. This has cost many lives.
- Evidence that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes acute myocarditis is largely absent.
- Interrogation of continuous patient registries and large data sources (e.g., UK Biobank, openSafely, SwedeHeart, NICOR) and digitized health systems have accurately highlighted the disparities in risk and outcomes of COVID-19 and provided the infrastructure for undertaking pragmatic randomized controlled trials.

- Once corrected for age, diabetes, obesity and social deprivation, the excess risk of coronavirus disease 2019 (COVID-19) death conferred by CVD is relatively small. The impact of the pandemic on non-COVID-19 mortality has been significant. This may have contributed to the excess non-COVID-19-related mortality observed during the first wave of the pandemic.

LDL-C MANAGEMENT: TARGET-BASED OR DOSE-BASED?

Dr Sadanand Shetty, Mumbai

I will continue with high-dose statin irrespective of low LDL cholesterol.

Why is longer therapy with high-intensity statin required?

- Longer the better: Takes time for complete clinical benefit from the time of LDL-lowering.
- Lowest LDL levels are best: No safety concerns with low LDL levels.
- The incremental benefit with absolute LDL reduction: Reduce residual risk.

I WILL NOT RECOMMEND ABPM ROUTINELY

Prof (Dr) Vitull K Gupta, Bathinda

- Hypertension is one of the most prevalent CVD risk factors. Accurately measuring BP is essential for proper diagnosis and management.
- Recent guidelines recommend that the diagnosis of hypertension (HTN) should be based on repeated office BP measurements or ambulatory BP monitoring (ABPM) if economically feasible.
- Evidence substantiates the value of ABPM and home BP monitoring (HBPM) but does not recommend universal use of ABPM for diagnosis and management of HTN.

So, I will not recommend ABPM to all the patients routinely because of the paucity of available resources, both human and financial, and guidelines do not suggest universal use of ABPM.

ACUTE CORONARY SYNDROME

Prof (Dr) PS Banerjee, Kolkata

- Acute coronary syndrome (ACS) is a potentially life-threatening condition that affects millions of individuals each year.
- Diagnosis is based on serial ECG and cardiac marker levels, particularly using new, highly sensitive troponin T estimation.
- Initial ACS management should include risk stratification, appropriate pharmacologic management including dual antiplatelet therapy, anticoagulation and appropriate adjuvant therapies and a decision to pursue early invasive or conventional treatment strategy.
- Long-term management following an ACS event should follow evidence-based recommendations and should be individualized to each patient.

EGGS AND CARDIOVASCULAR HEALTH

Dr S Sivasankaran, Thiruvananthapuram

Egg yolk rich in cholesterol should be avoided in the diet to ensure vascular health. Cholesterol is unique to the animal kingdom and is insoluble in water. It is a crucial component of the cell membrane and steroid hormones. All cells synthesize adequate cholesterol. Dietary cholesterol reaches the cells via transport proteins and receptors. Downregulation of receptors allows cholesterol in the transport protein LDL to remain in circulation for longer, which can turn out to be vasculotoxic. Keeping LDL (a protein that transports cholesterol) below 70 mg/dL is ideal to preserve vascular health. Therefore, avoiding egg yolk in the diet is a key dietary prevention strategy for Indians at high risk for vascular disorders and diabetes.

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