STATE-OF-THE-ART REVIEW

JACC Cardiovascular Imaging

Vulnerable or High-Risk Plaque

A *JACC: Cardiovascular Imaging* Position Statement

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Disclosure

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- No industry relationship

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Background

1. Widespread use of lipid-lowering therapies and other preventive measures → changes in plaque phenotype (rupture↓ erosion↑) and epidemiology (STEMI↓ NSTE ACS↑)

2. Definitions of VP

3. Controversy over plaque characteristics vs. plaque burden

HRP: A Position Statement

- History
- Definition
- Pathology: rupture, erosion, eruptive calcified nodule
- Plaque burden
- Clinical relevance
- Silent plaque disruption
- Location of HRP
- Diagnosis
- Treatment

Definition of "Vulnerable Plaque" in clinical trials

A plaque that is prone to rapid progression leading to progressive angina requiring revascularization, AMI, or cardiac death.

Definition of “High-risk Plaque”

A plaque that is prone to disruption (rupture, erosion, eruptive calcified nodule) leading to acute occlusive thrombosis resulting in cardiac death or MI.

- plaque characteristics, plaque burden (anatomy), inflammation (biology), thrombogenicity, flow dynamics (physiology), myocardium at risk

Minami Y, Jang IK. Braunwald Heart Disease Companion. In press

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Rupture-prone plaque

- **TCFA**: FCT < 65 μm + lipid arc > 90º
- Compared to ruptured plaque, TCFA has a smaller necrotic core, thicker fibrous cap, fewer macrophages, less plaque burden
- → FCT determines rupture, while plaque burden is a key factor for occlusive thrombosis.

Erosion-prone plaque

- No known precursor

Eruption-prone calcified plaque

- No known precursor

HRP: A Position Statement

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Plaque burden

- PROSPECT
  - Most powerful predictor for MACE
    - PB < 40%: 0%
    - PB < 60%: < 0.5%
    - PB ≥ 70%: 9.5%
- PROSPECT II
  - PB < 55%: MACE 0%
  - PB ≥ 70% + lipid-rich: high-risk for MACE
- VIVA
  - PB: one of the strongest predictors for MACE

Relative Risk of MI

- Presence of atheroma: 2.95
- Presence of HRP: 3.33
- Non-extensive plaque: 4.22
- Obstructive non-extensive plaque: 8.28
- Obstructive extensive plaque: 12.48

Fuchs A. Ann Intern Med 2023

Plaque characteristics vs. Plaque burden

The greater the atherosclerotic disease burden, the larger the number of high-risk plaques, and the higher the probability that one of them will destabilize and eventually cause a clinical manifestation.

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The “Vulnerable Plaque” Facts

- Atherosclerosis is a pan-vascular process*.
- Plaque phenotype changes over time.
- Three quarters of plaques regress with medical therapy.
- Plaque erosion is responsible for 30-40% of ACS.
- Subclinical plaque disruption and healing contribute to plaque progression*.

Pan-vascular Inflammation

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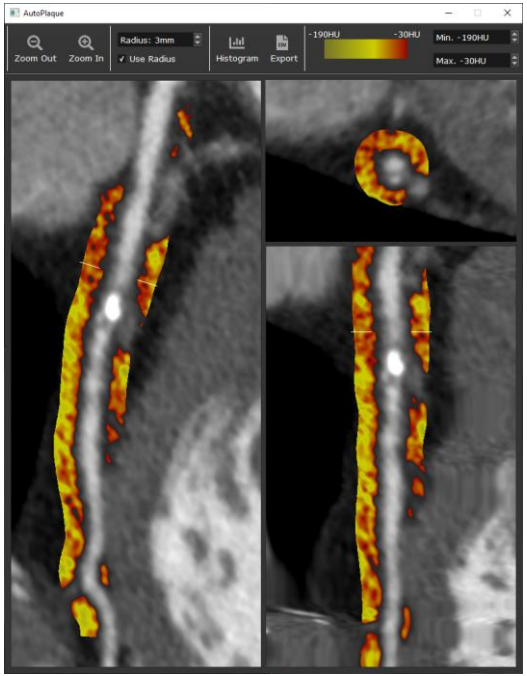
CCS

ACS



Araki M, Jang IK. Circ Img 2022

Healed (Layered) Plaque

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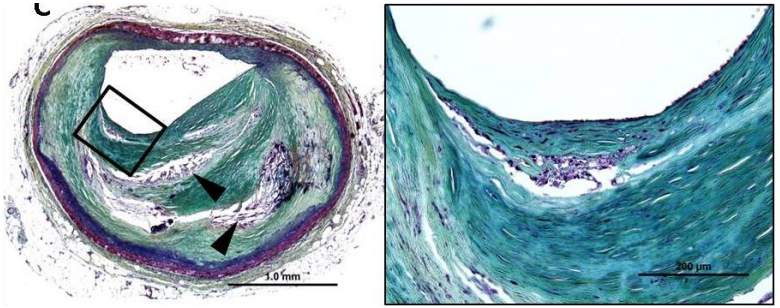

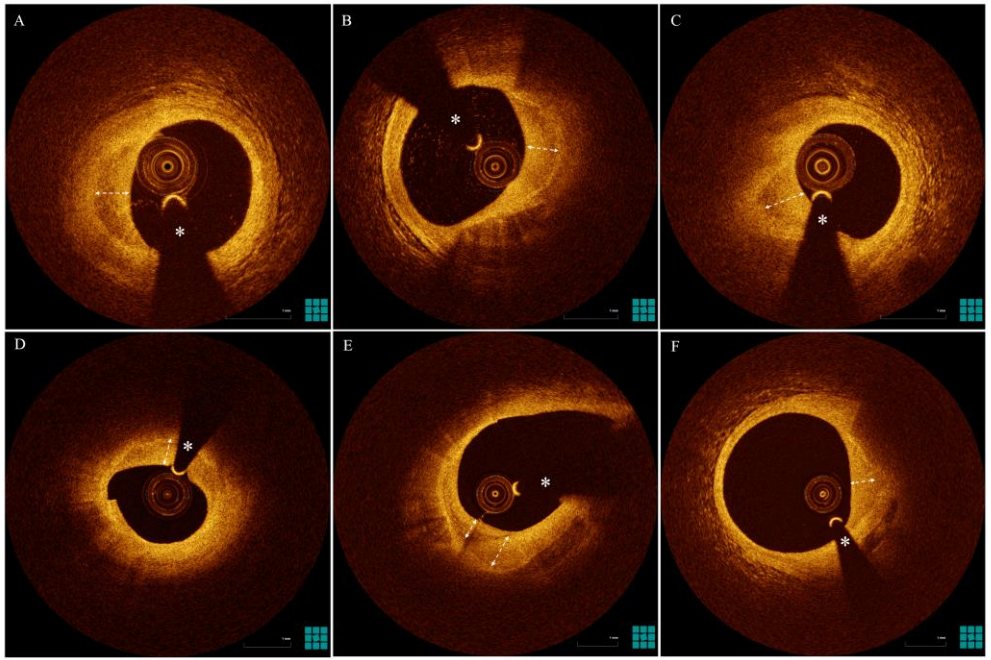

Evidence of previous plaque disruption was present in up to 73% in autopsy cases

Fracassi F. JACC 2019
Vergallo R. JAMA Card 2019
Russo M. ATVB 2020

Prevalence of Layered Plaque

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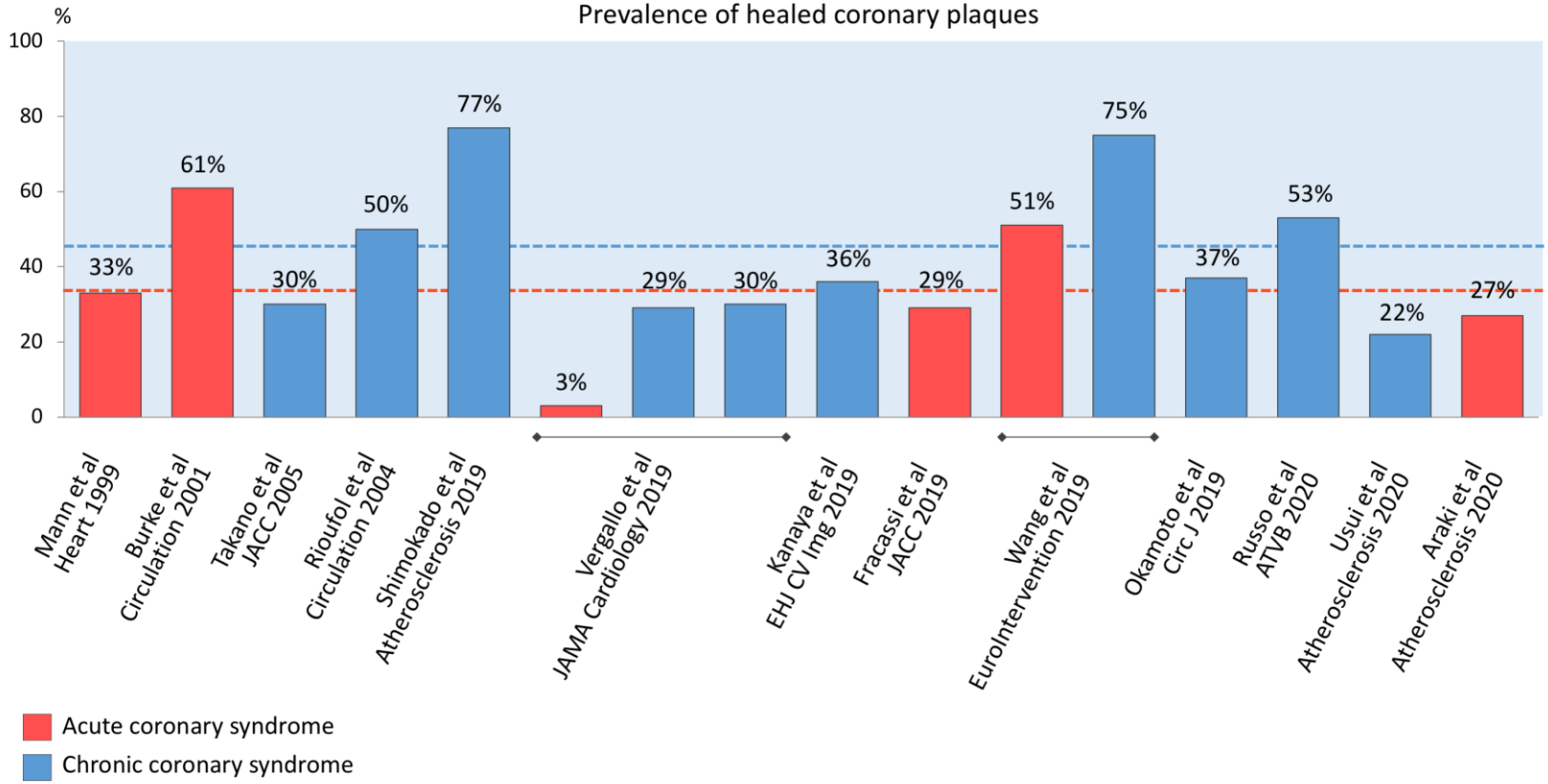

Conclusion

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- Atherosclerosis is a pan-vascular process with a local manifestation.

  - Araki M, … Jang IK. Nature Reviews Card. 2022

- Detection of VP helps to risk stratify patients.

  - Gallone G, d'Ascenzo F. JACC img 2023

- Plaque burden is a strong predictor for future revascularization.

  - Stone G. NEJM 2011
  - Park SJ. The Lancet 2024

- 75% of plaques can be stabilized by medical therapy.

  - Fujimoto D, Fuster V, Jang IK. Nature CV Res. In press.