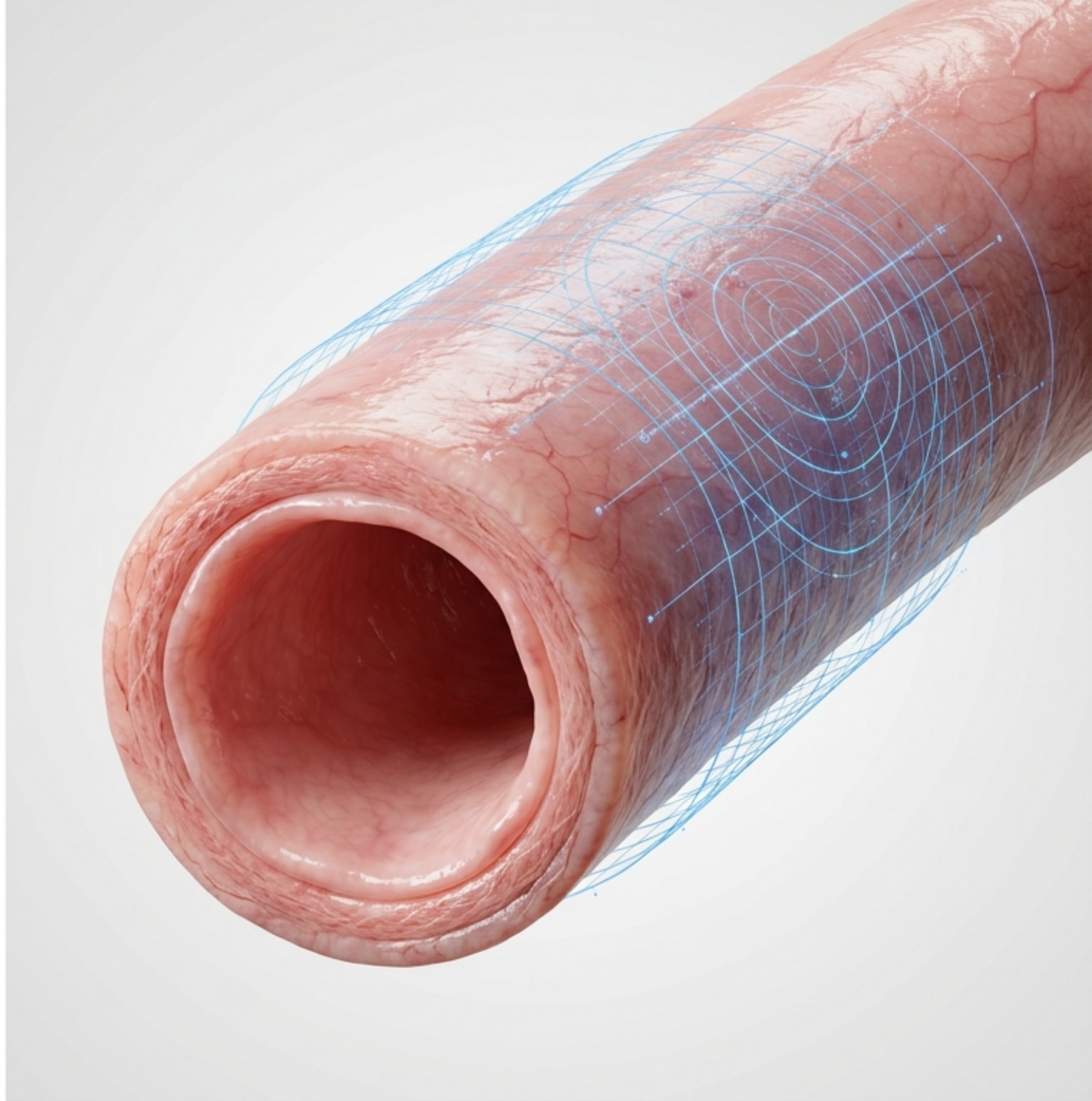
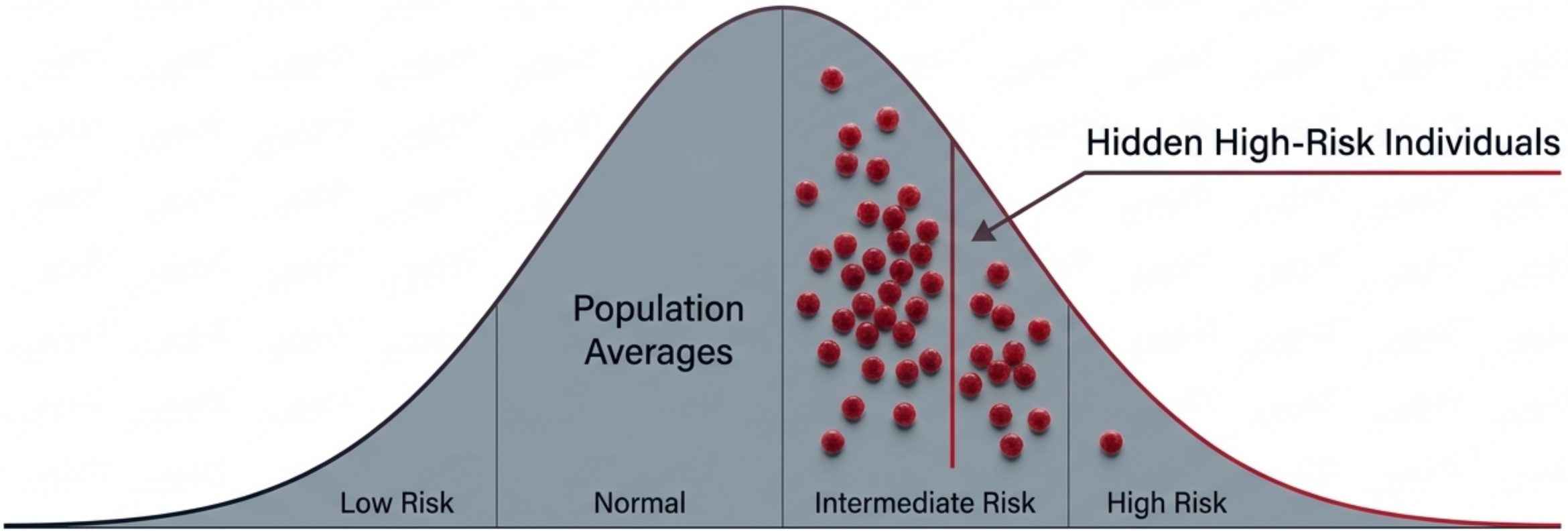
The Future of Precision Cardiology

Biomarkers, AI Imaging, and the End of Population Averages.



The Limitation of Population Averages

> Traditional models (Framingham, PCE) leave significant numbers of high-risk individuals in a clinical “blind spot.”
>
> Recent models like the 2024 AHA PREVENT tool improve calibration (adding eGFR, removing race variables), yet standard assessments still fail to detect residual biological and anatomical risks at the individual level.



The Precision Cardiology Paradigm

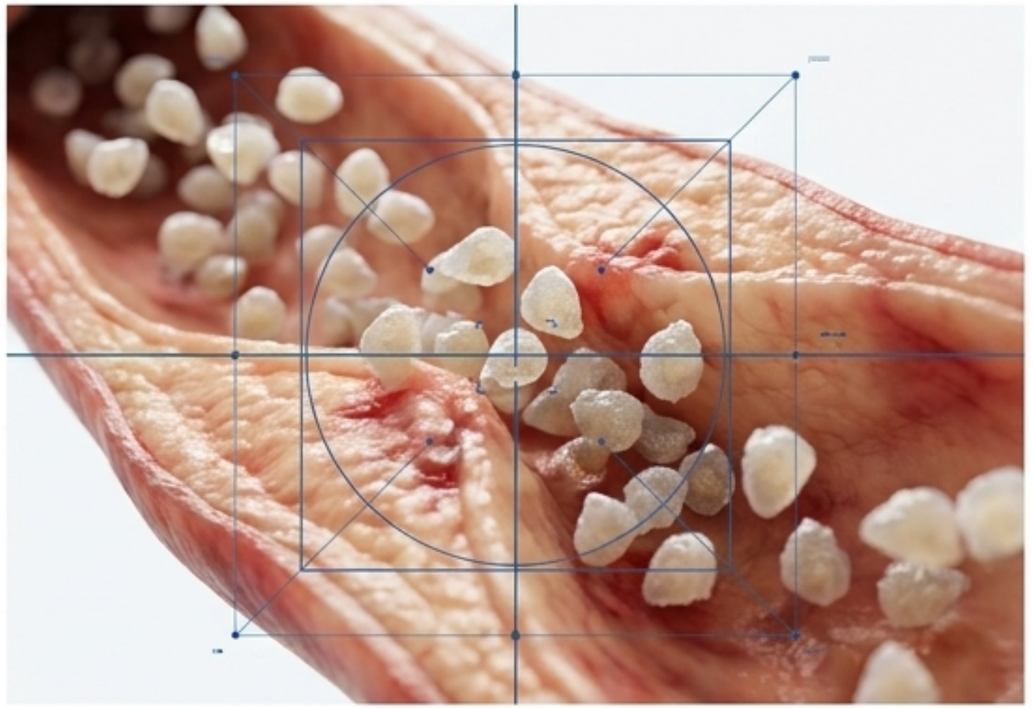
Cardiovascular prevention is shifting from estimating broad risk factors to directly measuring biological pathways and visualizing exact atherosclerotic disease progression.

The Old Era

Weight-Based Lipids & Indirect Guessing

The New Era

Particle Dynamics, AI Imaging & Direct Visualization



Standard Lipids vs. The Particle Number Paradigm

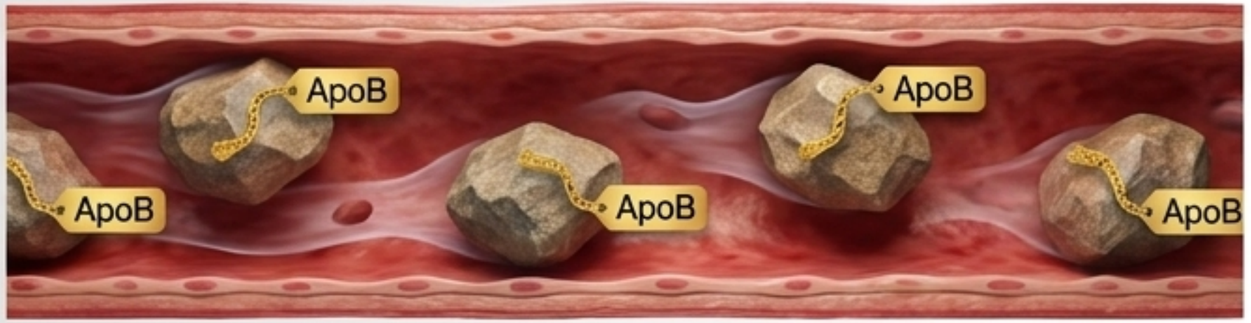
Standard lipid panels measure the weight of cholesterol (Total, HDL-C, Triglycerides).

Atherosclerosis is driven by the number of atherogenic particles penetrating the arterial wall, rendering standard LDL-C concentrations dangerously deceptive in many patients.

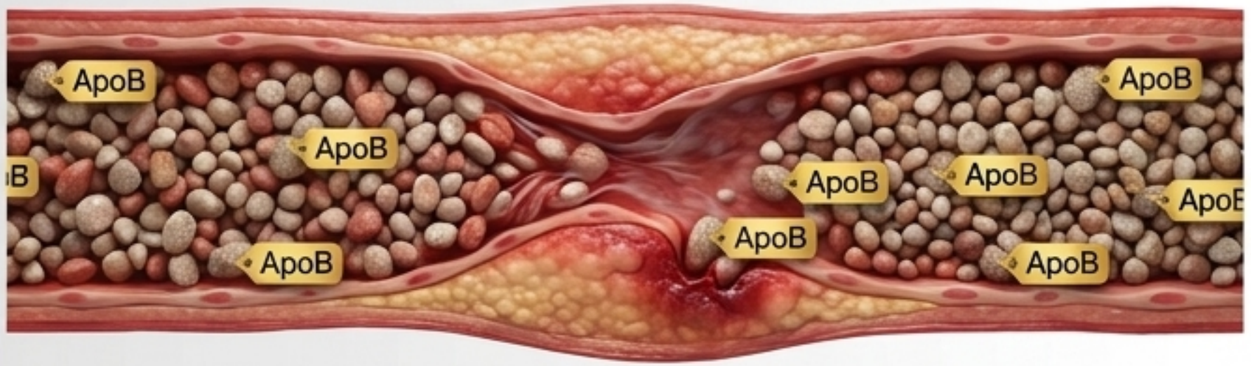
Apolipoprotein B (ApoB) & The Traffic Jam

Every atherogenic particle (VLDL, IDL, LDL) carries exactly one ApoB molecule.
ApoB provides a precise count of total disease-causing particles.

Concordant



Discordant

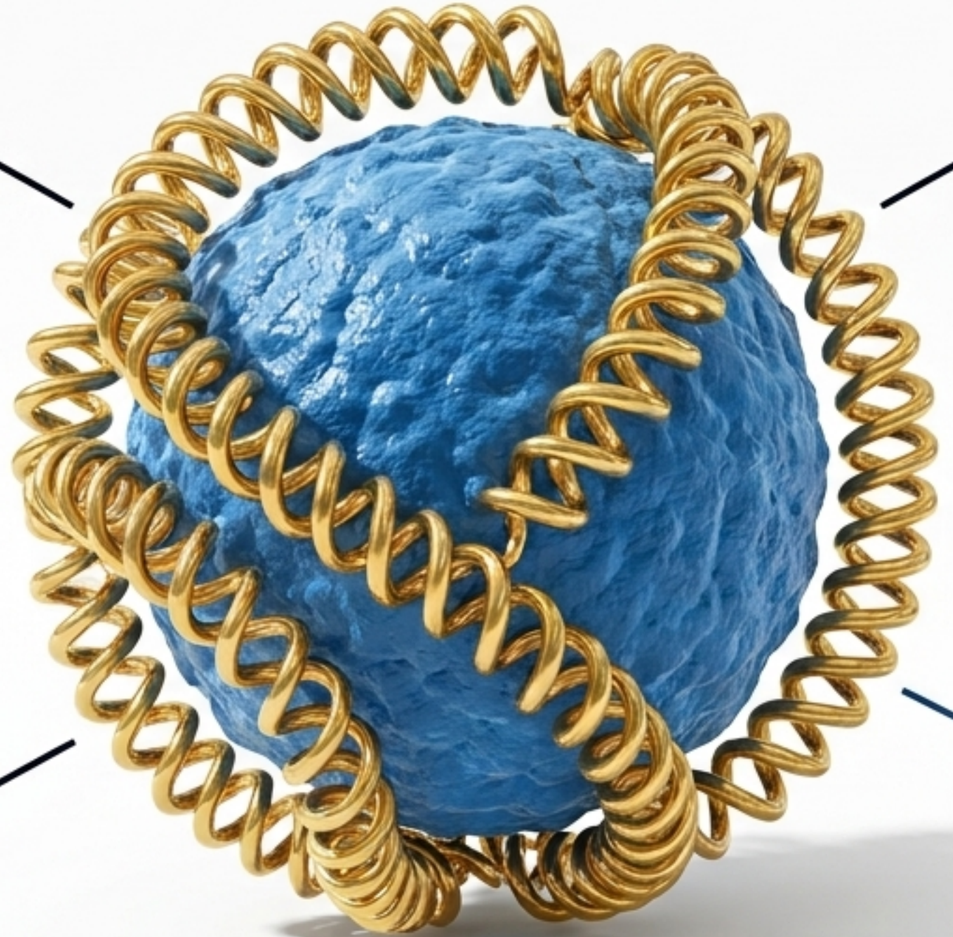


Discordance:
When LDL-C weight is low, but ApoB particle count is high (common in metabolic syndrome).

Guideline Recommendation:
Assigned a Class 2a recommendation in 2026 ACC/AHA guidelines for treatment intensification.

Lipoprotein(a): The Genetic Wildcard

Affects **~20%** of the global population with risk equivalent to familial hypercholesterolemia.



Genetically determined; unaffected by **diet**, **exercise**, or **standard statins**.

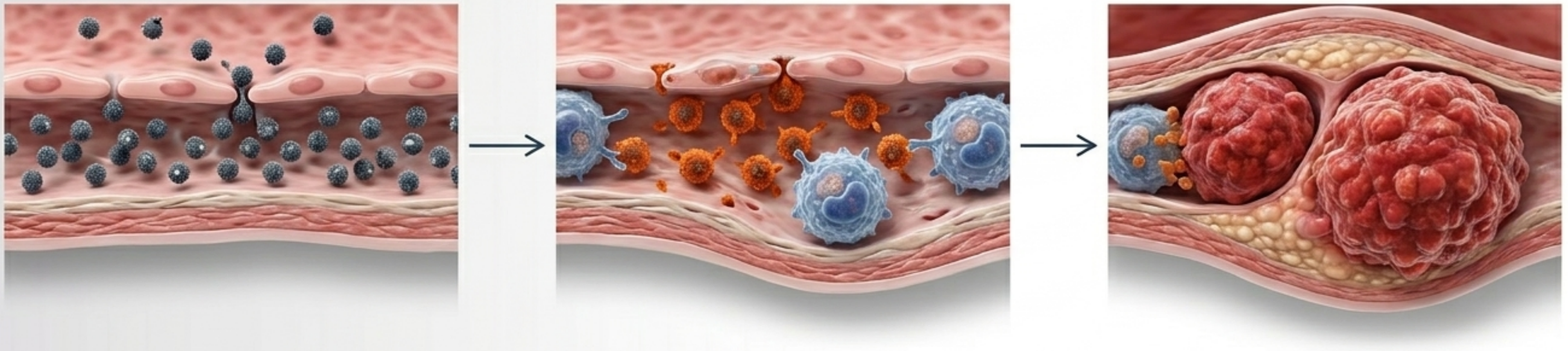
Highly **pro-thrombotic** and **pro-inflammatory** structure.

Guideline Update: 2025 ESC/EAS and 2026 ACC/AHA mandate testing at least once in every adult's lifetime to uncover hidden premature risk.

The Plaque Triggers: sdLDL & oxLDL

- **Penetration:** Small dense LDL (sdLDL) particles easily breach the endothelium and become trapped.
- **Oxidation:** Trapped particles oxidize (oxLDL), triggering scavenger receptors to transform macrophages into plaque-building foam cells.
- Elevated levels are **independent predictors** of CVD events and **plaque rupture**.

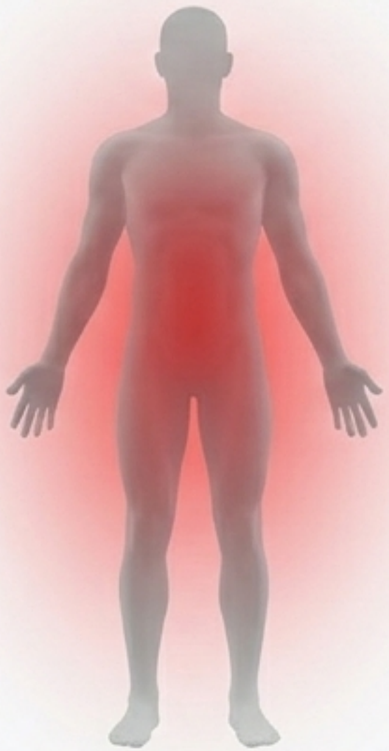
1. sdLDL → **2. oxLDL** → **3. Foam Cells**



The Inflammatory Axis: Systemic vs. Vascular

hs-CRP

The standard marker of **systemic inflammatory residual risk**. Identifies patients needing high-intensity statins.



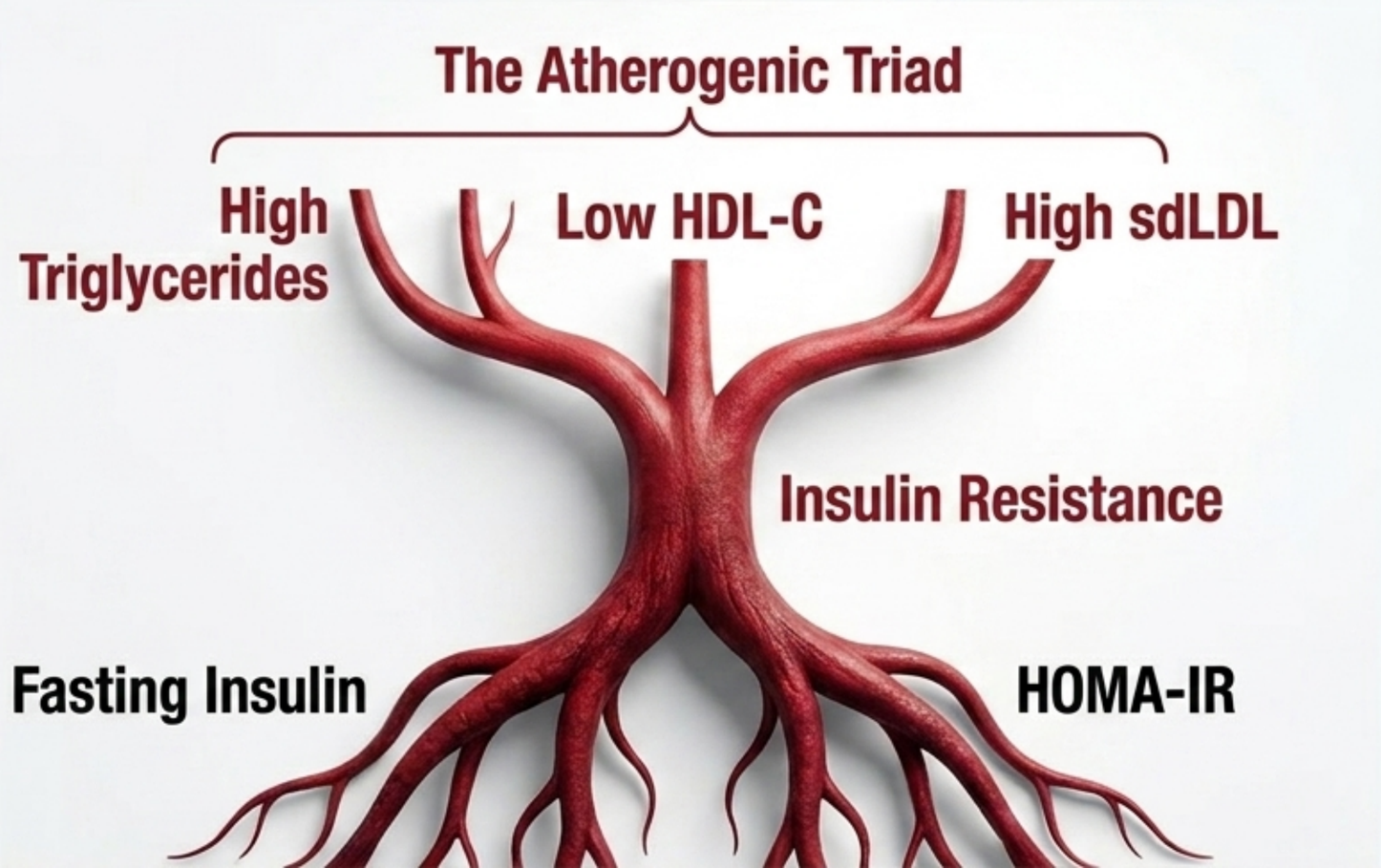
Lp-PLA2

A vascular-specific enzyme produced directly by macrophages inside the plaque. Strongly predicts stroke and myocardial infarction by identifying active plaques.

Unmasking Metabolic Risk

Metabolic dysfunction drives the ‘atherogenic triad’ long before clinical diabetes develops.

Integrating Fasting Insulin and HOMA-IR exposes the hidden metabolic roots of high ApoB and sdLDL, enabling targeted lifestyle intervention earlier.



Cardiac-Specific Stress Markers

Originally reserved for acute settings, these markers reveal immense prognostic value in asymptomatic adults.

NT-proBNP

Predicts subclinical heart failure and improves risk reclassification by gauging ventricular wall stretch.

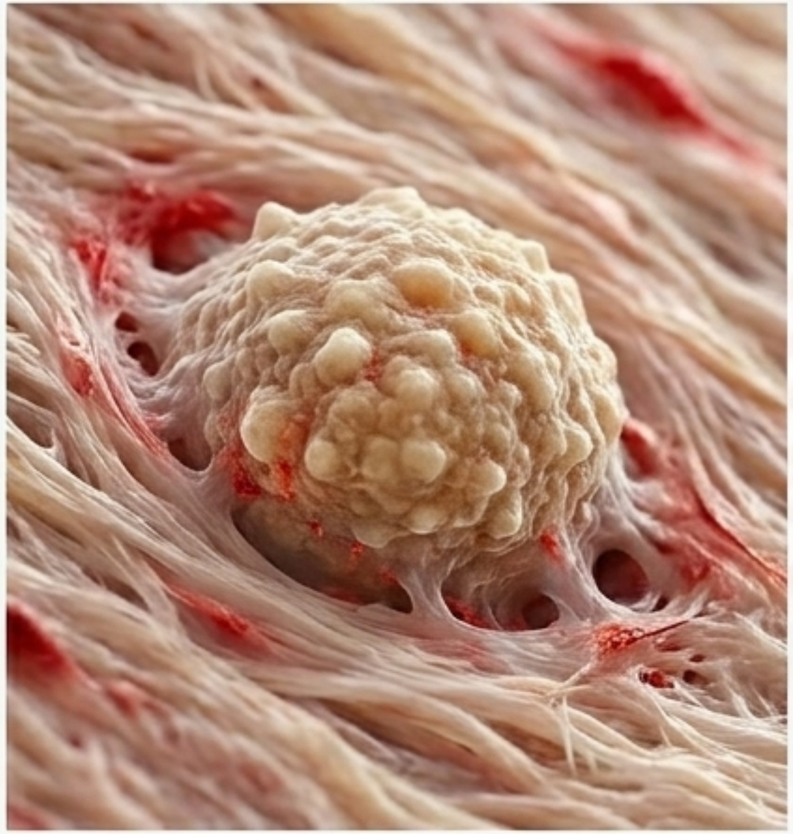
hs-Tn (Troponin)

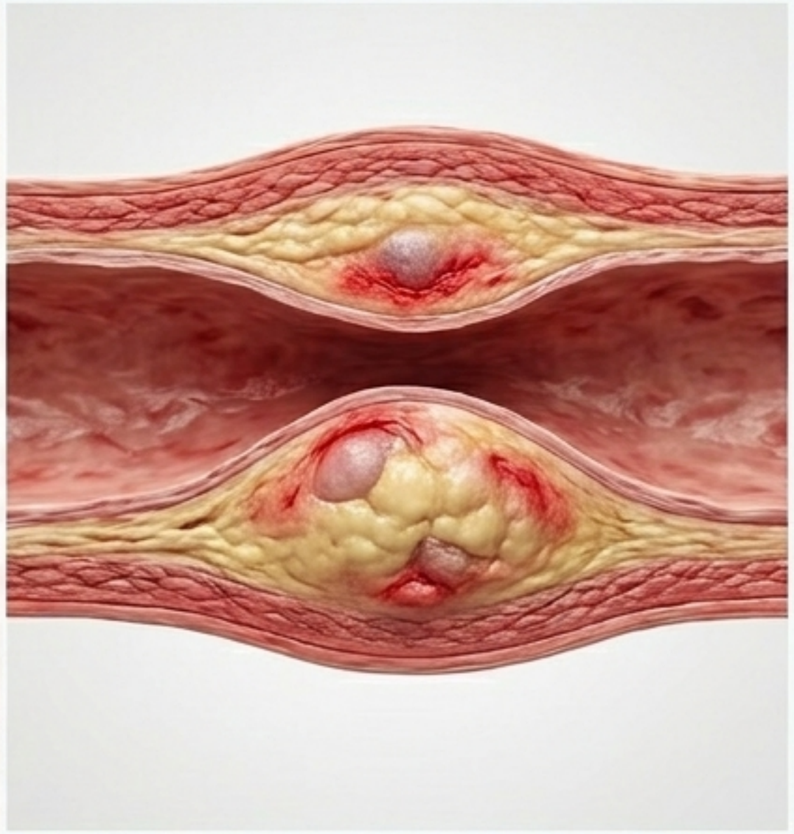
Detects chronic myocardial injury. Integrating with traditional models significantly enhances predictive accuracy, particularly for patients with diabetes.

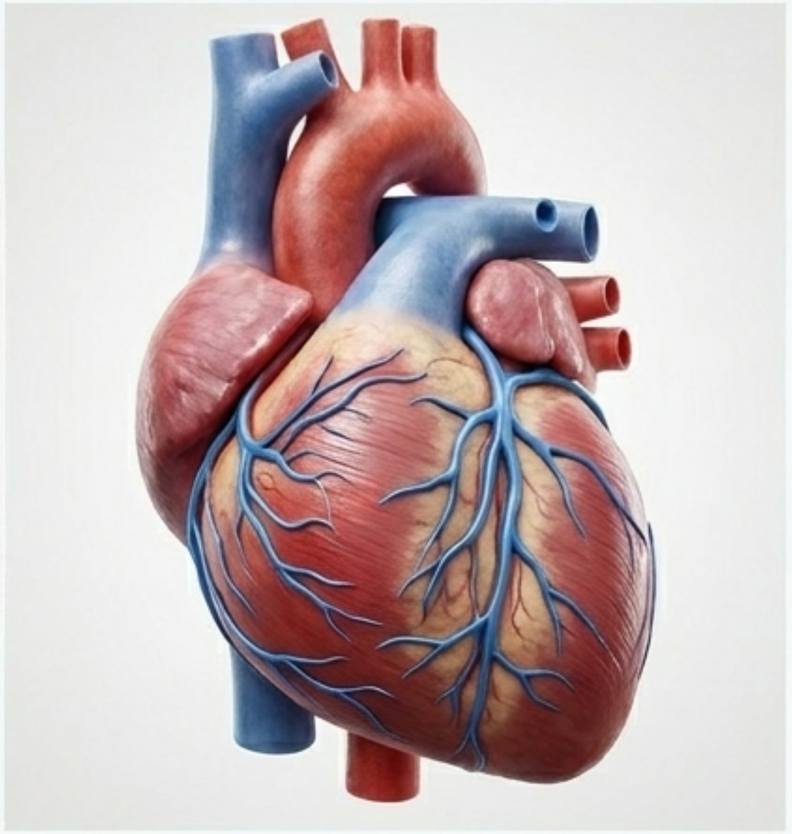
The Anatomical Frontier

Moving beyond indirect blood biomarkers to direct visualization.

Assessing the actual burden, geometry, and characteristics of disease at the target organ.





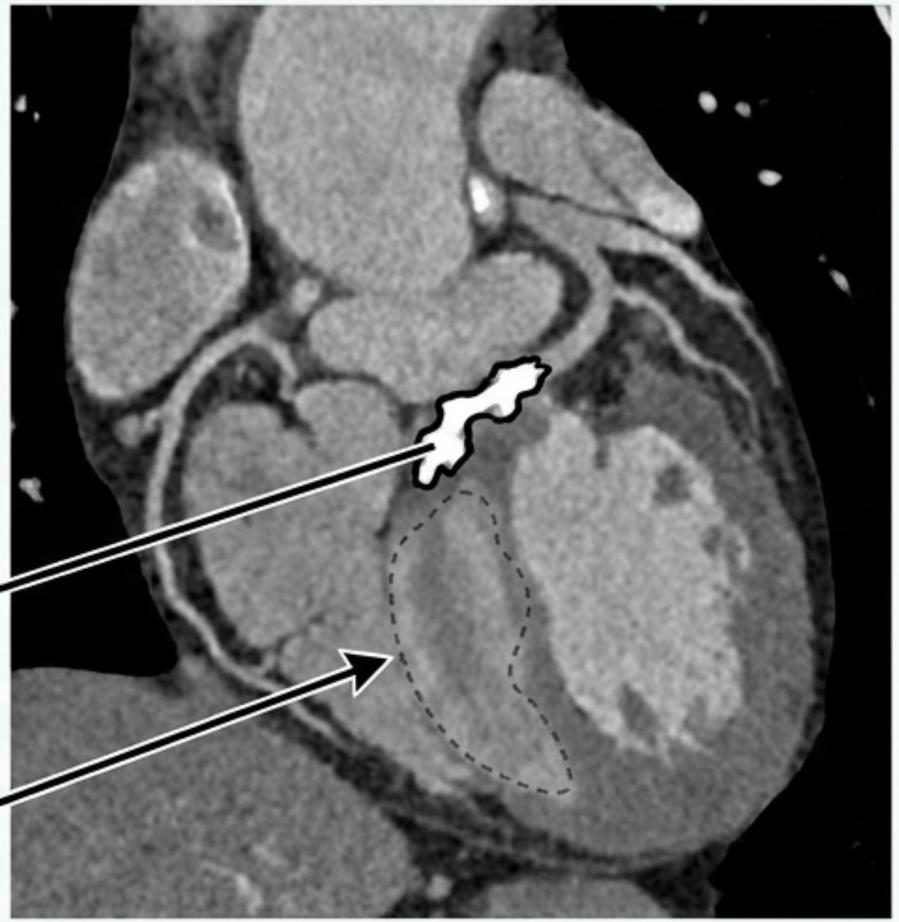


Coronary Artery Calcium (CAC): The Gatekeeper

A powerful, yet strictly limited, tool for cardiovascular risk assessment.

The Power of Zero

A CAC score of 0 indicates very low 10-year probability of events, often deferring statin therapy.



The Critical Limitation

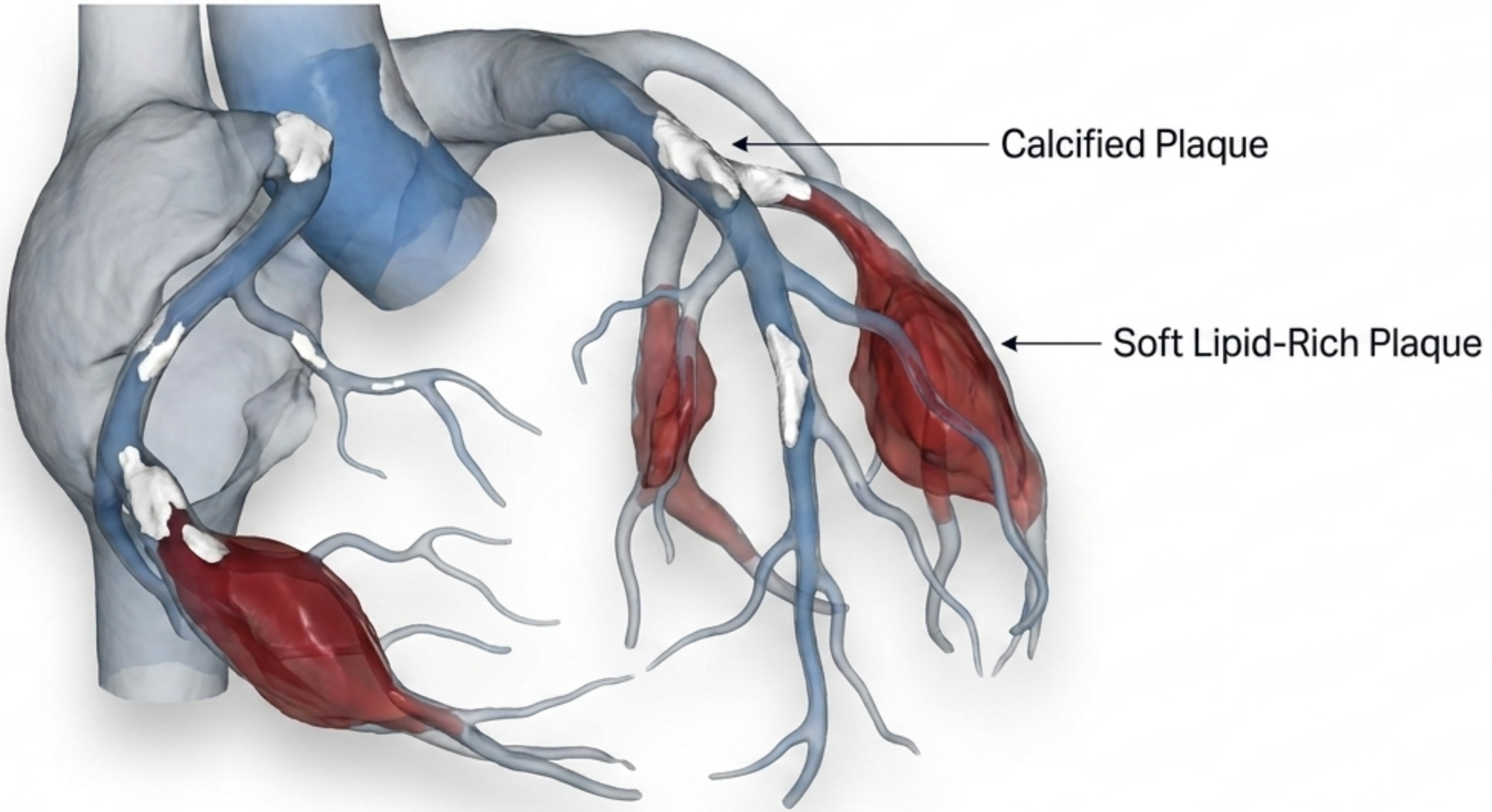
CAC strictly detects calcified (‘healed’) plaque.

It is blind to the non-calcified, lipid-rich ‘soft’ plaques responsible for acute infarctions in younger individuals and women.

CCTA: The Complete Anatomical Picture

Contrast-enhanced CT Coronary Angiography (CCTA) maps both stenosis severity and underlying plaque composition.

Directly detects the dangerous, non-calcified soft plaque that standard calcium scoring leaves entirely unseen.



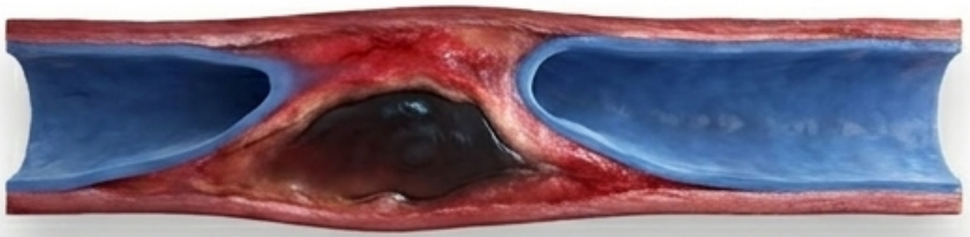
Direct Imaging Diagnostics Compared

Feature	CAC Scoring	CCTA
Primary Measurement	Calcified plaque volume only	Stenosis, calcified, AND soft plaque
Clinical Context	Asymptomatic screening	Symptomatic evaluation & high-risk screening
Advantages	Low cost, low radiation, no contrast	Detailed plaque phenotyping, rules out stenosis
Limitations	Misses non-calcified soft plaque entirely	Higher cost, contrast requirement, higher radiation
Predictive Value	Excellent for long-term risk	Excellent for near-term acute events

High-Risk Plaque (HRP) Phenotypes via CCTA

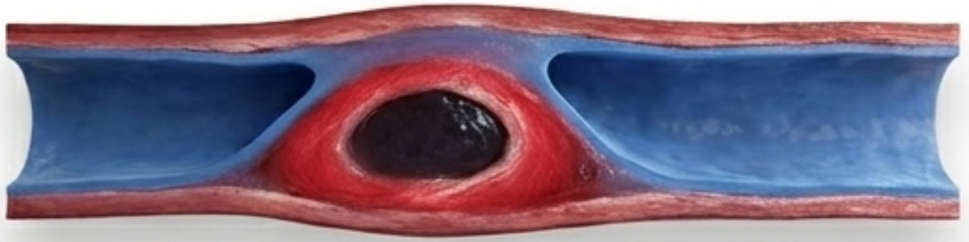
CCTA identifies features associated with 3- to 12-fold increased risk of rupture, independent of luminal narrowing.

Low Attenuation Plaque (LAP)



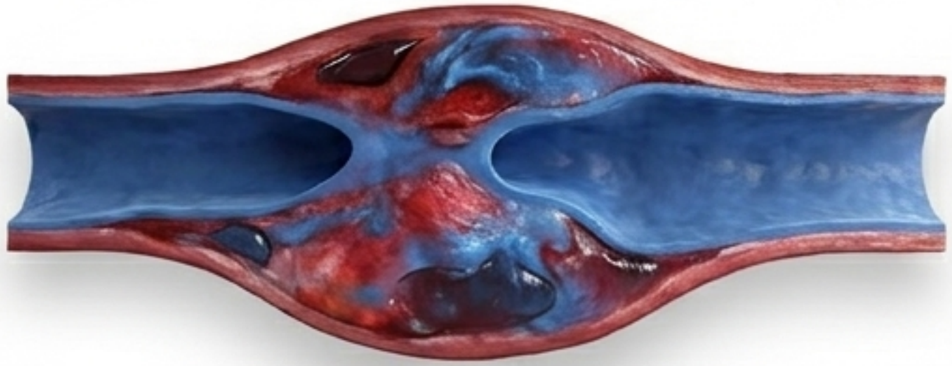
Deep, dark lipid core associated with inflammation and increased rupture risk.

Napkin-Ring Sign (NRS)



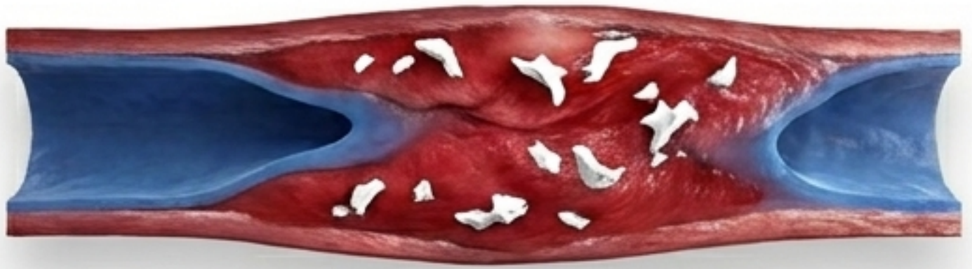
Thin, fibrous cap surrounding a large lipid core, highly vulnerable to rupture.

Positive Remodeling (PR)



Arterial wall expands outward, concealing large plaque burden while maintaining luminal patency.

Spotty Calcification (SC)

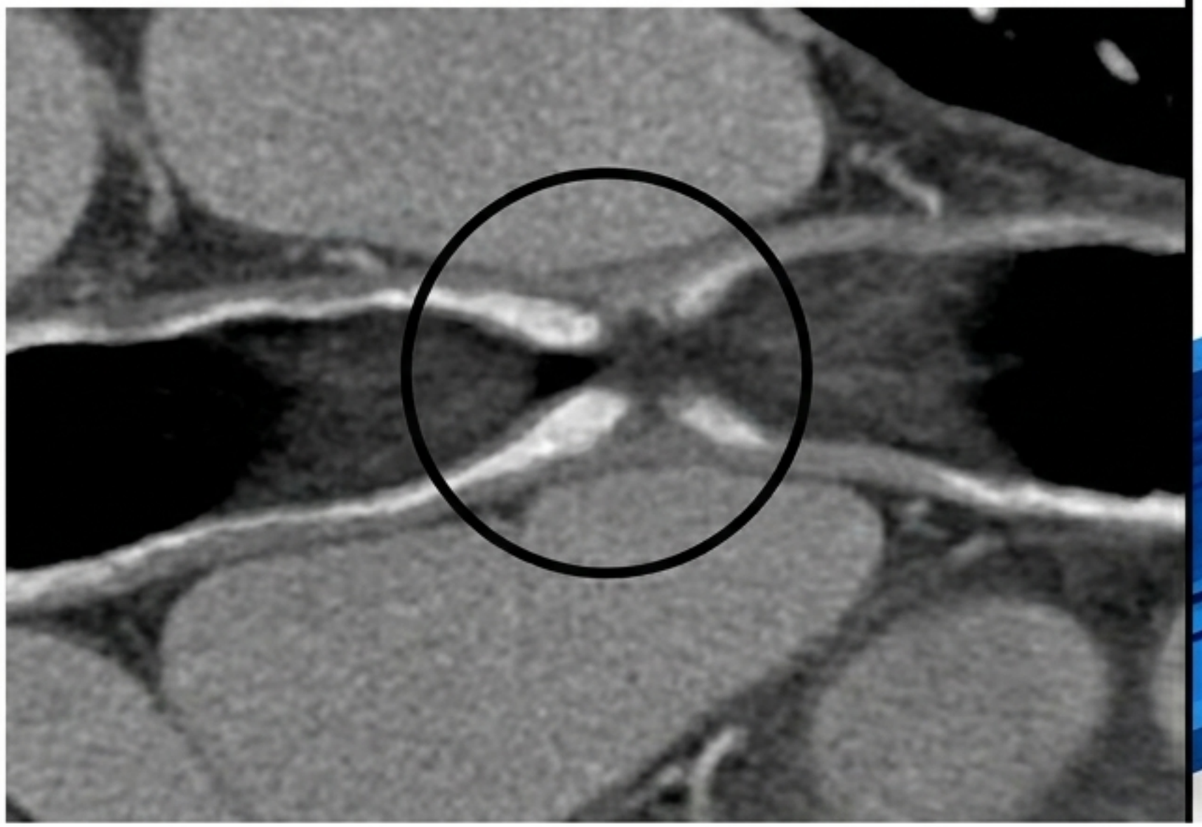


Multiple small, sharp calcium deposits embedded within inflamed soft plaque.

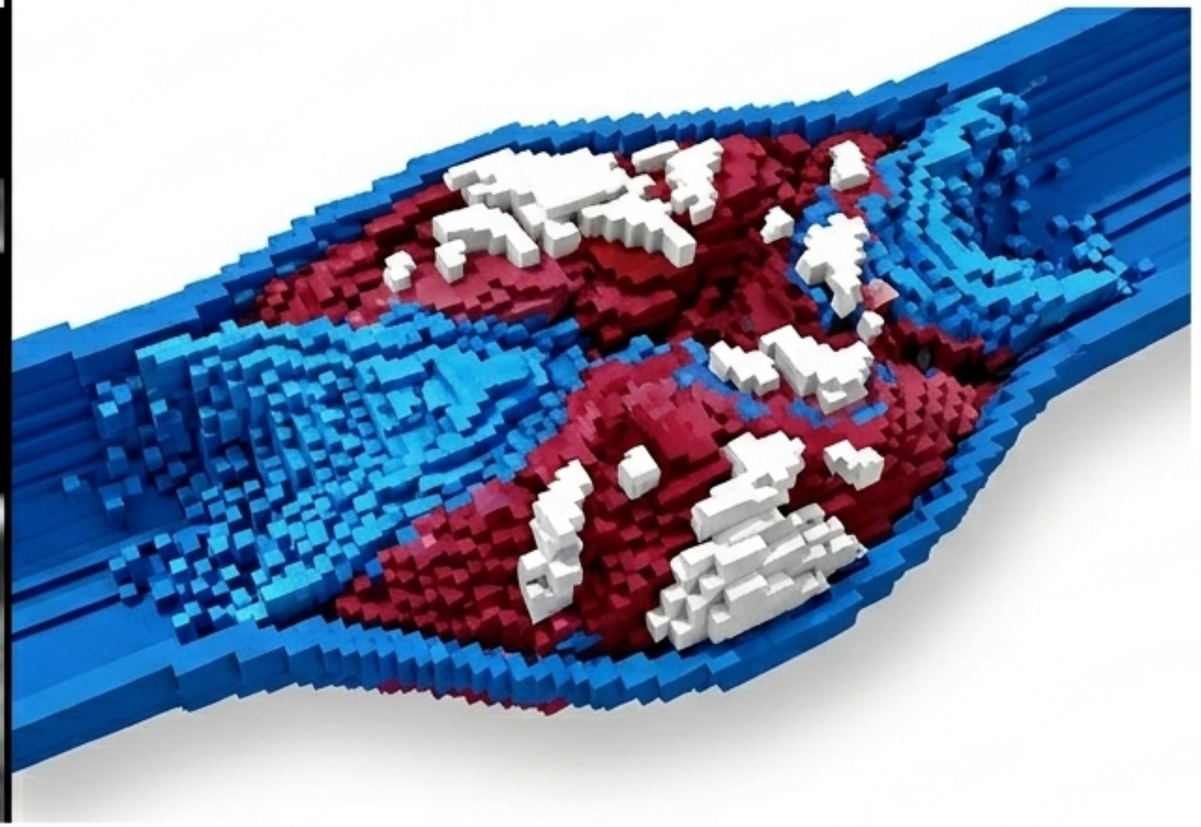
AI in Imaging: AI-Guided Quantitative CT (AI-QCT)

- Automates detection, segmentation, and characterization of plaque burden.
- Outperforms expert human readers in determining stenosis severity and precise plaque composition.

Human Visual Assessment



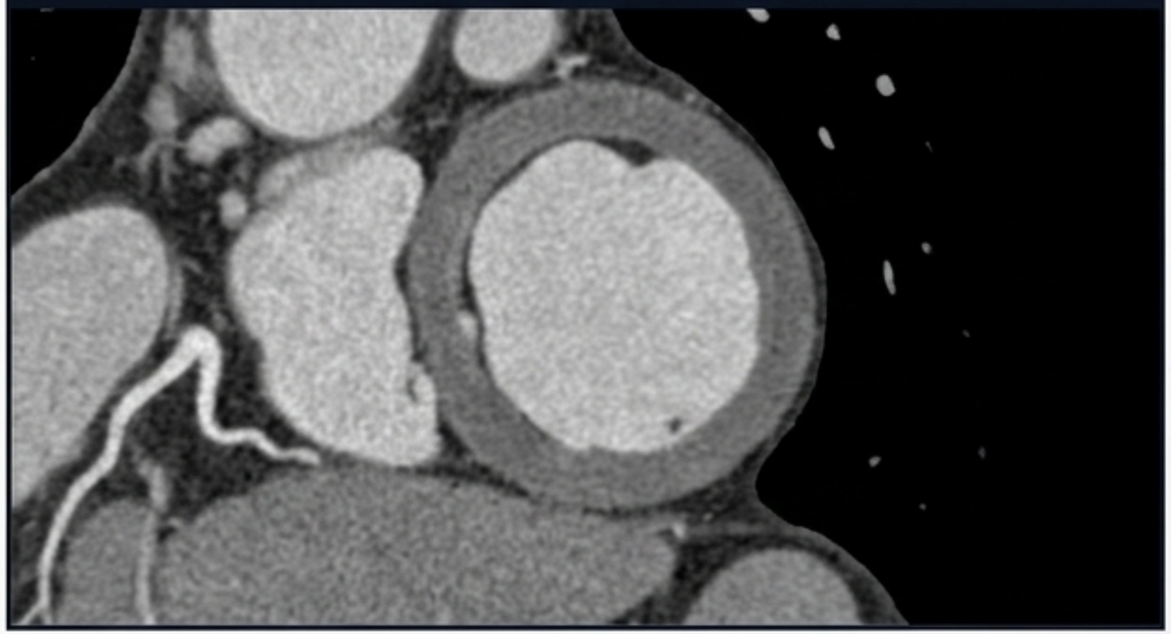
AI-QCT Segmentation



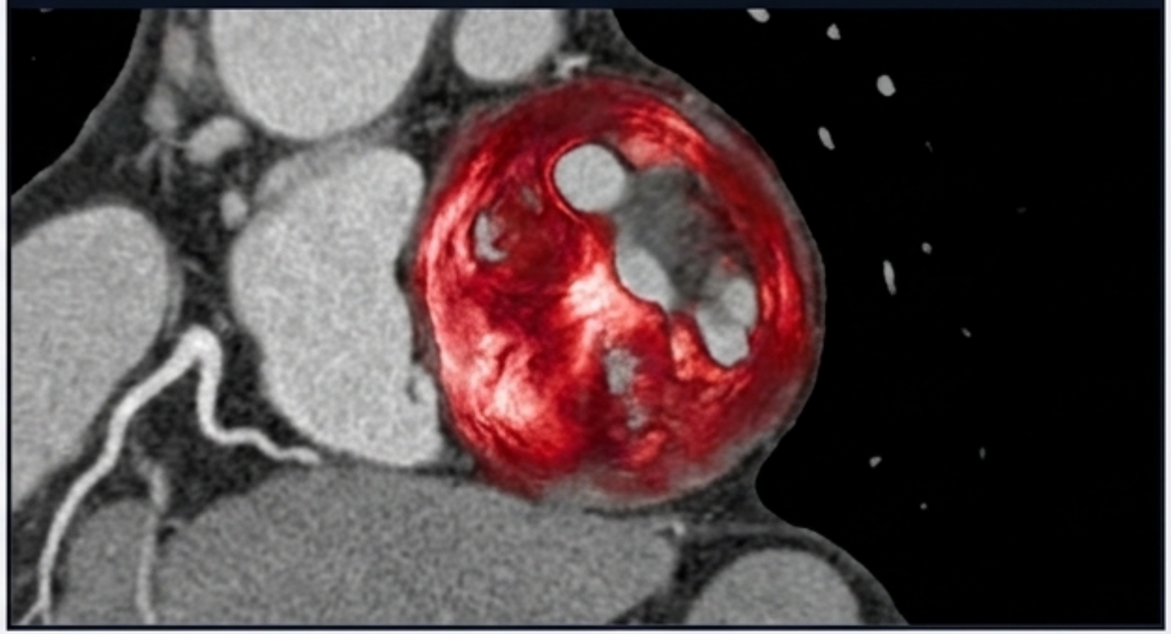
The ‘Zero Calcium’ Paradox

Clinical practice often over-relies on a CAC score of 0 to stop preventative efforts.

CAC = 0 (Patient Cleared)



AI-QCT: High-Risk Plaque Detected

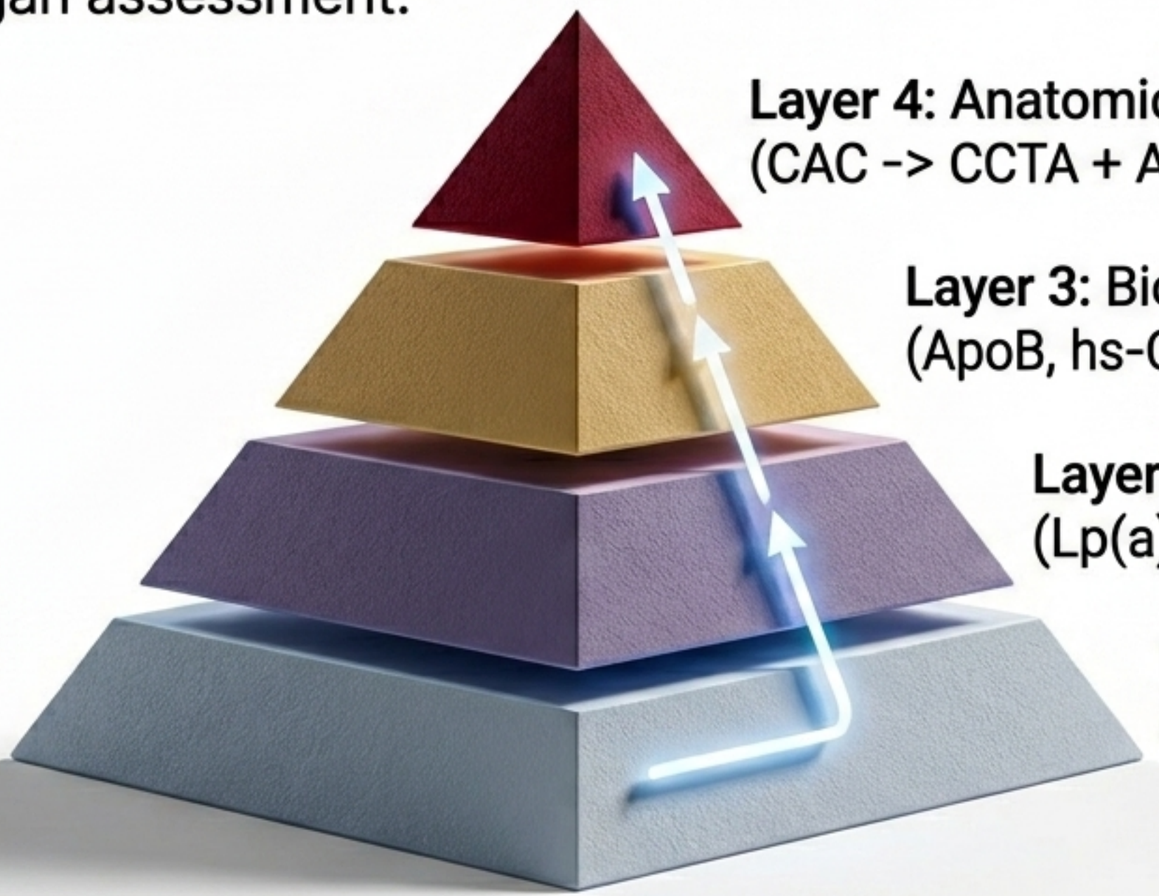


AI-QCT reveals that 11-16% of patients cleared by ‘CAC = 0’ harbor clinically relevant, dangerous non-calcified plaque.

Synthesis: The 4-Layer Risk Fusion Model

Integrating clinical baseline, genetics, biology, and anatomy into a unified workflow.

- Eliminates the “blind spots” of isolated testing by combining systemic traffic/inflammation with direct target-organ assessment.



Layer 4: Anatomical Disease
(CAC -> CCTA + AI)

Layer 3: Biological Activity
(ApoB, hs-CRP, HOMA-IR, Lp-PLA2)

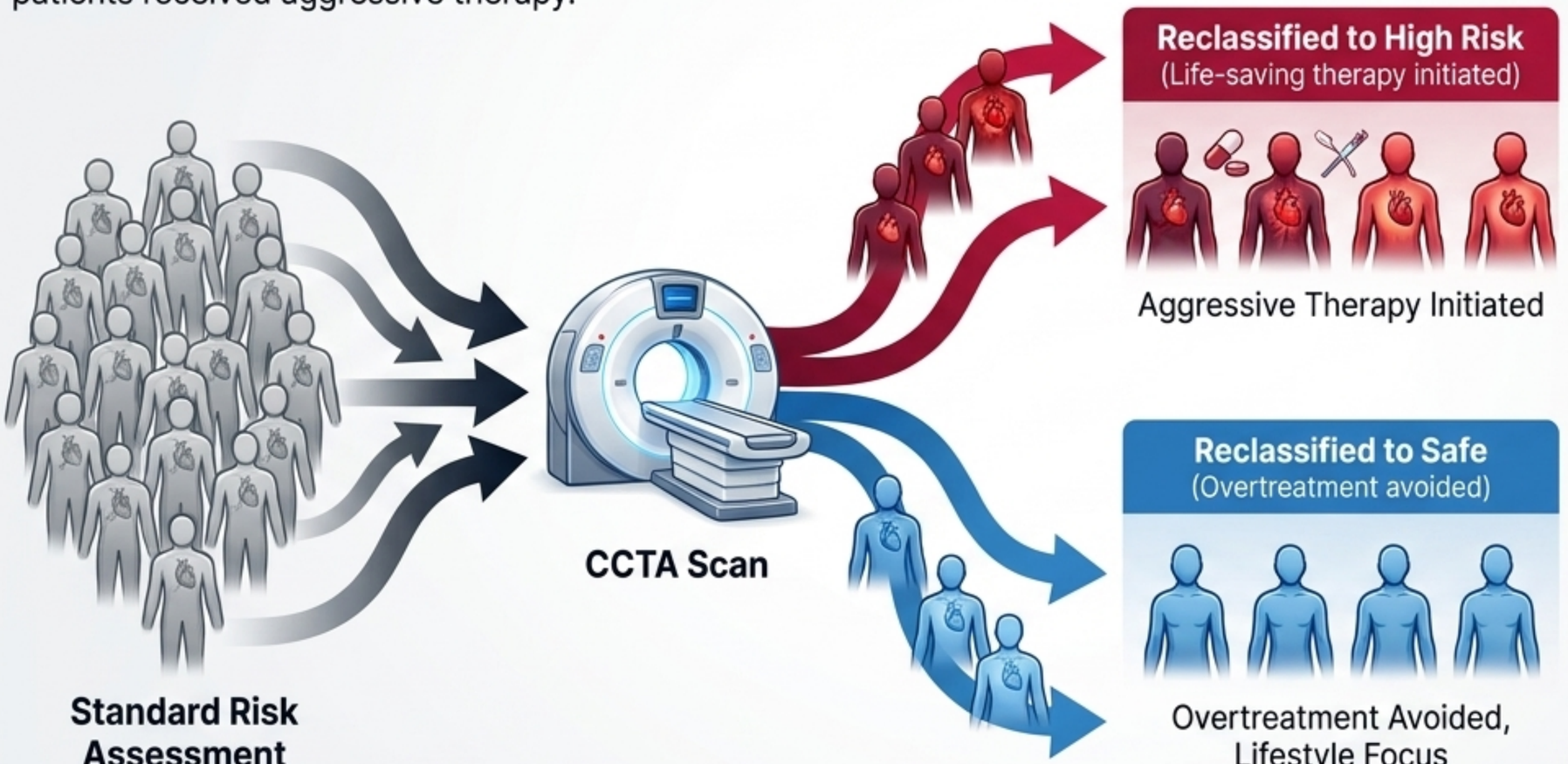
Layer 2: Genetic Predisposition
(Lp(a), PRS)

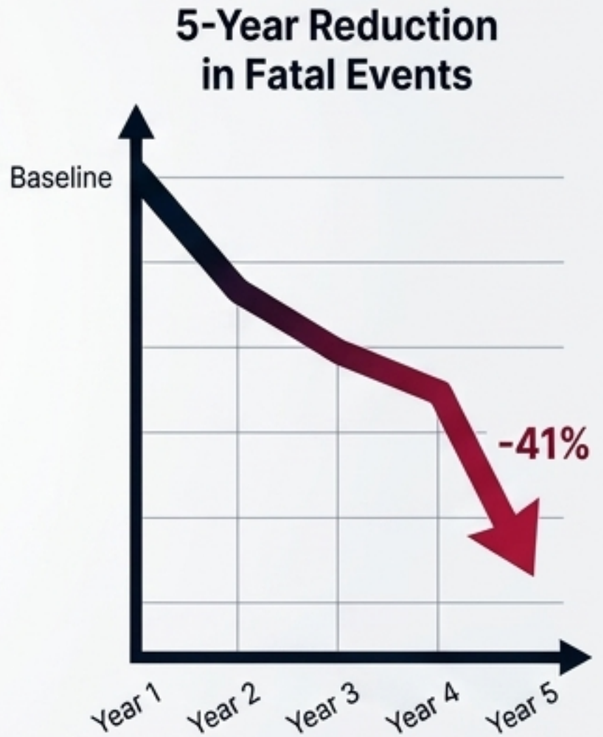
Layer 1: Clinical Baseline
(PREVENT tool)

The Clinical Benefit: Reclassification & Prevention

The landmark SCOT-HEART trial proved that advanced imaging (CCTA) drives massive patient reclassification.

Resulted in a significant relative reduction in fatal and non-fatal myocardial infarctions over 5 years by ensuring the right patients received aggressive therapy.





The ROI: Cost-Effectiveness

- Despite higher upfront costs, advanced diagnostic strategies demonstrate highly favorable Incremental Cost-Effectiveness Ratios (ICER).
- By preventing downstream acute events (infarctions, strokes), precision screening proves strictly viable for large-scale healthcare economics.

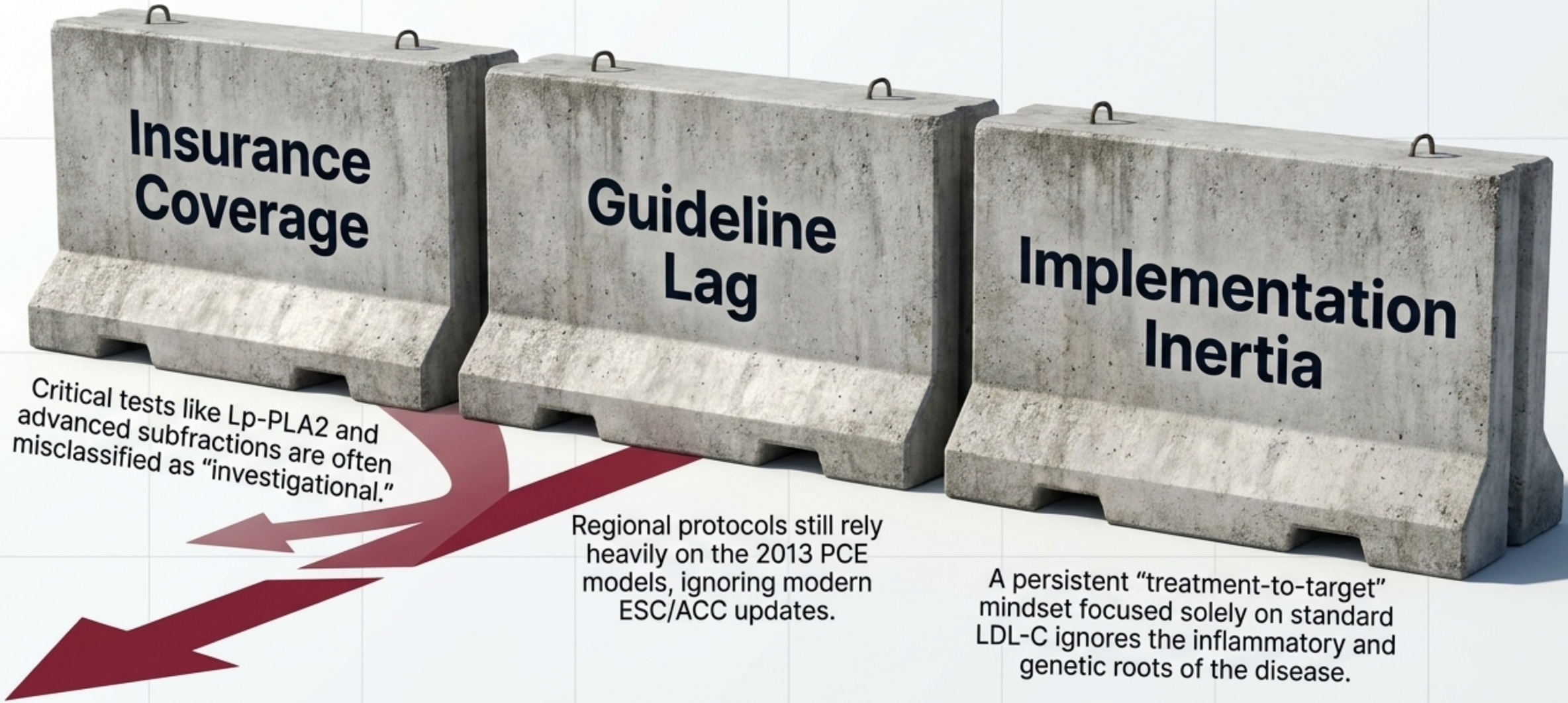
CAC-based Strategy

Viable ICER threshold in diabetic populations.

hs-TnI-guided Strategy

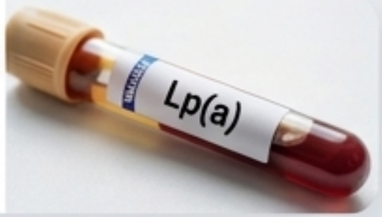
Viable ICER tied to direct reduction in CVD events.

Bridging the Implementation Gap



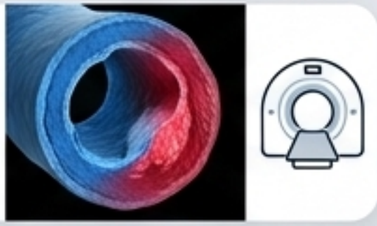
Clinical Recommendations for Immediate Adoption

1. **Universal Lp(a) Testing:** Test every adult at least once to identify genetic outliers.



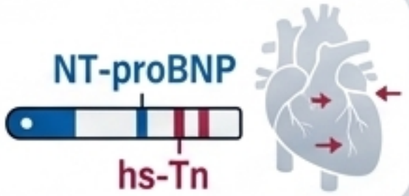
2. **ApoB as Primary Target:** Replace LDL-C with ApoB for patients with metabolic syndrome/obesity.

3. **Expanded Role for CCTA:** Deploy earlier for intermediate-risk patients with high biological markers.



4. **AI Integration:** Mandate AI-QCT to quantify plaque and eliminate human visual error.

5. **Subclinical HF Screening:** Use NT-proBNP and hs-Tn to catch pre-heart failure in asymptomatic diabetics.



Lower for longer, earlier the better.

The era of estimating average risk is over. By unifying advanced biological markers with AI-driven direct visualization, we can identify exact risk in the exact patient—preventing the disease decades before it strikes.