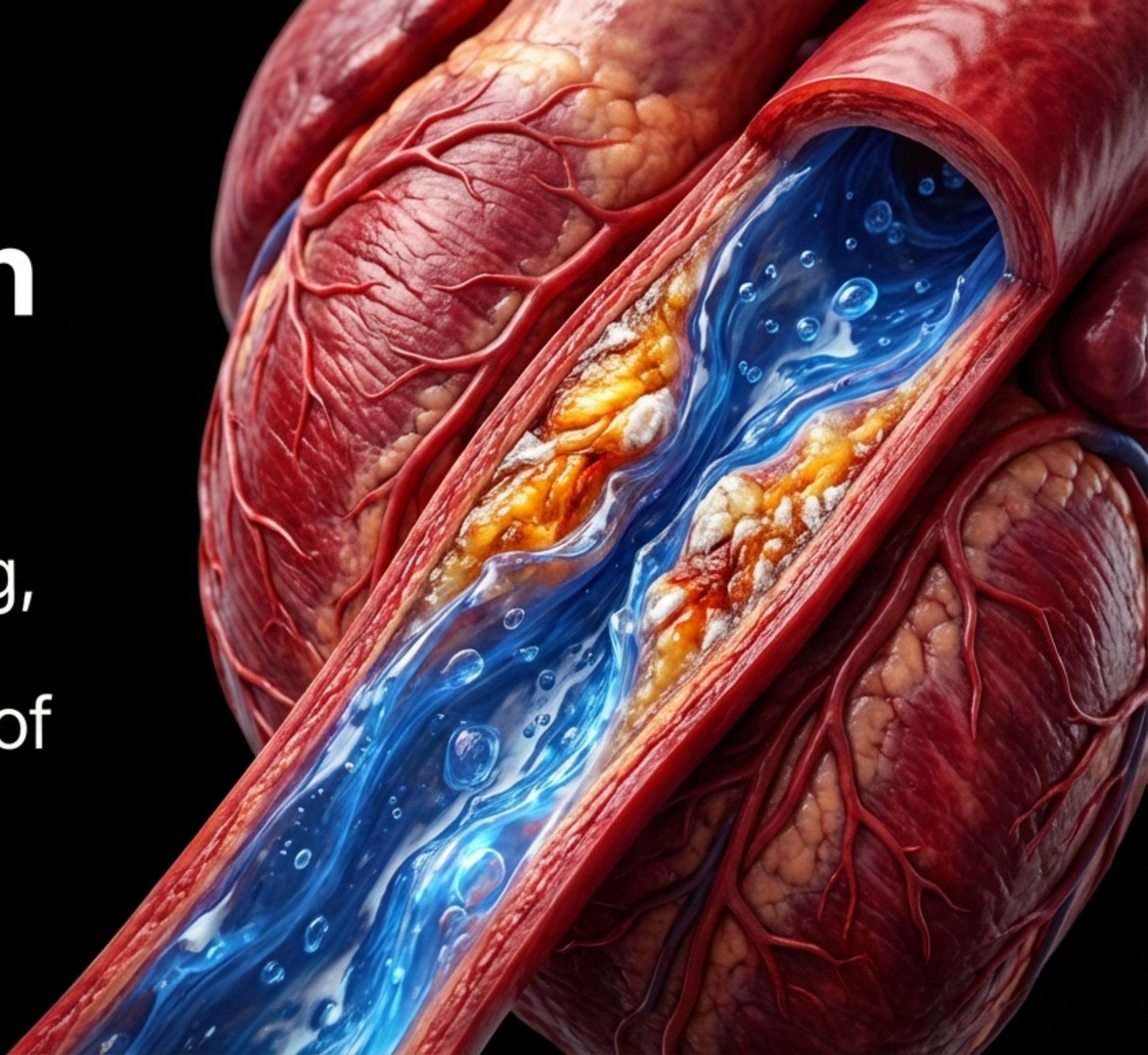


# The Athlete Calcification Paradox

Vascular Remodeling,  
Structural Disease,  
and the Uncoupling of  
Cardiovascular Risk  
in Masters Athletes



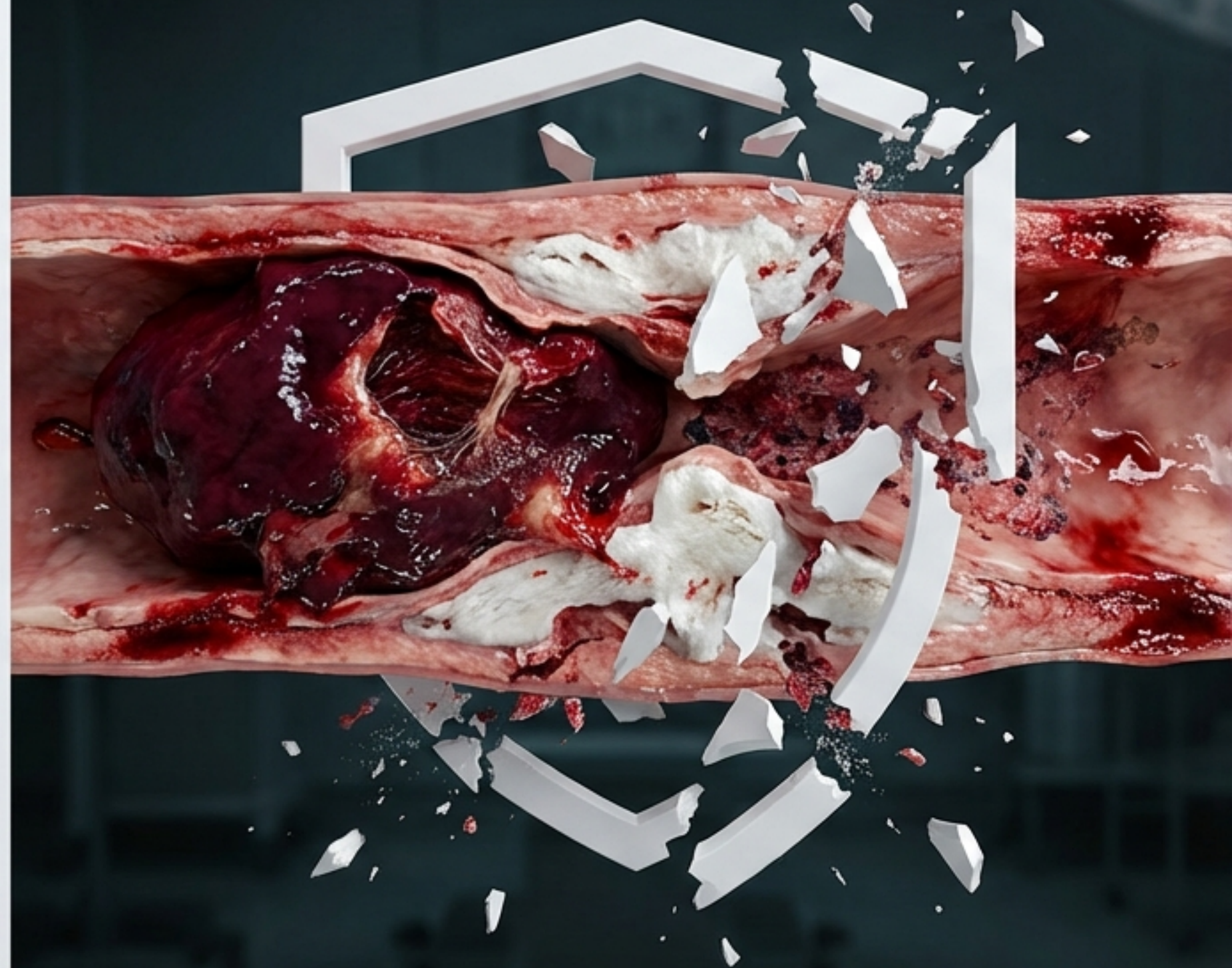
## THE BASSLER HYPOTHESIS (1970s)

**The assumption:** Completing a 42km marathon confers absolute immunity against fatal coronary atherosclerosis.



## THE AUTOPSY REALITY (1980s-PRESENT)

**The forensic truth:** Fatal, histologically proven coronary atherosclerosis is routinely documented in marathon runners dying suddenly during exertion.



# DEFINING THE ATHLETE CALCIFICATION PARADOX

**The Masters Athlete:** >35-40 years old, engaged in prolonged, systematic, high-volume endurance training.

## Structural Disease

Significantly higher prevalence of Coronary Artery Calcification (CAC) and overall atherosclerotic plaque burden than sedentary peers.



## Functional Health

Substantially lower all-cause and cardiovascular mortality rates.



# Traditional risk stratification masks the true atherosclerotic burden in runners

Data from the Heinz Nixdorf Recall Marathon Study

The Illusion

## Median Framingham Risk Score (FRS)



Marathon Runners: 7% | Controls: 11%

Runners exhibit a highly favorable, low-risk metabolic profile.

The Reality

## Median CAC Score



Runners: 36 | FRS-Matched Controls: 12

Despite "low risk" scores, athletes harbor **3x the calcification** of matched controls ( $P=0.02$ ).

# Lifelong endurance training accelerates all coronary plaque morphotypes

Master@Heart Study: Lifelong Athletes vs. Controls



# The Coronary Phenotype Matrix

Activity strata dictate distinct physical plaque presentations



**Sedentary / Moderate**



**Late-Onset Masters**



**Lifelong Masters**

**Dominant Type:**  
Mixed / Non-calcified

**Dominant Type:**  
Predominantly calcified

**Dominant Type:**  
Calcified, with higher  
absolute non-calcified volume

**CAC Distribution:**  
High prevalence of zero

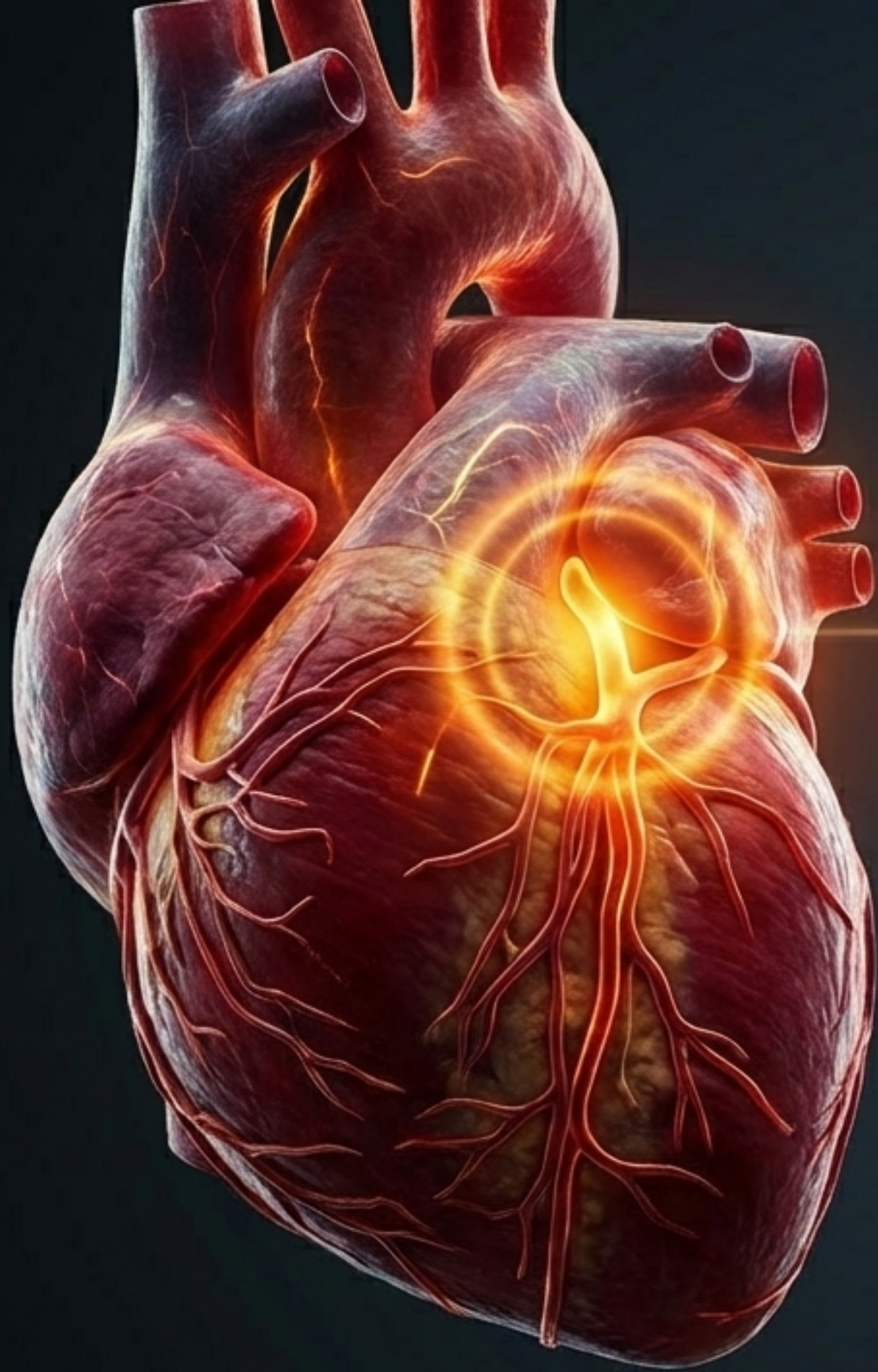
**CAC Distribution:**  
Elevated absolute scores

**CAC Distribution:**  
Highest prevalence of >100 and  $\geq 300$  AU

**High-Risk Lesions:**  
Tied to traditional risk factors

**High-Risk Lesions:**  
Rare without traditional risks

**High-Risk Lesions:**  
Higher absolute prevalence



Lifelong athletes exhibit a **severe proximal anatomical risk profile**

### The Anatomical Threat:

Plaques located in **proximal** segments **jeopardize massive** territories of distal myocardium in the event of an acute occlusion.

### Master@Heart Data:

Lifelong athletes possess an Odds Ratio of **5.92** for a **≥50% stenosis** in a proximal segment compared to late-onset athletes (95% CI 1.22–28.80).

# The sex-specific disparity of **exercise-induced calcification**

## Male Masters Athletes



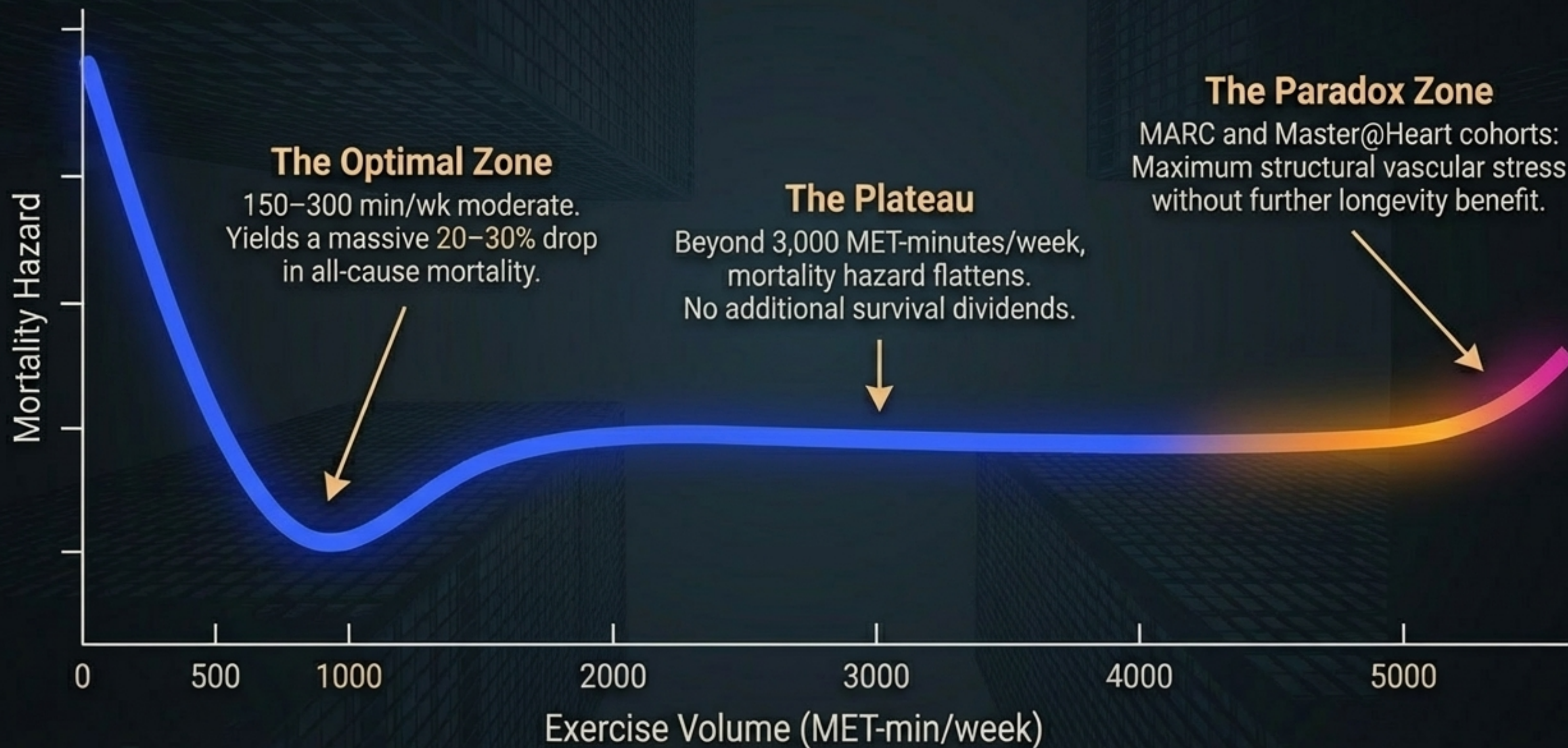
- High prevalence of extreme CAC.
- High prevalence of extreme CAC.
- Driven entirely by mechanical stress and cumulative years of endurance training.
- Higher prevalence of mixed-morphology plaques.

## Female Masters Athletes



- Significantly lower prevalence of CAC >50<sup>th</sup> percentile.
- Complete absence of obstructive CAD (>50% stenosis).
- Plaque burden shows **NO** association with exercise volume or intensity.
- Driven exclusively by traditional aging risks (BP, age, low HDL).

# The **Reverse J-Curve**: Diminishing returns at the extremes of human endurance



# Intensity, not total volume, drives the calcification cascade

MARC-2 Follow-up Data (6-year trajectory)



# The Mortality Disconnect

Extreme activity neutralizes the risk of severe calcification

Low Activity + Low CAC (<100)



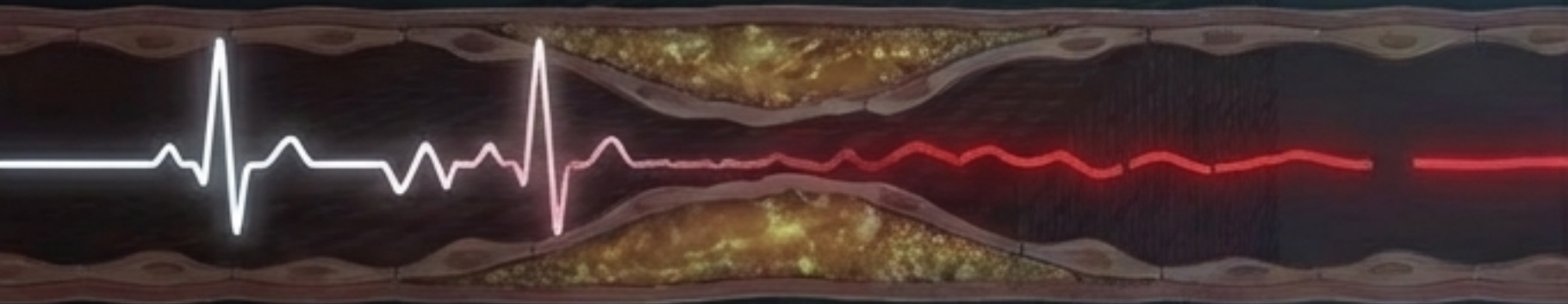
Baseline Risk (HR 1.0)

High Activity ( $\geq 3000$  MET-min) + Low CAC



Peak Longevity (HR 0.52): Half the baseline risk of death.

Low Activity + High CAC ( $\geq 100$ )



The Fatal Trajectory (HR 1.93):  
Nearly double the risk of cardiovascular death.

High Activity + High CAC ( $\geq 100$ )



The Paradox (HR 0.77):  
No significant mortality increase compared to the least active men with the exact same high CAC burden.

# Subclinical **myocardial damage** arises from **demand ischemia**, not classic rupture



Ultra-high-fidelity 3D CMR) with Late Gadolinium Enhancement (LGE)

## **The Finding:**

14% of male masters athletes exhibit myocardial scarring (LGE) on CMR, compared to 0% of matched controls.

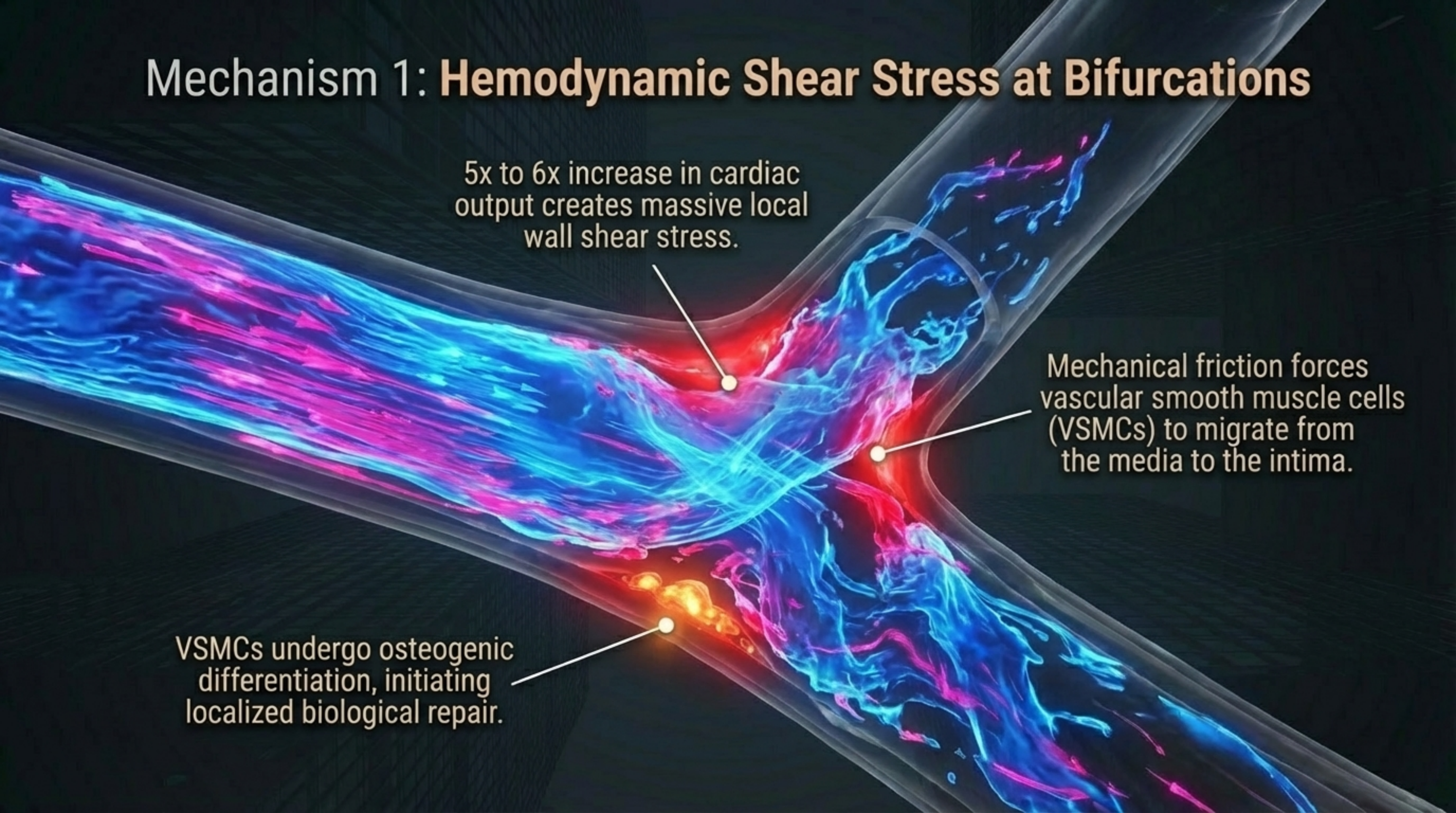
## **The Disconnect:**

Of the athletes with an infarct pattern, only 43% had a corresponding obstructive lesion ( $\geq 50\%$  stenosis) in the supplying artery.

## **The Mechanism:**

Myocardial scarring in these extreme athletes is frequently driven by profound demand ischemia, microvascular trauma, or transient spasm during peak exertion, rather than classical atherosclerotic plaque rupture.

# Mechanism 1: Hemodynamic Shear Stress at Bifurcations



5x to 6x increase in cardiac output creates massive local wall shear stress.

Mechanical friction forces vascular smooth muscle cells (VSMCs) to migrate from the media to the intima.

VSMCs undergo osteogenic differentiation, initiating localized biological repair.

# Mechanism 2: The Parathyroid Hormone (PTH) Calcium Cascade

Systemic Trigger



**Step 1:** Extreme exertion triggers acute, proportional spikes in Parathyroid Hormone (PTH).

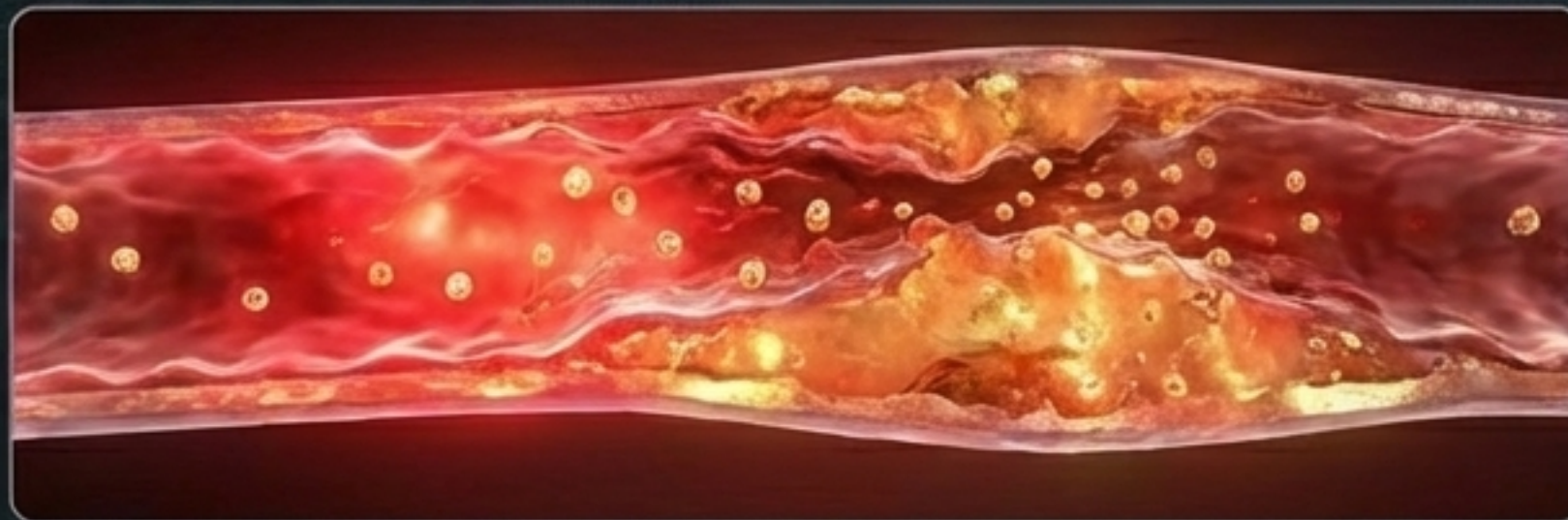
Mobilization



**Mobilization**

Step 2: Recurrent PTH spikes continuously mobilize serum calcium from bone mineral reserves.

Deposition



**Deposition**

Step 3: Free calcium substrate is deployed directly to sites of mechanically traumatized endothelium to build vascular armor.

# Mechanism 3: **The Neo-Media and Fibrous Cap Hypertrophy**

Why athlete plaques resist rupture despite high mechanical stress



## **The Lipid Core:**

The inner atherosclerotic necrotic pool.

## **The Neo-Media:**

The hypertrophied, mechanically reinforced fibrous cap.

## **The Outcome**

The sheer density of this calcified armor protects the underlying plaque from hemodynamic shear forces, explaining why vulnerable plaques are rare (OR 0.11).

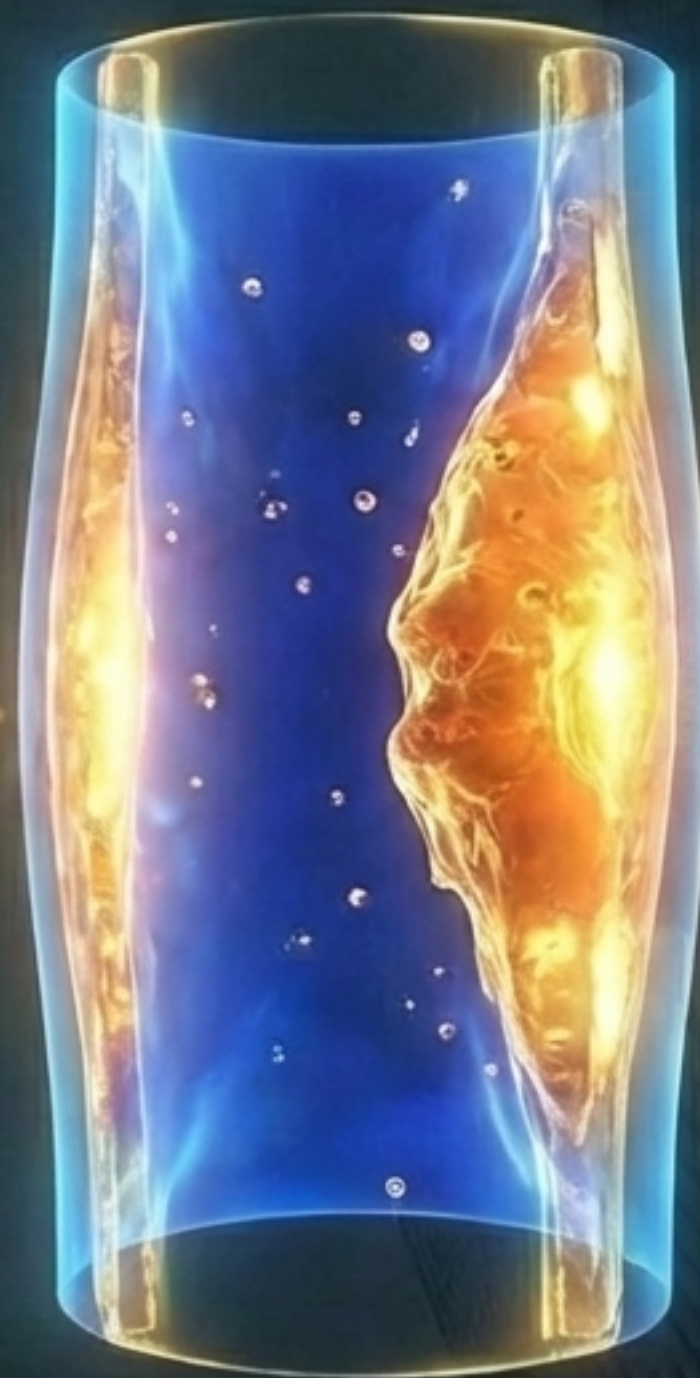
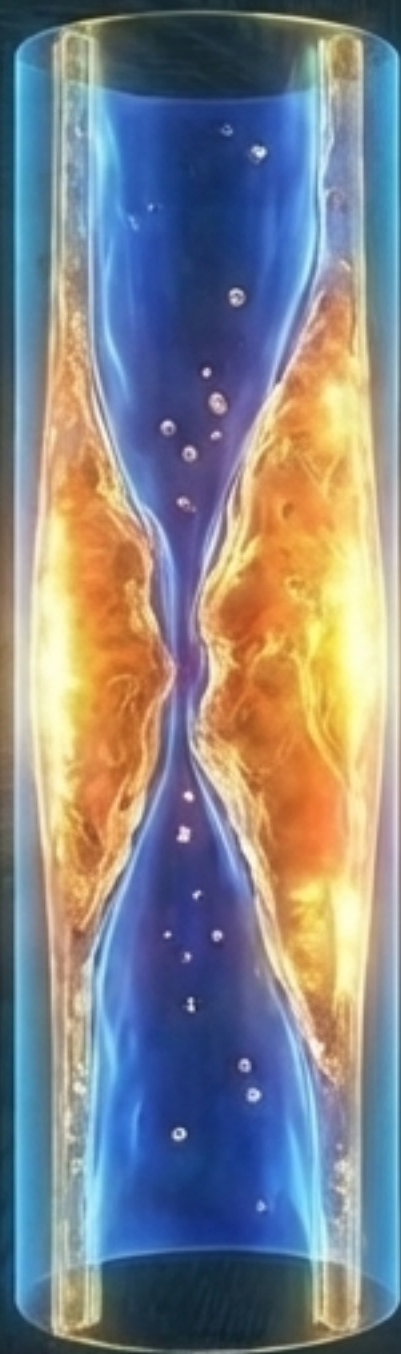
# Mechanism 4: **Luminal Dilation and Absolute Space**

Identical relative stenosis yields vastly different functional outcomes

Sedentary Artery

Athlete Artery

Narrow baseline resting diameter. A 50% stenosis leaves



**Favorable structural remodeling** massively dilates resting diameter.

A 50% stenosis leaves an absolute luminal area larger than the entirely healthy sedentary artery.

# Mechanism 5: **Supranormal Flow Reserve and Collateral Redundancy**

The biological failsafe against acute occlusion

**Coronary Flow Reserve (CFR):** Athletes structurally enhance their capacity to increase blood flow exponentially above resting levels.



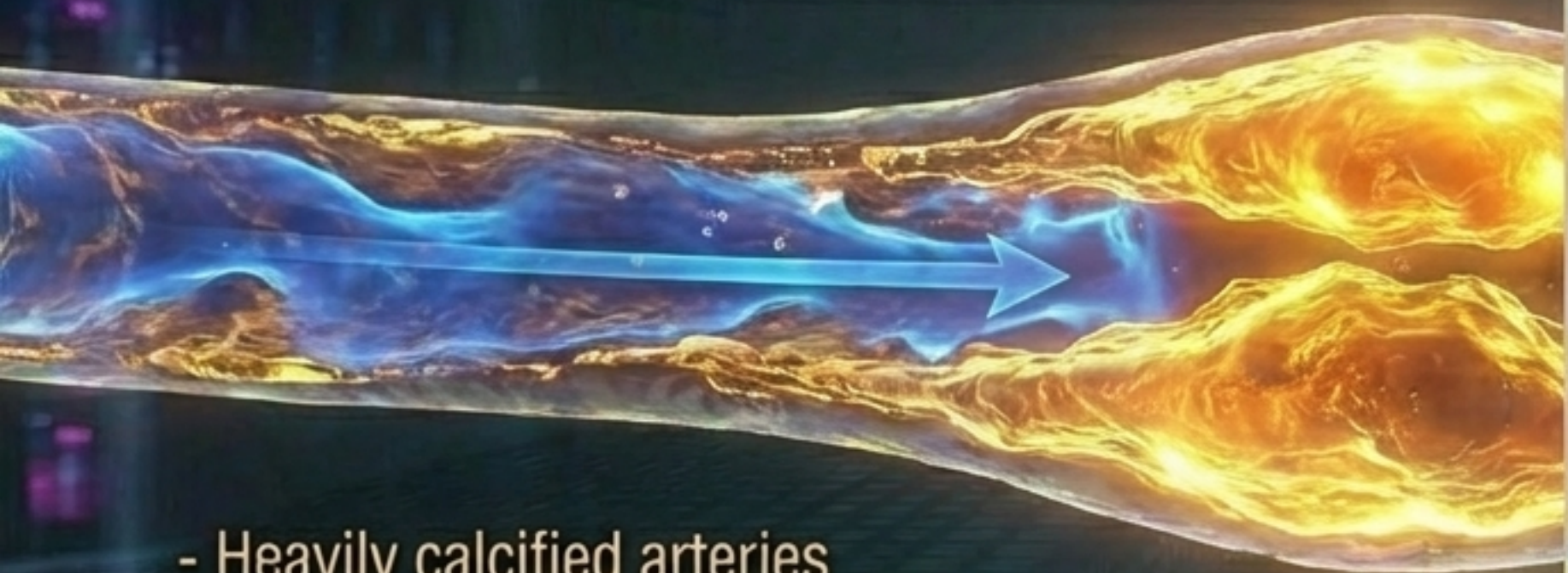
**Collateral Circulation:** The development of vast, redundant microvessel networks.

**The Failsafe:** In the event of acute plaque rupture, pre-existing collaterals immediately bypass the epicardial blockage, providing instant perfusion and minimizing infarct size.

# Synthesis: The Structural Uncoupling of Anatomical Risk

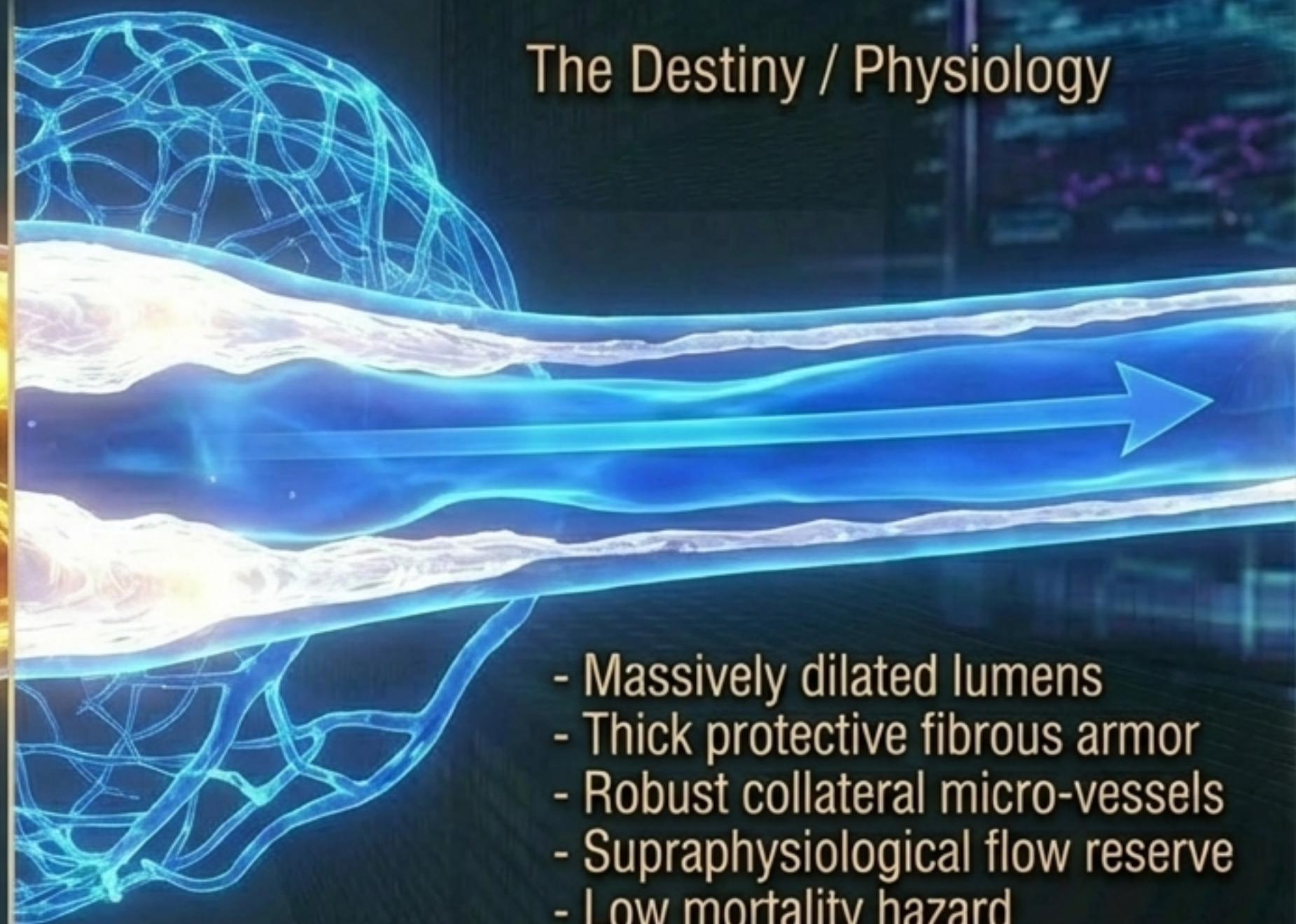
Athlete calcification is an extreme biological reinforcement process, uncoupling anatomy from destiny.

## The Disease / Anatomy



- Heavily calcified arteries
- High absolute plaque volume
- Proximal anatomical lesions
- Elevated CAC scores

## The Destiny / Physiology

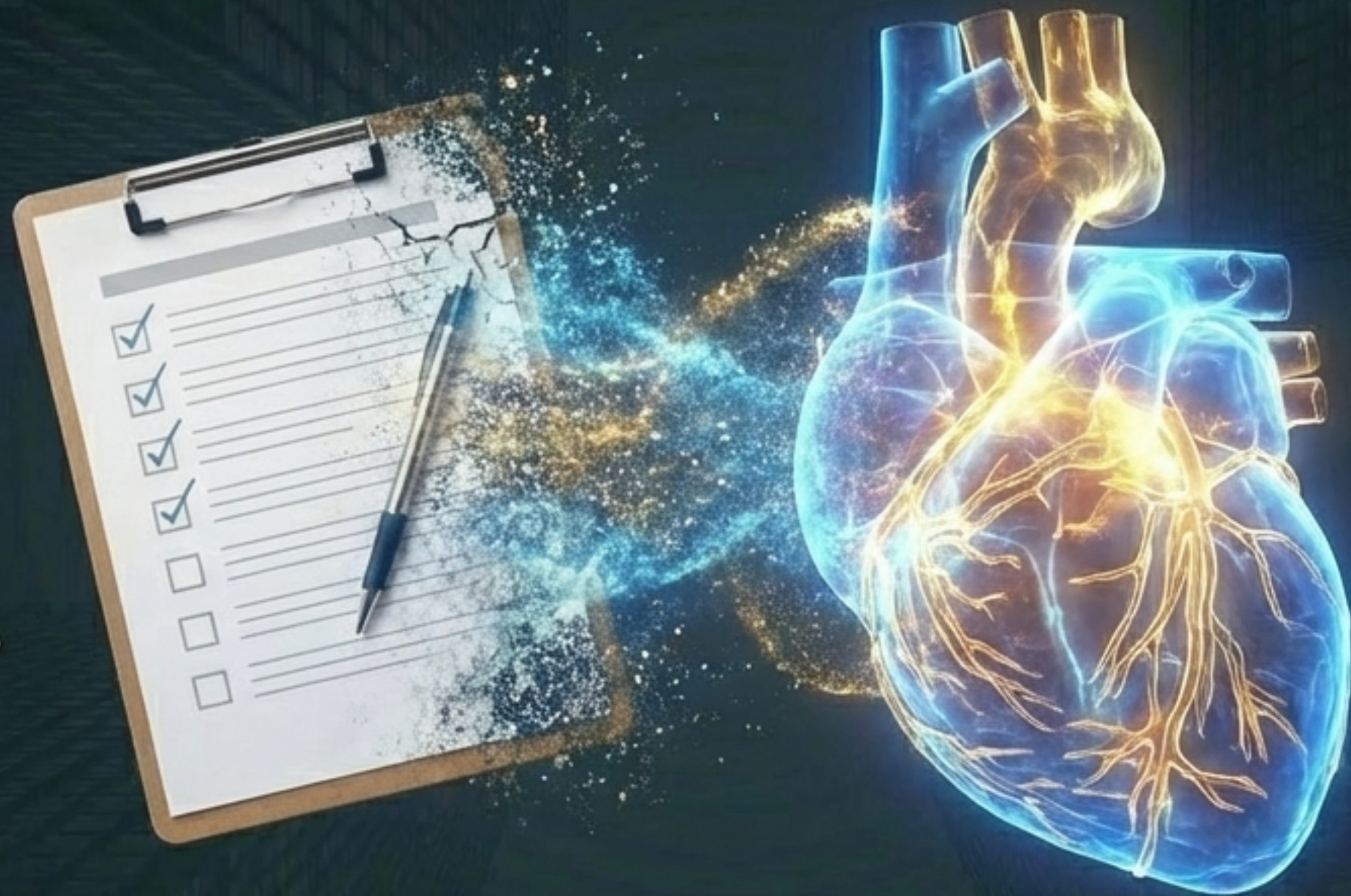


- Massively dilated lumens
- Thick protective fibrous armor
- Robust collateral micro-vessels
- Supraphysiological flow reserve
- Low mortality hazard

# Conventional risk calculators inherently fail the Masters Athlete

## The Input

Traditional algorithms (FRS / SCORE) rely heavily on chronological age, standard lipid profiles, smoking status, and resting blood pressure.



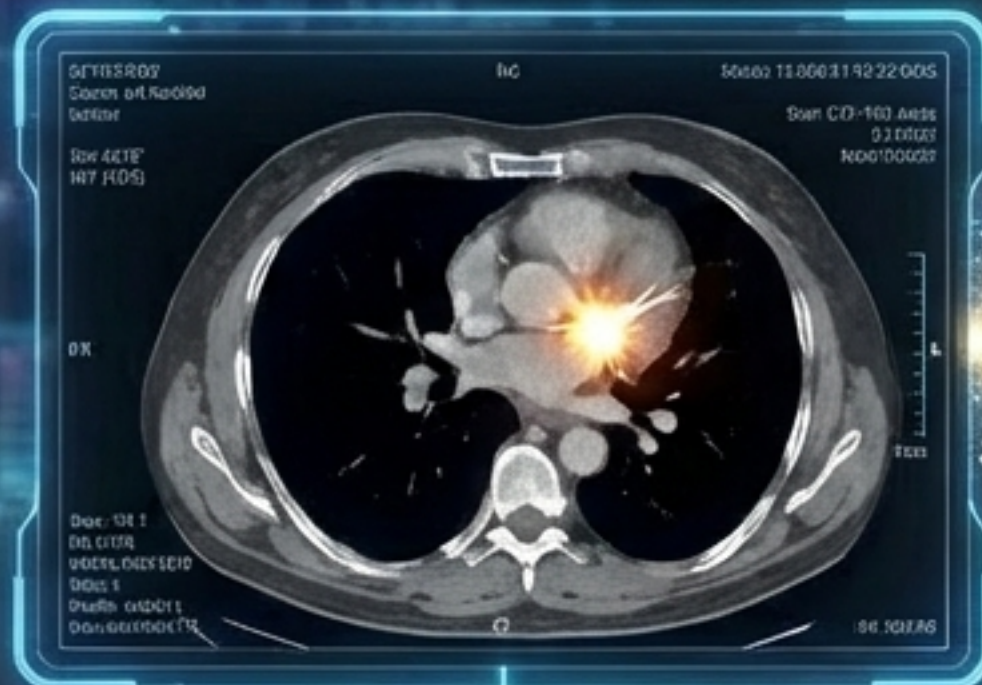
## The Blindspot

Masters athletes uniformly present with ideal metabolic parameters, automatically placing them in the lowest possible risk strata.

**The Clinical Danger:** Relying solely on basic lipid panels and blood pressure to clear an aging athlete for extreme competition severely underestimates the risk of exercise-induced calcification and demand ischemia.

# The Advanced Screening Architecture: A Multimodal Approach

## Non-Contrast CAC Scan



Used for primary risk reclassification.  
Shifts athletes out of assumed 'low risk' categories.  
Limitation: Cannot detect non-calcified lipid plaques.

## CCTA (CT Angiography)



Indicated for symptomatic athletes.  
Visualizes complete plaque morphology, soft non-calcified volume, and precise arterial narrowing.

## CPET (Cardiopulmonary Exercise Testing)



Correlates anatomical findings with functional outcomes.  
Detects silent demand ischemia or arrhythmic triggers during peak physiological stress.

# 2025 AHA/ACC Guidelines: Shared Decision-Making replaces paternalism

## Permissive Continuation



Increased physical activity does not exacerbate mortality in the presence of CAC. If ischemia and arrhythmias are excluded via stress testing, continued athletic participation is strongly supported.

## Shared Decision-Making (SDM)



Clinicians must openly balance statistical risk against the athlete's personal values, psychological well-being, and the massive systemic benefits of continued extreme exercise.

## Emergency Action Plans



Sudden cardiac arrest risk remains. Guidelines mandate the universal deployment of AEDs and high-quality CPR training in all athletic and endurance environments.

# The Clinical Mandate: Secondary Prevention in the Athlete

Extreme fitness **does not grant immunity** from secondary prevention.

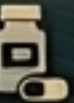

## The Reality:

The global cardiovascular benefits of exercise dominate and endure, even in the unmistakable presence of severe structural coronary disease markers.

## The Mandate:

Significant Coronary Artery Calcification, even in elite, asymptomatic masters athletes, warrants aggressive pharmacological management.

## Clinical Action Items:

- Immediate initiation of lipid-lowering therapy (statins). 
- Rigorous, uncompromising blood pressure control. 
- Deployment of advanced predictive models (AstroCHARM, hs-CRP) to personalize and escalate secondary prevention.

