NCD Newsletter

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Men at high risk of cardiovascular disease face brain health decline 10 years earlier than women, study finds

Men with cardiovascular disease risk factors, including obesity, face brain health decline a decade earlier from their mid 50s to mid 70s than similarly affected women who are most susceptible from their mid 60s to mid 70s, suggest the findings of a long term study, published online in the Journal of Neurology, Neurosurgery & Psychiatry.

The most vulnerable regions of the brain are those involved in processing auditory information, aspects of visual perception, emotional processing and memory, with the damaging effects just as evident in those who didn't carry the high risk APOE ε4 gene as those who did, the findings show.

It's clear that cardiovascular disease risk factors, such as type 2 diabetes, obesity, high blood pressure, and smoking are associated with a heightened risk of developing dementia. But when might be the best time to intervene with appropriate treatment to stave off the associated neurodegeneration, and whether this timing might differ between the sexes, isn't clear, say the researchers. To explore this further, they drew on 34,425 participants of the UK Biobank all of whom had both abdominal and brain scans. Their average age was 63, but ranged from 45 to 82.

Cardiovascular disease risk was assessed using the Framingham Risk Score, which is based on: age, blood fats, systolic blood pressure, the maximum arterial pressure exerted when the heart contracts and pumps blood, and represented by the first higher number in a reading blood pressure medication, smoking and diabetes.

Additionally, changes in brain structure and volume were recorded using a neuroimaging technique called Voxel-based morphometry (VBM) to identify the influence of cardiovascular risk, abdominal fat, and the fat that surrounds body organs (visceral adipose tissue) on brain neurodegeneration.

Analysis of the data showed that higher levels of abdominal fat and visceral adipose tissue were associated with lower brain gray matter volume in both men and women. The strongest influence of cardiovascular risk and obesity on brain neurodegeneration occurred a decade earlier in men than in women and was sustained over two decades, the data revealed. The effects were also stronger in men than they were in women. Men were most susceptible to the damaging effects between the ages of 55 and 74, while women were most susceptible between the ages of 65 and 74.

High cardiovascular risk and obesity predisposed to gradual loss of brain volume over several decades, occurring in a bell-shaped curve over time, with susceptibility lower at younger (under 55) and older ages (75+), although there were relatively few participants of either sex in these age groups, note the researchers. Importantly, the associations remained, irrespective of whether or not those affected were carriers of the high risk APOE ε4 gene. The most vulnerable regions of the brain were the temporal lobes, located in the cerebral cortex, the brain's outer surface. These regions are involved in aural, visual, and emotional information processing, and memory regions affected early on in the development of dementia.

The detrimental impact of cardiovascular risk was widespread throughout cortical regions, highlighting how cardiovascular risk can impair a range of cognitive functions, note the researchers.

Therefore, modifiable cardiovascular risk factors, including obesity, deserve special attention in the treatment/prevention of neurodegenerative diseases, including Alzheimer's disease they add.

This highlights the importance of aggressively targeting cardiovascular risk factors before the age of 55 years to prevent neurodegeneration and Alzheimer's disease, in addition to the benefit of preventing other cardiovascular events, such as myocardial infarction [heart attack] and stroke they emphasize.

One such possibility may be in the repurposing of agents used for obesity and type 2 diabetes mellitus for the treatment of Alzheimer's disease they suggest, adding that other drugs used for the treatment of cardiovascular disease have also shown promise.

This is an observational study, so no firm conclusions can be drawn about cause and effect. And the researchers acknowledge various limitations to their findings, including that the UK Biobank didn't record specific biomarkers for Alzheimer's disease.

Atrophy of frontal, parietal, and temporal brain regions is also typical of normal aging, making it difficult to precisely differentiate between the impact of cardiovascular risk on general aging processes and the risk of specific neurodegenerative conditions, they add.

But there are plausible biological explanations for the observed neuronal damage, they explain. These include inflammation, central leptin and insulin resistance, as well as the breakdown of the blood-brain barrier.

They conclude, Targeting cardiovascular risk and obesity a decade earlier in males than females may be imperative for potential candidates to achieve a therapeutic benefit in preventing neurodegeneration and cognitive decline.

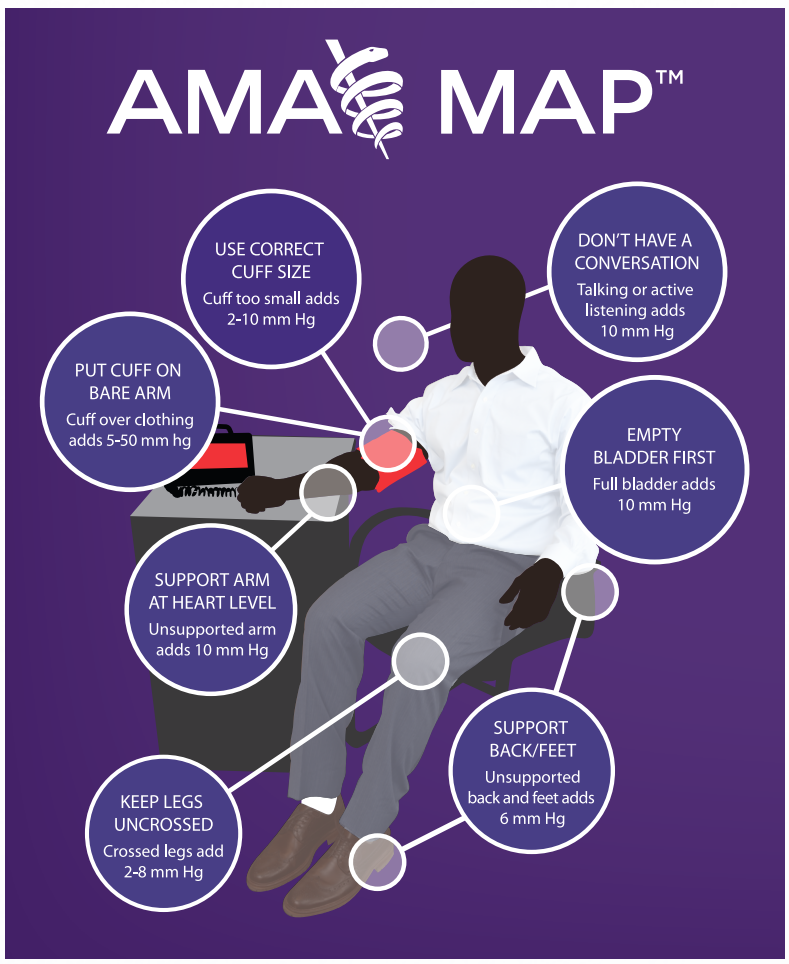
Reference: Cardiovascular risk and obesity impact loss of grey matter volume earlier in males than females, Journal of Neurology, Neurosurgery & Psychiatry (2024). DOI: 10.1136/jnnp-2024-333675

From Clinical Care To Clinical Trials: The Importance of Proper Clinic BP Assessment Methods

Source: Clario

Awareness of one's blood pressure (BP) is critical for cardiovascular health and overall well-being. There's overwhelming evidence that untreated high blood pressure (hypertension) is associated with adverse consequences such as stroke, heart attack, kidney disease and death. Often when thinking of hypertension, one pictures sitting in their clinician's office with a blood pressure cuff around their arm and a nurse or physician with a stethoscope and manometer assessing their blood pressure. This picture is now evolving within both the clinical care and clinical trials environment. Over the last few years, there's been a trend towards the use of validated automated oscillometric BP devices, rather than the previous standard of a manometer (aneroid/mercury) and a stethoscope to manually assess the brachial blood pressure.

Implementing automated oscillometric BP assessments with a validated device has a number of benefits, including standardization of assessment methodology, digital data capture, and ability to collect and average multiple replicate inflations. While BP assessment is typically considered straightforward, it is important that the fundamentals to successful and reliable measurement are not overlooked. Whether it's measuring the circumference of an individual's arm to select the correct cuff size, ensuring an adequate pre-assessment rest period, or providing an appropriately quiet environment, there are a number of variables that can impact the accuracy of results. The American Medical Association (AMA)/American Heart Association (AHA) and other scientific groups have highlighted the importance of these considerations as outlined in the infographic below:



7 SIMPLE TIPS TO GET AN ACCURATE BLOOD PRESSURE READING

The common positioning errors can result in inaccurate blood pressure measurement. Figures shown are estimates of how improper positioning can potentially impact blood pressure readings.

Sources:

1. Pickering. et al. Recommendations for Blood Pressure Measurement in Humans and Experimental Animals Part 1: Blood Pressure Measurement in Humans. Circulation. 2005;111: 697-716.
2. Handler J. The importance of accurate blood pressure measurement. The Permanente Journal/Summer 2009/Volume 13 No. 3 51

This 7 simple tips to get an accurate blood pressure reading was adapted with permission of the American Medical Association and The Johns Hopkins University. The original copyrighted content can be found at www.ama-assn.org/ama-johns-hopkins-blood-pressure-resources.

This resource is part of AMA MAP™ Hypertension, a quality improvement program. Using a single or subset of AMA MAP™ tools or resources does not constitute implementing this program. AMA MAP™ includes guidance from AMA hypertension experts and has been shown to improve BP control rates by 10 percentage points and sustain results.

AMA, September 29, 2021

Blood pressure assessment in clinical trials

Specifically looking at the clinical trials arena, clinic blood pressure assessment (often referenced as a vital sign time point in a protocol) can contribute to a primary safety or efficacy endpoint, depending on the therapeutic indication.

Whether as an efficacy endpoint (development of anti-hypertensive medications) or as a safety endpoint, there continues to be increased focus in the industry on the technology and methodology for BP assessment. Interest increased even further after release of the updated draft FDA Pressor Effect Guidance in February of this year.

Blood pressure, as with other cardiovascular assessments, includes consideration around variability with the measurement. As it is applicable with healthcare use, the benefits of an automated, validated oscillometric device are only further magnified in clinical trial use. The standardization of technology and methodology can reduce the potential variability within a study participant, and across participants at all study sites. This is achievable by implementing the following in a clinical trial:

- Implementation of a single, well validated and standardized BP device across all clinical trial sites.
- Establishing a well-defined BP assessment procedure across all sites which includes the rest period and defined number of inflations with rest between readings.
- Optionally completing the BP assessment in an "unattended" scenario to reduce the potential of white coat hypertension (elevated BP in the presence of a clinician). The approach of "attended vs unattended" was a discussion point around the SPRINT trial.
- The BP data is a calculated average of the pre-defined readings, i.e., capture 4 readings and generate an average of the last 3 readings.
- Centralized, digital capture of the BP assessments at each scheduled clinic visit.
- Proper training and reinforcement of the clinic BP procedures defined for the study with the clinical research team at the site.
- Maintenance and functional testing of the standardized BP devices at a pre-defined schedule.
- Ensuring the selected device is appropriate for the study population and the algorithm within the oscillometric device has been validated specific to the study population (i.e., adult versus pediatric).

FDA DRUG APPROVALS

1. U. S. FDA Approves Rapiblyk™ (Landiolol) for Critical Care Treatment of Atrial Fibrillation and Atrial Flutter

November 27, 2024

AOP Health has announced that the U.S. Food and Drug Administration (FDA) has approved Rapiblyk™ (landiolol), a novel therapeutic option for patients in critical care settings suffering from supraventricular tachycardia (SVT), including atrial fibrillation and atrial flutter. This landmark approval marks AOP Health's first entry into the U.S. market, reinforcing its commitment to delivering solutions for rare diseases and critical care.

Clinical Efficacy and Safety

The approval of Rapiblyk™ was supported by five randomized, double-blind, placebo-controlled clinical studies involving 317 adult patients with SVT. Results demonstrated that 40-90% of patients treated with landiolol achieved a significant reduction in heart rate within approximately 10 minutes, compared to only 0-11% in the placebo group. Heart rate reduction was defined as a >20% decrease in heart rate, a heart rate of <100 bpm, or intermittent cessation of arrhythmia. The most common adverse event reported was hypotension, observed in 9.9% of landiolol-treated patients versus 1% in the placebo group.

A New Solution for Critical Care Settings

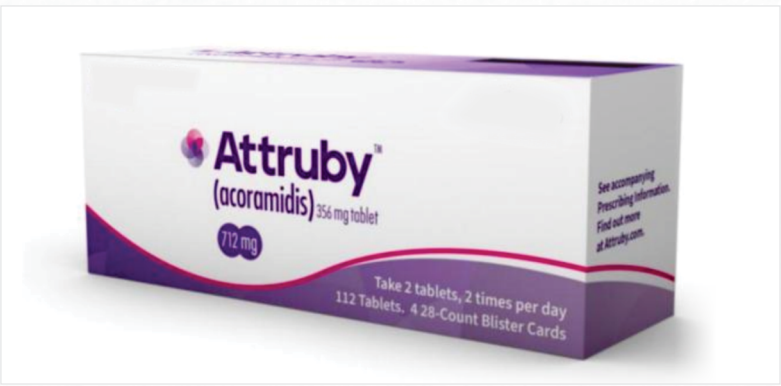
Landiolol is an ultra-short-acting beta-adrenergic receptor antagonist with a beta 1/beta 2 selectivity ratio of 255. This high selectivity enables rapid heart rate control with minimal impact on blood pressure, making it suitable for emergency and critical care environments such as intensive care units, cardiac critical care units, and operating rooms. Rapiblyk™ is not intended for chronic treatment but provides a fast-acting option for short-term management of supraventricular tachycardias.

Key Features of Rapiblyk™:

- Rapid onset of action.
- Minimal impact on blood pressure.
- Indicated for short-term ventricular rate control in adults with SVT, including atrial fibrillation and atrial flutter.

2. FDA Approves Attruby™ (acoramidis) for the Treatment of ATTR-CM: A New Option for Patients

November 22, 2024



The U.S. Food and Drug Administration (FDA) has approved BridgeBio's Attruby™ (acoramidis) for the treatment of transthyretin amyloid cardiomyopathy (ATTR-CM), bringing hope to patients with this life-threatening condition.

A Milestone for ATTR-CM Treatment

The FDA's decision is based on the groundbreaking results from the ATTRibute-CM Phase 3 study. Attruby demonstrated its ability to significantly reduce death and cardiovascular-related hospitalizations while improving the quality of life for patients. This approval marks an important milestone in addressing the unmet medical needs of those living with ATTR-CM.

Understanding ATTR-CM

ATTR-CM is a progressive disease caused by the misfolding of the transthyretin (TTR) protein, which leads to harmful amyloid deposits in the heart. Over time, these deposits impair the heart's function, potentially resulting in heart failure. With limited treatment options available until now, the approval of Attruby offers a much-needed solution.

How Does Attruby Work?

Attruby acts as a TTR stabilizer by binding to the TTR protein and preventing it from misfolding into amyloid fibrils. This stabilization helps slow amyloid formation, reducing disease progression and supporting improved heart health.

Why This Approval Matters?

The introduction of Attruby adds a powerful option to the existing treatments for ATTR-CM, such as Vyndamax/Vyndaqel. This expanded arsenal provides more choices for patients and healthcare providers to manage this challenging disease effectively.

3. FDA approves new treatment for uncomplicated urinary tract infections in adult women who have limited or no alternative oral antibiotic treatment options

October 24, 2024

Food and Drug Administration (FDA) has approved Iterum's new drug application for Orlynvah (sulopenem etzadroxil and probenecid) for the treatment of uncomplicated urinary tract infections (uUTIs) caused by the designated microorganisms Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis in adult women who have limited or no alternative oral antibacterial treatment options. This is the first approved indication for Orlynvah and the first FDA-approved product for Iterum.

ORLYNVAH a combination of sulopenem etzadroxil, a penem antibacterial, and probenecid, a renal tubular transport inhibitor, is indicated for the treatment of uncomplicated urinary tract infections (uUTI) caused by the designated microorganisms Escherichia coli, Klebsiella pneumoniae, or Proteus mirabilis in adult women who have limited or no alternative oral antibacterial treatment options.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ORLYNVAH and other antibacterial drugs, ORLYNVAH should be used only to treat uUTI that are proven or strongly suspected to be caused by susceptible bacteria. Culture and susceptibility information should be utilized in selecting or modifying antibacterial therapy. The recommended dosage of ORLYNVAH is one tablet (sulopenem etzadroxil 500 mg and probenecid 500 mg) orally twice daily for 5 days.

ORLYNVAH is a combination of sulopenem etzadroxil, a penem antibacterial drug and probenecid, a renal tubular inhibitor. Probenecid inhibits OAT3-mediated renal clearance of sulopenem, resulting in increased plasma concentrations of sulopenem.

The FDA approval of Orlynvah was based on a clinical development program supported by a robust data package, including two pivotal, Phase 3 clinical trials (known as SURE 1 and REASSURE) that evaluated the safety and efficacy of Orlynvah compared to ciprofloxacin (SURE 1) and Augmentin™ (REASSURE) in the treatment of adult women with uUTI. SURE 1 showed superiority to ciprofloxacin in fluoroquinolone resistant infections, while REASSURE showed non-inferiority and statistical superiority to Augmentin™ in the Augmentin™ susceptible population. Orlynvah was generally well tolerated in both SURE 1 and REASSURE clinical trials.

4. US FDA approves Hikma's generic version of Novo's diabetes drug Victoza

December 23, 2024

The FDA has approved the first generic of Victoza (liraglutide injection) for adults and pediatric patients older than 10 with type 2 diabetes, according to a recent news release. This 18 mg / 3 mL injection, glucagon-like peptide-1 (GLP-1), is approved for use in combination with diet and exercise. This approval was granted to Hikma Pharmaceuticals USA Inc.

The first generic GLP-1, Byetta (Exenatide), was approved by the FDA last month. More than 38 million Americans have diabetes, with type 2 being the most common, accounting for 90% to 95% of all diabetes cases, according to the Centers for Disease Control and Prevention.

PRODUCT UPDATES

1. Repurposing Semaglutide and Liraglutide for Alcohol Use Disorder

This study highlights the promising potential of glucagon-like peptide-1 (GLP-1) receptor agonists, specifically semaglutide and liraglutide, as a novel treatment for alcohol use disorder (AUD). Here are the main takeaways:

Key Insights:

1. **Efficacy of GLP-1 Receptor Agonists**
   - Semaglutide showed the most significant reduction in the risk of AUD-related hospitalizations.
   - Liraglutide followed with a slightly lesser but still substantial impact.
   - Both medications also reduced hospitalizations related to substance use disorder (SUD) and somatic reasons.
2. **Comparison with Traditional AUD Medications**
   - Traditional AUD medications had only modest effectiveness, underscoring the innovative potential of GLP-1 agonists.
3. **Lack of Association with Suicide Risk**
   - Neither semaglutide nor liraglutide increased the risk of suicide attempts, suggesting a favorable safety profile in this context.
4. **Study Design and Scope**
   - Conducted in Sweden, this cohort study analyzed data from over 220,000 individuals with AUD across a median follow-up of 8.8 years.
   - This is one of the largest studies to examine the real-world effectiveness of repurposing GLP-1 agonists for AUD.
5. **Real-World Implications**
   - Repurposing these drugs for AUD treatment could address gaps in current pharmacological therapies, especially for patients with coexisting type 2 diabetes or obesity.
   - Given their dual benefits for metabolic and alcohol-related outcomes, these medications could provide a holistic approach to patient care.

Clinical Relevance:

Healthcare providers may consider these findings when managing patients with comorbid AUD and metabolic conditions, although further evidence from controlled trials will be necessary before widespread adoption.

This study not only expands the understanding of GLP-1 agonists' therapeutic versatility but also opens doors to innovative approaches in managing AUD-a condition with significant public health impact.

2. Rosuvastatin appears better than atorvastatin for mortality, cardio, liver outcomes in large database

Six-year all-cause mortality was lower among patients taking rosuvastatin than atorvastatin, but the difference was only about a percentage point, a study of patients in the United Kingdom and China found.

Rosuvastatin may have lower rates of all-cause mortality, major adverse cardiovascular events (MACE), and major adverse liver outcomes than atorvastatin, a study found.

To compare the real-world effectiveness and safety of the two statins, researchers conducted an active comparator cohort study using target trial emulation for data from the China Renal Data System and UK Biobank databases. Results were published Oct. 29 by Annals of Internal Medicine.

Among 285,680 eligible participants in both databases, six-year all-cause mortality was lower with rosuvastatin than atorvastatin (2.57 vs. 2.83 per 100 person-years in the Chinese database and 0.66 vs. 0.90 per 100 person-years in the UK database), with differences in cumulative incidence of -1.03% (95% CI, -1.44% to -0.46%) and -1.38% (95% CI,-2.50% to -0.21%), respectively. Rosuvastatin was also associated with lower risks for MACE and major adverse liver outcomes. In the UK database, risk for type 2 diabetes was higher with rosuvastatin, and the two drugs had similar risks for chronic kidney disease and other statin-related adverse effects.

The association between rosuvastatin use and lower all-cause mortality compared to atorvastatin may be largely attributable to its stronger cardiovascular protective effect, which in turn may stem from it being more effective than atorvastatin at reducing low-density lipoprotein cholesterol and inflammatory markers, such as C-reactive protein, the study authors said. Other studies have suggested but not confirmed a difference between rosuvastatin and atorvastatin in protecting against MACEs, and rosuvastatin has a lower likelihood for drug interactions than other statins, they noted.

The lower risk of adverse liver outcomes might be attributable to rosuvastatin's antioxidant and anti-inflammatory activities, but specific differences in hepatic effects between rosuvastatin and atorvastatin have not been comprehensively examined, the study authors cautioned. They also noted that despite use of a target trial emulation with two large national cohorts linked to national death registries, only small differences were found in important outcomes, and the confidence intervals did not always meet the requirements for statistical significance.

However, the associations between rosuvastatin and the outcomes remained similar across sensitivity analyses and persisted when defined daily dose and the indications for statin therapy were accounted for, the authors concluded. These findings emphasize that some of the clinical outcomes associated with starting rosuvastatin treatment differ from the clinical outcomes associated with starting atorvastatin treatment, and clinicians might want to consider these differences when prescribing one of these drugs to individual patients.

STUDY UPDATES

1. Persistently short sleep during and after pregnancy associated with Cardiometabolic Disorders: JAMA

In recent years, the significance of sleep health has gained increasing attention, particularly in the context of maternal well-being. Sleep is a critical component of overall health, and its disruption can have profound implications for both mothers and their children. The Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be Heart Health Study (NuMoM2b-HHS) has provided valuable insights into how sleep duration during and after pregnancy can influence long-term health outcomes. Conducted across eight academic medical centers in the United States, this ongoing prospective cohort study has shed light on the relationship between sleep patterns and the risk of developing hypertension and metabolic syndrome (MetS) in new mothers.

The study involved 3,922 participants, all of whom were nulliparous women-those who had not given birth before-enrolled during their first pregnancy between 2010 and 2013. These women were followed for an average of 3.1 years post-delivery. A key focus of the research was on self-reported sleep duration, specifically identifying those who experienced persistent short sleep, defined as less than seven hours per night during pregnancy and for two to seven years after delivery.

Key Findings

Study Population

- 3,922 nulliparous women (first-time mothers) participated in the study.
- Average age of participants was 27.3 years.

Prevalence of Persistent Short Sleep

- 14.4% of participants reported experiencing persistent short sleep (defined as less than 7 hours per night) during pregnancy and for 2 to 7 years after delivery.

Higher prevalence of persistent short sleep was observed in

- Non-Hispanic Black women (adjusted odds ratio [aOR], 2.17; 95% CI, 1.59-2.97).
- Unmarried participants (aOR, 1.68; 95% CI, 1.29-2.19).

Association with Metabolic Syndrome

- Women with persistent short sleep had a 60% higher odds of developing metabolic syndrome (aOR, 1.60; 95% CI, 1.21-2.11).

Association with Hypertension

- No significant association was found between persistent short sleep and incident hypertension (aOR, 0.91; 95% CI, 0.69-1.19).

Follow-Up Duration

Participants were followed for an average of 3.1 years after delivery.

The implications of these findings are particularly concerning. The study found that women who reported short sleep duration had a significantly higher risk of developing metabolic syndrome, while the association with hypertension was not statistically significant. This distinction is crucial for healthcare providers as they develop strategies to support maternal health during and after pregnancy.

The research also highlighted the importance of considering various factors that may contribute to sleep health. The study acknowledged limitations, including the lack of comprehensive data on other sleep characteristics such as regularity and satisfaction. Additionally, factors such as pre-pregnancy sleep patterns, infant feeding methods, and mental health conditions were not fully explored, indicating a need for future studies to address these variables. The authors emphasized that understanding the multifaceted nature of sleep health is essential for guiding targeted interventions aimed at improving outcomes for mothers and their children.

As the study progresses, it is clear that the findings have significant implications for maternal healthcare. The association between sleep duration and metabolic health underscores the need for healthcare providers to prioritize sleep education and support for expectant and new mothers. By addressing sleep health, providers can help to mitigate the risk of long-term health issues, ultimately contributing to healthier families and communities.

In conclusion, the NuMoM2b-HHS study provides critical insights into the relationship between sleep duration and maternal health outcomes. As we continue to explore the complexities of sleep and its impact on health, it is imperative that we recognize the importance of sleep as a vital component of maternal care. By fostering a greater understanding of sleep health, we can empower mothers to prioritize their well-being, leading to improved health outcomes for themselves and their children. The findings from this study serve as a call to action for healthcare professionals to integrate sleep health into their practice, ensuring that mothers receive the comprehensive care they need during this pivotal time in their lives.

Reference: Kim M, Wiener LE, Gilbert J, et al. Persistent Short Sleep Duration From Pregnancy to 2 to 7 Years After Delivery and Metabolic Health. JAMA Netw Open. 2024;7(12):e2452204.

2. New Study Reveals Two-Thirds of Diabetic Men Suffer from Erectile Dysfunction

A recent study published in BMC Public Health sheds light on a significant health issue affecting diabetic men: 65.8% of them suffer from erectile dysfunction (ED). This condition, often underreported and overlooked, has profound implications for both physical and emotional well-being. Early detection and better diabetes management are essential in mitigating this common yet serious problem.

Understanding the Link Between Diabetes and ED

Erectile dysfunction, characterized by the consistent inability to achieve or maintain an erection for sexual satisfaction, has long been associated with chronic conditions like cardiovascular disease (CVD), depression, and diabetes mellitus (DM). The study underscores how diabetes, in particular, exacerbates ED risk through multiple mechanisms:

- Endothelial Dysfunction: High blood sugar damages blood vessels, impairing their ability to support regular erectile responses.
- Oxidative Stress and Neuropathy: Chronic diabetes leads to the accumulation of harmful sugar byproducts and cell waste, causing oxidative stress and nerve damage.
- Impaired Nerve Signals: Peripheral neuropathy affects the communication between the brain and penis, while autonomic nerve damage restricts blood flow essential for maintaining an erection.
- Cardiovascular Impacts: Conditions like hypertension and atherosclerosis further impede blood flow, linking ED to potential silent heart disease and increased cardiovascular risks.

Study Insights

The study, titled The Global Burden of Erectile Dysfunction and Its Associated Risk Factors in Diabetic Patients: An Umbrella Review, aggregated data from 108,030 male diabetic patients. Researchers conducted a meta-analysis using seven systematic reviews and determined a global prevalence of ED among diabetic men at 65.8%.

Key findings

- **Risk Factors:** Age over 40, diabetes duration longer than 10 years, peripheral vascular disease, and a body mass index (BMI) above 30 kg/m^2 significantly increase ED risk.
- **Geographical Variations:** Lower ED prevalence was observed in Africa, while higher rates were noted in regions with older diabetic populations, such as Ethiopia, India, and Japan. Countries like Kuwait and Italy, with younger study populations, reported lower prevalence.
- **Diagnostic Stringency:** Studies using stricter diagnostic criteria reported higher ED prevalence.

Implications for Awareness and Treatment

The study's findings highlight the urgent need to:

- **Encourage Routine Screening:** Early diagnosis of ED in diabetic men can lead to timely interventions.
- **Promote Diabetes Management:** Effective blood sugar control may alleviate ED symptoms and enhance quality of life.
- **Facilitate Open Conversations:** Addressing the stigma around ED can improve mental health outcomes, confidence, and relationships for those affected.

Moving Forward

This comprehensive review emphasizes the interconnectedness of chronic conditions like diabetes and ED. By prioritizing education, screening, and treatment, healthcare professionals can support diabetic patients in managing this condition more effectively.

Reference: Kitaw, T. A., Abate, B. B., Tilahun, B. D., et al. (2024). The Global Burden of Erectile Dysfunction and Its Associated Risk Factors in Diabetic Patients: An Umbrella Review. BMC Public Health, 24(2816)

GUIDELINE UPDATES

1. The American Diabetes Association Releases Standards of Care in Diabetes-2025

Dec 09, 2024

The American Diabetes Association® released the Standards of Care in Diabetes-2025 (Standards of Care) the gold standard in evidence-based guidelines for diagnosing and managing diabetes and prediabetes. Based on the latest scientific research and clinical trials, the Standards of Care includes strategies for diagnosing and treating diabetes in both youth and adults, methods to prevent or delay type 2 diabetes and its associated comorbidities like obesity, and care recommendations to enhance health outcomes.

Notable updates to the Standards of Care in Diabetes-2025 include:

- Consideration of continuous glucose monitor (CGM) use for adults with type 2 diabetes on glucose-lowering agents other than insulin.
- Guidance on actions to take during circumstances of medication unavailability, such as medication shortages.
- Additional guidance on the use of GLP-1 receptor agonists beyond weight loss for heart and kidney health benefits.
- Guidance on continuation of weight management pharmacotherapy beyond reaching weight loss goals.
- Guidance for treatment of metabolic dysfunction-associated steatotic liver disease (MASLD) with moderate or advanced liver fibrosis using a thyroid hormone receptor-beta agonist.
- Emphasis on the use of antibody-based screening for presymptomatic type 1 diabetes in those who have a family history or known genetic risk.
- Guidance on the use of recreational cannabis for type 1 diabetes and those with other forms of diabetes at risk for diabetic ketoacidosis (DKA).

- Key updates highlighting potentially harmful medications in pregnancy and guidance for appropriately modifying the care plan.
- Expanded nutrition guidance to encourage evidence-based eating patterns, including those incorporating plant-based proteins and fiber, that keep nutrient quality, total calories, and metabolic goals in mind.

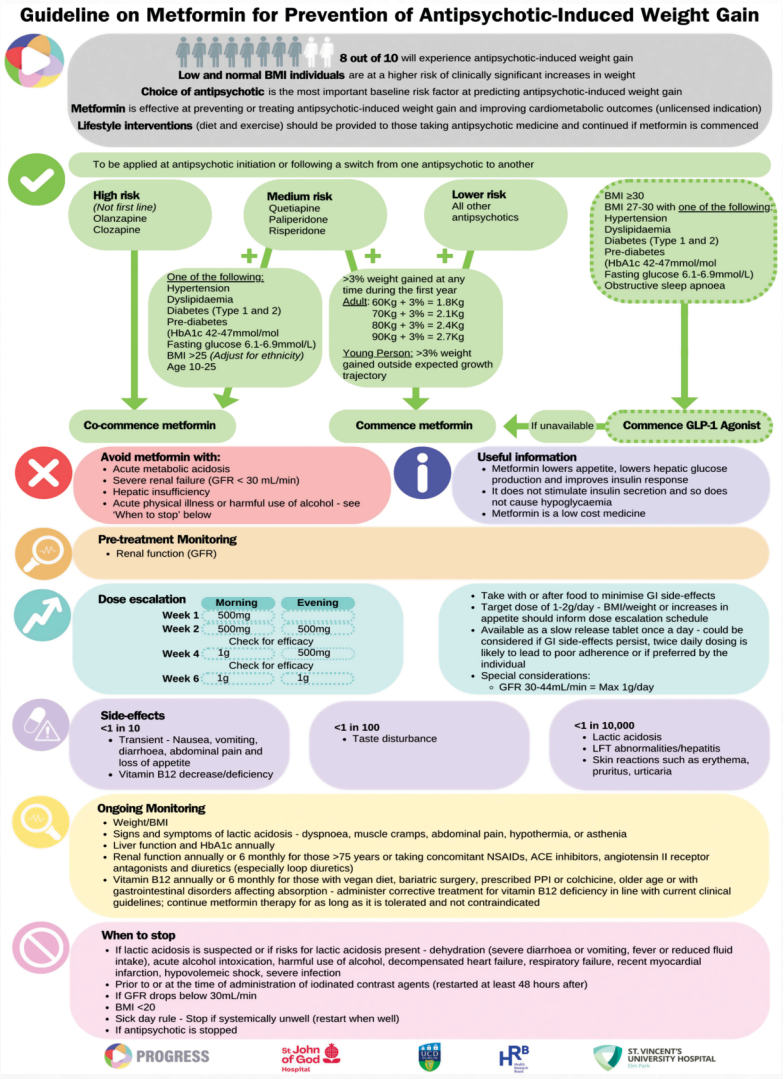
The ADA annually updates its Standards of Care through the efforts of its Professional Practice Committee (PPC). Comprising global experts from diverse professional backgrounds, the PPC includes physicians, nurse practitioners, certified diabetes care and education specialists, registered dietitian nutritionists, pharmacists, and methodologists. Its members hold expertise in a range of related fields. The 2025 Standards of Care has garnered endorsements from the American College of Cariology (Section 10), the American Geriatrics Society (Section 13), the American Society of Bone and Mineral Research (Bone Health, Section 4), and the Obesity Society (Section 8).

Other noteworthy changes include:

- Emphasis on water intake over nutritive and nonnutritive sweetened beverages; and the use of nonnutritive sweeteners over sugar-sweetened products in moderation and for the short term to reduce overall calorie and carbohydrate intake.
- Importance of meeting resistance training guidelines for those treated with weight management pharmacotherapy or metabolic surgery.
- Guidance for DKA and hyperglycemic hyperosmolar state (HHS) in the outpatient and inpatient settings.
- Screening updates for fear of hypoglycemia, diabetes distress, and anxiety.
- Improved approach for diabetes care delivery for older adults.
- Guidance on the use of GLP-1 receptor agonists and dual GIP and GLP-1 receptor agonists in the perioperative care setting.

2. Metformin for the Prevention of Antipsychotic-Induced Weight Gain: Guideline Development and Consensus Validation

Overweight and obesity are prevalent among individuals with severe mental illness (SMI), with antipsychotic-induced weight gain (AIWG) being a common and distressing side effect. Metformin has shown efficacy in preventing AIWG, yet its clinical use remains underutilized due to a lack of clear guidelines.



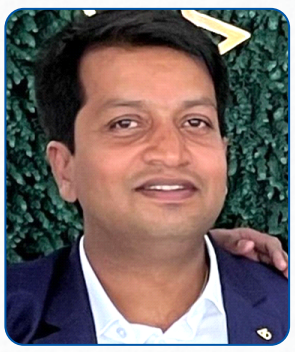
This study developed evidence-based guidelines for using metformin to prevent AIWG, following the AGREE II framework and GRADE methodology. A literature review and a consensus meeting led to recommendations, including the co-commencement of metformin with antipsychotic treatment, which can reduce weight gain by an average of 4.03 kg compared to controls. The guidelines were graded as strong by consensus and incorporate shared decision-making tools to facilitate implementation and address barriers. This initiative represents a significant step toward translating evidence into practice to mitigate AIWG in patients with SMI.

Reference: Aoife Carolan,et al., Metformin for the Prevention of Antipsychotic-Induced Weight Gain: Guideline Development and Consensus Validation, Schizophrenia Bulletin, 2024; sbae205, https://doi.org/10.1093/schbul/sbae205

CASE STUDY - 1

Retraction of Hypertension in a Young Woman with Middle Aortic Syndrome after Stent Implantation

DR. E. SRIKANTH
MD, DM, Consultant Cardiologist,
Padmavathi Cardiac Clinic,
Chittoor, Andhra Pradesh



Introduction

Middle Aortic Syndrome is a rare condition with a frequency of 0.5-2% in the general population. The characteristic feature of this clinical entity is the narrowing of the abdominal or distal thoracic aorta. Of the branches of the aorta, the renal and visceral arteries are commonly involved followed by the celiac and superior mesenteric arteries. The inferior mesenteric arteries are rarely involved. The symptoms vary based on the severity and the extent of narrowing of the aorta and visceral vasculature. It usually manifests as refractory hypertension, or with the claudication of the lower limbs, mesenteric angina. On literature review very few cases have reported the survival age of patients beyond 40 years with this clinical entity. If left untreated, this condition leads to life-threatening complications like renal or cardiac failure or intracerebral hemorrhage. The etiology of this syndrome is congenital, genetic with mendelian inheritance i.e., neurofibromatosis, Williams syndrome, or acquired secondary to Takayasu arthritis and fibromuscular dysplasia.

Case

A 27 years old female hypertensive for three years with an episodic headache and a 7-month history of amenorrhea and accelerated hypertension on triple antihypertensive drugs, who had delivered a stillborn baby, was referred to us for control of hypertension. On physical examination, there was no evidence of facial dysmorphism and lower limb pulses were absent. There was a difference of 10mmHg of SBP between the right and left upper limbs. Fundus examination suggested stage I hypertension-induced retinopathy. Blood and urine profiles were normal. Ultrasound evaluation revealed no organomegaly and ruled out the tumor and renal parenchymal disease. The electrocardiogram showed left ventricular hypertrophy. An echocardiogram confirmed left ventricular hypertrophy with grade II diastolic dysfunction. An Aortogram of the patient through the right radial approach with 6F pigtail catheter revealed the coarctation in the descending thoracic aorta at the diaphragm (atypical site) with a diameter of 3.4mm and a length of 13.4 mm and luminal diameter stenosis of >70% (Figure-1). On Computed tomography (CT) angiography, there was coarctation at an atypical site, diffuse renal artery disease, total block of the mid-segment of superior mesenteric artery, and mild disease of the proximal part of the iliac art.

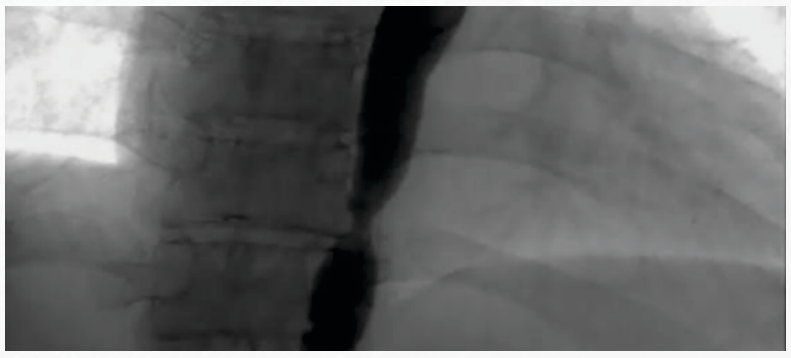


Fig-1: Aortogram showing significant stenosis in the thoracic aorta

Balloon angioplasty was done through the right femoral approach using a 7F-long femoral sheath. The lesion was crossed with 0.035 extra stiff wire. The lesion was dilated with a 7 x 40 mm carotid stent balloon at 8 atm for 10 sec and later with a 14 x 60 mm TYSHAQ balloon (BVM Medical Limited, Leicestershire, Leicester, UK) at 6 atm for 15 sec. CORDIS S.M.A.R.T. CONTROL (Cordis Vascular Stent system, Santa Clara, California, U.S.) self-expanding stent was deployed (Figures 2 and 3). After this procedure, the peak systolic gradient decreased from 100 to 40 mmhg, the Coarctation site diameter increased from 3.4 to 7.4 mm and percentage stenosis decreased from 70 to 50%. Despite the residual gradient, no further dilatation was done as deployment to normal size may result in aortic rupture and also because staged correction with further dilatation at a later date after healing may be a better approach. After two months of follow-up, both lower limb pulses were felt and blood pressure was controlled on triple antihypertensive drugs Follow up aortogram (figure 4) showed an increase in diameter of the coarctation segment to 8.4 mm from 7.4 mm and percentage stenosis decreased from 50 to 42% on using quantitative analysis software. The automated pressure gradient calculated showed a decrease in gradient to 36 mm Hg. No stent migration and no restenosis were detected.

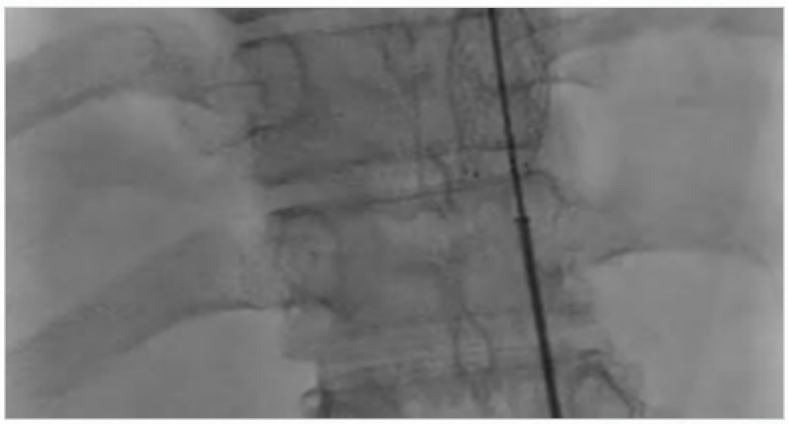


Fig-2: Aortogram showing stent deployment

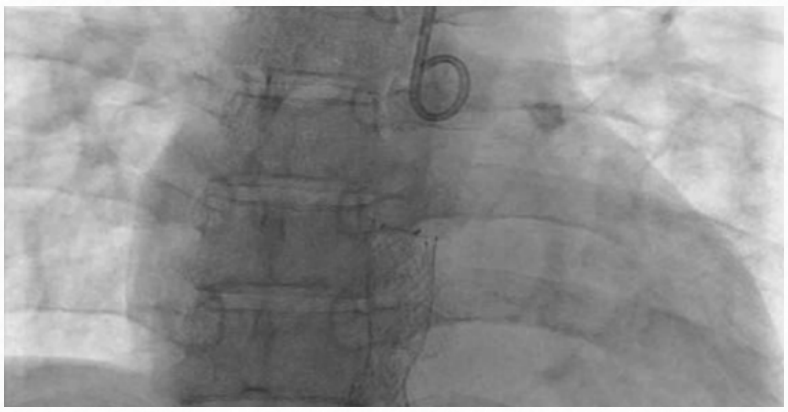


Fig-3: Aortogram showing the deployed stent

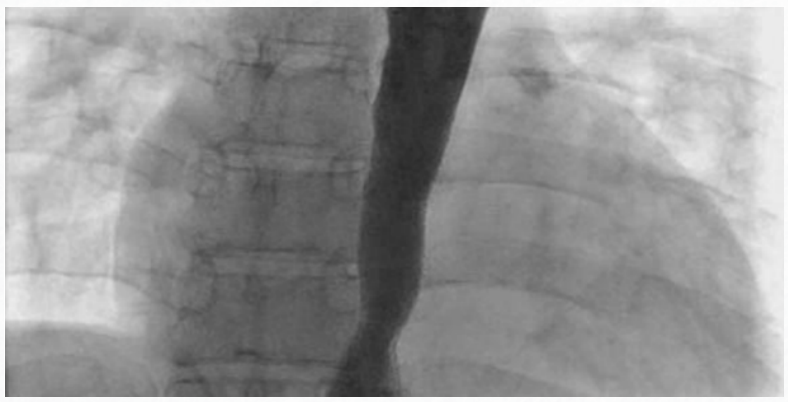


Fig-4: Aortogram showing good result

Discussion

Onset before 40 years, abnormal arteriogram, absence of inflammation or symptoms of myalgia, pleuritis, pericarditis, fever, and rashes, and observation of no neurological and dermatological abnormalities, and, normal range of CRP and ESR levels of our patient suggest a congenital type of etiology. Management modalities of this syndrome include aortoaortic bypass, prosthetic or autologous venous graft vascular reconstruction, or percutaneous transluminal angioplasty. In the Indian context, Sen et al., from Bombay in 1964 have reported 16 patients with the middle aortic syndrome in whom blood pressure was controlled by surgical bypass and nephrectomy. As 75% had a history of tuberculosis, these patients were also maintained on antituberculosis and corticoid regimens. From Calcutta in 1979 Gupta has informed the survival of five patients out of seven who underwent corrective surgery. Difficulty in fashioning an appropriate graft and the extensive nature of vascular abnormality may be responsible for high surgical mortality. Unresponsiveness of the hypoplastic segment to balloon dilatation, aneurysm formation, dissection of the aorta, pseudoaneurysm, and rupture of the aorta leading to death are the disadvantages of balloon dilatation. Controlled dilatation of stenotic segment and limited intimal injury are advantages reported for stent implantation. In our case, stent implantation after balloon dilatation improved hemodynamic parameters and controlled blood pressure. Further, observation of no stent migration and restenosis as revealed by follow-up angiogram, suggested the successful management of aortic syndrome with endovascular stent implantation. To the best of our knowledge, this case serves as a reference for aortic syndrome managed invasively with stent implantation in the Indian context.

Conclusion

Middle Aortic Syndrome is rare in the general population which can be either congenital or acquired. It manifests as uncontrolled hypertension with varying involvement of the renal and superior mesenteric arteries. Surgery is the usual treatment of choice, though individual cases like the one reported can be managed successfully by a percutaneous approach.

CASE STUDY - 2

Acute Myoglobinuric Renal Failure Following Gastroenteritis: A Case Study

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Introduction

Acute myoglobinuric renal failure is a potentially fatal condition characterized by acute kidney injury secondary to rhabdomyolysis.
Myoglobinuria, a hallmark feature, results from the release of myoglobin into the circulation due to muscle injury, leading to nephrotoxicity. This condition was first described in 1941 by Bywaters and Beall. Early diagnosis and aggressive intervention are crucial to prevent progression to acute tubular necrosis. We report a case of acute myoglobinuric renal failure in a young Indian male following severe gastroenteritis complicated by compartment syndrome and pancreatitis.

Case Presentation

A 35-year-old Indian male presented with a three-day history of anorexia, vomiting, and diarrhea, occurring approximately 20 times daily, accompanied by abdominal discomfort. His stools were liquid and yellow in color. Physical examination revealed a temperature of 38.6°C, dry mucous membranes, a heart rate of 100 beats per minute, blood pressure of 112/84 mmHg, and low jugular venous pressure. Notably, his calf muscles were tender and hard on palpation. The urine was dark brown, with a total output of 20 mL over 24 hours.

Laboratory Investigations

Initial blood tests revealed hemoglobin of 13.2 g/dL, platelets at 125 × 10^9/L, lymphocytes at 0.28 × 10^9/L, neutrophils at 1.52 × 10^9/L, sodium of 124 mmol/L, potassium of 2.2 mmol/L, urea of 220.2 mg/dL, bicarbonate at 12 mmol/L, corrected calcium at 1.35 mmol/L, phosphate at 5.16 mmol/L, creatinine at 6.5 mg/dL, bilirubin at 1.1 µmol/L and albumin at 28 g/L. C-reactive protein was elevated at 34 mg/L. Coagulation parameters were normal. Urine analysis was positive for blood (+++) without red cells or casts on microscopy, and myoglobin levels were pending. Serum creatine kinase levels were elevated. Imaging studies, including chest radiographs and Doppler ultrasound of the lower limb, revealed cellulitis without arterial block. CT imaging of the pancreas showed swelling suggestive of acute pancreatitis.

Treatment

Initial management involved aggressive fluid resuscitation with crystalloid solutions, achieving a central venous pressure of 8 cm H_2O write as per IUPAC. Despite this, oliguria persisted. Intravenous piperacillin and metronidazole

were administered to address sepsis. Torsemide infusion at 5 mg/h was attempted but failed to improve urine output. Hemodialysis via a jugular catheter was initiated, with three sessions performed over seven days. Fasciotomy of the right leg revealed serosanguinous discharge and necrotic muscle, necessitating debridement. Following these interventions, urine output and color improved significantly within 48 hours.

Discussion

This case highlights the interplay between severe gastroenteritis, rhabdomyolysis, and acute myoglobinuric renal failure. Rhabdomyolysis, characterized by elevated creatine kinase and electrolyte disturbances such as hyperphosphatemia and hypocalcemia, can lead to acute renal failure due to myoglobin's nephrotoxic effects. Hypokalemia in this patient exacerbated muscle injury. While forced alkaline diuresis is a recognized treatment, it carries risks of fluid overload and compartment syndrome. In this patient, early fluid resuscitation and hemodialysis were critical in managing acute renal failure. Fasciotomy and debridement further alleviated compartment syndrome, improving muscle perfusion and reducing myoglobin release.

Conclusion

This case underscores the importance of prompt recognition and intervention in acute myoglobinuric renal failure. Severe gastroenteritis, combined with metabolic derangements and compartment syndrome, poses a high risk of acute tubular necrosis. Aggressive fluid resuscitation, hemodialysis, and surgical intervention were pivotal in this patient's partial recovery. Clinicians should remain vigilant for rhabdomyolysis and its renal complications in patients presenting with severe dehydration and muscle tenderness.

CASE STUDY - 3

A Rare Relapse of Kikuchi-Fujimoto Disease from Tertiary Care Hospital in Southern Rajasthan

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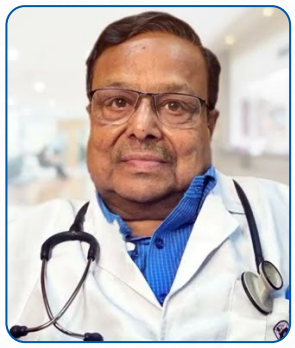


Introduction

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare condition of unknown etiology presenting with cervical lymphadenopathy along with associated symptoms of fever, and weight loss. It is often misdiagnosed due to its rare existence. We report a case of a 21-year-old female who presented with painful cervical lymphadenopathy and low-grade fever on and off for 6 months. Examination revealed left-sided multiple, tender, matted lymph nodes measuring a maximum of 2 cm in size, firm and mobile. The patient underwent a panel of investigations including cervical biopsy, which revealed findings of KFD.

Kikuchi-Fujimoto disease (KFD) is a rare form of painful lymphadenopathy, which is more common in Southeast Asia. KFD is not very well described in Africa, with very few reports described in the literature. The lymphadenopathy is usually cervical with associated nonspecific symptoms of fever and night sweats, which makes the diagnosis more challenging as the differential diagnosis is wide.1 We describe the case of a young female, who presented with painful multiple cervical lymphadenopathy in the cervical region and later confirmed to have KFD on lymph node biopsy.

Case presentation

A 21-year-old female presented with features of multiple, tender, soft to firm, mobile, nonadherent to adjacent tissue, matted, left cervical lymph node enlargement for about 6 months duration, and associated low-grade fever off and on. There was no history of weight loss, night sweats, cough, breathlessness, any swellings in other sites, generalized weakness and fatigue, butterfly rash, photosensitivity, oral ulcers, hair loss, palpitations, heat intolerance, or dry mouth. Examination revealed enlarged lymph nodes in the left cervical region measuring a maximum of 2 cm in size, firm, and mobile. There was no pallor, icterus, or clubbing.

Respiratory system examination revealed no abnormality and on per abdomen examination, no hepato-splenomegaly was found. The patient underwent a panel of investigations including complete blood count (CBC) with peripheral smear, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and thyroid profile. The Mantoux test was found to be indeterminate. The urine routine was normal, and microscopy showed no sediments.

Ultrasonography (USG) of the abdomen did not show any lymphadenopathy. The USG left cervical region showed few enlarged level V cervical lymph nodes. The patient underwent a cervical lymph node biopsy, which revealed histiocytic necrotizing lymphadenitis suggestive of KFD (Figs. 1 and 2).

On detailed history, it was found that the patient had a similar complaint 1.5 years ago for which she underwent an excisional biopsy that showed KFD, and the patient was treated for it. The disease subsided after treatment with complete regression of lymph nodes. We report this case of relapse of KFD, as there are very few reports of relapse (3%) making it rare. The patient was started on nonsteroidal anti-inflammatory drugs (NSAIDs) along with oral corticosteroids, hydroxychloroquine, and leflunomide with symptomatic improvement.

Figure 1. Profile picture of patient showing scar mark on lateral side of neck (post-excisional).

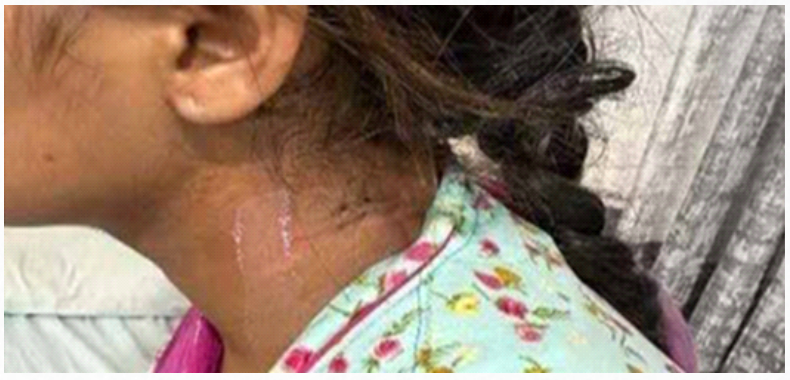
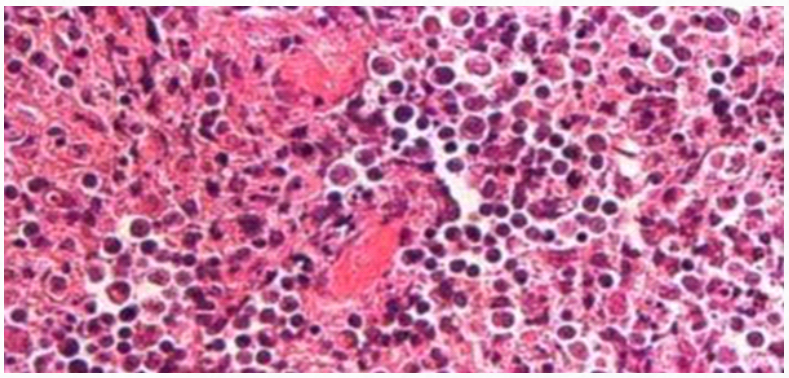


Figure 2. Lymph node biopsy showing numerous foci of necrosis with apoptotic bodies and scattered histiocytes. Absence of acute inflammatory infiltrate and hematoxylin bodies are suggestive of Kikuchi's disease.



Discussion

Kikuchi-Fujimoto disease, also known as histiocytic necrotizing lymphadenitis, is commonly seen in females of the 20 to 30 years age group with self-limiting lymphadenopathy (which disappears within 1 to 4 months). A low but possible recurrence rate of 3% to 4% has been seen. Recurrence has been recorded over a period of 2 to 10 years after the initial presentation. Our case represents a shorter recurrence course (within 1.5 years). The exact pathophysiology of KFD is not known, and postulated theories are of infectious and autoimmune origins. KFD is commonly found in association with systemic lupus erythematosus (SLE), Still's disease, Grave's disease, and Sjogren's disease. Clinical features include lymphadenopathy, fever, fatigue, joint pain, high ESR, CRP, and erythematous rashes. The cervical region is the most common site for lymphadenopathy and is usually painful.

The clinical picture is often nonspecific and should be differentiated from tuberculosis (TB) infectious mononucleosis, lymphoma and metastatic cancer. Due to the frequent association with SLE (30%) regular follow-ups and screening for diagnosis of SLE are recommended. The diagnosis is confirmed in histopathology showing architecture of follicular hyperplasia and necrotic abundant karyorrhectic nuclear debris. Histiocytes are positive for lysozyme, myeloperoxidase, CD68, CD163, and CD4 cells.

Patients with mild disease respond to supportive care with antipyretics and NSAIDs. Treatment options for aggressive and recurrence cases include the use of corticosteroids and immunosuppressors. Symptomatic treatment is the main medical intervention but there are documented cases of recurrence,

who need treatment with corticosteroids and other immunosuppressant drugs.

Conclusion

Kikuchi's disease can present with infective lymphadenopathy and therefore should be considered in the differential diagnoses of enlarged lymph nodes. Histological examination is the gold standard to diagnose the condition and avoid unnecessary treatment. Usually, complete regression of disease occurs, but it can rarely recur in 3% of cases. A high degree of clinical suspicion is required to make the diagnosis and a detailed history with lymph node biopsy reports should not be missed out.

CASE STUDY - 4

A Difficult Bifurcation Coronary Artery Stenosis Tackled by the "Mini-Crush Technique"

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Background

The field of interventional cardiology has evolved significantly, allowing operators to address increasingly complex coronary lesions percutaneously. However, the treatment of bifurcation lesions remains a challenge due to procedural and clinical complexities, including a high burden of adverse events such as in-stent restenosis (ISR), stent thrombosis, and periprocedural myocardial infarction.

The "Mini-Crush Technique" is a modification of the traditional "Crush Technique" aimed at reducing the volume of crushed stent by limiting the side branch (SB) stent protrusion to approximately 2 mm. Recent evidence has demonstrated favorable outcomes, with low rates of major adverse cardiac events (MACE) and restenosis in both the main and side branches when using this technique with drug-eluting stents (DES).

Case Description

A 52-year-old male patient, known to have hypertension and diabetes for the past 10 years, presented to the emergency department with sudden-onset severe chest pain and profuse sweating lasting eight hours. He had a history of chronic smoking, dyslipidemia, and a family history of atherosclerotic cardiovascular disease (ASCVD).

Initial investigations revealed the following:

- **Electrocardiogram (ECG):** Extensive anterior wall myocardial infarction.
- **2D Echocardiography:** Regional wall motion abnormalities (RWMA) in the left anterior descending artery (LAD) territory with a left ventricular ejection fraction (LVEF) of 40%.

Following thrombolytic therapy as a pharmaco-invasive approach, coronary angiography was performed. The angiogram revealed critical stenosis at the LAD-D1 bifurcation (MEDINA 1, 1, 1). It was decided to address the lesion using the "Mini-Crush Technique.

Procedure

Percutaneous Transluminal Coronary Angioplasty (PTCA) to the LAD-D1 bifurcation was performed using the "Mini-Crush Technique" with two stents. The left main coronary artery (LMCA) was engaged using a 7F EBU 3.0 guiding catheter, and the lesions in the LAD and diagonal branch (D1) were crossed with Runthrough NS and BMW PTCA wires. The diagonal and LAD lesions were pre-dilated with Artimes 1.5 × 10 mm and 2.0 × 10 mm balloons, followed by the first kissing balloon inflation using diagonal and LAD balloons at 10 atm pressure. Subsequently, the D1 lesion was stented with a zotarolimus-eluting stent (2.75 × 14 mm), with 2-3 mm of the stent protruding into the LAD. The proximal portion of the D1 stent was crushed using a 3.0 × 12 mm balloon inflated at 10 atm pressure in the LAD, employing the Mini-Crush Technique.

The proximal to mid-segment of the LAD lesion was then stented with a zotarolimus-eluting stent (2.75 × 18 mm), and final kissing balloon inflation (FKBI) was performed using 2.5 × 12 mm and 3.0 × 12 mm balloons inflated at 14 atm pressure. Intracoronary nitroglycerin (200 mcg) and tirofiban (10 ml) were administered during the procedure. The intervention achieved excellent angiographic results with TIMI 3 flow in the LAD-D1 bifurcation and no complications.

Results

The "Mini-Crush Technique" successfully addressed the critical LAD-D1 bifurcation lesions, achieving excellent angiographic results without any periprocedural complications. At an 8-month follow-up, the patient was asymptomatic and doing well.

Conclusion

The "Mini-Crush Technique" with drug-eluting stents provides complete coverage of the side branch ostium while optimizing side branch access. It is a refined and effective modification of the traditional "Crush Technique" with demonstrated safety and efficacy.

Experimental studies using intravascular imaging modalities like IVUS and OCT have validated its favorable outcomes. Its application in both bifurcation and trifurcation lesions holds significant promise for improved procedural success and clinical outcomes.

GLP1RA, the "It" Drug Class

Glucagon-like protein 1 receptor agonists (GLP1RAs) have emerged as the "it" drug class of 2024. Few medications have garnered as much attention — both positive and negative — in the mainstream press. Ozempic, Wegovy, and Mounjaro have become social media sensations, symbolizing a cultural moment in medicine. Remarkably, the first GLP1RA was approved nearly 20 years ago, although these drugs were initially confined to the realm of endocrinologists treating type 2 diabetes. While GLP1RAs gained approval for weight loss in 2014, their transformative potential wasn't fully realized until the introduction of higher doses, such as 2.4-mg semaglutide and tirzepatide, which delivered 15% to 20% weight loss. These breakthroughs propelled GLP1RAs into the center of a national conversation.

The science of GLP1RAs is evolving rapidly, with over 50 new articles appearing in PubMed each week. What do we know so far? GLP1, a gut hormone, is a potent regulator of satiety and metabolism, exerting effects on the brain and multiple organ systems. At pharmacologic doses, GLP1RAs improve hyperglycemia, promote weight loss, and reduce inflammation. In type 2 diabetes, they are a first-line therapy for glucose control and significantly lower cardiovascular event risk. The SELECT trial 1 demonstrated that semaglutide 2.4 mg reduced cardiovascular events in patients with obesity or overweight and atherosclerotic cardiovascular disease (ASCVD), while also improving renal outcomes in patients with chronic kidney disease (CKD). Additionally, semaglutide and tirzepatide have shown benefits in heart failure with preserved ejection fraction (HFpEF), reduced sleep apnea severity, and alleviated osteoarthritis pain. Emerging research suggests these drugs could address a wide range of conditions, including substance use disorders, atrial fibrillation, Alzheimer's disease, Parkinson's disease, metabolic-associated liver disease, and polycystic ovary syndrome (PCOS).

Despite these advancements, fundamental questions remain about GLP1RAs and their mechanisms of action. The relationships of weight loss, glucose control, and clinical outcomes are complex and are likely to vary by condition. For instance, some GLP1RAs deliver cardiovascular benefits with only modest glucose-lowering effects. Conversely, weight loss appears to play a larger role in the benefits observed in HFpEF trials.

The next wave of incretin therapies will feature dual or triple agonists, combining GLP1RAs with an agent such as gastric inhibitory polypeptide (GIP), glucagon, amylin, FGF21, or PYY. To succeed clinically, these combinations will likely need to achieve greater than 20% weight loss. Whether they offer superior cardiovascular, renal, or other systemic benefits - or reduce side effects - will be determined by the outcomes of head-to-head trials.

A bigger challenge looms: how to afford these medications in a society grappling with the consequences of poor-quality diets and sedentary lifestyles. GLP1RAs can profoundly enhance life expectancy and quality when used appropriately, but they are no panacea for society's broken relationship with food. Striking a balance between their promise and practicality will require collaboration across medicine, industry, and society.

HEALTHY LIVING

1. Making cellphone calls may increase heart disease risk, study finds

- A new study finds an association between making cellphone calls and increased cardiovascular risk.
- Compared with those who made the fewest calls, those who used their phones the most had a 21% increased risk of experiencing a cardiovascular event.
- This relationship was most pronounced in people with diabetes and those who smoke.
- However, the study has a number of limitations, and more research is needed.

A new study published in the Canadian Journal of Cardiology, which included data from almost half a million participants, measured an association between making cellphone calls and cardiovascular disease risk.

Specifically, the more time an individual spends making calls each week, the greater their risk of experiencing a cardiovascular event, such as stroke or heart failure.

According to the paper, sleep, psychological distress, and neuroticism are important drivers of the association.

What are the health implications of cellphone use?

As cellphones continue their path to world domination - there are now more cellphone contracts than humans on Earth- scientists are keen to understand their effects on health and happiness.

Research has focused on many potential effects of smartphones. For instance, there were once widespread fears that using a cellphone might cause brain cancer, and a recent World Health Organization (WHO) review of 63 studies has dismissed the link. Previously, the Food and Drug Administration (FDA) also found no data to support this link.

As smartphones are here to stay, understanding how they impact our health is clearly important. Much of the research today focuses on the impact of social media apps or chat rooms on mental health rather than the effects of mobile technology itself.

However, the latest study takes a step back and asks whether phone calls might be linked to cardiovascular risk.

To investigate, the researchers took data from 4,44,027 participants from the UK Biobank. This dataset included self-reported details about how much time they spent making calls on cell phones.

The scientists defined "regular" phone use as taking or making at least one call per week. More than 85% of participants fit into this classification, and the rest were defined as nonregular users.

Using hospital records, the scientists tracked participants' health conditions and deaths over an average of 12.3 years of follow-up.

Is mobile phone use linked to cardiovascular disease?

The researchers combined cases of stroke, coronary heart disease, atrial fibrillation, and heart failure to give a composite outcome of cardiovascular disease risk.

After controlling for various factors, they found that, compared with nonregular cellphone users, regular users had a small increase in composite cardiovascular disease risk (4%). However, the longer people spent on phone calls, the larger this difference became.

Compared with people who made or received calls for 5 minutes or less each week, those who used their phone for:

- 5–29 minutes had a 3% increased risk.
- 30–59 minutes had a 7% increased risk.
- 1–3 hours had a 13% increased risk.
- 4–6 hours had a 15% increased risk.
- 6 or more hours had a 21% increased risk.

According to the paper, three factors seemed to play an important part in the relationship between cell phone usage and cardiovascular disease:

- Psychological distress explained 11.5% of the association.
- Sleep quality 5.1%.
- Neuroticism 2.3%.

A poor sleep pattern and poor mental health may adversely affect the development of cardiovascular diseases through disrupted circadian rhythm, endocrine and metabolic disruption, and increased inflammation, explains Xianhui Qin, MD, one of the study's authors.

Interestingly, the scientists also found that the link between phone usage and cardiovascular disease risk was most pronounced in people who smoke and those with diabetes. The authors suggest that this link may be because RF-EMF exposure from mobile phones in combination with smoking and diabetes may have a stronger effect in increasing [cardiovascular disease] risk.

How cellphones raise heart disease risk?

The relationship between cell phone usage and heart disease risk was examined in an observational study, though causation could not be established. It was suggested that the effects of phone usage on mental health and sleep might contribute to the observed relationship. Additional factors, such as smoking and diabetes, were identified as potential confounders, as increased mobile phone usage was more prevalent among individuals with these conditions. This raises the possibility that the reported cardiovascular risk could be linked to these pre-existing factors rather than phone usage itself.

The impact of extensive phone use on sleep was highlighted, noting that disruptions to the body's circadian rhythm can lead to stress on the heart and blood vessels. Additionally, prolonged phone use may elevate stress and anxiety levels, potentially increasing blood pressure and inflammation, both of which are associated with cardiovascular disease.

Should people be worried about their cellphones?

The findings of the study were viewed with caution, as further research is needed to confirm the connection between mobile phone use and cardiovascular disease. It was emphasized that the study primarily assessed the frequency of phone calls during a specific period (2006–2010), without accounting for the broader range of activities now commonly performed on mobile devices, such as messaging, video conferencing, and social media use. While awaiting additional studies, individuals are encouraged to mitigate cardiovascular risks by following recommendations such as adopting a healthy balanced diet, engaging in regular physical activity, ensuring sufficient quality sleep, maintaining a healthy weight, avoiding tobacco and alcohol, and reducing stress levels.

2. Habit of Daily Flossing may help Lower Cardiovascular Risk and Mortality: Study

Daily Flossing may lower cardiovascular risk and mortality suggests a new study published in The Journal of the American Dental Association. Increasing evidence suggests that daily oral hygiene self-care measures may alleviate cardiovascular disease (CVD) risk. The authors aimed to determine the influence of self-reported dental flossing behavior on the prevalence of CVD events, CVD-linked mortality, and a CVD risk marker of inflammation (ie, C-reactive protein [CRP]). Data from 18,801 adult participants of the 2009-2016 National Health and Nutrition Examination Surveys were analyzed about flossing behaviour, prevalence of CVD events, mortality cause data, and CRP levels. Information on mortality was obtained from the US mortality registry, updated to 2019. Participants who answered the flossing question were divided into 4 groups (model 1 to 4) according to their frequency of flossing: not flossing (0 d/wk); occasional flossing (1-3 d/wk); frequent flossing (4-6 d/wk); and daily flossing (7 d/wk). Multiple logistic regression and Cox proportional hazard regression were used for analysis.

Results

Daily flossing was associated with lower prevalence of CVD events after adjusting for age, sex, sociodemographic factors, and lifestyle habits (model 2); the odds ratio was 0.71 (95% CI, 0.59 to 0.85) for CVD prevalence in

the daily flossing group compared with the not flossing group. The odds ratio for CVD prevalence for each additional day of flossing was 0.95 (95% CI, 0.93 to 0.98; P for linear trend <%E2%80%89.001) in model 2, and remained statistically significant after model 2 was further adjusted for metabolic syndrome. Daily flossing compared with not flossing was associated with lower risk of experiencing CVD mortality (hazard ratio, 0.64; 95% CI, 0.49 to 0.84) in model 2. The hazard ratio of CVD mortality for each additional day of flossing was 0.94 (95% CI, 0.90 to 0.98; P for linear trend = .002) in model 2. Participants in the not flossing group had significantly elevated CRP levels, even after multivariable adjustments. Poor flossing behavior is associated with higher prevalence of cardiovascular events, increased risk of experiencing CVD mortality, and elevated CRP levels. Improvement in flossing behavior can have an additional benefit in the prevention of CVD events. Cardiologists need to advise patients to improve their personal oral hygiene practices, in addition to the standard diet and exercise advice.

3. 4 or 5 minute bouts of intense exercise may slash cardiovascular risk

- Past studies show that getting enough physical activity can help lower a person's risk for major adverse cardiovascular events (MACE).
- Researchers from the University of Sydney have found that just 1.5 to 4 minute small bursts of high intensity exercise throughout the day may lower a person's MACE risk.
- This correlation was observed more significantly in female participants compared to male participants.

Past studies show that getting enough physical activity can help lower a person's risk for major adverse cardiovascular events (MACE), such as heart failure, stroke, and heart attack.

Physical inactivity is a major public health issue contributing to [up to] 6 million deaths per year globally, and is directly responsible for at least 15–20% of cardiovascular disease. There is a pressing need to identify feasible ways and support people to be physically active. Structured exercise such as gyms, running, classes, etc is fantastic towards these goals but only 20% of the middle aged and older population do it regularly, he pointed out.

Stamatakis is the lead and corresponding author of a new study recently published in the British Journal of Sports Medicine that has found that just 1.5 to 4 minute small bursts of high intensity exercise throughout the day - scientifically known as vigorous intermittent lifestyle physical activity (VILPA) - such taking the stairs instead of an elevator or carrying groceries a short distance may help lower a person's risk of MACE, especially in women.

What is vigorous intermittent lifestyle physical activity?

For this study, researchers analyzed UK Biobank data from more than 103,000 middle-aged men and women with an average age of 61. All participants had worn an activity tracker 24 hours a day for a full week between 2013 and 2015.

About 22,000 participants said they did not follow any structured exercise program or only took one recreational walk a week, while the remaining participants said they regularly exercised.

Researchers used the activity trackers to determine which participants had bouts of VILPA during the day and for how long.

Incidental physical activity, things we do as part of our daily routines, offers many untapped opportunities, but we do not understand what is the best way to promote, and how to support people - VILPA offers such an option, Stamatakis explained.

These are short bursts of vigorous incidental activity, typically lasting [between] 10 seconds [and] 1 minute, that are part of people's daily living. This kind of activity may be more feasible than structured exercise for many people as it does not require preparations, time commitment, or traveling to a facility to be active he detailed.

Using advanced wearable measurement methods that allow us to scrutinize the effects of daily movement at a very high resolution-10-second time windows - we wanted to understand what are the effects of VILPA on major cardiovascular disease events added Stamatakis. No such study has been published before.

3.4 VILPA minutes per day lowers MACE risk by 45% in women

Study participants' cardiovascular health was tracked until November 2022. Upon analysis, researchers found that female participants with no formal exercise regimen who recorded an average of 3.4 minutes of VILPA a day were 51% less likely to have a heart attack, 67% decreased risk for heart failure, and 45% less likely to develop any type of MACE compared to female participants who did not clock any VILPA during their day.

Additionally, scientists discovered for women that even VILPA amounts of 1.2 to 1.6 minutes a day were associated with a 40% decreased risk of heart failure, 33% lowered risk of heart attack, and 30% lower risk of all MACE.

This finding is significant for at least two reasons Stamatakis said. First, it represents a much lower amount of physical activity [than] any current exercise related recommendation, and this activity is incidental - which implies that it may be easier for many people to incorporate it into their daily routine.

The second noteworthy aspect of these findings is that we should not be fooled into thinking that small amounts of VILPA are a quick fix of a complex problem, like physical inactivity, he continued.

4. FDA Warns Against Using Newspapers and Cardboard Boxes for Food Packaging

The FDA has warned food operators against using newspapers and cardboard boxes for packaging, citing health risks from toxic inks and chemicals. Legal action and hefty fines await violators operating without mandatory licenses.

The Food and Drugs Administration (FDA) has cautioned food business operators (FBOs) against using newspapers for wrapping or serving food and cardboard boxes for delivering cooked or fried items. Banned by the Food Safety and Standards Authority of India (FSSAI), the practice poses significant health risks due to toxic substances in printing ink and packaging materials.

An FDA advisory highlighted that newspaper ink contains harmful bioactive materials, including lead and heavy metals, which can contaminate food and cause serious health issues when ingested. The advisory also warned FBOs of legal action if they continue such practices, urging immediate compliance.

Additionally, the FDA noted that many FBOs operate without mandatory registration or licenses, violating the Food Safety and Standards Act. Unlicensed operations can result in penalties of up to Rs 10 lakh. The FDA has directed FBOs to obtain licenses either online or by visiting the FDA office.

IS YOUR CRYING LUNG BREATH A SIGN OF IMPENDING HEART FAILURE OR SOMETHING ELSE?

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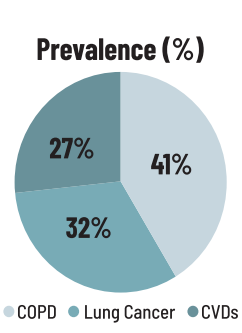
Dyspnoea, commonly known as shortness of breath, is a prevalent symptom that can arise from various medical conditions. In older adults, it often serves as a critical indicator of underlying health issues, particularly heart failure (HF). This article aims to explore the impact of dyspnoea on older adults, the challenges in diagnosing heart failure, and the importance of early detection and intervention.

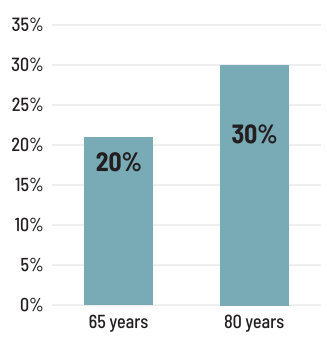
The Prevalence of Dyspnoea in Older Adults

As individuals age, the prevalence of moderate-to-severe dyspnoea also rises, making it a common reason for emergency visits. However, distinguishing between cardiac and respiratory causes of dyspnoea can be challenging due to the prevalence of comorbidities and the nonspecific nature of symptoms.

The Nidus Study estimates that **8-10 million people in India have heart failure.** The risk rises sharply after **age 50,** making older adults more vulnerable



Prevalence of chronic illnesses which are linked to dyspnea



Prevalence of moderate-to-severe dyspnea, increasing with age

Key Respiratory Symptoms Associated with Heart Failure

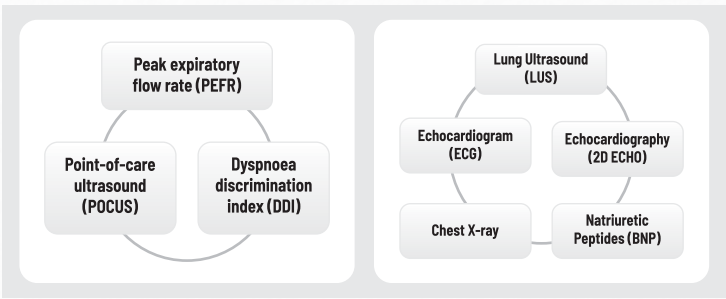
Several respiratory symptoms are frequently associated with heart failure, including:

- Dyspnea (Shortness of Breath)
- Paroxysmal Nocturnal Dyspnea (PND)
- Orthopnoea
- Treponema
- Cheyne-Stoke Respiration
- Nocturnal Cough
- Pulmonary Crackles (Rales)
- Wheezing
- Crepitant Moist Rales

These symptoms not only affect the quality of life but also complicate the diagnostic process for healthcare providers.

Diagnostic Tools for Early Detection

To differentiate heart failure from other causes of dyspnoea, several diagnostic interventions are recommended:



These tools enhance the clinician's ability to make timely and accurate diagnoses, ultimately improving patient outcomes.

Conclusion

In summary, recognizing dyspnoea as a key indicator of heart failure is vital for improving outcomes in older adults. Early detection and intervention can enhance survival and quality of life, emphasizing the importance of proactive and informed clinical care.

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