Future of Cardiology

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Future of Cardiology

- **Niels Bohr's** famous prediction statement:
- "Prediction is very difficult especially if it's about the future"
- **Benjamin Franklin's** famous prevention statement:
- "An ounce of prevention is worth a pound of cure"

Future of Cardiology

- Early Prevention (as early as childhood)
- New and advanced therapeutics (beyond traditional approaches)
- **Precision medicine**/Personalized healthcare/Genomics (tailor medical care to individual patient characteristics)
- **Identify high-risk/vulnerable individuals** (who would benefit most from aggressive treatment)
- AI and Digital innovation

Future of Cardiology

- Current effectiveness of statin therapy (Over 5 years of therapy):
- Primary Prevention: **Need to treat 104 patients** to prevent one heart attack; **Need to treat 154 patients** to prevent one stroke
- Secondary Prevention: **Need to treat 39 patients** to prevent one heart attack; **Need to treat 125 patients** to prevent one stroke
- Very High-Risk Individuals: **Need to treat 14** patients to prevent one heart attack

Future of Cardiology

- **Global obesity epidemic** – Root cause of cardiovascular disease (from adolescence through adulthood) reversing decades of progress in heart health
- **Cardiometabolic focus** – Appreciate that the cardiovascular and metabolic systems are an interconnected network, as opposed to separate, isolated conditions
- **Multi-organ approach** and multi-disciplinary care – Treat the whole patient; (holistic-approach); CVD interrelated with multi-organ involvement
- **Trending from a reactive, event driven field to a proactive prevention focused one**

Future of Cardiology

- The obesity epidemic acts as a major counterforce to declines in CVD mortality despite advances in medical care
- Obesity promotes hypertension, hyperlipidemia, diabetes/insulin resistance, metabolic syndrome, systemic and vascular inflammation, endothelial dysfunction and atherosclerosis
- Obesity/**increased visceral fat** is at the core of the metabolic derangements that occur in the body that lead to the increased risk of CVD

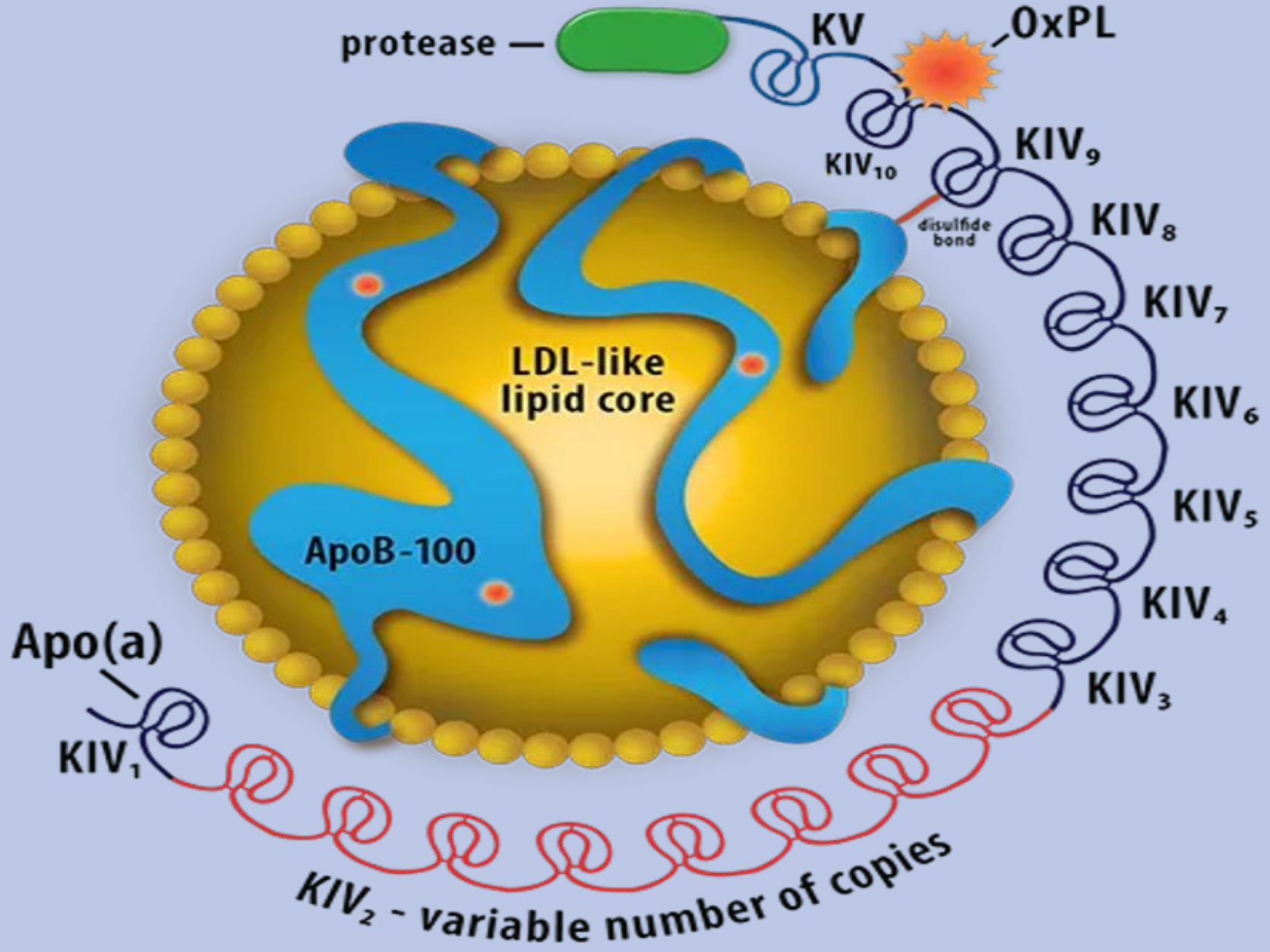
Future of Cardiology

Lp(a)

Future of Cardiology - Lp(a)

- Lipoprotein similar to and looks like LDL cholesterol
- Contains an added “sticky” glycoprotein **(apolipoprotein(a) or apo(a))**
- Contains **oxidized phospholipids (OxPL)**
- These components result in a lipoprotein that promotes and accelerates atherosclerosis development

Lipoprotein(a) Structure

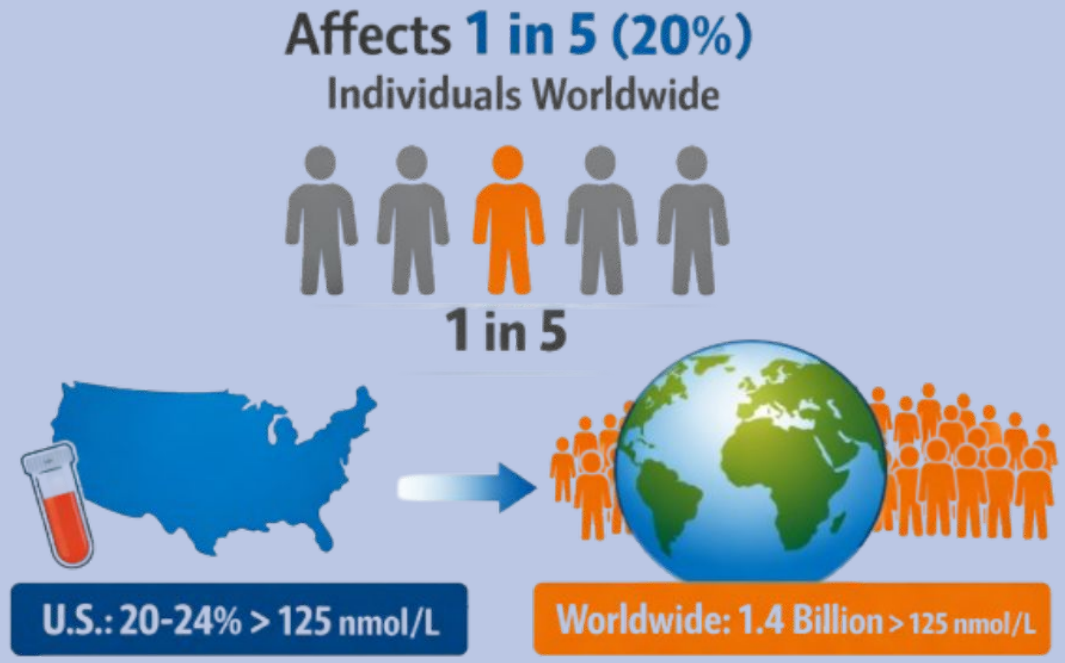


Future of Cardiology - Lp(a)

Risk Categories for Lp(a)		
Risk Level	**nmol/L**	**mg/dL** (approx.)
Low risk	< 30	< 10
Borderline	30–75	10–30
High risk	75–125	30–50
Very high risk	> 125	> 50
Extreme risk	> 180	> 70

Lp(a) Prevalence

- Affects 1 in 5 (20%) individuals worldwide
- US: 20-24% of population > 125 nmolL
- Worldwide: 1.4 billion have levels > 125 nmol/l
- Prevalence may be greater because testing is not routine and therefore, undiagnosed
- More common in females, Black population and South Asians
- Level goes up post menopause and during times of illness



Lp(a) – Detrimental Effects

- Promotes atherosclerosis
- Promotes inflammation
- Promotes thrombosis

Future of Cardiology - Lp(a)

- Independent risk factor for atherosclerotic cardiovascular disease (ASCVD) (**Heart Attacks and Strokes** – 2 to 3 fold) (May contribute more than diabetes, smoking and other lipid parameters)

- Independent risk factor for **peripheral arterial disease**

- Independent risk factor for **calcific aortic stenosis**

Future of Cardiology Lp(a)

- Elevated Lp(a) associated with **imaging findings** consistent with **subclinical ASCVD** (i.e. carotid intima-media thickness, carotid plaque, coronary artery calcification and subclinical brain infarcts)

- Elevated Lp(a) associated with presence of focal **vulnerable plaques**

Lp(a) Who Should be Screened?

- 2019: ESC and EAS Guidelines for the Management of Dyslipidemias: Recommends one-time screening for Lp(a) for the general adult population

- 2026: ACC/AHA/Multisociety Guideline on the Management of Blood Cholesterol strongly recommends that all adults have their Lipoprotein(a) [Lp(a)] measured at least once in their lifetime for atherosclerotic cardiovascular disease (ASCVD) risk assessment.

Future of Cardiology - LP(a) & Calcific Aortic Stenosis

- Lp(a) accumulates in aortic valve leaflets
- Lp(a) mediates **pro-inflammatory and pro-calcifying** responses in valvular interstitial cells.
- Lp(a)'s oxidized phospholipids bind to exposed lysine on aortic valve endothelial cells.
- Lp(a) can then bind tightly and deliver its cargo of **oxidized phospholipids** that then mediate **pro-calcifying responses**.

Future of Cardiology – Lp(a) & Calcific Aortic Stenosis

- European Heart Journal; February 21, 2026:

- Prospective study of 6598 participants enrolled in the US-based cohort Multi-Ethnic Study of Atherosclerosis(Mesa); Participants were **men and women age aged 45-84 years.**
- **Regular aspirin use** (at least X3/week) was associated with markedly lower risk of developing aortic valve calcium or worsening aortic valve calcium and severe aortic stenosis in individuals with **significantly elevated Lp(a)**
- Proposed mechanism of action involves a potentially Lp(a) specific, platelet mediated pathway
- **Particularly associated with a specific Lp(a) gene variant (the "risk allele")**

Future of Cardiology – Lp(a) Case Presentation

- Jeremy is a 52 y/o male
- Julie is a 56 y/o female
- B/P 130/80 mmHg
- Hs CRP 1.8 mg/L
- LDL 110 mg/dl
- Lp(a) 200 nmol/L



- A - Mild calcific aortic stenosis noted on echocardiogram
- B - No calcific aortic stenosis noted on echocardiogram
- Would you treat Jeremy and/or Julie with aspirin? (A and/or B)
- Would you test for presence of the specific high risk genetic variant" (also called the "genetic aspirin test")

Future of Cardiology - Treatment of Elevated Lp(a)

- Lp(a) levels cannot be controlled by healthy eating and exercising.
- Lipoprotein apheresis is the only therapy approved by the Food and Drug Administration (FDA) for treating high Lp(a) (no outcome data)
- PCSK9 Inhibitors
- Niacin
- HRT (Estrogen)
- Supplements (Berberine, Ginko Biloba and others)

Future of Cardiology: Treatment of Elevated Lp(a)

- Most of the drugs in development for lowering Lp(a) work by **interfering with RNA**
- Currently, there are four RNA-based drugs that effectively silence the gene that makes Lp(a) in liver cells: **lepodisiran, olpasiran, pelacarsen, and zerlasiran.**
- All are **administered by injection** every one to six months and have been shown to lower Lp(a) levels 80% and 100%. The **side effects appear to be limited to mild**, short-lived pain at the injection site.
- Larger, longer trials looking at whether these drugs will help prevent heart-related problems are currently under way, with results expected within the next one to two years.

Future of Cardiology: Treatment of Elevated Lp(a)

- Muvalapin: Not RNA-based
- **Prevents the assembly** of the Lp(a) particle.
- Leads to dramatic drops in Lp(a), and is **taken as a daily pill**.
- Side effects include headache, back pain, and fatigue.
- While some people prefer pills over shots, injectable drugs have the advantage of much less frequent dosing.

Future of Cardiology – Lp(a)

Conclusion:

- Common Lipid disorder
- >125 nmol/L considered high risk
- Associated with increased CVD risk and progressive calcific aortic stenosis
- Screen everybody, at least once
- Help is on the way!

Future of Cardiology

Hyperlipidemia

The Future of Cardiology - Hyperlipidemia

Current Treatment Modalities:

- Statins (HMG-CoA Reductase Inhibitors)
- Ezetimibe (Zetia) (Inhibits absorption of dietary and biliary cholesterol in the small intestine)
- Bempedoic Acid (Nexletol) (Inhibits enzyme upstream of HMG-COA reductase in the hepatic cholesterol synthesis pathway)
- PCSK9 Inhibitors (Monoclonal Antibodies: Praluent; Repatha)
- RNA Interference (siRNA) Inclisiran (Leqvio)
- Bile Acid Sequestrants
- Fibrates and Niacin

Future of Cardiology - Hyperlipidemia

- **Shift Towards Earlier Treatment:**

- JACC 01/10/26: Impact of Early, Delayed, or Interrupted Treatment in Children With Familial Hypercholesterolemia

- **Early Cholesterol Treatment May Lower Lifetime Heart Risk**

- Starting therapy later or stopping it was associated with an increase in LDL-cholesterol exposure, more lifetime CVD events, and fewer life-years than continuous therapy starting in childhood.

Future of Cardiology - Hyperlipidemia

Cholesterol Treatment/Management Guidelines:

- 1988: Adult Treatment Panel (ATP) I
- 1993: Adult Treatment Panel (ATP) II
- 2001: Adult treatment Panel (ATP) III
- 2004: Adult treatment Panel (ATP) III Update
- 2013: ACC/AHA Cholesterol Treatment Guidelines
- 2018: ACC/AHA Cholesterol Management Guidelines



2026 ACC/AHA Guideline on the Management of Dyslipidemia

ACC/AHA Release New Clinical Guideline For Managing Dyslipidemia; Mar 13, 2026

2026 ACC/AHA Guideline on the Management of Dyslipidemia

- ACC/AHA Release New Clinical Guideline For Managing Dyslipidemia; Mar 13, 2026

- Replaces 2018 Guidelines

- A major focus of the guideline is earlier intervention through healthy lifestyle changes, starting in childhood and early initiation of pharmacotherapy as indicated

2026 ACC/AHA Guideline on the Management of Dyslipidemia

- The 2026 ACC/AHA guidelines recommend the **P**revent (Predicting **R**isk of cardiovascular disease **EVENT**s) online calculator for estimating 10-year (ages **30**–79) and 30-year (ages **30**–59) ASCVD risk

- Risk of ASCVD should be calculated beginning at age 30 rather than age 40 years old

2026 ACC/AHA Guideline on the Management of Dyslipidemia

- Measurement of Lp(a)
- Measurement of ApoB
- Dietary supplements
- Referral to nutritionist/RD
- PREVENT – ASCVD Equations:
    - Low risk: <3%
    - Borderline risk: 3% to < 5%
    - Intermediate risk: 5% to <10%
    - High risk: 10% or greater

2026 ACC/AHA Guideline on the Management of Dyslipidemia

- **Risk enhancers** for borderline or intermediate risk: Personalize CVD risk assessment:
- Family history of ASCVD in a parent or sibling
- Higher risk ancestry: e.g. South Asian, Fillipino
- Reproductive Risk Markers (Early menopause/Gestational diabetes/Pre-eclampsia/Pre-term delivery)
- Chronic inflammatory disease (RA/SLE/Psoriasis/Hepatitis/AIDS)
- Lp(a) > 125 nmol/L or 50 mg/dl; ApoB 130 or above mg/dl
- HS CRP 2 mg/L or greater
- Non fasting triglycerides 175 mg/dl or greater (Metabloic syndrome)
- Fasting triglycerides 150 mg/dl or greater

2026 ACC/AHA Guideline on the Management of Dyslipidemia

- Management of **subclinical coronary atherosclerosis:**
- **Coronary artery calcium (CAC) scans** recommended for adults (men 40 y/o or older and women 45 y/o or older) at intermediate risk and select adults at borderline risk with no prior ASCVD in whom the decision to initiate LLT is in question
- Lipid-lowering therapy recommended for **CAC score >0 AU** (especially if it is ≥100 AU or ≥75th standardized percentile) in adults at intermediate risk and select adults at borderline risk.
- For moderate subclinical atherosclerosis (CAC score ≥100 AU): Goal: lower LDL cholesterol to <70 mg/dL
- For severe subclinical atherosclerosis: CAC score ≥300 AU): Optional goal: Lower LDL cholesterol to <55 mg/dL

2026 ACC/AHA Guideline on the Management of Dyslipidemia

Key Takeaways:

- Endorses the PREVENT equations to guide lipid-lowering therapy in primary prevention in adults.
- Endorses using the PREVENT equations beginning at age 30
- Lipid-lowering therapy can be considered with a 10-year PREVENT-ASCVD risk estimate of 3% to <5% (borderline) and should be considered for those at 5% to <10% (intermediate) 10-year risk.
- For **secondary prevention**, ezetimibe (Zetia), a PCSK9 monoclonal antibody, and bempedoic acid (Nexletol) are equally recommended as adjunct therapies for bringing LDL cholesterol down to **<55 mg/dL** in adults with clinical ASCVD already on statin therapy

CENTRAL ILLUSTRATION 2026 Dyslipidemia Guideline-at-a-Glance

Lipid Lowering to Reduce ASCVD Risk

Screen EARLIER



- Screen at **age ≥2y** if family history of premature ASCVD, severe hypercholesterolemia, or FH
- Screen at **ages 9–11y** to identify FH and other lipid disorders

Check REGULARLY



- Screen lipids again at age **19y**
- Recheck at least every **5y** and use PREVENT-ASCVD to identify risk

Aim for LOWER LDL-C



LDL-C goal:

- **<100 mg/dL** for PREVENT-ASCVD <10%
- **<70 mg/dL** for PREVENT-ASCVD ≥10%, FH, DM with risk factors, CAC ≥100 AU
- **<55 mg/dL** for clinical ASCVD at very high risk*

Treat LONGER



- Check lipids **4–12wk** after start or dose change of lipid-lowering therapy, then **every 6–12mo** thereafter
- Benefits increase with longer therapy; tailor duration to individual risk

Promote lifelong healthy lifestyle behaviors

Wiggins BS, et al. JACC. 2026;■(■):■-■.

*Very high risk includes a history of multiple major ASCVD events (ACS within the past 12 months; prior myocardial infarction [other than ACS above]; prior ischemic stroke; or symptomatic peripheral artery disease) or 1 major ASCVD event and multiple high-risk conditions (age >65 years of age; prior coronary artery revascularization; current smoking; diabetes; history of heart failure; hypertension; or LDL-C >100 mg/dL despite maximally tolerated statin plus ezetimibe). ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; DM = diabetes mellitus; FH =familial hypercholesterolemia; LDL-C = low-density lipoprotein cholesterol; PREVENT = Predicting Risk of cardiovascular disease EVENTs.

Future of Cardiology - Hyperlipidemia Case Presentation



36 y/o Female

Mei

Pre-menopausal

- B/P: 130/80
- Hs CRP: 1.8
- LDL: 150 MG/dL
- **Lp(a): 200 nmol/L**

Would you treat with statin?



Would you first test for the presence of specific Lp(a) gene variants?

Future of Cardiology - Hyperlipidemia

- Patients with very high Lp(a) levels remain at increased risk of MACE regardless of whether they carry the specific Lp(a) gene variant
- Very high Lp(a) levels is still a strong independent risk factor of CVD risk.
- The actual concentration of Lp(a) in the blood is the primary driver of risk (proinflammatory and prothrombotic)

Future of Cardiology – Hyperlipidemia Case Presentation

- While a low 10-year risk (<3%) traditionally suggests lifestyle modification alone, the 2026 guidelines emphasize using Lp(a) to reclassify risk
- Therefore, statin therapy is reasonable to consider for primary prevention in low-risk individuals with high Lp(a) to reduce cumulative lifelong exposure to atherogenic particles.

Future of Cardiology - Hyperlipidemia Case Presentation



36 y/o Male

Greg

- B/P 130/80 mmHg
- Hs CRP 1.8 mg/L
- LDL 150 mg/dl
- Lp(a) 25 nmol/L
- **CAC Score 2 AU**

? Would you treat with statin?



Future of Cardiology – Hyperlipidemia Case Presentation

- According to the 2026 ACC/AHA guidelines a coronary artery calcium score of 1-99 indicates subclinical atherosclerosis and favors treatment with a moderate intensity statin (in borderline or moderate risk individuals)
- In a low-risk individual ordinarily this would fall under shared-decision-making, any CAC score >0 indicates elevated risk compared to a risk of zero
- This is especially true for younger individuals

Future of Cardiology - Hyperlipidemia

- Revisions to the new guideline are already being planned in the wake of the recent VESALIUS-CV trial report

- Addition of the PCSK9 inhibitor evolocumab (Repatha) to stable lipid-lowering therapy reduced cardiovascular risk in patients with atherosclerosis but no history of MI or CVA

- Future updates to the 2026 Dyslipidemia Guidelines should include a single care for all patients with ASCVD: an optimal LDL-C goal of <55 mg/dL to be achieved via pharmacotherapy as well as lifestyle optimization

Future of Cardiology - Hyperlipidemia

- **Shift Towards Lower Targets:**
- Shift towards extremely low LDL-C targets (<55 mg/dl)
- 2025 ECS/EAS targets levels below 40 mg/dl for extreme risk individuals
- “Lower is Better” (Without a floor)
- “Lower for Longer”
- Achieve plaque regression
- Beyond statin monotherapy

Future of Cardiology - Hyperlipidemia

- **Future Therapeutic Goals:**
- Improve efficacy
- Improve convenience and adherence
- Reduce side effects
- Alternate targets/pathways/delivery systems

Future of Cardiology - Hyperlipidemia

Address Residual Risk:

- Lp(a)
- Anti-inflammatory therapy (Colchicine; Ziltivekimab (Il-6inhibitor)
- Mixed hyperlipidemia
- Functional measures (of lipoprotein particles)

Future of Cardiology - Hyperlipidemia

RNA Based Therapies:

- LEQVIO (Inclisiran)
- The siRNA binds to the mRNA responsible for producing the PCSK9 protein, preventing its synthesis
- PCSK9 degrades LDL receptors in the liver which clears LDL from the blood stream
- With less PCSK9 available to degrade LDL receptors on the liver, more receptors are available to pick up and clear LDL cholesterol from the blood.

Future of Cardiology - Hyperlipidemia

RNA Based Therapies:

- Continuously prevents PCSK9 production (long duration of action)
- Oral PCSK9 (Inhibitor (Enlicitide) – NEJM 02/04/26: Phase 3 trial completed – Received FDA approval April 2026; Coming to market by the summer of 2026)
- Offers significantly greater LDL reduction compared to standard statin alone

Future of Cardiology - Hyperlipidemia

Targeting New Targets:

- PCSK9 – Promotes the degradation of LDL receptors in the liver allowing it to more effectively remove LDL from the blood stream (Monoclonal antibodies Repatha and Praluent)

- ApolipoproteinC-III – Amino Acid produced in liver and intestine which inhibits lipoprotein lipase

- ANGPTL3 – Protein secreted by liver that inhibits lipoprotein and endothelial lipase

Future of Cardiology – Hyperlipidemia

Targeting New Technologies:

- **Gene-editing** technology (CRISPR-Cas9)
- Acts like "molecular scissors" to precisely cut and modify DNA at specific locations
- Can add, remove, or alter genetic material to potentially correct disease-causing mutations
- One-time infusion of gene-editing therapy (e.g., CTX310) can significantly reduce LDL cholesterol and triglycerides, potentially offering a one-time, long lasting, possibly permanent treatment

Future of Cardiology – Hyperlipidemia

Targeting New Targets and New Technologies:

- Results from Phase 1, first in human trial of a CRISPR – Cas9 **gene editing** therapy
- Targets **ANGPTL3**, cas9 gene shown to regulate LDL and triglyceride metabolism (mixed hyperlipidemia)
- Results of a single intravenous infusion to patients with elevated lipids despite standard therapies were striking
- Dose dependent reduction of LDL of up to nearly 50% and 55% for triglycerides
- Could a single infusion eliminate the need for life-long lipid lowering therapy?

Future of Cardiology - Hyperlipidemia

Targeting New Delivery Mechanisms:

- **Nanoparticles** (undetectable by the human eye) are not inherently a form of gene editing itself, but rather a leading **non-viral delivery mechanism** used to transport gene-editing tools (like CRISPR/Cas9, DNA, or mRNA) into cells.
- They act as protective carriers that improve the efficiency and safety of delivering genetic material to target tissues, bypassing the need for viral vectors
- **Nanotheranostics:** Some nanoparticles can simultaneously act as **diagnostic** imaging tools (to detect vulnerable plaques) and carriers for **therapeutic** drugs to treat the lipid disorder

Future of Cardiology – Hyperlipidemia

- **Precision Medicine: (Tailored to an individual's metabolic and genetic profile)**
- PCSK9 Inhibitors and other pharmacologic agents
- Targeting LDLR Mutations which cause Familial Hypercholesterolemia in which LDL receptors are disrupted
- Gene editing to turn off genes which can drastically (and permanently) lower cholesterol and triglycerides; i.e., a **curative approach**

Future of Cardiology - Hyperlipidemia

Conclusion:

- Treat early (Screen early and regularly)
- Treat to lower thresholds
- Address residual risk
- Newer targets
- Newer delivery mechanisms
- Improved convenience/adherence
- Longer lasting effects of treatment
- Driven by precision medicine and AI

Future of Cardiology

Hypertension

History of Hypertension Guidelines

- 1977: First guidelines for hypertension were published introducing a standardized approach for detection, evaluation and treatment. (JNC)
- 2013: AHA/ACC publishes their own guidelines (Pre-hypertension established)
- 2014: Eighth and final JNC Report
- 2017: Definition of hypertension lowered from ≥140/90 mmHg to ≥130/80 mmHg, changing how patients are classified and treated

AHA/ACC Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults: August 14, 2025

Hypertension Guidelines: 2025

Takeaways:

- Adopts PREVENT-ASCVD Risk Calculator to guide treatment
- Targets B/P <130/80 mmHg for most individuals
- Targets B/P <120/80 mmHg for high risk individuals
- Stage I: 130-139/80-89: **Borderline ASCVD risk:** Lifestyle modifications for 3-6 months; Initiate medical therapy if target not met after 3-6 months
- Stage I: 130-139/80-89: **Intermediate ASCVD risk:** Initiate medical therapy immediately
- Stage II: 140/90 mmHg or greater: Initiate medical therapy immediately

Hypertension Guidelines: 2025

Takeaways:

- Advocates single pill combination therapy (better adherence)
- Strong focus on lifestyle modification
- Discusses role of GLP1 agonists to aid in weight loss and hypertension control
- Recommends broader evaluation for secondary hypertension including primary hyperaldosteronism
- Promotes remote home (ambulatory) blood pressure monitoring
- Emphasizes blood pressure control to reduce dementia risk

Hypertension Guidelines: 2025

Takeaways:

- Severe Hypertension: 180/120 or greater: Treatment can be initiated/titrated as outpatient if no organ damage evident (hypertension urgency vs hypertension emergency (with organ involvement))

- Renal denervation recommendations for severe/resistant hypertension

Future of Cardiology - Hypertension

- 2024 European Society for Cardiology (ESC) and 2025 AHA/ACC hypertension guidelines demonstrate a shift towards lower and more intensive targets for blood pressure control

- "Lower is better"

Future of Cardiology - Hypertension

- Essential hypertension: 85-90%
- Secondary hypertension: 10-15%
- Primary Hyperaldosteronism: 5-10% in patients with hypertension
- Primary Hyperaldosteronism: More common: 30-60 y/o; Women
- Primary Hyperaldosteronism: 20% of resistant hypertension
- Consider mineralocorticoid receptor anatogonist (MRA; e.g. spironolactone/eplerenone) in treatment of hypertension

Future of Cardiology - Hypertension

What's in store for the future?

Future of Cardiology - Hypertension

- **Long Acting Injectables:**
- Gene silencing technology (reversible) such as small interfering RNA targeting angiotensin (Sc Q 6 months)

- **Device Based Therapies:**
- Renal denervation (Minimally invasive; FDA approved in 2023)

- **Innovative Drug Therapies:**
- Aldosterone synthase inhibitors (2026: FDA approved review of Lorundrostat)
- Dual endothelin receptor antagonists

Hypertension: Future

Digital Health Monitoring/Telemedicine/AI:

- Cuffless remote B/P monitoring; Wearable, real-time, digitally connected devices enabling continuous monitoring, replacing need for intermittent traditional cuff measurements

Focus on Adherence, Precision, and Holistic Approaches:

- Incorporating lifestyle adjustments, digital tracking, and personalized medicine

Future of Cardiology - Hypertension

Conclusion:

- Stricter guidelines
- Innovative therapies
- Longer acting therapies
- Holistic/Precision therapies
- Digital (home/ambulatory) monitoring

Future of Cardiology

Diabetes

Future of Cardiology - Diabetes

- 2026: Comment paper in the Lancet Diabetes and Endocrinology: Proposed new classification of Type II Diabetes: Replace the concept of "prediabetes" with a more actionable, disease-based framework with the aim of **promoting earlier treatment and risk reduction**

- Stage 1: A gradual increase in fasting plasma glucose but within currently defined normal limits(i.e. <100 mg/dl or < 5.7 nmol/L)
- Stage 2: Glucose above normal but < defined T2D, A1c 5.7%-6.4%; Stage 2a and 2b further define "slow" vs "fast"
- Stage 3: Overt T2D

Future of Cardiology - Diabetes

- CVD risk equivalent
- High incidence of CVD
- CVD leading cause of death
- Increased chronic inflammation/oxidative stress

Future of Cardiology - Diabetes

Newer Non-Insulin Medical Therapies:

- Next generation incretins (metabolic gut hormones); Triple agonists
- Dual SGLT1/2 inhibitors
- AMPK activators & FGF21 analogs to improve insulin resistance

Future of Cardiology - Diabetes

Non Pharmacological Therapies:

- Non-surgical endoscopic procedures to rejuvenate the lining of the duodenum to improve insulin sensitivity
- Gene Editing to edit cells to be more insulin responsive
- Stem cell therapy & Immunotherapy

Future of Cardiology - Diabetes

Conclusion:

- CVD Risk equivalent
- Next generation medical therapies
- Next generation non-pharmacological therapies

Future of Cardiology

CAD

Future of Cardiology - CAD

- Despite all of the advances made over the past several decades heart disease is still the leading cause of death in the United States and worldwide as well.

- CAD or ischemic heart disease is the leading cause of death due to heart disease

Future of Cardiology - CAD

Women and Heart Disease:

- CVD remains the leading cause of death in women, yet much of our risk prediction framework has been derived predominantly from male populations
- Women often do not experience traditional chest pains making it more difficult to suspect ischemic heart disease
- Women more often have non obstructive CAD and microvascular disease
- Women in general have lower plaque burdens than men yet have similar risks for MI or death

Future of Cardiology - CAD

Women and Heart Disease:

- Circulation; Promise Trial; February 2026:
- As plaque levels increased, women's risk rose more sharply than men
- In women, low to moderate plaque burden should not automatically be assumed to be indicative of low risk
- The study raises awareness for evaluation and treatment of women with symptoms suggestive of CAD and to appreciate the nuances in plaque burden between men and women

Future of Cardiology - CAD

- ACC Scientific Sessions; March 2026:

- Myocardial Infarction with nonobstructive coronary arteries **(MINOCA)** have similar rate of MACE compared to patients with M.I. with obstructive CAD (4.17 median years of follow up)
- Highlights the importance of endothelial/microvascular dysfunction
- Women are significantly more likely than men to experience MINOCA and nonobstructive CAD

Future of Cardiology - CAD

Future Goals:

- **Address Gaps:** Traditional scores often miss events in asymptomatic patients; we need new tools for **early detection**
- **Precision Prevention:** Move from broad guidelines to **personalized strategies**, targeting high-risk individuals with specific treatments.
- **Revolutionize Care:** Aim to shift focus from treating heart attacks to **preventing** them through early, accurate identification and intervention.

Future of Cardiology - CAD

Future Goals:

- Revolutionize **primary prevention**
- Determine **new risk factors** beyond traditional ones
- More accurately identify **high risk patients**
- Identify which patients would benefit most from:
  - Lifestyle changes
  - Medical therapy
  - Interventional modalities

Future of Cardiology - CAD

- Genetics – Genetic risk scores
- Biomarkers – Lp(a), hs-CRP, troponins, B-type natriuretic hormone
- Advanced imaging – Going beyond calcium scoring
- Cardiac CT – Assess plaque characteristics/vulnerability
- Integrated modules – Combing anatomical and functional (CT perfusion) - All-in-one-CT
- Machine learning – Using complex algorithms to enhance predictive accuracy
- AI – Analyzing characteristics on imaging modalities missed by human eye

Future of Cardiology - CAD

CAD & Inflammation:

- 01/28/26: ACC: Scientific Statement:
- Atherosclerosis is a chronic inflammatory disease
- Inflammation is now considered a modifiable risk factor
- Comparable to cholesterol and blood pressure
- Routine measurement of hsCRP now recommended

Future of Cardiology - CAD

CAD & Biomarkers:

- Measurement of NT-ProBNP
- Can guide implementation of preventive measures in individuals with hypertension and diabetes
- Predictive value for future cardiovascular events
- Can help determine if individual's outlook is improving or deteriorating

Future of Cardiology - CAD

- **GLP-1 Agonists: Provide Cardio-protection**
- **Target population:**
- Individuals with diabetes and/or established CVD

- **Beneficial Effects:**
- Reduce MACE

- **Mechanism of Action: (Beyond weight loss and glycemic control)**
- Reduce inflammation; improve endothelial function; reduce plaque formation

Future of Cardiology – Aspirin and Primary Prevention

- ASPREE Trial (**ASP**irin in **R**educing **E**vents in the : **E**lderly)
- Published in NEJM in September 2018

- Daily low-dose aspirin does not prolong healthy, disability-free life in the elderly (aged 70+ or 65+ for US minorities – Black and Hispanic)
- Increased bleeding risk
- Higher mortality rates
- Did not provide significant CVD benefits
- Findings led to recommendations against initiating daily aspirin for primary prevention in older adults

Future of Cardiology – Aspirin and Primary Prevention

- September 2023: Sub-analysis of the **ASPREE** trial:

- Individuals with high Lp(a) levels have higher risk of MACE that were abrogated by aspirin 100 mg/day without an increased risk of bleeding
- Individuals with **genetically** significantly high Lp(a) levels may benefit more from low-dose aspirin therapy than the general population
- Benefit attributed to aspirin negating the antiplatelet and prothrombotic effect of Lp(a)
- Aspirin may also lower Lp(a) by inhibiting its production in the liver by suppressing apo(a) mrna expression



Future of Carfiology – Asprin and Primary Prevention

- Women's Health Study (WHI): Secondary analysis published in 2010
- Low dose aspirin reduced MACE in Women aged 45+ who had **genetically** significantly elevated Lp(a)

- Multi-Ethnic Study of Atherosclerosis (MESA): Published in 2024
- Daily aspirin reduced MACE in men/women ages 40-70 with **genetically** significantly elevated Lp(a)

Future of Cardiology – Aspirin and Primary Prevention

- **Genetically Elevated Lp(a):**

- Carriers of specific Lp(a) genotype variants: (“High-risk allele”)
- rs3798220
- rs3798220
- Test offered by Quest Diagnostics and Boston Heart Diagnostics: “genetic aspirin test”
- Cardio IQ® LPA Aspirin Genotype

Future of Cardiology – Aspirin and Primary Prevention

- Risk of bleeding with aspirin usage in the ASPREE, WHS and MESA studies:
- Net benefit in reducing MACE without a significant corresponding increase in major bleeding
- Proposed mechanism: Aspirin, which has anti-platelet effects may uniquely counteract/offset the pro-thrombotic/anti-fibrinolytic effect of Lp(a)

Future of Cardiology - CAD Case Presentation



70 y/o Male

Jose

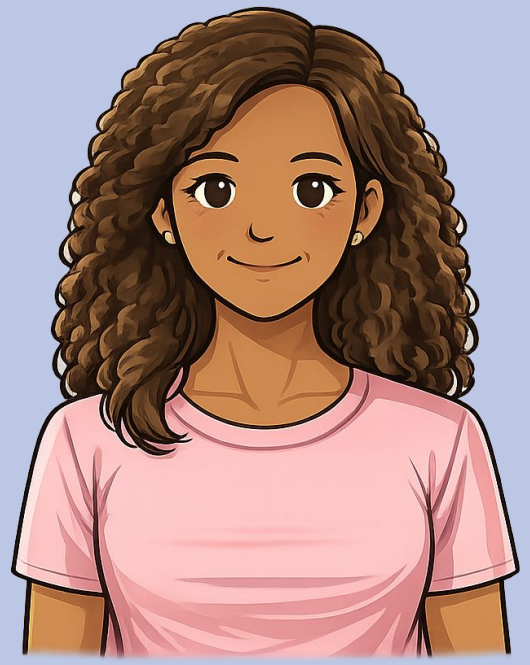
- B/P 130/80 mmHg
- Hs CRP 2.0 mg/L
- LDL 110 mg/dl
- Lp(a) 200 nmol/L



Would you treat with low dose aspirin for CVD protection?

Would you first test for the presence of specific Lp(a) gene variants?

Future of Cardiology - CAD Case Presentation



52 y/o Female

Mia

- B/P 120/80 mmHg
- Hs CRP 1.2 mg/L
- LDL 120 mg/dl
- Lp(a) 200 nmol/L



Would you treat with low dose aspirin for CVD protection?

Would you first test for the presence of specific Lp(a) gene variants?

Future of Cardiology - CAD

CAD: New Approach:

- For many years we have been using various modalities of stress testing to diagnose CAD in patients with chest pain

- We have been searching for a focal stenosis that may be amenable to medical and/or interventional therapy.

Future of Cardiology - CAD

- The Ischemia Trial: 2020
- Patients with stable CAD and moderate to severe ischemia
- Initial revascularization (PCI: 74%; CABG surgery 24% - Multi-vessel disease) vs OMT approaches
- Initial revascularization approach: Better reduction in angina and improvement in quality of life
- Initial revascularization approach: Does not reduce MACE

Future of Cardiology - CAD

CAD: New Approach:

- Lack of relationship between severity of ischemia and severity of CAD for different stress test modalities in the ISCHEMIA Trial
- Lack of any impact of ischemia severity on outcome
- Coronary CTA is now recommended as a first line diagnostic tool for patients with chest pain
- Anatomic imaging preferable to quantify extent of CAD and determine outcomes (risks)

Future of Cardiology - CAD

CAD: New Approach:

- Currently The ACC/AHA maintain a Class 1, Level A recommendation for CCTA as the frontline test for both stable and acute chest pain in the appropriate risk groups
- Assess coronary anatomy
- Assess hemodynamically significant stenoses
- Calculation of CT derived fractional flow reserve (FFR; Normal > .80)
- **Plaque burden**/volume/analysis

Future of Cardiology - CAD

CAD: New Approach:

- CCTA derived plaque analysis and FFR both correlate well with **future occurrence of MACE**
- CCTA derived FFR can help determine **necessity for interventional procedure**
- CCTA plaque analysis can determine plaque burden/volume as well as the presence of **vulnerable plaques**, defined as those plaques who demonstrate high risk characteristics: low attenuation, napkin-ring sign, spotty calcification and positive remodeling

Stage	Total Plaque Volume	Lipid Biomarkers Thresholds/Goals	Medical Management Under clinical evaluation in the DECIDE Registry
Mild[†]	1-100	LDL-C: 100 mg/dL Non-HDL: 130 mg/dL Apo-B: 90 mg/dL	• Statin • ± Aspirin
Moderate[†]	>101–250	LDL-C: 70 mg/dL Non-HDL: 100 mg/dL Apo-B: 70 mg/dL	• High intensity statin ± PCSK9I ± Bempedoic Acid ± Ezetimibe • ± Aspirin • If DM: Intensify therapy with GLP1 ± SGLT2I
Severe[†]	>251–750	LDL-C: 55 mg/dL Non-HDL: 85 mg/dL Apo-B: 60 mg/dL	• High intensity statin ± PCSK9I ± Bempedoic Acid ± Ezetimibe • Aspirin • Aggressive BP Rx • If DM: Intensify therapy with GLP1 ± SGLT2I • If elevated BMI: weight loss treatment • If elevated CRP & LDL at target: consider anti-inflammatories
Extensive	>750	All as low as can be achieved: LDL-C: <50 mg/dL Non-HDL: <80 mg/dL Apo-B: <50 mg/dL	• Same as severe • ± Colchicine ± Icosapent Ethyl

Heartflow **Plaque Overview**

John Doe

Birth Date: 06/05/1968 (55 years)
Sex: Male
CT Study Date: 06/26/2023

Heartflow ID: ANYH-23FQRD-KRNT
Patient ID: 111ECAA13D2C4F5498305
Referring Physician: John Smith

Total Plaque Summary

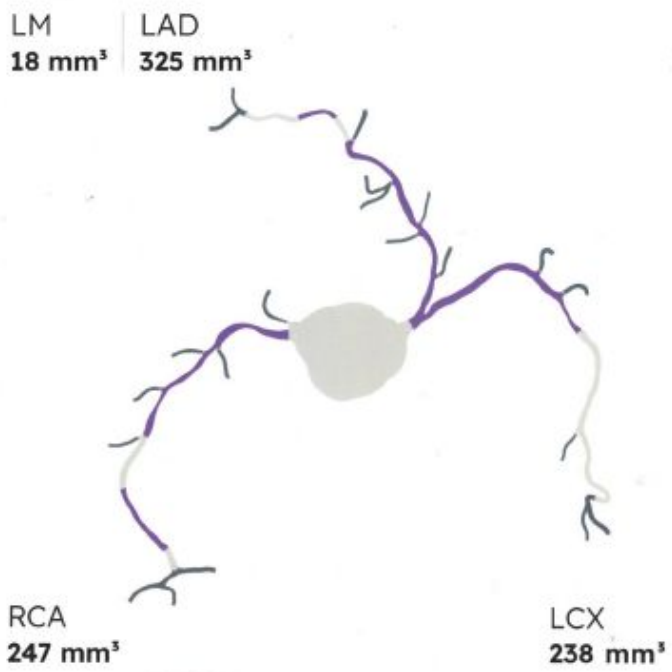
828 mm³
Total Plaque Volume

94th
Patient Percentile[1]

Plaque Types

Calcified	384 mm³	(46%)
Non Calcified	444 mm³	(54%)
Low attenuation	0 mm³	(<1%)

2D Model - Plaque Volume by Vessel Territory



Legend

- Regions of identified plaque
- Lumen
- Non-reportable

Heartflow **Plaque Overview**

John Doe

Birth Date: 06/05/1968 (55 years)
CT Study Date: 06/26/2023

Heartflow ID: ANYH-23FQRD-KRNT
Patient ID: 111ECAA13D2C4F5498305

LM and LAD Vessel Territory Analysis

18 mm³
LM Total Plaque Volume

Plaque Types

Calcified	8 mm³	(44%)
Non Calcified	10 mm³	(56%)
Low attenuation	0 mm³	(<1%)

325 mm³
LAD Total Plaque Volume

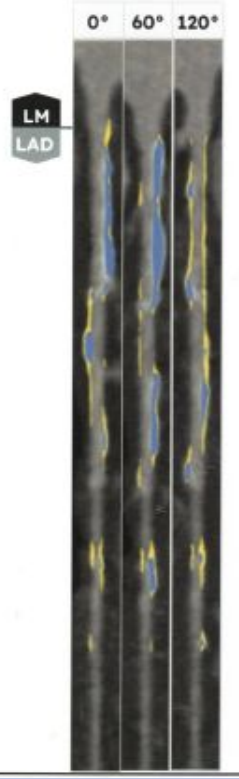
Plaque Types

Calcified	202 mm³	(62%)
Non Calcified	123 mm³	(38%)
Low attenuation	0 mm³	(<1%)

2D Model



sCPR



Legend

2D Model legend

- Regions of identified plaque
- Lumen
- Non-reportable

Future of Cardiology - CAD

CAD: New Approach:

- We are entering a new era of plaque determination, where endothelial characterization and plaque vulnerability are the new targets

- Since vulnerable plaques are associated with higher degrees of MACE **should we revascularize all of them**?

Future of Cardiology - CAD

Is there a role for pre-emptive coronary revascularization

in patients with high-risk vulnerable plaques ?

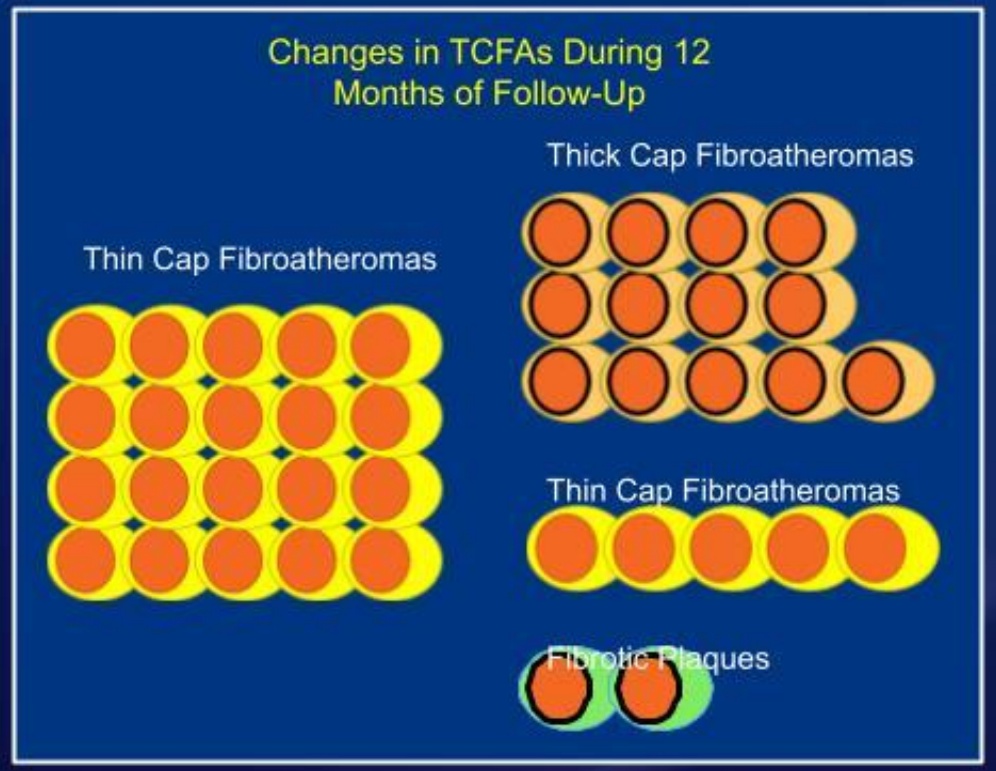
Future of Cardiology - CAD

- **Not so fast!**
- Plaque phenotype may dynamically change over time, but is often assessed at a single time point
- Vulnerable plaques with thin cap fibroatheromas (high risk) may become thick cap fibroatheromas (low risk) or fibrotic plaques (low risk
- Vulnerable plaques may disrupt leading to an MI or a clinically silent/benign occurrence
- Multiple vulnerable plaque are often found in non-culprit arteries post ACS - Are we to stent all of them?

The Dynamic Nature of Coronary Lesion Morphology

The Dynamic Nature of Coronary Lesion Morphology

- 99 pts – 212 non-culprit lesions plaque burden 40%
- 20 lesions
- IVUS were TCFA (thin-capped fibroatheroma)
- Baseline and 12 mth follow0up



Redrawn from: Arbab-Zadeh & Fuster: JACC, 2015

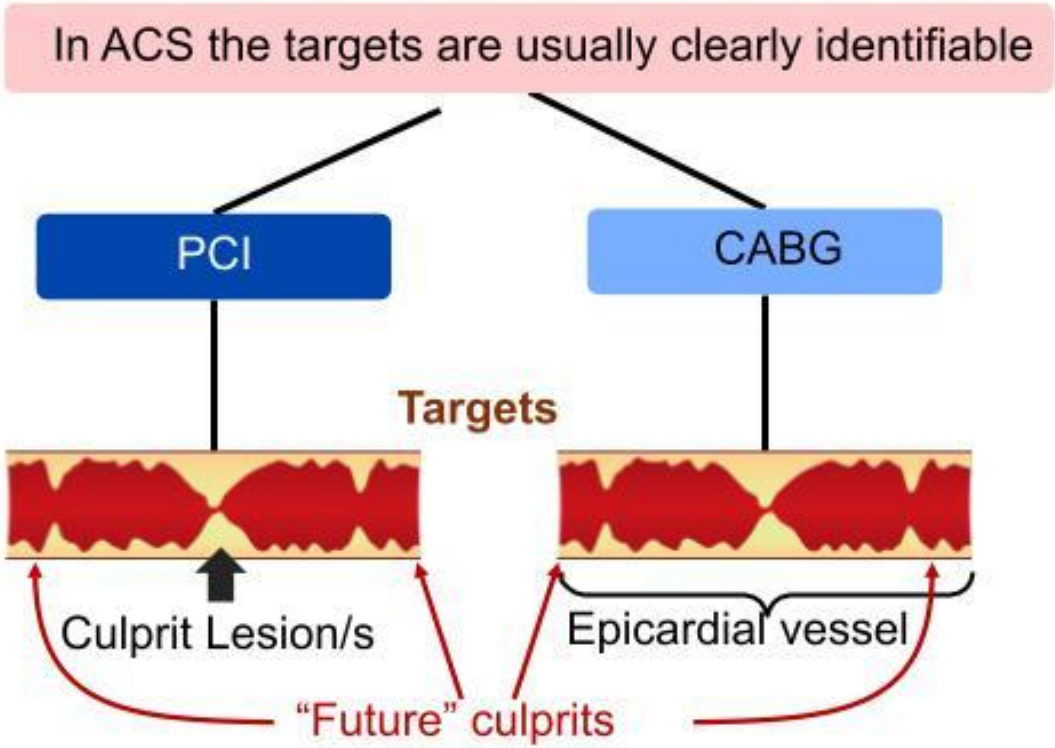
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Future of Cardiology - CAD

- Why has PCI not led to reduction in MACE (ISCHEMIA TRIAL)
- Why is CABG surgery superior to PCI in diabetic patients with MVD?
- PCI addresses focal stenotic stenosis; Many vulnerable plaques remain
- CABG surgery bypasses the entire diseased artery

Discordance Between the Impact of PCI in Pts With ACS vs CCS and Why CABG is Superior to PCI in Pts with MVD and Diabetes



Modified from Gersh and Frye: NEJM, 2005

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Future of Cardiology - CAD

- Perhaps the future will bring us the answer by addressing two main areas of focus:

- Identify **other high risk vascular characteristics** that can be addressed by lifestyle and/or medical therapy

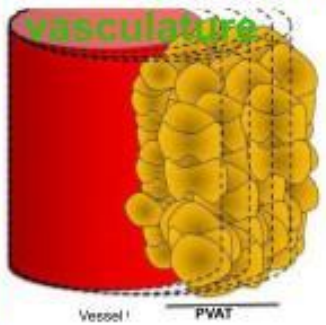
- Look beyond identifying the vulnerable plaque and instead identifying the **vulnerable patient**

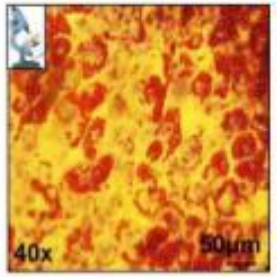
Future of Cardiology - CAD

- CCTA will be able to identify **perivascular adipose tissue (PVAT)**
- CCTA will be able to distinguish between healthy non-inflamed vasculature and diseased, inflamed vasculature by quantifying the **fat attenuation index (FAI)**
- Determination of **plaque volume/burden** and **high risk plaque** will lead to appropriate modes of therapy including aggressive lipid lowering, aggressive modification of all risk factors and possibly anti-inflammatory therapy and revascularization modalities

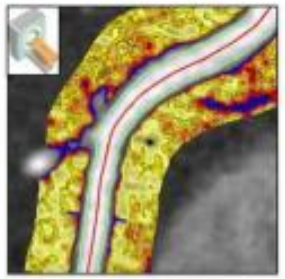
Assessing CV Risk by Using the Fat Abbreviation Index on

Healthy, non-inflamed vasculature

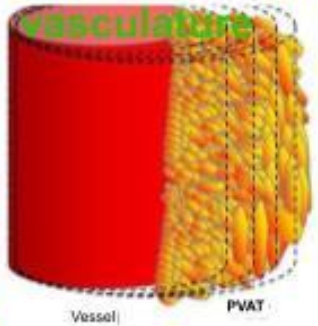


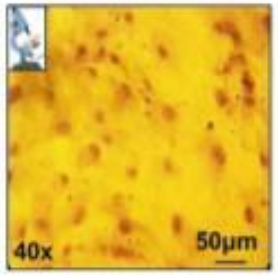


Mature, lipid-laden adipocytes

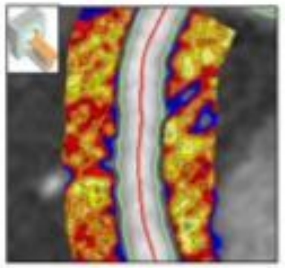

In vivo perivascular FAI mapping using CT

Diseased, inflamed vasculature





Lipid-laden adipocytes


In vivo perivascular FAI mapping using CT

Klüner et al: Radiology Cardiothoracic Imaging, 2021

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Future of Cardiology - CAD

- JACC Feb 2026:

- High epicardial adipose tissue volume (EATv) on CCTA is independently associated with the presence and progression of CAD

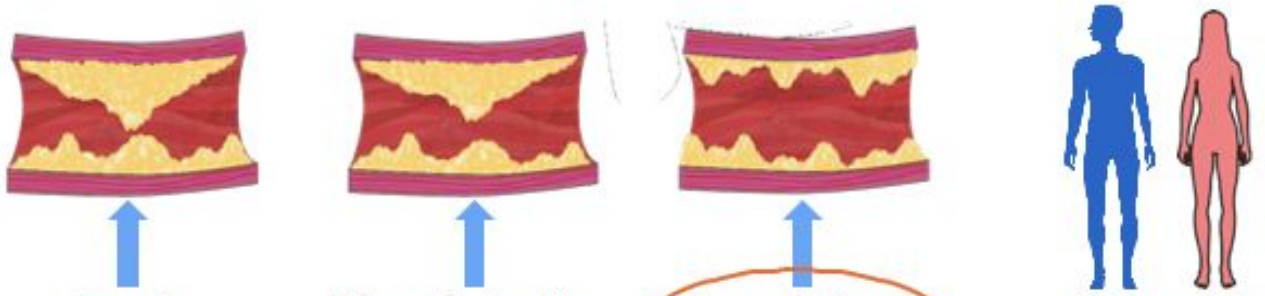
- Future potential risk-stratification marker for MACE and a therapeutic target for earlier or more intensive intervention

Future of Cardiology - CAD

Approach to CAD in the future:

- Identify high risk vulnerable vascular characteristics
- Identify the vulnerable patient
- **Preventive modalities** in the asymptomatic patient rather than **reactive measures** in the symptomatic patient

Evolving approaches to therapeutic targets:
From focal stenoses to plaque vulnerability to overall plaque burden



Focal stenosis

Non-obstructive "vulnerable" plaque

Overall plaque burden

Vulnerable patients

? Indications for Revascularization

Risk factor reduction – lipid lowering therapies

? Pre-emptive revascularization (ongoing trials)

? Glucose-lowering agents

- ***Early*** detection of impact of atherosclerosis risk factors
  - Imaging
  - "Omics"
- Aggressive ***early*** prevention to inhibit plaque development, progression and stabilization

Modified from Libby et al Circ 2024

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Future of Cardiology – CAD

The Future Cath Lab:

- **CTA** for PCI planning
- Use of **AI** to improve detection of coronary occlusion by EKG
- AI enabled fluoroscopy
- Spatio-temporal enhancement processing (STEP)
- **Intra-coronary imaging**:
- AI for procedural planning with intravascular ultrasound **(IVUS)**
- AI for procedural planning with optical coherence tomography **(OCT)** – Automated calcium detection

Future of Cardiology - CAD

The Future Cath Lab:

- Applications of endovascular robotic systems
- Telerobotic Mitral Transcatheter Edge-to-Edge Repair (TEER)
- Telerobotic transthoracic echocardiogram (with or without sonographer)

Future of Cardiology - CAD

Conclusion:

- Focus on prevention
- Identify novel high-risk vascular characteristics (Plaque analysis and beyond)
- Identify the vulnerable patient

Future of Cardiology

Anomalous Coronary A

Anomalous Aortic Origin of Coronary Arteries (AAOCA)

- Prevalence: 1% of population
- 2nd leading cause of sudden cardiac death (SCD) in young competitive athletes
- Wide range of anomalies and symptoms
- Usual presenting symptoms include chest pains, shortness of breath, dizziness, palpitations or SCD. Murmur may be present.
- CCTA allowing for increased diagnosis and risk assessment and determine appropriate management

The Future of Cardiology – Anomalous Coronary Arteries

- Myocardial bridging included in this condition
- Wide range of anomalies and symptoms make general recommendations limited
- Coronary CTA essential for morphologic risk assessment
- **Future:** Standardized pathways for early detection, consistent evaluation and individualized decisions

Future of Cardiology

Cardiac Surgery

Future of Cardiology – Cardiac Surgery

- Minimally invasive surgery
- Transcatheter surgery
- Robotic surgery
- AI and personalized medicine
- Heart "team"/multidisciplinary approach

Future of Cardiology – Aortic Stenosis

- March 2026: SENSE-AS Study
- Proof of Concept Study
- Chest worn multimodal sensors can accurately detect the presence and severity of aortic stenosis
- Uses ECG, seismocardiogram and phonocardiogram signals and machine learning predictive models

Future of Cardiology – Aortic Stenosis

- March 2026: Randomized trials of 145 patients with severe aortic stenosis in South Korea:

- Early surgical aortic valve replacement (SAVR) showed significant mortality benefit (improved survival) compared with those who received conservative care

Future of Cardiology

Atrial Fibrillation

The Future of Cardiology

- 2023 ACC/AHA Guidelines for the Detection and Management of Atrial Fibrillation

- Published in Circulation and JACC in January 2024

Future of Cardiology – Atrial Fibrillation

- Key Point #1
- **Stages of A Fib:**

- At risk for A Fib
- Pre- A Fib
- A Fib (Paroxysmal, Long-standing & persistent)
- Permanent A Fib

Future of Cardiology – Atrial Fibrillation

- Key Point #2:
- **Lifestyle Modification**

- Obesity
- Alcohol
- Hypertension
- Diabetes
- Smoking
- OSA
- Sleep
- Exercise
- CHF

Future of Cardiology - Atrial Fibrillation

- Key Point #3:
- **CVA Risks and Anticoagulation:**
- Risk factors in addition to CHA2DS2-VASc Score:

- Higher A Fib burden/Long duration
- Persistent/Permanent A Fib vs Paroxysmal
- Obesity
- HCM
- Poorly controlled HTN
- CKD (GFR<45 ml/h)
- Proteinuria (>150 mg/24 h)
- Enlarged LA volume/diameter

Future of Cardiology – Atrial Fibrillation

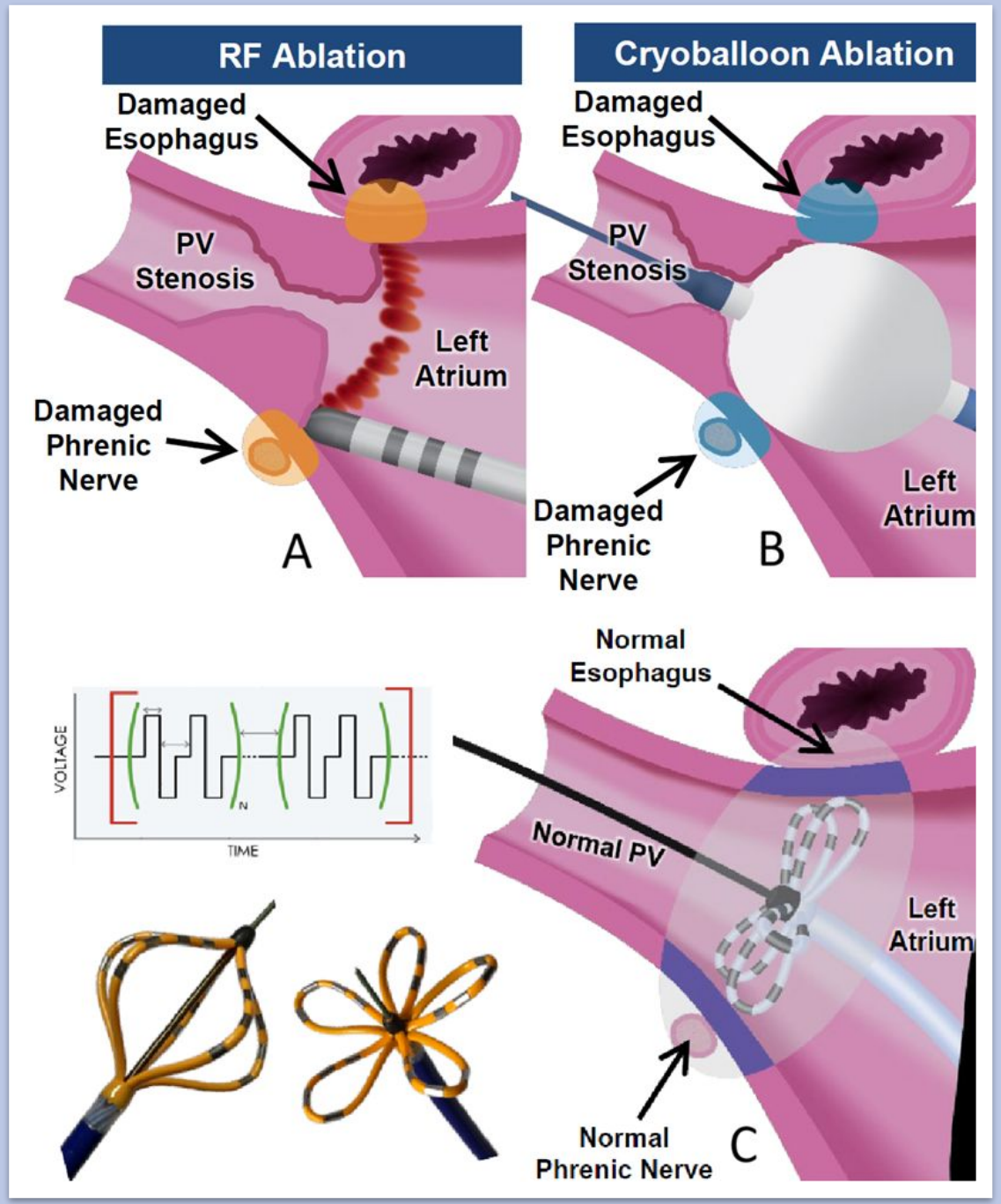
- Key Point #4
- Paradigm Shift from Rhythm Control:

- Ablation Superior to rhythm medications
- Early ablation better than delayed ablation:

- Prevents irreversible atrial remodeling
- Prevents A Fib related strokes, heart failure and death

Pulse Field Ablation: the New Kid on the Block

Application of **high voltage** currents for microseconds causing **non-thermal electroporation** of cells and cell death.



Future of Cardiology – Atrial Fibrillation

- Left Atrial Appendage Closure (LAAC):

- Will become more mainstream/First-Line
- Expansion of indications
- Technological advances (minimize peri-device leaks/thrombosis)
- AI: Smart devices to monitor for risk of stroke and CHF

Future of Cardiology – Atrial Fibrillation

Conclusion

- Shift towards rhythm control
- Expand indications for anticoagulation
- Focus on lifestyle modifications
- Left atrial appendage closure may become more mainstream

Future of Cardiology

Cardiomyopathy

Future of Cardiology - Cardiomyopathy

- Dilated
- Hypertrophic (HCM/HOCM)
- Restrictive
- Infiltrative - **Amyloid**
- Arrhythmogenic right ventricular dysplasia (ARVC) (Often affects left ventricle as well
- **Myocarditis**

The Future of Cardiology - Cardiomyopathy

- Genetic etiologies (Up to 40% of all dilated cardiomyopathies)
- Genetic testing-including myocarditis (Up to 15% have genetic etiology)
- Genetic counseling/Family screening
- Early detection – AI-ECG
- Early detection – Identify pre-clinical/sub-clinical disease
- Early Treatment – Reversal of pathological findings
- New Treatment options – Pharmacological/Interventional/Gene therapy
- Sports cardiology has evolved in complexity; Shared decision making now a fundamental principle

Future of Cardiology - Cardiomyopathy

Amyloidosis:

- **Earlier Improved Diagnosis:**
- Highly sensitive biomarkers
- Advanced Imaging (MRI & PET Scan)
- AI
- **Improved Treatment:**
- Novel antibody therapies
- Novel anti-fibril (anti-fibrotic) therapies
- Gene therapy

Future of Cardiology - Cardiomyopathy

Myocarditis:

- **Earlier Improved Diagnosis:**
- Advanced imaging (MRI & PET scans)
- Improved endomyocardial biopsy techniques
- AI
- **Improved Treatment:**
- Multidisciplinary approach (immunosuppression/antiviral
- Stem cell therapy
- Gene therapy

Future of Cardiology – Cardiomyopathy

Hypertrophic Cardiomyopathy:

- **Prevalence:** 1 in 200 to 1 in 500 globally; 70% are obstructive
- Genetic etiology can be identified in 30-70% of cases
- Current first line therapies: Beta blocker or non-dihydropyridine calcium blocker
- Advanced therapies: Disopyramide, Mavacamten/Aficamten (cardiac myosin inhibitor), Surgical myomectomy, Septal ablation

Future of Cardiology – Cardiomyopathy

- **Hypertrophic Cardiomyopathy: Novel Approaches:**
- Identify preclinical disease (Before development of hypertrophy):
- Novel biomarkers
- New imaging modalities: Diffusion Tensor Imaging (Advanced cardiac MRI technique that detects early subclinical myocardial microstructural changes
- AI: ECG diagnosis
- AI: SCD risk stratification

Future of Cardiology – Cardiomyopathy

- **Hypertrophic Cardiomyopathy: Novel Therapies:**
- Mitotropes (Enhance mitochondrial function)
- Percutaneous myomectomy
- Minimally invasive alternatives for removing obstructive muscle
- Gene therapy: (targeted gene modulation of the hypertrophic response)

Future of Cardiology

CHF

Future of Cardiology - CHF

- Systolic Heart Failure (HFrEF)
- Weakened poorly contracting keart muscle

- Diastolic Heart Failure (HFpEF)
- Stiffened poorly relaxation of heart muscle

Future of Cardiology - CHF

HFrEF: Current

- More early, consistent application of GDMT
- Four "pillars" of medications
- ARNI/ARB/ACE-I/B-Blockers/MRAs/SGLT2 Inhibitors
- Additional pharmacological alternatives

HFrEF: Future

- More early AI driven diagnosis
- Personalized treatments
- Intracellular therapies
- Regenerative/Reversal/Repair therapies (Utilizing gene editing technologies)

Future of Cardiology - CHF

- **HFpEF: Current**
- More early recognition/diagnosis
- More early initiation of treatment
- More early initiation of non-pharmacological & lifestyle management
- More complete management of co-morbidities

- **HFpEF: Future**
- More widespread clinician education
- AI-driven personalized and phenotype specific diagnosis and treatment
- Newer multidisciplinary and non-pharmacological therapies
- Advance device therapies

Future of Cardiology

Heart Transplant

Future of Cardiology – Heart Transplant

- The best ways to improve patient outcomes is to avoid transplantation
- Primary prevention (gene Rx, GLP1, tobacco)
- Secondary prevention (excellent use of GDMT)

Future of Cardiology – Heart Transplant

- Increase the donor pool
- Improve peri-transplant care (advanced mechanical support)
- Improve Immuno-suppression and surveillance modalities
- Xenotransplantation
- Robotic Surgery
- Personalized Medicine and AI
- Goal: Increase accessibility, reduce complications and improve (short and long term) survival

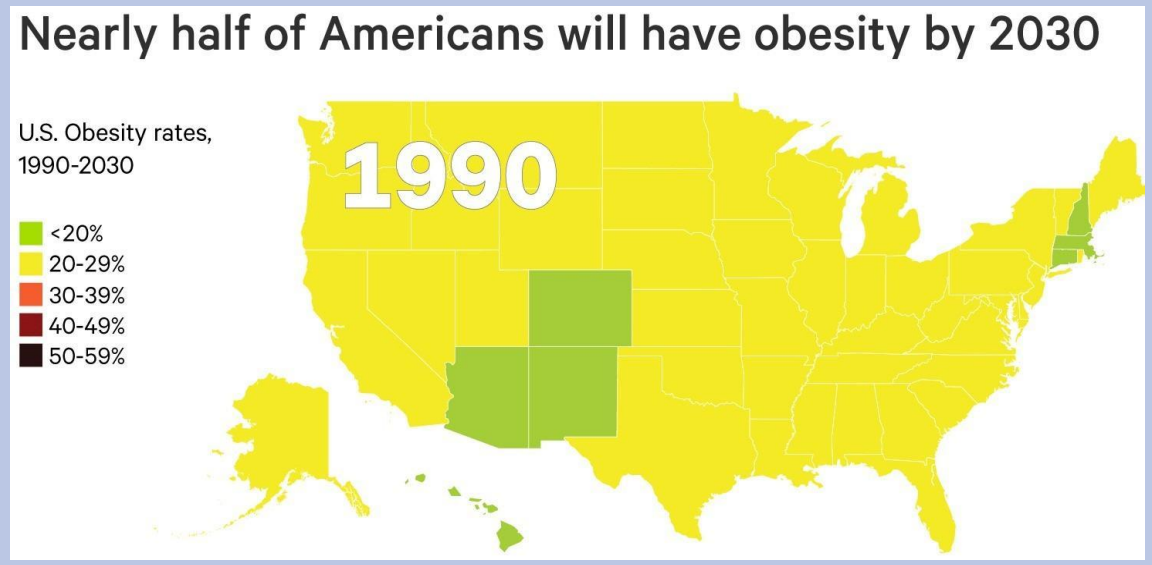
Future of Cardiology

Obesity

Future of Cardiology - Obesity

Obesity is a growing national epidemic!!

- Currently affects ~40% of US adults



Future of Cardiology - Obesity

- Recognition that adipose tissue is not inert organ whose function is solely for fat storage
- Recognition of the adipocyte as being metabolically active
- Recognition of the many substances secreted by adipose tissue

Future of Cardiology - Obesity

- Recognition of relationship between adipose tissue and multiple body organs and systems

- Recognition of obesity as being an excess of dysfunctional/pathogenic adipose tissue (visceral fat or "sick fat"/"adiposopathy")

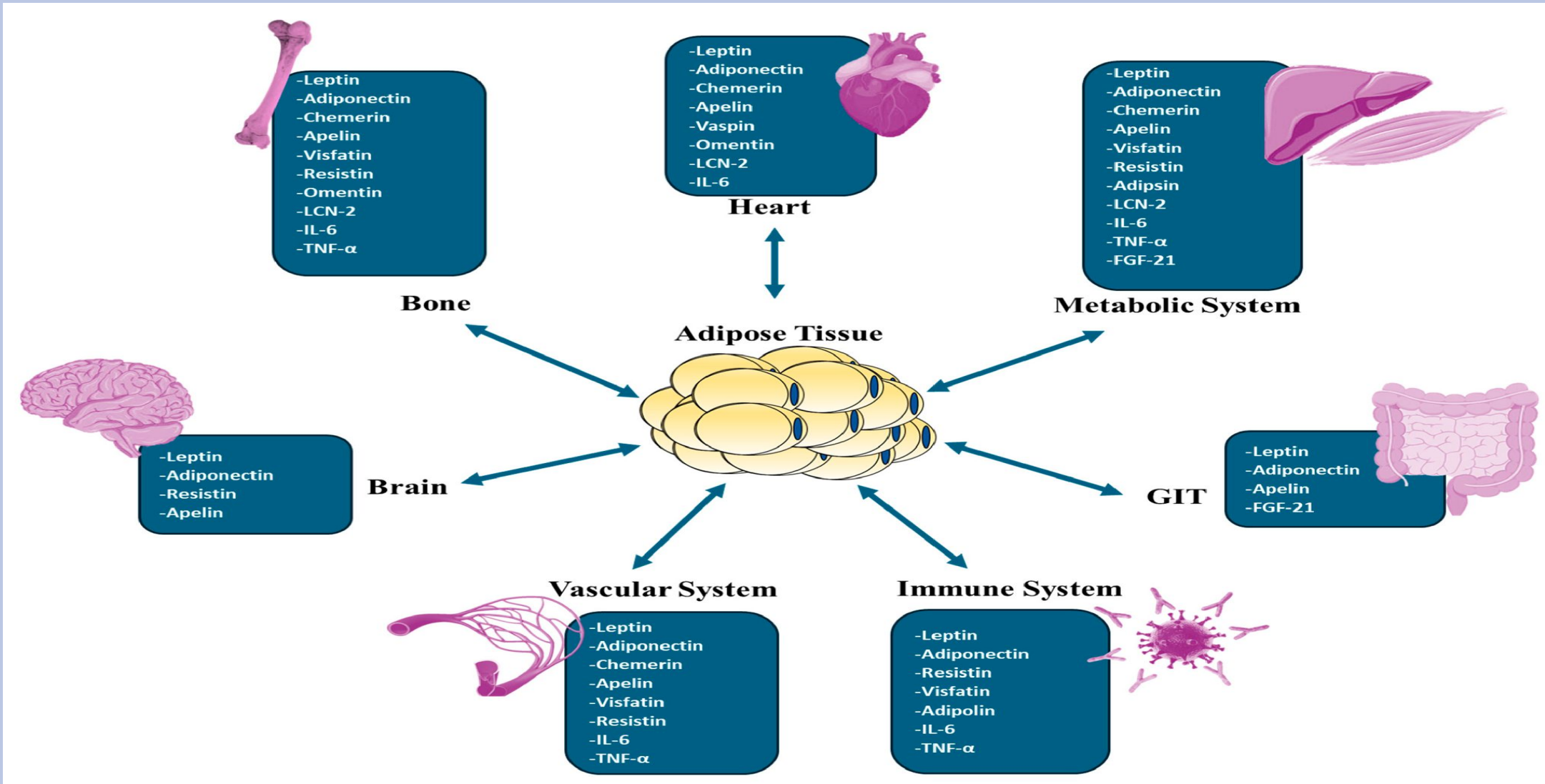
Future of Cardiology - Obesity

- Visceral fat secretes cytokines promoting inflammatory responses throughout the body and immune system disorders
- Obesity or adiposopathy is the root cause of cardiometabolic dysfunction, insulin resistance, type 2 diabetes, and contributes to hypertension, mixed hyperlipidemia, liver dysfunction and cardiovascular disease
- Obesity management will shift from a focus on short term weight loss to a long term "Obesity–First" chronic disease model

Future of Cardiology - Obesity

- Definition of Obesity:
- BMI
- Waistline circumference
- Waist-to-hip ratio
- Measurement of fat percentage
- "Clinical" vs Pre-clinical" (presence vs absence of organ dysfunction secondary to excess adiposity)

Future of Cardiology - Obesity



Future of Cardiology - Obesity



Future of Cardiology - Obesity

- 2025 ACC Expert Consensus Statement on Medical Weight Management for Optimization of Cardiovascular Health

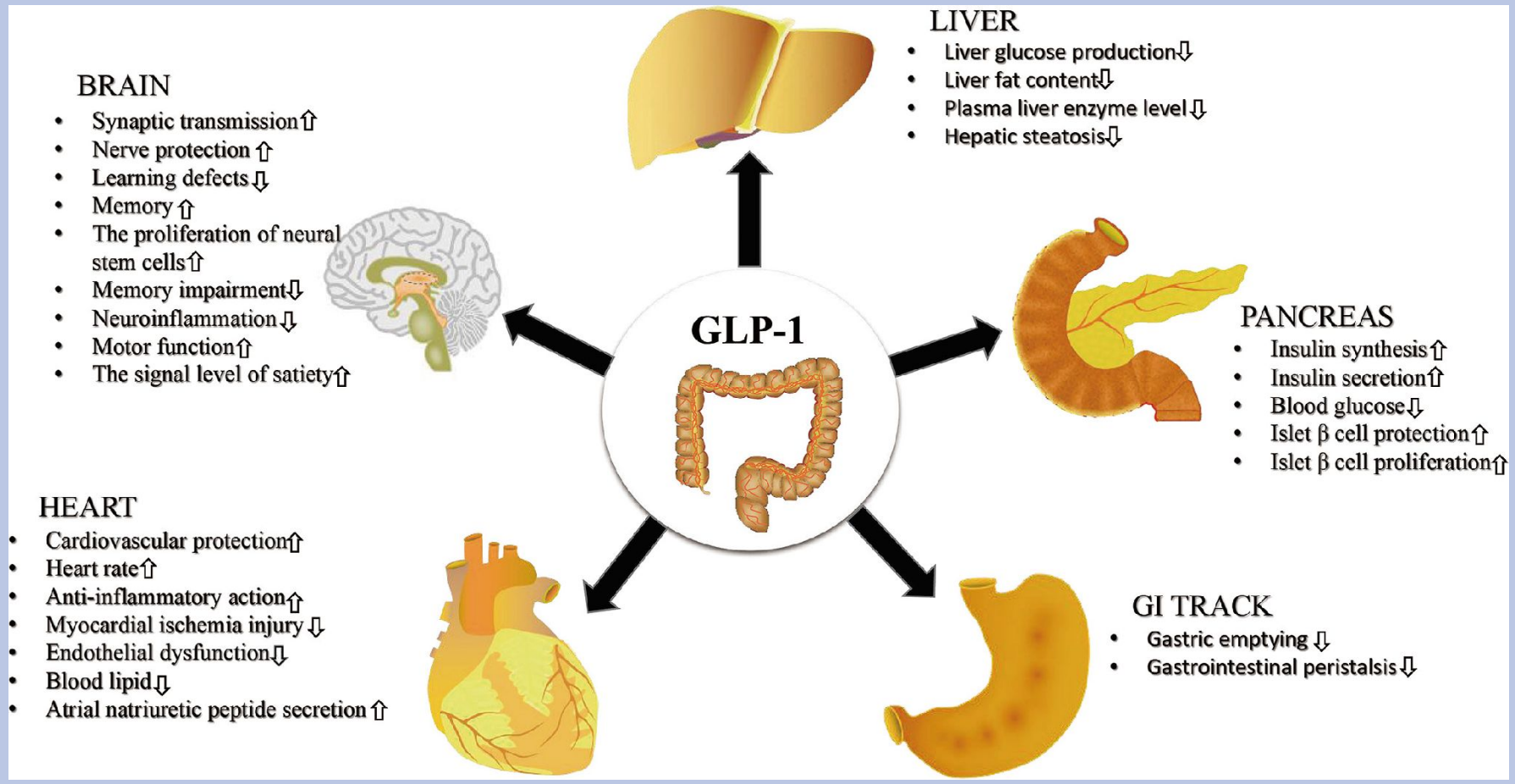
- Key Takeaway:

- It is no longer recommended that all patients try lifestyle modification alone before adding pharmacologic treatment for weight loss

Future of Cardiology - Obesity

- GLP-1 Agonists: Beneficial effects beyond blood sugar lowering
- Reduce MACE (Heart attacks/strokes)
- Slow CKD progression
- Lower blood pressure
- Improve lipid profiles
- Help with PAD
- Reduce inflammation

Future of Cardiology - Obesity



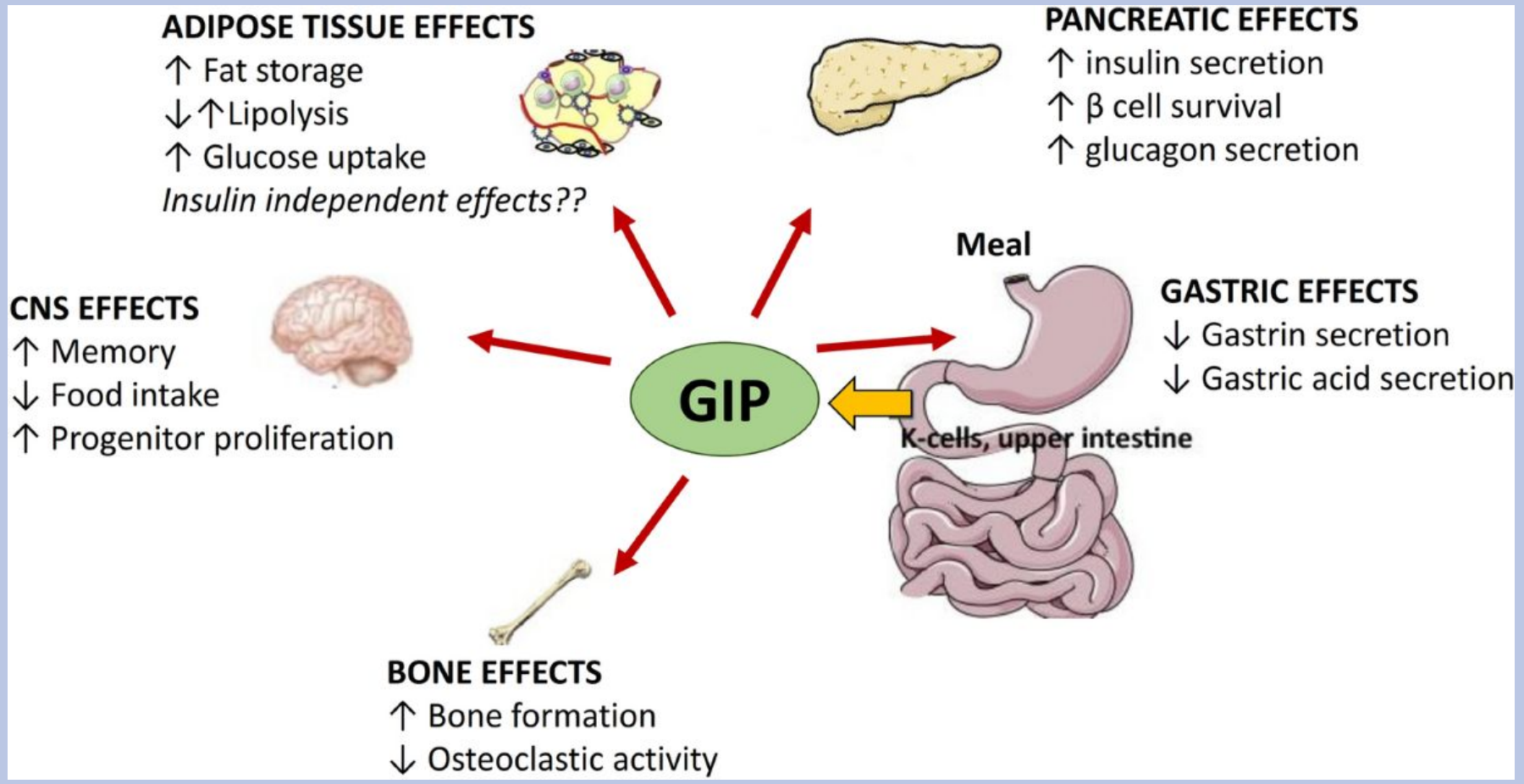
Future of Cardiology - Obesity

- GLP-1 agonists my help reduce both microvascular and macrovascular complications in individuals with diabetes

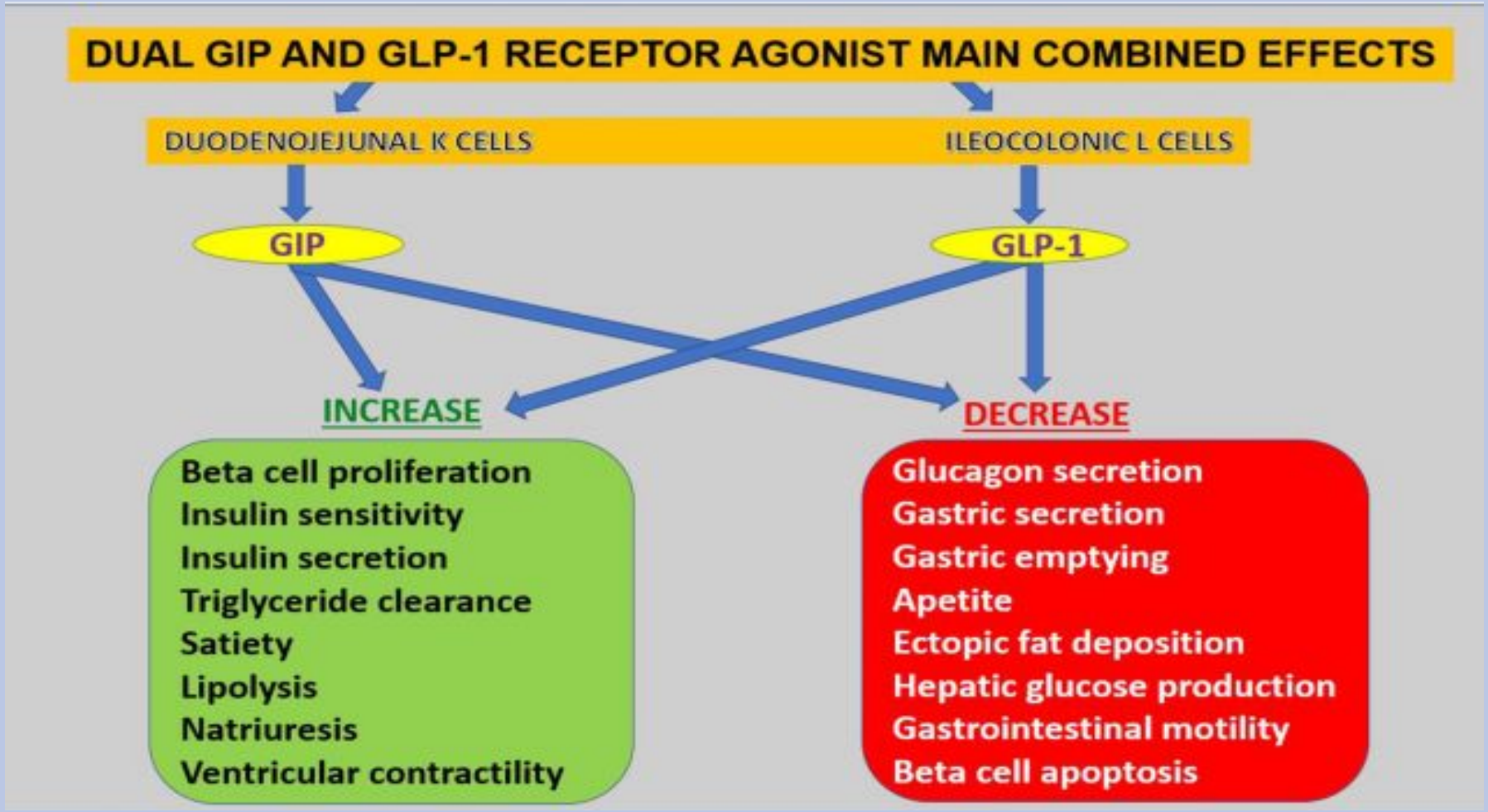
- Microvascular Complications:
- Retinopathy, Neuropathy, CKD, Diabetic foot complications & amputation

- Macrovascular Complications:
- Heart attacks, strokes, CVD death, PAD

Future of Cardiology - Obesity



Future of Cardiology - Obesity



Future of Cardiology - Obesity

- **High-dose semaglutide**, 7.2 mg, which is triple the highest doses of what is currently on the market for weight loss.
- Development of **multi-hormone receptor agonists:**
- **Triple Agonists:** Retatrutide: Targets GLP-1, GIP and glucagon receptors
- **Combination Therapies:** CagriSema: Combines semaglutide and amylin analogue (polypeptide co-secreted by pancreas with insulin); Key regulator of glucose metabolism; Promotes satiety and delays gastric emptying
- **Muscle preservation:** Combining GLP-1s with myostatin inhibitors to prevent loss of lean muscle during rapid weight loss

Future of Cardiology - Obesity

Oral alternatives:

- Wegovy; must be taken on an empty stomach with no more than a few ounces of water; must wait a half hour before eating or drinking. It received FDA approval on 12/22/25

- Orforglipron, (Brand name Foundayo) a different GLP-1 receptor agonist; small-molecule drug that can be taken with or without food. It received FDA approval on 04/01/26

Future of Cardiology - Obesity

- Endoscopic Procedures: Less invasive bariatric surgery
- Hybrid Models: Combination of pharmacotherapy and surgical procedures (In either order)

Future of Cardiology - Obesity

Digital health and AI integration:

- Precision nutrition and machine learning: Tailor a diet to an individual's genetic and gut microbiome profile (Personalized medicine)
- Gene therapy: Technologies that may alter metabolic processes at the genetic level
- Remote monitoring/wireless scales: Allows real time tracking by clinicians
- AI Apps: Provide counseling and motivation

Future of Cardiology - Obesity

Conclusion:

- Prevalence
- Adipocyte metabolically very active - "Adiposopathy"
- Root cause of cardiometabolic dysfunction/CVD
- Chronic disease treatment approach
- Novel treatments: pharmacological/interventional/hybrid
- Gene therapy
- Digital health and AI integration

Future of Cardiology

Hormone Replacement Therapy

Future of Cardiology - Hormone Replacement Therapy (HRT)

- Heart and Estrogen-Progestin Replacement Study (HERS):
- HERS I: 1998; HERS II: 2002
- HRT vs placebo in women **with CAD**; Lack of benefit on MACE and increased risk of DVT

- Women's Health Initiative (WHI): 2002
- HRT vs placebo in Women **without CAD**: Increased risk of MACE and DVT

Future of Cardiology - Hormone Replacement Therapy (HRT)

- 75 million women in US are peri-or post-menopausal (estimated 90 million by 2060)
- 75% of peri-/post- menopausal women have symptoms
- HRT is the most effective treatment for menopausal symptoms

Future of Cardiology - HRT

February 2026:

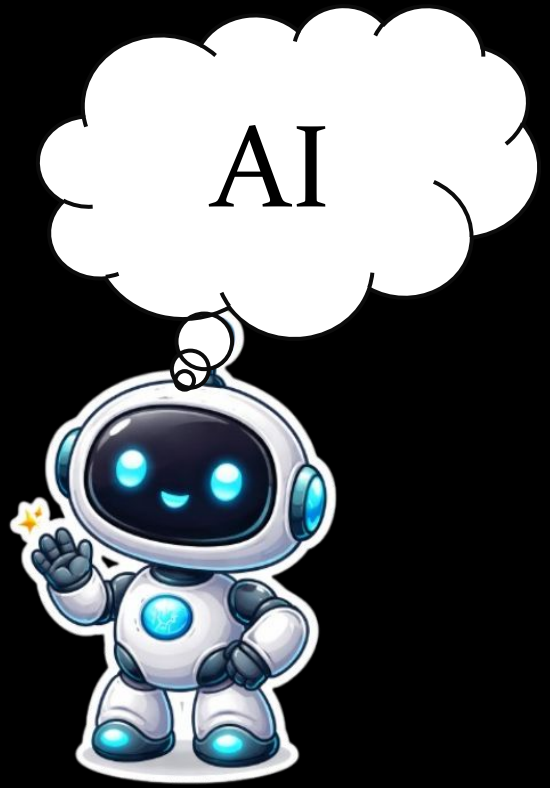
- FDA removed boxed warnings for HRT on CVD, breast cancer and dementia

- No new randomized clinical trials to further address HRT use

Hormone Replacement Therapy

- Not recommended for primary prevention
- Not recommended for high risk patients
- Shared decision making
- Lowest dose and shortest duration possible if use HRT

Future of Cardiology



The Future of Cardiology – AI & Digital Inovation

- Early risk prediction
- Early disease detection
- Enhance preventive measures
- Enhanced diagnostic modalities

The Future of Cardiology – AI & Digital Innovation

- Enhanced therapeutic modalities (medical and interventional)
- Patient education
- Personalized medicine
- Transform field from reactive to proactive

Future of Cardiology

GENE EDITING

Future of Cardiology – Gene Editing

- March 26 2026: ACC Scientfic Statement:

- Technological innovations- Most notably "clustered regularly interspaced short palindromic repeats" CRISPR-associated protein 9 (Cas9) have enabled the precise and targeted editing of a patient's genome
- Raises the possibility of durable or even curative treatments for selective cardiovascular conditions
- The development of lipid nanoparticles offers a promising nonviral startegy for cardiovascular diseases with hepatocyte-expressed treatment targets

Future of Cardiology

Lifestyle Management

Future of Cardiology - Lifestyle Management

- **AHA: Life's Essential Eight":**
- Diabetes/Hypertension/Hyperlipidemia/Cigarette Smoking
- Diet/Weight/Physical activity/**Sleep health**

- **Doc I: "The Great Eight":**
- Diabetes/Hypertension/Hyperlipidemia/Cigarette smoking
- Diet/Weight/Physical activity/**Mental well being**

Future of Cardiology – Lifestyle Management

- Circulation March 2026; AHA updates the guidance on dietary patterns for cardiovascular health optimization
- AHA Scientific Statement supersedes it's 2021 statement
- Emphasizes the adoption of heart-healthy dietary patterns instead of focusing on single foods or nutrients
- Examples include healthy versions of the DASH or Mediterranean-style diets, pescetarian, and lacto-ovo vegetarian diets
- Shift from meat to plant sources of protein

The AHA guidance offers 9 key steps for achieving a *heart-healthy eating pattern:*



Balance calories and activity to maintain a healthy weight.



Choose plenty of **vegetables and fruits**, **healthy** proteins, whole grains, and unsaturated fats;



Minimize added sugars, sodium, ultraprocessed foods, and alcohol.

Future of Cardiology – Lifestyle Management

- Focus on personalized, tech-enabled preventive care
- Focus on personalized and early lifestyle management
- Focus on remote monitoring
- Focus on AI and wearable technology

Future of Cardiology –Lifestyle Management

- **Precision Nutrition:** Instead of "one-size-fits all" dietary advice recommendations are based on an individual's unique biology, lifestyle and environment and response to food
- **Nutritional Genomics**: How your DNA influences how you metabolize certain nutrients
- **The Microbiome**: The gut microbiome functions as a metabolic organ. It influences numerous physiologic provesses, help breakdown food and regulate inflammation
- **Metabolomics**: Measuring small molecules in blood/urine to create a "metabolic signature" of your current metabolic and overall health status
- **Dynamic Phenotype:** Takes into account how parameters such as sleep patterns, physical activity and stress impact how your body handles food

Future of Cardiology – Lifestyle Management

Dietary Recommendations:

Complementing Precision Nutrition:

- Plant based/Fiber rich
- Elimination of ultra-processed food
- Focus on fruits/vegetables/legumes/nuts/whole grains
- Emphasize healthy proteins and fats


LET FOOD BE
THY MEDICINE.
—HIPPOCRATES

Future of Cardiology – Lifestyle Management

Victor Lindlahr in 1942 published a book beginning with: “You are what you eat"

Doc I in 2026 says:

"Eat well to be well"

"Make your food colorful – Not calorieful”

Future of Cardiology Conclusion: (or to be continued...)

Future of Cardiology

- **Identify the High Risk ("Vulnerable") Individual**
- **Proactive/Preventive Approach**
- **Precision Medicine**
- **Adress Inflammation**

The Future of Cardiology

- **Bob Dylan: 1964:**
- "The Times They Are A–Changin'"
- **Aristotle: Circa 300's BCE:**
- "The more you know, the more you realize you don't know"

The Future of Cardiology

- **Niels Bohr's** famous prediction statement:
- "Prediction is very difficult especially if it's about the future"
- **Benjamin Franklin's** famous prevention statement:
- "An ounce of prevention is worth a pound of cure"

Future of Cardiology

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