U.P Chapter of Cardiological Society of India

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From the desk of the Editor – Dr Roopali Khanna

Dear Readers,

We are glad to embark on this new issue of the Newsletter in September 2024. This issue is an amalgamation of critical reviews of recently published cardiology trials and their impact on daily clinical practice.

This issue features a diverse range of topics, from the latest drugs in the management of heart disease to the newer domain of artificial intelligence. In the end, there is a take-home message of recently released guidelines from the European Society of Cardiology. Our contributors have worked tirelessly to bring you relevant and resonant content.

Thank you for your continued support. I hope this issue provides you with knowledge, inspiration, and perhaps even a new perspective.

We also anticipate an excellent Midterm Intervention Conference, UPCSI-2024, by Dr. Awadhesh Sharma, at Hotel Taj Mahal, Lucknow, on 22nd September 2024.



Statins in Heart Failure: What is the evidence

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Data from two prospective, large RCTs performed exclusively in chronic systolic HF:

- The Corona (Controlled Rosuvastatin Multinational Trial in Heart Failure) included 5,011 patients (≥60 years of age) with ischemic systolic HF, LVEF < 40% (mean 31%), NYHA class II-III (~63% in Class III) and randomly assigned them to either 10 mg rosuvastatin (*n* = 2,514) or placebo (*n* = 2,497). At a median follow-up of 32.8 months, there was no significant reduction in the primary endpoint (a composite of CV death, nonfatal MI, and nonfatal stroke. ***The study concluded that despite having favorable biological effects (i.e., reduction in LDLc, TG, and hsCRP and an increase in HDLc) and an acceptable safety profile in moderate-to-severe HF, the long-term clinical outcomes were unaffected.***

- The Gissi-HF (Gruppo italiano per lo studio della sopravvivenza nell'infarto miocardico–Heart Failure) included 4564 patients (mean age 68 years, 44% >70 years),mean LVEF 33%, NYHA class II-IV (36% class III) with chronic systolic heart failure). In contrast to the CORONA study, patients were younger, with mixed etiologies of HF (40% ischemic, 35% DCM, 18% HT), had less advanced HF (37% in NYHA class III-IV), and 10% had LVEF > 40%. At a median of 3.9 years, although there was a reduction in LDLc and hsCRP, there was no reduction in the primary endpoints of time to death and time to death or admission to hospital for CV reasons. ***Similar to what was reported by the CORONA study, the GISSI-HF study also established the safety of statins in patients with chronic systolic HF but did not show any incremental benefits in reducing adverse clinical outcomes.***

Possible reasons for the lack of benefits in CORONA and GISSI-HF:

- Patients were older and sicker: CORONA: mean age 73 years, 41% > 75 years, GISSSI-HF: mean age 68 years, 43% > 70 years) and it was probable that many had established CAD. Over 60% in CORONA and 35% in GISSI-HF had NYHA class II-IV HF. Hence, the patients had moderate to severe symptomatic HF rather than symptomatic CAD.
- The annualized mortality was ~ 10% and ~ 7.4% in the CORONA and GISSI-HF respectively.
- The majority of CV deaths were driven by worsening HF and sudden deaths, while the rate of nonfatal MI and stroke were relatively lower in this population.

Message: The plaque stabilisation and pleiotropic effects of rosuvastatin are more likely to modify atherothrombotic vascular events like MI and stroke rather than CV deaths/sudden death, possibly explaining its lack of benefit in the two studies. It is possible that these patients may have had atherosclerotic or myocardial disease that was too advanced to modify, and rosuvastatin might have had more favorable effect in patients with milder HF.

Pooled data analysis of both trials

Feinstein et al. pooled the data from the CORONA and GISSI-HF to improve the power to detect any statistically significant differences in atherothrombotic events by competing risk analyses. In this pooled analysis of CORONA study (all of whom had ischaemic HF) and GISSI-HF study participants with ischemic etiology of HF, a 19% risk reduction in first incident MI's was observed (HR 0.81, 95% CI 0.66–0.99, *P* <0.05) with rosuvastatin, with a number needed to treat to prevent one MI as 94. ***This significant reduction in risk for MI amongst those with ischaemic etiology of HF is consistent with previous findings of pooled data of non-HF patients.*** However, the absolute risk reduction for MI was comparatively small since only a few patients had an MI due to their elevated risks from other causes of death.

Which subset of HF patients would benefit?

Two sub-analyses of the CORONA study focused on the possibility of assessing a threshold point for cardiac biomarkers below which patients with HF would demonstrate a favorable outcome and greater benefit with rosuvastatin.

- Of the 5,011 patients enrolled in the CORONA study, 73% had an available NT-proBNP level. This was measured in 3,664 (73%). Cleland et al. divided the patient population into tertiles of NT-proBNP (< 868, 868–2,347, and > 2,347 pg/ml). Log NT-proBNP was the strongest predictor of every clinical outcome, with the HR for death from worsening HF as 1.99; 95% CI 1.71 to 2.30). ***The maximum benefit with rosuvastatin was observed in patients in the lowest tertile of NT-proBNP (< 868 pg/ml) with a 35% risk reduction in the primary endpoint*** (HR: 0.65; 95% CI: 0.47 to 0.88). The effect was entirely driven by fewer MIs, strokes, and CV deaths in the lowest tertile, reflecting fewer atherothrombotic events with rosuvastatin. This benefit was seen independent of the effect of rosuvastatin on lipid profile and hsCRP in each tertile of NTproBNP.
- Plasma galectin-3, which is part of the family of b-galactoside-binding lectins and plays a regulatory role in fibrogenesis, inflammation, and cell proliferation, is thought to be a marker for irreversible myocardial fibrosis and poor prognosis in HF. It was measured in 29% of the CORONA participants. Gullestad et al. reported that ***patients with median galectin-3 (≤19.0 ng/mL), when assigned to rosuvastatin, had lower primary event rate*** (HR 0.65; 95% CI, 0.46–0.92; P = 0.014), lower total mortality (HR 0.70; 95% CI, 0.50–0.98; p = 0.038), and lower event rate of all-cause mortality and HF hospitalizations (HR 0.72;95% CI, 0.54–0.98; P = 0.017) compared with placebo. No benefit was observed in patients with higher levels of galectin-3. ***A combination of both low galectin-3 and NT-proBNP identified patients with the largest benefit with rosuvastatin*** (HR 0.33; 95% CI, 0.16–0.67; p = 0.002), reflecting the fact that a combination of biomarkers was perhaps a better prognostic marker.

Message: ***Biomarkers like NT-proBNP and galectin-3 can help identify a subset of ischemic HF patients who might benefit from treatment with statins***. Initiating statins early in the course of ischemic HF (when the biomarkers are not very high: tertile 1 of CORONA, NT-pro BNP < 868 pg/ml, and galectin-3 ≤19.0 ng/mL), may be associated with maximum clinical benefit.

Meta-analysis of statins in HF:

- Data from 10 prospective RCTs of statins in HF (n=10,192 patients) was analyzed by Lipinski et al. to assess the effect on hospitalization for worsening HF, LVEF, major adverse cardiovascular events, and safety outcomes. Rosuvastatin was used in 3 trials, atorvastatin in 6, and simvastatin in 1. ***No impact on all-cause or cardiovascular mortality was observed; statins significantly reduced hospitalizations for worsening HF*** (OR 0.67, p = 0.008) ***and improved LVEF*** (+ 4.2% increase in LVEF, 95% CI 1.3 to 7.1, p = 0.004). ***Lipophilic statin (atorvastatin) significantly reduced all-cause mortality*** (OR 0.39, p = 0.004) ***and decreased hospitalization for worsening HF*** (OR 0.30, p < 0.000 01), ***while no benefit was seen in those receiving hydrophilic statin (rosuvastatin)***.
- Meta-analysis of 17 studies (n = 88,100; 2 RCTs and 15 cohort studies) by Bielecka-Dabrowa et al revealed that ***statin use in HF was associated with lower all-cause mortality*** (HR 0.77, 95% CI 0.72–0.83, p < 0.0001) ***CV mortality*** (HR 0.82, 95% CI: 0.76–0.88, p < 0.0001) and ***CV hospitalization*** (HR 0.78, 95% CI: 0.69–0.89, p = 0.0003). [38] Benefit was seen in patients with EF<40% and EF ≥ 40% (reduction in all-cause mortality 23% and 25%, reduction in CV mortality 14% and 17%, and reduction in CV hospitalizations 20% and 24%, respectively). ***The favorable effects on clinical outcomes were larger in magnitude for lipophilic than hydrophilic statins.***

Message: Cumulative evidence from these meta-analyses suggested that statins may benefit CV outcomes irrespective of HF etiology. Although lipophilic statins seem more favorable for patients with heart failure, one must remember that rosuvastatin (a hydrophilic statin) was associated with a significant decrease in CV hospitalization in the CORONA trial.

Although data ***showed that lipophilic statins were more effective in HF*** in terms of improvement in LVEF, reduction in BNP, all-cause mortality, cardiovascular mortality, and hospitalisation for worsening HF, ***no randomized trial has been performed with lipophilic statins like atorvastatin in HF, and more studies are needed to clarify this issue.*** In contrast to these studies, a modestly ***reduced risk of incident HF in a large US national database of HF patients initiated on high-intensity hydrophilic statins*** (mainly rosuvastatin) when compared to lipophilic statins was reported.

HF preserved EF:

Limited data are available on the role of statins in patients with HF and preserved systolic function (HFpEF). In light of the paucity of data from RCTs in patients with HFpEF, the decision to start statins should be based on other indications, like the presence or absence of ASCVD and LDL-c above guideline cutoffs.

Guidelines

The European Society of Cardiology (ESC) guidelines recommend that, based on current evidence, routine administration of statins in patients with HF without other indications for their use (e.g., CAD) is not recommended. Since there is no evidence of harm in patients on statin treatment ***after the occurrence of HF***, there is

no need for discontinuation of therapy if the patients are already on statins. Treatment with statins is recommended in patients at high risk of CV disease or with CV disease in order to prevent or delay the onset of HF and to prevent HF hospitalizations as a Class I indication.

The LAI guidelines offer the following comprehensive and detailed recommendations for patients with HF:

1. Patients with ischemic HF (NYHA Class II-III) should be started on statins.
2. If a patient with CAD develops symptomatic HF, statins can be continued to achieve a 50% reduction in LDLc.
3. Patients of ischemic HF awaiting cardiac transplantation should be given statins.
4. Statin therapy is not recommended in advanced HF patients who have a short life expectancy (e.g., Because of comorbidities like malignancy).
5. Statins are not recommended for advanced severe HF (NYHA Class IV), if there are no other indications for starting statins.
6. Patients with advanced symptomatic HF need individualized therapy. Although rosuvastatin 10 mg/day was found to be safe in advanced HF patients in CORONA and GISSS-HF, no benefit was observed. Since significantly fewer hospitalizations were noted with rosuvastatin in the CORONA study, a statin with potency equivalent to rosuvastatin 10 mg is recommended if statin therapy is deemed necessary for advanced HF patients.
7. Statins are not recommended in patients with dilated cardiomyopathy or non-ischemic HF solely for the management of HF.

Suggested Reading

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Long-Term Beta Blockade After Myocardial Infarction: *To Interrupt Or Continue?*

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Introduction

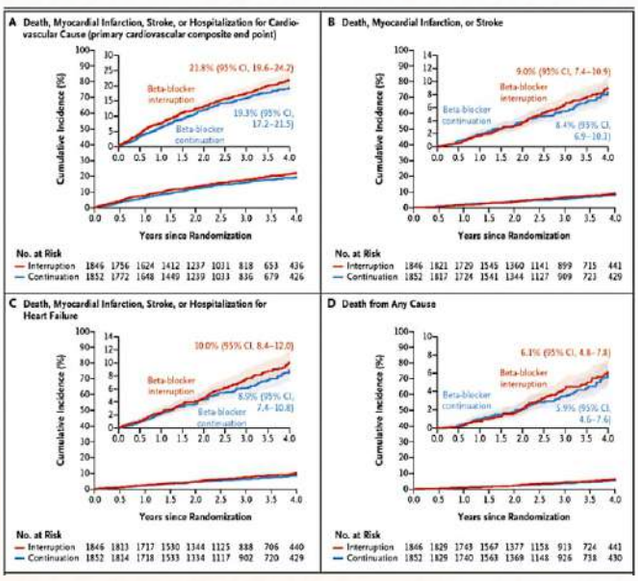
The efficacy and duration of beta-blocker treatment after myocardial infarction, a topic of significant importance, is well documented. The lack of contemporary large-scale randomized trials and consensus recommendations on the duration of beta-blocker therapy after myocardial infarction underscores the need for further research in this area. This gap has resulted in lifelong therapy in many patients, making this class of drugs one of the most prescribed worldwide. The efficacy of beta-blocker therapy in myocardial infarction patients is rooted in trials conducted before the modern era of myocardial reperfusion and pharmacotherapy. This historical context is crucial in understanding the evolution of this treatment, especially considering the significant decrease in heart failure and death risks post-myocardial infarction due to early coronary reperfusion therapy. Two recent trials published this year (2024) have endeavoured to throw some light on long term beta-blockade following MI.

ABYSS trial

This study was a multicentre, open-label, randomized, non-inferiority trial conducted at 49 sites in France. The patients had a left ventricular ejection fraction of at least 40% and were receiving long-term beta-blocker treatment. They had no history of cardiovascular events in the previous six months. The primary endpoint was a composite of death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for cardiovascular reasons at the longest follow-up (minimum one year), according to an analysis of non-inferiority (defined as a between-group difference of <3 percentage points for the upper boundary of the two-sided 95% confidence interval). The secondary endpoint was the change in the quality of life as measured by the European Quality of Life–5 Dimensions questionnaire.

A total of 3698 patients underwent randomization – 1856 to the interruption group and 1852 to the continuation group. The median time between the last myocardial infarction was 2.9 years, and the median follow-up was 3.0 years. A primary outcome event occurred in 432 (23.8%) in the interruption group and 384 (21.1%) in the continuation group (risk difference 2.7 percentage points; 95% confidence interval, <0.1 to 5.5), for a hazard ratio of 1.16 (95% CI, 1.01 to 1.33; p=0.44 for non-inferiority). Beta-blocker interruption did not seem to improve the patients' quality of life. Beta-blocker interruption did not seem to improve the patient's quality of life.

To sum up, in patients with a history of myocardial infarction, interruption of long-term beta-blocker treatment was not found to be non-inferior to a strategy of beta-blocker continuation.



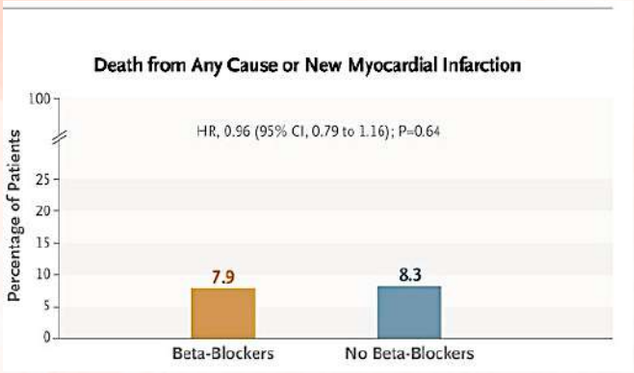
REDUCE-AMI study

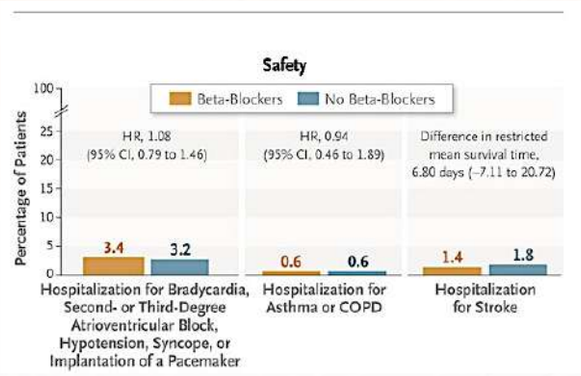
It was another clinical trial conducted at 45 centers in Sweden, Estonia, and New Zealand assessed the effectiveness and safety of long-term oral beta-blocker treatment started early in patients with acute myocardial infarction and preserved left ventricular ejection fraction. The trial was registry-based, prospective, parallel-group, open-label, and randomized.

020 patients (95% of whom were from Sweden) who had experienced an acute myocardial infarction and had undergone coronary angiography with a left ventricular ejection fraction of ≥50% were divided into two groups: one receiving beta-blocker treatment (with either metoprolol or bisoprolol) and the other receiving no beta-blocker treatment. The primary outcome studied was a combination of death from any cause or new myocardial infarction.

The study had a median follow-up period of 3.5 years. Out of 2508 patients in the beta-blocker group, 199 (7.9%) experienced a primary endpoint event, while in the no–beta-blocker group, 208 out of 2512 patients (8.3%) experienced the same (hazard ratio, 0.96; 95% confidence interval, 0.79 to 1.16; P=0.64). The use of beta-blocker treatment did not result in a lower cumulative incidence of secondary endpoints such as death from any cause (3.9% in the beta-blocker group and 4.1% in the no–beta-blocker group), death from cardiovascular causes (1.5% and 1.3%, respectively), myocardial infarction (4.5% and 4.7%), hospitalization for atrial fibrillation (1.1% and 1.4%), and hospitalization for heart failure (0.8% and 0.9%). Regarding safety endpoints, hospitalization for bradycardia, second- or third-degree atrioventricular block, hypotension, syncope, or pacemaker implantation occurred in 3.4% of the patients in the beta-blocker group and 3.2% of those in the no–beta-blocker group. Hospitalization for asthma or chronic obstructive pulmonary disease was observed in 0.6% of patients in both groups, and hospitalization for stroke occurred in 1.4% of the beta-blocker group and 1.8% of the no–beta-blocker group.

In a nutshell, among patients with acute myocardial infarction who underwent early coronary angiography and had a preserved left ventricular ejection fraction (≥50%), long-term beta-blocker treatment did not lead to a lower risk of the composite primary end point of death from any cause or new myocardial infarction than no beta-blocker use.





Guidelines

The ACC/AHA guidelines recommend that physicians start beta-blockers in ACS patients with STEMI (class I recommendation, level of evidence B) and NSTE-ACS patients with and without impaired systolic function (class IIa, level of evidence C). However, for the management of chronic coronary disease, it's essential to reassess the need for long-term regular beta-blocker use (beyond one year) in post-MI patients to reduce MACE (class IIb, level of evidence B). The 2024 European Society of Cardiology guidelines for the management of chronic coronary syndrome acknowledge that there is a gap in the evidence regarding the long-term benefit of beta-blocker therapy in post-MI patients. The duration of beta-blocker therapy is a matter of debate in MI patients with preserved LVEF.

Conclusion

The duration of long term betablocker therapy after acute MI still remains a grey area. For patients with LV dysfunction, beta blocker therapy is sine-qua-none while with preserved ejection fraction the indications are not so strong. A patient-physician discussion and use of third generation beta blocker (with high selectivity & vasodilatory properties) will be the way forward in such cases.

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Insights On Dapt Abbreviation And De-Escalation From Ultimate Dapt Trial-

Are we heading towards an aspirin-free strategy

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The recently presented ULTIMATE-DAPT trial by Zhen G. et al, at the ACC Congress 2024, which was simultaneously published in the LANCET journal, has brought this question again into the light. The trial examined both the clinically significant bleeding endpoints and ischemic endpoints in post-percutaneous coronary intervention (PCI) acute coronary syndrome (ACS) patients from the IVUS-ACS study. Around 3400 post-PCI ACS patients

were randomized to either continue dual antiplatelet therapy (DAPT) (ticagrelor with aspirin) for 12 months or de-escalate to ticagrelor (P_2Y_{12} inhibitor) monotherapy after one month of DAPT and compared for study endpoints after 12 months of follow up. The results showed that there were no significant differences between the two groups in terms of either bleeding or ischemic events. Compared to earlier trials, the ULTIMATE DAPT trial was different in being a double-blind placebo-controlled trial, and besides studying safety endpoints, it also investigated the efficacy endpoints with ticagrelor monotherapy in ACS patients presenting within 1-month of the index event [1]. The earlier published Korean study T-pass trial, enrolling around 2823 ACS patients including 40% ST-segment elevation in Myocardial Infarction (STEMI) cases, had presented similar results. It evaluated the effects of early aspirin discontinuation within 1-month post-PCI in these ACS patients. The study achieved both the non-inferiority and superiority margins for ticagrelor monotherapy over 12-month DAPT for combined ischemic and bleeding endpoints, results being primarily driven by the bleeding endpoints. In this trial, aspirin was discontinued as early as the median 16th day post-randomization. The trial was, however, criticized for being open-label and enrolling low-risk ACS patients [2]. Further, the T-PASS trial had fewer major bleeding and ischemic endpoints during the study period, limiting its power for results. The lower-than-anticipated rates of ischemic endpoints could be due to the lower complexity of the coronary lesions, the higher utilization of imaging modalities for PCI, and the use of biodegradable polymer sirolimus-eluting stents [2]. While the ULTIMATE-DAPT trial addressed the issue of blinding, the trial population enrolled in it, was again a lower-risk population with fewer clinical events and the majority (around 70%) having single vessel disease and employed intravascular ultrasound (IVUS) based revascularization strategies in 99% cases [1]. This concept of more potent P_2Y_{12} inhibitor monotherapy to maintain a trade-off between ischemic events and major bleeding has been tested in earlier trials as well. However, the timing of de-escalation was suggested to be after 3 months. This was first demonstrated by the TWILIGHT trial [3]. The trial enrolled a high-risk PCI patient population of around 4000 patients mainly non-ST-segment-elevation myocardial infarction (NSTEMI) and unstable angina cases. Its primary analysis showed that there was a significant reduction in the BARC 2, 3, or 5 bleeding without any increased risk of major adverse cardiovascular events. Another previous landmark trial was the GLOBAL LEADERS trial. It enrolled both ACS and stable angina patients and although it failed to show the superiority of ticagrelor monotherapy against the continuation of DAPT for ischemic endpoints at 12 months, its post-hoc analysis suggested that de-escalation to ticagrelor monotherapy at 1 month in high bleeding risk ACS patients may work in reducing major bleeding episodes [4]. More recently TICO trial evaluated around 3000 ACS patients who were deescalated to ticagrelor monotherapy after 1-month post-PCI

and compared them with the DAPT continuation group after 12 months. The trial showed that ticagrelor monotherapy after 1month of DAPT was again non-inferior to 12 DAPT. Although the trial suffered from open label non-placebo-controlled design and had enrolled low-risk patients utilizing biodegradable polymer drug-eluting stents (DES). Thus the message was clear [5]. The results of these trials together suggested that not only ticagrelor monotherapy was feasible in post-PCI patients without an added risk of ischemic events but it could be implemented as early as 1-3 months of the index procedure. This was reflected in both the European and ACC guidelines. European guidelines favoured de-escalation to monotherapy after 3-6 months of DAPT in post-PCI patients having high bleeding risk while ACC guidelines recommended an earlier de-escalation at 1-3 months [6] [7].

The choice of P_2Y_{12} inhibitors however has been limited to more potent molecules namely ticagrelor and prasugrel. STOP-DAPT-2-ACS trial employing clopidogrel monotherapy 1-3 months post-PCI ACS patients failed to show non-inferiority between clopidogrel monotherapy and 12-month DAPT for ischemic endpoints [8]. This may be because of the direct action of ticagrelor and genetic variability in response to the clopidogrel molecule.

Can prasugrel work as monotherapy in such patients? Perhaps yes. However, STOP-DAPT-3 using prasugrel monotherapy in lower doses failed to achieve superiority margins against 12 months of DAPT and there was a hint towards increased coronary events [9]. Then another question that surfaces is can aspirin itself work as monotherapy in the post-PCI period while achieving lower bleeding endpoints? This was evaluated in the SMART DATE trial. The SMART DATE trial, however, failed to show non-inferiority with aspirin monotherapy after 6 months of DAPT against 12 months of DAPT [10].

Thus, so far, only the trials using ticagrelor monotherapy have succeeded in achieving the balance between the major bleeding events and ischemic endpoints namely, the GLOBAL LEADERS, TWILIGHT, TICO, T-PASS, and now the ULTIMATE DAPT trial adds to this accumulating evidence.

Some further inferences to be drawn from these trials can be that with the availability of newer DES technology and the use of imaging modalities in PCI, probably we can have a subset of post-PCI patients who have low anatomical complexity and post-procedural risk for coronary events where continuing with ticagrelor monotherapy alone after 1 month of DAPT may suffice. A time may come when this corollary may extend to a wider population and such monotherapy can be implemented as early as immediate post-PCI. One study named OPTICA evaluated such

concept of P2Y12 inhibitor (ticagrelor or clopidogrel) monotherapy directly after OCT-guided PCI showing no increase in safety concerns, and highlighted the need for further randomized controlled trials [11]. But as of now, this decision to start with a single antiplatelet remains unanswered and invites more clinical evidence before there is a change in recommendations.

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The Triple Threat: Semaglutide's Efficacy in Diabetes, Obesity, and Heart Failure

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Introduction

Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that has garnered significant attention due to its efficacy in treating multiple chronic conditions, including type 2 diabetes, obesity, and heart failure. Initially developed as a diabetes drug, semaglutide has since shown substantial benefits beyond glycaemic control, notably in weight reduction and cardiovascular health. Its broad-spectrum effects have led to a rethinking of how metabolic and cardiovascular diseases are treated. This presentation will explore semaglutide's role in managing obesity, diabetes, and heart failure, backed by clinical evidence, and its potential to redefine therapeutic approaches to these interrelated conditions.

Mechanism of Action

Semaglutide mimics the natural hormone GLP-1, which is secreted by the intestine in response to food intake. GLP-1 enhances insulin secretion, suppresses glucagon release, slows gastric emptying, and promotes satiety. These effects not only lead to improved glucose control but also have profound impacts on weight reduction and cardiovascular protection.

1. Glycaemic Control: Semaglutide stimulates insulin release in a glucose-dependent manner, making it an effective treatment for type 2 diabetes. Its ability to lower blood glucose levels with a reduced risk of hypoglycaemia is a significant advantage over traditional therapies.

2. Weight Loss: Semaglutide action on the brain's appetite regulation centres leads to reduced appetite and promoting early satiety. It also affects the reward pathways, helping individuals better control their food intake, which leads to significant weight loss in patients, making it a valuable option for individuals with obesity, both with and without diabetes.

3. Cardiovascular Benefits: Semaglutide's cardiovascular effects are attributed to a combination of glycaemic control, weight loss, anti-inflammatory properties, and improvements in endothelial function.

Semaglutide in Obesity

Obesity is a global public health issue, and traditional lifestyle interventions and pharmacotherapies often fall short in delivering sustainable results. Semaglutide has emerged as a promising therapy for long-term weight management.

The landmark STEP (Semaglutide Treatment Effect in People with Obesity) trials demonstrated that once weekly semaglutide at a higher dose (2.4 mg) led to significant weight loss in patients with obesity, regardless of diabetes status. Participants in the trial lost an average of 15-20% of their body weight over 68 weeks. This is particularly notable, as previous pharmacotherapies typically resulted in 5-10% weight loss.

Implications for Obesity Treatment: The success of semaglutide in weight loss has changed the landscape of obesity treatment. Its use in conjunction with lifestyle modifications has become a cornerstone of modern obesity management.

Semaglutide in Type 2 Diabetes

Type 2 diabetes is a metabolic disorder characterized by insulin resistance and hyperglycaemia. Effective management of blood glucose levels is crucial to reducing the risk of complications like cardiovascular disease, neuropathy, and retinopathy.

Numerous trials, including the SUSTAIN (Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes) program, have shown that semaglutide significantly lowers HbA1c levels, often leading to target achievement in more than 70% of patients. This glycaemic control is sustained over long periods, making semaglutide a durable option for diabetes management.

Compared to other GLP-1 receptor agonists like liraglutide and dulaglutide, semaglutide demonstrates superior efficacy in both glucose control and weight loss. Additionally, its once-weekly dosing offers greater convenience and adherence potential than daily options.

Beyond Glycaemic Control: Semaglutide's benefits extend beyond glycaemic control. Its weight reduction properties are particularly advantageous for people with type 2 diabetes, who often struggle with obesity. The dual effect on glucose and weight makes semaglutide a preferred treatment in diabetes guidelines.

Semaglutide in Heart Failure and Cardiovascular Disease

Heart failure and cardiovascular disease are leading causes of morbidity and mortality in people with diabetes and obesity. Traditional therapies for these conditions focus on managing symptoms and slowing disease progression, but semaglutide offers a novel approach by addressing the root metabolic causes.

Semaglutide's cardiovascular benefits were first noted in the SUSTAIN-6 and PIONEER-6 trials. These studies showed a significant reduction in major adverse cardiovascular events (MACE), including heart attack, stroke, and cardiovascular death, in patients treated with semaglutide compared to placebo. The cardiovascular protection observed in these trials led to its approval for reducing cardiovascular risk in people with type 2 diabetes and established cardiovascular disease.

The STEP-HFpEF trial (Semaglutide Treatment Effect in People with obesity and Heart Failure with Preserved Ejection Fraction) investigated its efficacy in heart failure patients, particularly those with heart failure with preserved ejection fraction (HFpEF), a condition often associated with obesity. In the trial, semaglutide showed promising results in improving physical function, reducing symptoms and improving exercise capacity in patients with HFpEF. Participants also experienced substantial weight loss (around 13% over 52 weeks). Semaglutide led to improvements in quality of life compared to the placebo group. Semaglutide's weight reduction effect is thought to play a critical role in alleviating heart failure symptoms, as excess body weight can exacerbate cardiac workload and inflammation, contributing to HFpEF progression.

The STEP-HFpEF trial represents a significant step toward expanding the use of GLP-1 receptor agonists like semaglutide in managing heart failure, especially for those with comorbid obesity, which may further shape the landscape of heart failure treatment.

Safety and Tolerability

Common side effects include gastrointestinal symptoms such as nausea, vomiting, and diarrhoea, particularly when starting treatment. These side effects are typically transient and can be managed by gradual dose escalation.

1. Gastrointestinal Issues: The most common adverse effects of semaglutide are related to the gastrointestinal tract, primarily nausea and vomiting. However, these side effects tend to diminish over time as the body adjusts to the medication.

2. Rare but Serious Risks: There is some concern about the potential for pancreatitis and thyroid C-cell tumours, though these risks appear to be very low based on clinical trial data. Long-term surveillance is ongoing to assess any potential risks more thoroughly.

3. Contraindications: Semaglutide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2.

Conclusion

- Semaglutide has emerged as a powerful therapeutic agent with broad-spectrum benefits across obesity, type 2 diabetes, and cardiovascular disease, including heart failure.
- Its ability to improve glycaemic control, induce significant weight loss, and reduce cardiovascular risks marks a paradigm shift in how these interrelated conditions are treated.
- As ongoing research continues to uncover more of its potential benefits, semaglutide is poised to become a cornerstone in the management of metabolic and cardiovascular disorders.
- With its impressive efficacy and expanding indications, semaglutide represents a major advancement in therapeutic options for patients struggling with diabetes, obesity, and heart failure. As healthcare systems continue to grapple with the growing burden of these chronic conditions, semaglutide's role in comprehensive care will likely grow.

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Insights Into Management of Femoral Artery Pseudoaneurysm: An Achilles Heel of Femoral Interventions

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ABSTRACT

Pseudoaneurysms are vascular abnormalities caused by defects in the arterial wall. Prompt diagnosis and intervention are crucial to prevent serious complications. Diagnostic methods include duplex ultrasonography, CT angiography (CTA), and digital subtraction angiography (DSA). Treatment options encompass ultrasound-guided compression (UGC), surgical repair, and minimally invasive percutaneous techniques.

Keywords: Pseudoaneurysm, Diagnosis, Endovascular repair, surgical repair

INTRODUCTION

A pseudoaneurysm, or false aneurysm, is a hematoma enclosed by a thin fibrous capsule rather than vessel walls. When blood is leaked through the damaged wall, it accumulates in the surrounding tissue and creates a persistent connection between the artery and the adjacent cavity, linked by a neck that allows bidirectional blood flow. Patient-related risk factors include hypertension, renal dysfunction, age over 65, obesity (BMI > 28 kg/m^2), female sex, peripheral artery disease (PAD), and use of antiplatelets, anticoagulants, thrombolytics or having a coagulopathy. Procedural risk factors involve arteriotomy location (especially at bifurcations or below), use of large sheaths (> 6 F), prolonged or urgent procedures, and inadequate manual compression during sheath removal. The incidence of percutaneous procedure is around 4%.

CASE-1

A 70-year-old male with an unremarkable medical history experienced a domestic fall in 2022, resulting in an intertrochanteric fracture of the right femur. He underwent Dynamic Hip Screwing (DHS) the following day. Since then, he has developed pulsatile swelling in his right thigh. Examination findings reveal he had a pulsatile bulge on the medial side of the right thigh with a systolic bruit but no signs of inflammation, venous stasis, or neurological and vascular compromise of the right lower leg, with typical vital signs. Imaging with arterial color Doppler (figure 1) and CTA (figure 2) diagnosed a pseudoaneurysm of the profunda femoris artery (PFA). The Doppler revealed turbulent flow within pseudoaneurysm with a wide-neck communication to the PFA, and the size measured on CTA 7.6 × 8 × 7 cm. Selective arteriography of the superficial femoral and Profunda femoris arteries via the contralateral approach showed a prominent dye jet into the pseudoaneurysm (figure 3A). The patient was successfully treated endovascularly with a self-expanding Fluency stent graft (6 × 20 mm) deployed in the feeding vessel (figure 3B).

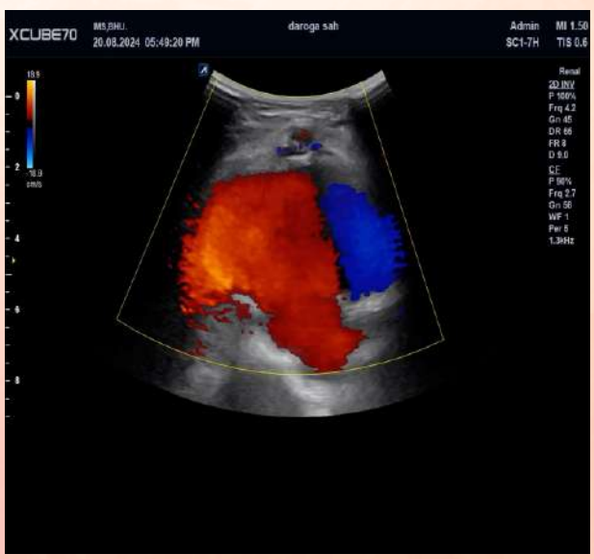


Fig 1: Color Doppler of CASE- 1 shows Pseudoaneurysm from Profunda femoris artery with 'Yin - Yang' sign within the lesion, which represents the Swirling motion of the turbulent blood flow within the lesion

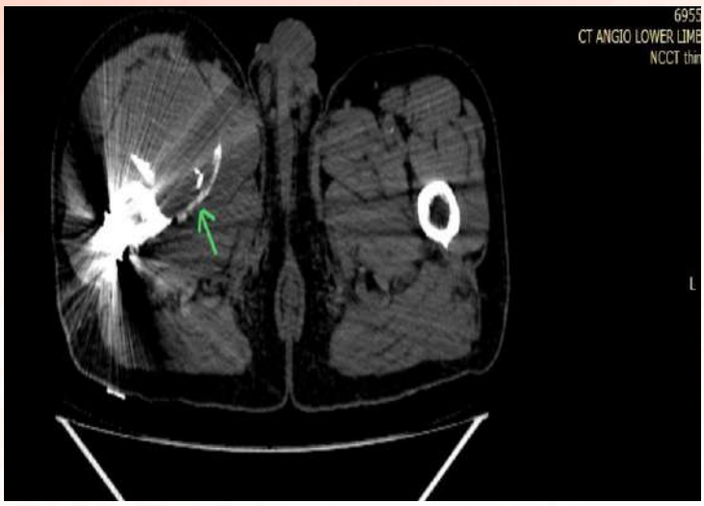


Fig 2: Axial section of non contrast CT (CASE-1) of bilateral upper thigh reveals a well defined iso dense lesion in antero-medial aspect of right femur below muscle plane. The lesion show rim calcification along its posterior margin (green arrow).



Fig 3A: **Fig 3B:**

Fig 3A: Selective angiogram (case 1) of profunda femoris artery showing large pseudoaneurysm (red border) and its neck showing spurt of dye (blue arrow) Fig 3B: Post stent graft no flow into pseudoaneurysm from profunda femoris artery (Green arrow)

CASE-2

A 60-year-old male with type 2 diabetes was admitted with chest pain and shortness of breath and diagnosed with acute anterior wall myocardial infarction. After angiography, he underwent percutaneous transluminal coronary angioplasty (PTCA) with stent placement in the mid-left anterior descending artery, achieving TIMI-3 flow and no residual stenosis. 4 days after discharge, he developed severe sharp pain in the right groin. Arterial color Doppler confirmed a pseudoaneurysm of the common femoral artery (CFA) with a narrow neck. Compression with an ultrasound probe for 60 minutes successfully obliterated the flow through the pseudoaneurysm neck.

DISCUSSION

Conventional angiography remains the gold standard for diagnosis, but non-invasive imaging methods such as duplex Doppler ultrasonography, MR angiography, and CTA are also effective. Small (< 2 cm) asymptomatic cases can often be managed conservatively with blood pressure control, discontinuation of anticoagulants, and regular ultrasound monitoring. Larger (> 2 cm) or symptomatic pseudoaneurysms generally require intervention. Complications of femoral artery pseudoaneurysm may include compression of the femoral vein, leading to deep vein thrombosis, hemorrhage causing acute compartment syndrome, arteriovenous fistula, local ischemia, critical limb ischemia, skin necrosis, neuropathy, infection and rupture.

MANAGEMENT STRATEGIES

1) **Ultrasound-guided compression (UGC)**
   After accurately locating the neck of the pseudoaneurysm, bedside compression is done by placing the ultrasound probe above the neck and applying pressure for 10 to 20 minutes. This pressure should occlude flow through both the neck and the pseudoaneurysm, leading to thrombosis within the cavity, maintaining steady pressure to stop the flow while ensuring that blood supply to the limb is preserved.

2) **Percutaneous thrombin injection**

   An ultrasound-guided 19- to 22-gauge needle is guided into the center of the pseudoaneurysm for thrombin injection, typically at a concentration dose of 100 to 1,000 IU/mL. Thrombin injections are suitable for small pseudoaneurysms with narrow necks.

3) **Endovascular approach**

   Factors such as the pseudoaneurysm's location and proximity to bifurcations are critical in deciding endovascular treatment. The two primary endovascular techniques are embolization and stent placement. A covered stent excludes a pseudoaneurysm from circulation, especially in wide-necked or multilobed pseudoaneurysms. If the artery is expendable and lacks collateral circulation, embolization of the afferent artery may be performed. This can be achieved using coils, detachable balloons, or N-butyl 2-cyanoacrylate (glue).

4) **Open Surgical repair**

   Surgical treatment is indicated in rapid expansion of the pseudoaneurysm, where there is insufficient time for non-invasive treatments, distal ischemia or neurological deficits caused by local pressure or distal embolization, and Failure of percutaneous interventions. While surgery remains the traditional gold standard for treating femoral pseudoaneurysms, offering a high success rate, it involves longer recovery times and a higher risk of wound infections and bleeding. Surgical repair should be considered if other treatments fail.

CONCLUSION

Understanding the anatomy of the upper part of the lower extremity is crucial for recognizing complications associated with a Femoral artery pseudoaneurysm. Timely diagnosis and intervention are vital to prevent severe complications. High clinical suspicion, coupled with duplex ultrasonography and CTA, can accurately diagnose the condition in over 90% of cases, providing details on size, extent, and thrombus presence. DSA remains the gold standard for diagnosis and treatment. While traditional surgical repair was once the primary method, it is now reserved for complex cases or unstable patients. Less invasive techniques, such as covered stent placement, offer high technical success and lower complication rates.

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Ischemia In Open Artery: Current Status

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INTRODUCTION

Ischemic cardiovascular disease remains the major public health problem in the entire world. Clinically, ischemic heart disease (IHD) may present as an acute coronary syndrome (e.g., unstable angina, myocardial infarction, or as a chronic coronary syndrome with more stable symptoms like angina pectoris).

There is emerging evidence that many patients, especially females with chronic IHD, have open or non-obstructed epicardial arteries. Hence, the term "open artery ischemia" (OAI) is coined for that [1]. The various clinical phenotypes include ANOCA (Angina with Open Coronary Arteries), INOCA (Ischemia with Non-Obstructive Coronary Arteries) and MINOCA (Myocardial Infarction with Open Coronary Arteries). Different mechanistic endotypes are there, and one is coronary microvascular dysfunction (CMD), defined by endothelial dysfunction, vascular smooth muscle dysfunction, or both [2]. Another is Heightened coronary vasoreactivity (vasospasm) occurring at the epicardial or microvascular levels.

Atherosclerosis plays a mechanistic role in most cases with OAI, and nonobstructive plaque with positively remodeled epicardial coronary arteries may be the rule rather than the exception [3]. More recently, CMD with nonobstructive disease has been suggested to represent a "pre-heart failure with preserved ejection fraction" (HFpEF) endotype [4].

Traditionally, the OAI was thought to be a "benign syndrome," but this is not Correct. A lot of these patients undergo invasive or non-invasive coronary anatomic imaging, which documents no or nonobstructive disease. However, considerable evidence now shows that they have an increased risk of hospitalization for recurrent angina, heart failure, or both. The ischemia related to microvascular dysfunction is often "patchy," and none of the abnormalities (angina, wall motion abnormality, ECG changes) have been well validated in patients with CMD. These patients are often missed with the use of only traditional angiograms. The only currently available, clinically useful methods that avoid these pitfalls are P31-cMR spectroscopy and coronary venous blood sampling for metabolites of anaerobic metabolism [5].

Women represent up to 65 % of these OAI syndromes. For MINOCA, mortality can approach 5 % at 1 year with 1-year MACE rates like those of patients with acute myocardial infarction due to an obstructive coronary artery [6]. Interestingly, in the WISE IVUS sub-study, designed to evaluate 100 women with coronary angiograms locally read as "normal," there was evidence for plaque in >80 % of proximal left coronary artery segment using intracoronary imaging.

Furthermore, ESC guidelines 2024 recommends that for persistently symptomatic patients despite medical treatment with suspected ANOCA/ INOCA (i.e., anginal symptoms with normal coronary arteries or non-obstructive lesions at non-invasive imaging, or intermediate stenoses with normal fractional flow reserve(FFR)/instantaneous flow reserve (iFR) at coronary arteriography) and poor quality of life, invasive coronary functional testing is recommended to identify potentially treatable endotypes and to improve symptoms and quality of life, considering patient choices and preferences (class I indication)[7,9]

DIAGNOSIS

The diagnosis of ANOCA/INOCA is exclusively based on invasive, functional evaluation of the coronary microcirculation. Non-invasive tests (stress echocardiography, PET, perfusion CCTA, and CMR) allow for diagnosing ANOCA/INOCA by measuring the coronary flow reserve(CFR), which has a high negative predictive value. Intracoronary pressure and flow measurements can assess the hemodynamic significance of focal or diffuse coronary lesions by measuring FFR or iFR and of microcirculatory function by measuring CFR and index of microvascular resistance (IMR), hyperemic microvascular resistance (HMR), or microvascular resistance reserve (MRR)[9][Fig 1]. A Doppler-derived CFR of <2.5 in non-obstructive CAD, an increased IMR (≥25), HMR value of >2.5 mmHg/cm/s by Doppler, and MRR values <2.7 indicates microvascular dysfunction [10]. The diagnosis of microvascular angina(MVA) and vasospastic angina(VSA) due to microvascular or macrovascular vasospasm is made owing to coronary vasomotor testing by acetylcholine.

The test is considered positive for macrovascular spasm if symptoms occur, accompanied by ischaemic ECG changes and an angiographic ≥90% reduction of the coronary lumen. If the lumen reduction is <90%, the diagnosis of microvascular spasm is to be entertained.

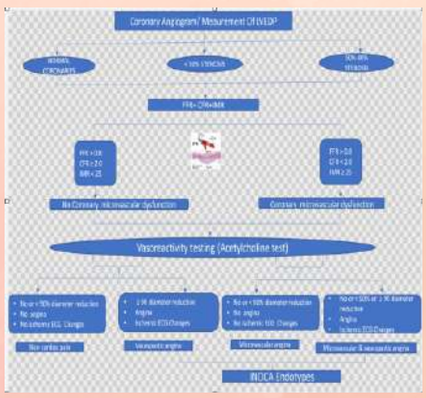


Fig.1 Diagnostic Algorithm for INOCA (taken from ESC 2024 guidelines)

MANAGEMENT

The management of these patients needs an individualized approach. There are two types of obstruction: fixed, which corresponds to plaque or an obstructive lesion, and dynamic, which corresponds to spasm. In fixed ones, beta blockers and dynamic calcium channel blockers (CCBs), nicorandil, play an upfront role. Figure 2 is a flow chart from the latest ESC guidelines for the management of such patients.

The first step is to counsel the patient on lifestyle and risk factors modification (DM, HTN) to improve the quality of life. For patients with MVA and reduced CFR and/or increased IMR (reflecting arteriolar remodeling), beta-blockers, CCBs, ranolazine, and angiotensin-converting enzyme inhibitors (ACE-I) are used [10].In patients with either epicardial or microvascular spasm following Ach testing, CCBs should be considered as first-line therapy. Zibotentan, an oral endothelin A receptor antagonist, is a new drug that may provide benefit by opposing the vasoconstrictor response of coronary microvessels to endothelin (PRIZE trial).

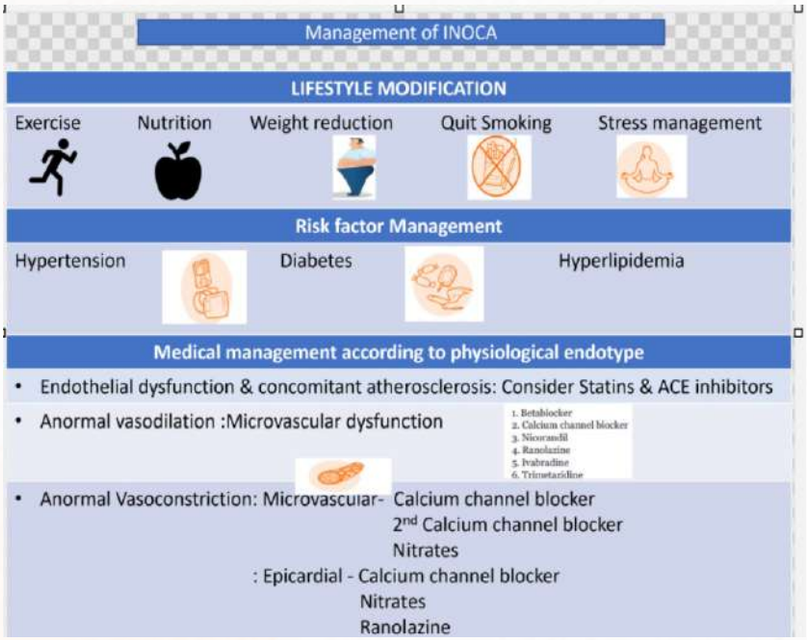


Fig.2 Treatment of ANOCA and INOCA

CONCLUSION

These Patients exhibit a wide array of presentations that can currently be diagnosed and treated with effective individualized therapies. Invasive diagnostic tests, as well as CMR with adenosine, constitute a new option. In conclusion, specific actions need to be taken by all health centers to create diagnostic and therapeutic protocols for managing these patients.

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Digital Health in Cardiology

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Introduction

In 2020, an estimated 6.95 billion mobile phones and 3.5 billion smartphone users are worldwide. There are 1.12 billion cellular connections in India, and there will be 751.5 million internet users in 2024. This reflects the scope of the population that can be reached with digital health initiatives (DHI). DHI is an umbrella term that includes text message programs, mobile apps, teleconsultation, wearable devices, and electronic decision support tools (Figure 1). These aid in better diagnosis, enhanced healthcare access, therapy titration, and follow-up.

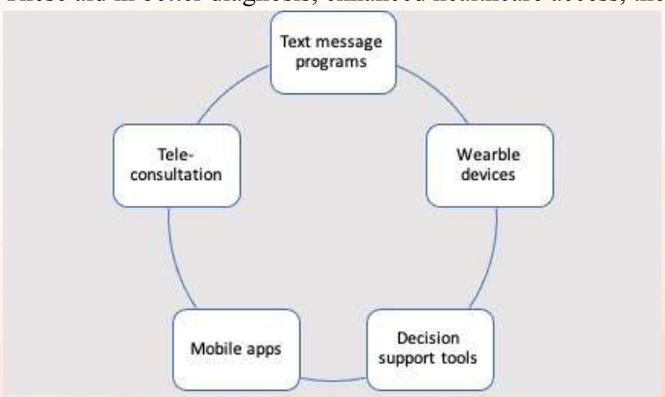


Figure 1: Components of digital health

Mobile text messages

Text messages can reinforce medication adherence and management of hypertension and diabetes. This works through repetitive messages using behavioral psychology techniques. The TEXTME randomized controlled trial (RCT) showed that sending four semi-personalized messages at random times and days a week significantly improved smoking cessation rates, blood pressure control, better physical activity, body mass index, and adherence to a healthier diet.

Mobile apps

Mobile health apps can help physicians strategize patients' risks, decide on specific therapies, and reduce hospitalizations. The HERB Digital Hypertension 1 (HERB-DH1) RCT showed that using a smartphone app helped improve ambulatory, home, and office blood pressure (BP) through home BP monitoring.

Telehealth

It refers to electronic communication between the health care provider and patient via phone, video, or text. The most promising uses of telemedicine include the management of chronic diseases like heart failure, hypertension, and diabetes and in arrhythmia detection. Better adherence to guideline-directed medical therapy (GDMT) was seen in the PROMPT-HF trial. The rural population benefits the most if provided with the essential devices and infrastructure. These patients primarily lack healthcare facilities due to several barriers like cost, travel time, loss of work, and lack of available transport. Telehealth has the potential to be used in secondary prevention for cardiac rehabilitation.

Wearable devices

The most common smartwatches, including the Apple Watch (from Apple Inc, Cupertino, CA), Samsung watch, Fitbit (Fitbit LLC, San Francisco, CA), and the Google Pixel Watch, can perform a single-lead electrocardiogram. Apple heart study showed that the Apple watch recording a single-lead electrocardiogram (ECG) resulted in highly accurate atrial fibrillation and sinus rhythm detection. Smartwatches improve daily steps and encourage physical activity through patient involvement on a daily basis. A systematic review of 28 RCTs, including 3646 participants across nine countries, investigated the effects of wearable activity trackers and found an average increase of 627 daily steps among the intervention group compared to controls. Wearable electronic patches work as extended Holter for the detection of rhythm disorders. The newest in this category is a smartwatch-based cardiopulmonary resuscitation (CPR) feedback device, which has been shown to enhance the quality of CPR. DHI is evolving to help patients with out-of-hospital cardiac arrest with wearables detecting fatal rhythms and drone-delivered automated cardiac defibrillators.

Heart failure and CIEDs

DHI holds a firm place in the effective management of heart failure. In the CardioMEMs system (St. Jude Medical, St. Paul, MN), a permanent pressure sensor is implanted in the main pulmonary artery, which sends data, including pressure waveforms and heart rate, to a distant web-based system and aids in the early detection of heart failure worsening. Voice recognition technology used in the follow-up of patients with chronic heart failure resulted in better sodium intake control and improved quality of life scores. Remote monitoring of cardiac electronic implantable devices (CIEDs), including pacemakers and implantable cardioverter-defibrillators, helps timely detect abnormal cardiac rhythms.

Electronic decision support tools

These are especially useful for empowering paramedical healthcare workers to efficiently diagnose and manage cardiovascular diseases and risk factors like hypertension. ‘mPower Health was a mobile app for healthcare providers to support clinical decision-making and maintain health records. It was successfully adopted by the states of Tripura and Mizoram in India and met all the recommendations as per the World Health Organization.

Electronic medical records

The government of India launched the Ayushman Bharat Digital Mission (ABDM) to facilitate easy access and sharing of medical records.

Artificial intelligence

The term ‘artificial intelligence’ refers to a machine mimicking the cognitive functions of a human mind. AI can integrate an extensive data pool and extract relevant information for an individual. It aids in faster interpretation of cardiac CT and MR images. Tele-stethoscopes can convert signals from stethoscopes to digital signals transmissible to smartphones. Recently developed ECG-AI model predicted HF risk within 10 years with the same accuracy as the established clinical factors-based risk calculators. Most of 12 lead ECG machines can make provisional diagnoses of myocardial infarction and cardiac arrhythmia by pre-defined algorithms. Recently, retinal images were used to predict the risk of cardiovascular diseases.

Evidence

CardioMEMs system was shown in clinical trials to reduce heart failure hospitalizations by 37% ($P < 0.0001$) over a 15-month mean follow-up period. It was found to be cost-effective as well. Liu et al. found that the time to revascularisation was significantly reduced by 30-40 minutes by tele-ECG while patients were transferred from a non-percutaneous coronary intervention (PCI) capable center to a PCI capable center. In a multicentre randomized controlled trial, IMMACULATE [IMproving reModeling in Acute myoCardial Infarction Using Live and Asynchronous Telemedicine], remote intensive monitoring of post-MI patients was found to be safe and effective. Another US and Indian multicentre trial evaluated the mHealth arm with smartphone-connected devices like ECG, BP devices, and handheld ultrasounds for in-person cardiology visits in patients with structural and rheumatic heart diseases. mHealth use was shown to be associated with a shorter time to referral for intervention with a lower risk of hospitalization and death on follow-up.

Concerns

Despite its numerous benefits, DHI poses several challenges (Figure 2). One challenge is to make it reach the distant population. It is extremely useful for the elderly who are unable to visit healthcare facilities regularly for follow-up. But certainly, those are the ones who are most hesitant to use digital means. Initial hesitation by both the patient and the physician to accept and adopt digital health is a real barrier. Data privacy in the background of massive data is concerning.

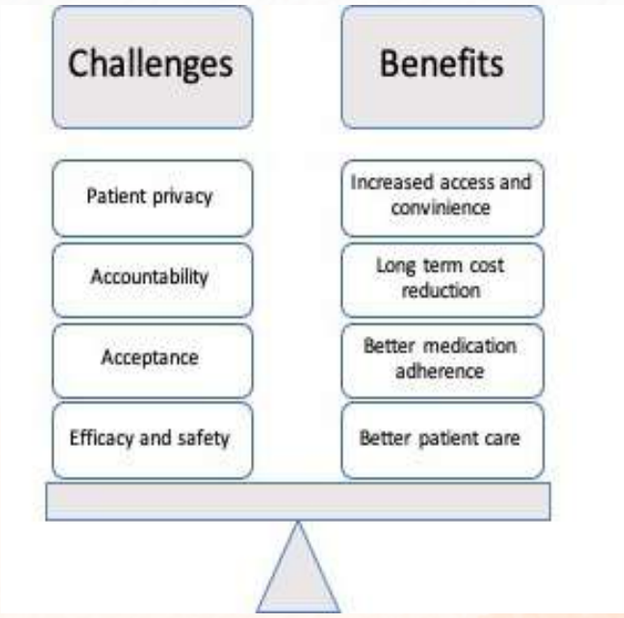


Figure 2: Challenges and benefits of Digital health initiatives.

As a long-term solution

Adequate resource allocation is needed for data management digitally and for it to be optimally used when needed. The healthcare workforce needs to be trained to retrieve meaningful information from it and use digital means efficiently. Patients need to be familiarised with the advancements and ensured about the privacy of their information. Medico-legal and ethical issues need regulatory laws to ensure justice. Regulation of digital health technologies is under the FDA.

Suggested Reading

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Highlights of ESC AF Management 2024 Guidelines

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The following are relevant important take-home messages from the 2024 European Society of Cardiology (ESC) guidelines for the management of atrial fibrillation (AF):

1. The guideline document recommends treatment using the AF-CARE pathway, which is comprised of:
    - [C] Comorbidity and risk factor management,
    - [A] Avoiding stroke and thromboembolism,
    - [R] Reducing symptoms by rate and rhythm control and
    - [E] Evaluating and reassessing as patients' disease and comorbidities progress.
2. Hypertension, heart failure (HF), diabetes mellitus, obesity, obstructive sleep apnea, physical inactivity, and high alcohol intake should be evaluated and managed to avoid recurrences and progression of AF, improve the success of AF treatments, and prevent AF-related adverse outcomes.
    - Appropriate medical therapy for HF is recommended in AF patients with HF and impaired left ventricular ejection fraction (LVEF) to reduce symptoms and/or HF hospitalization and prevent AF recurrence. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are recommended for patients with HF and AF, regardless of LVEF, to reduce the risk of HF hospitalization and cardiovascular death.
    - Metformin or SGLT2 inhibitors should be considered for individuals needing pharmacological management of diabetes mellitus to prevent AF.
    - Weight loss is recommended as part of comprehensive risk factor management in overweight and obese individuals with AF to reduce symptoms and AF burden, with a target of ≥10% reduction in body weight.
    - Management of obstructive sleep apnea may be considered part of the comprehensive management of risk factors in individuals with AF to reduce recurrence and progression. When screening for obstructive sleep apnea in individuals with AF, using only symptom-based questionnaires is not recommended.
    - A tailored exercise program is recommended in individuals with paroxysmal or persistent AF to improve cardiorespiratory fitness and reduce AF recurrence. Maintaining an active lifestyle is recommended to prevent AF, with the equivalent of 150–300 minutes per week of moderate-intensity or 75–150 minutes per week of vigorous-intensity aerobic physical activity.
    - Reducing alcohol consumption to ≤3 standard drinks (≤30 grams of alcohol) per week are recommended as part of comprehensive risk factor management to reduce AF recurrence.
3. Assessment of the risk of thromboembolism may be done with locally validated risk tools or the CHA_2-VA score and assessment of other risk factors.
    - Oral anticoagulants are recommended for all eligible patients: if CHA_2-VA = 1, anticoagulation should be considered; if CHA_2-VA ≥2, anticoagulation is recommended.
    - Direct oral anticoagulants (DOACs) (apixaban, dabigatran, edoxaban, and rivaroxaban) are preferred over vitamin K antagonists, except in patients with mechanical heart valves and mitral stenosis.
    - Adding antiplatelet treatment to oral anticoagulation is not recommended in AF patients for the goal of preventing ischemic stroke or thromboembolism. Anticoagulants and antiplatelet agents should not be combined unless the patient has an acute vascular event or needs interim treatment for procedures.
    - Anticoagulation should be pursued according to the patient's risk of thromboembolism, irrespective of whether they are in AF or sinus rhythm.
    - Oral anticoagulation is recommended in all patients with AF and hypertrophic cardiomyopathy or cardiac amyloidosis, regardless of CHA_2-VA score.
    - A reduced dose of DOAC therapy is not recommended unless patients meet DOAC-specific criteria to prevent underdosing and avoidable thromboembolic events.

- All patients should be on an oral anticoagulant for ≥2 months after an AF ablation procedure, irrespective of estimated thromboembolic risk.
- For a formal risk-score-based assessment of bleeding risk, the HAS-BLED score should be considered to help address modifiable bleeding risk factors and to identify patients at high risk of bleeding (HAS-BLED score ≥3) for early and more frequent clinical review and follow-up.

4. Beta-blockers (any EF), digoxin (any EF), or diltiazem/verapamil (LVEF >40%) may be used as initial therapy, as an adjunct to rhythm control therapies, or as a sole treatment strategy to control heart rate and symptoms.
5. Rhythm control should be considered in all suitable AF patients, including cardioversion, antiarrhythmic drugs, and catheter or surgical ablation to reduce symptoms and morbidity.
   - The primary indication for rhythm control is a reduction in AF-related symptoms and an improvement in the quality of life.
   - Implementation of a rhythm-control strategy should be considered within 12 months of diagnosis in selected patients with AF at risk of thromboembolic events to reduce the risk of cardiovascular death or hospitalization.
   - Electrical cardioversion as a diagnostic tool should be considered in patients with persistent AF where there is uncertainty about the value of sinus rhythm restoration on symptoms or to assess improvement in LV function.
   - Catheter ablation should be considered as a second-line option if antiarrhythmic drugs fail to control AF in persistent AF or as a first-line option in patients with paroxysmal AF.
   - Repeat AF catheter ablation should be considered in patients with AF recurrence after initial catheter ablation, provided the patient's symptoms were improved after the initial pulmonary vein isolation (PVI) or after failed initial PVI to reduce symptoms, recurrence, and progression of AF.
6. Endoscopic or hybrid ablation should be considered if catheter ablation fails or as an alternative to catheter ablation in persistent AF despite antiarrhythmic drugs.
   - Continuation of oral anticoagulation is recommended in patients with AF at elevated thromboembolic risk after concomitant, endoscopic, or hybrid AF ablation, independent of rhythm outcome or left atrial appendage exclusion, to prevent ischemic stroke and thromboembolism.
   - AF ablation during cardiac surgery should be performed in centers with experienced teams, especially for patients undergoing mitral valve surgery.
   - Surgical closure of the left atrial appendage should be considered as an adjunct to oral anticoagulation in patients with AF undergoing endoscopic or hybrid AF ablation to prevent ischemic stroke and thromboembolism.
7. Patients should be periodically reassessed with attention to new modifiable risk factors that could slow or reverse the progression of AF, increase quality of life, and prevent adverse outcomes.

Suggested reading –

ESC Scientific Document Group, 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): Developed by the task force for the management of atrial fibrillation of the European Society of Cardiology (ESC), with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Endorsed by the European Stroke Organisation (ESO), European Heart Journal, 2024;, ehae176, https://doi.org/10.1093/eurheartj/ehae176.

Highlights of Chronic Coronary Syndrome ESC 2024 Guidelines

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The following are the most relevant messages of interest from the 2024 European Society of Cardiology (ESC) guidelines for the management of chronic coronary syndromes (CCS):

1. The term CCS describes the clinical presentations of coronary artery disease (CAD) during stable periods, particularly those preceding or following an acute coronary syndrome (ACS).
2. In-depth discussion about nonobstructive coronary arteries (ANOCA)/ischemia with nonobstructive coronary arteries (INOCA) patients; these entities are considered to be much more common in the European population

3. Managing individuals with suspected CCS involves four steps:
    - STEP 1. The first step is a general clinical evaluation that focuses on assessing symptoms and signs of CCS, differentiating noncardiac causes of chest pain and ruling out ACS. This initial clinical evaluation requires recording a 12-lead resting electrocardiogram, basic blood tests, and in selected individuals, chest X-ray imaging and pulmonary function testing. This evaluation can be done by the general practitioner.
    - STEP 2. The second step is a further cardiac examination, including echocardiography at rest to rule out left ventricular (LV) dysfunction and valvular heart disease. After that, it is recommended to estimate the clinical likelihood of obstructive CAD to guide deferral or referral to further noninvasive and invasive testing.
    - STEP 3. The third step involves diagnostic testing to establish the diagnosis of CCS and determine the patient's risk of future events.
    - STEP 4. The final step includes lifestyle and risk factor modification combined with disease-modifying medications. A combination of antianginal medications is frequently needed, and coronary revascularization is considered if symptoms are refractory to medical treatment or if high-risk CAD is present. If symptoms persist after obstructive CAD is ruled out, coronary microvascular disease and vasospasm should be considered.
4. CTA has been given more importance to rule out obstructive CAD by virtue of its negative predictive value being very high (95%)
5. CACS ,Clinical likelihood and Risk factors are being incorporated to classify patients into very low, low, moderate and high likelihood of CAD in addition to PTP ESC Score
6. The inclusion of risk factors to classic pretest likelihood models of obstructive atherosclerotic CAD improves the identification of patients with very low (≤5%) pretest likelihood of obstructive CAD in whom deferral of diagnostic testing should be considered.
7. First-line diagnostic testing of suspected CCS should be done by non-invasive anatomic or functional imaging. Selection of the initial non-invasive diagnostic test should be based on the pretest likelihood of obstructive CAD, other patient characteristics that influence the performance of non-invasive tests, and local expertise and availability.
8. Coronary computed tomography angiography (CCTA) is preferred to rule out obstructive CAD and detect nonobstructive CAD. Functional imaging is preferred to correlate symptoms to myocardial ischemia, estimate myocardial viability, and guide decisions on coronary revascularization. Positron emission tomography is preferred for absolute myocardial blood flow measurements, but cardiac magnetic resonance perfusion studies may offer an alternative. Selective second-line cardiac imaging with functional testing in patients with abnormal CCTA and and CCTA after abnormal functional testing may improve patient selection for invasive coronary angiography (ICA).
9. ICA is recommended to diagnose obstructive CAD in individuals with a very high pre- or post-test likelihood of disease, severe symptoms refractory to guideline-directed medical therapy (GDMT), angina at a low level of exercise, and high event risk. When ICA is indicated, evaluating the functional severity of 'intermediate' stenoses by invasive functional testing (FFR, IFR) before revascularization is recommended.
10. A single antiplatelet agent, aspirin or clopidogrel, is generally recommended long-term in CCS patients with obstructive atherosclerotic CAD(driven by data from HOST -EXAM Trial).
11. Ticagrelor was given as class IIb indication post PCI due to weak evidence only in the form of TWILIGHT Trial
12. Among CCS patients with normal LV function and no significant left main or proximal left anterior descending lesions, current evidence indicates that myocardial revascularization over GDMT alone does not prolong overall survival.
13. Intravascular Imaging (IVUS, OCT) during PCI of Complex PCI like left main,True bifurcation,long lesions given Class I indication (Major change driven by results from RENOVATE -PCI trial , ILUMIEN trial , OCTOBER trial)
14. Ivabradine was downgraded to class III in the case of CCS with normal LVEF due to negative data of increased events in the SIGNIFY Trial.

Suggested reading –

ESC Scientific Document Group , 2024 ESC Guidelines for the management of chronic coronary syndromes: Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC) Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS), European Heart Journal, 2024;, ehae177, https://doi.org/10.1093/eurheartj/ehae177



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