
بسم الله الرحمن الرحيم

Noninvasive detection of vulnerable coronary plaque

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Outline

- Introduction.
- What is vulnerable (V) plaque.
- Why is V plaque detection important.
- Non invasive imaging of V plaque (CT- CMR- PET).
- Conclusion.
- Recommendation.

Introduction

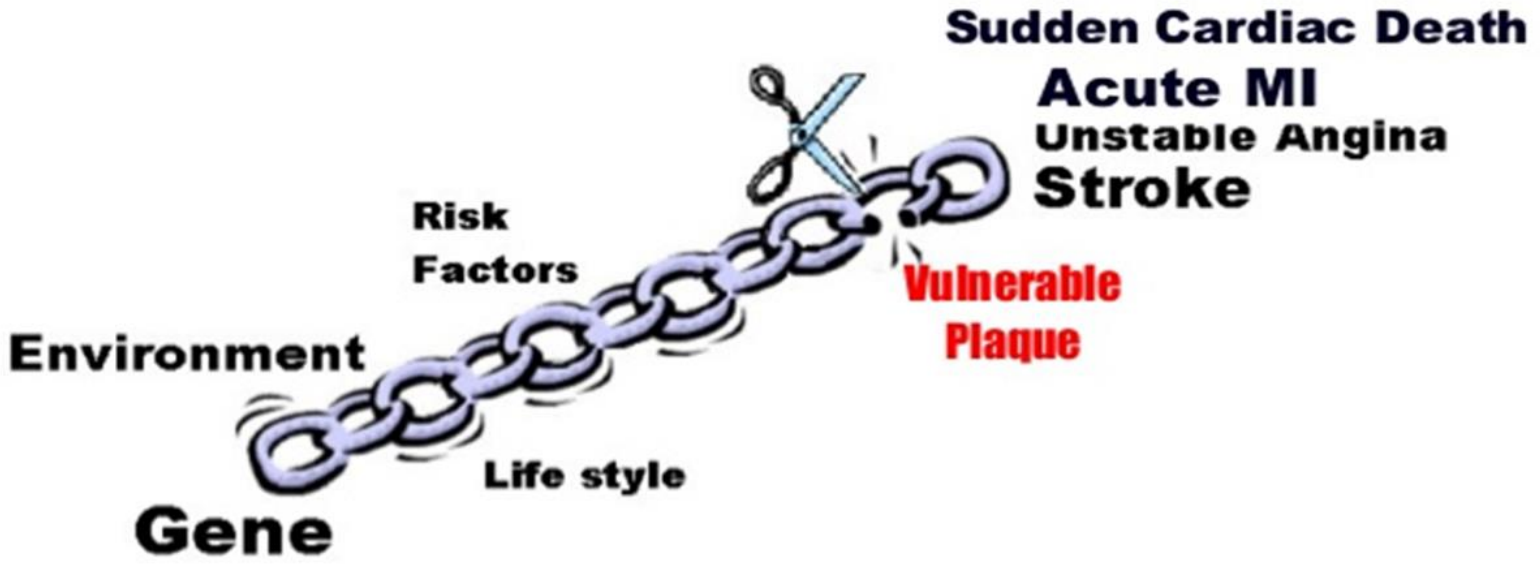
- The atherosclerosis is a highly complex multi-faceted disease process in which risk prediction is challenging.
- Combined assessments of plaque burden, plaque characteristic and disease activity are likely to be required to accurately identify patients at imminent risk of myocardial infarction and stroke.
- Technological advances in cardiovascular imaging in parallel with significant development in biomedical science has changed the way we assess coronary atherosclerosis.(Marc, et al., 2017) .

What is Vulnerable Plaque ?

High-risk plaque and dangerous form of atherosclerotic plaque that can rupture or induce thrombosis and lead to critical disruption of blood flow.

Vulnerable plaque = Future Culprit Plaque.

Breaking the Chain of Atherosclerosis



Everybody has atherosclerosis, the question is who has vulnerable plaque

PATHOPHYSIOLOGY

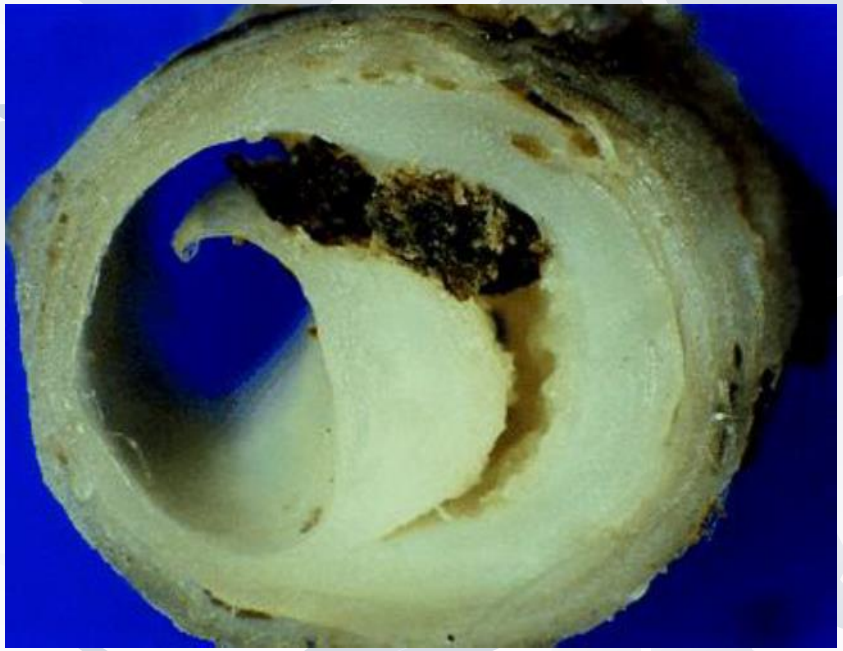
- In the early stage of atherogenesis, hypercholesterolemia accounts for the vascular endothelial dysfunction (Profumo, et al., 2016).
- The increased endothelial permeability allows lipids to penetrate across the arterial wall, especially oxidized low-density lipoprotein (ox.LDL).
- This in turn promotes recruitment of monocytes to the vessel wall where monocytes roll along the activated endothelium and continuously absorb ox.LDL through surface receptors, finally forming foam cells (Phinikaridou, etal., 2013) .

PATHOPHYSIOLOGY

- Its induce migration of macrophages to the lesion , Macrophages in subcutaneous space will secrete various kinds of inflammatory cytokines and proteolytic enzyme.
- That stimulate proliferation and migration of smooth muscle cells, degrade collagen and elastin, resulting in the thinning of the cap of the growing plaque and making the plaque susceptible to rupture (Amirbekian, etal.,2007) .

PATHOPHYSIOLOGY

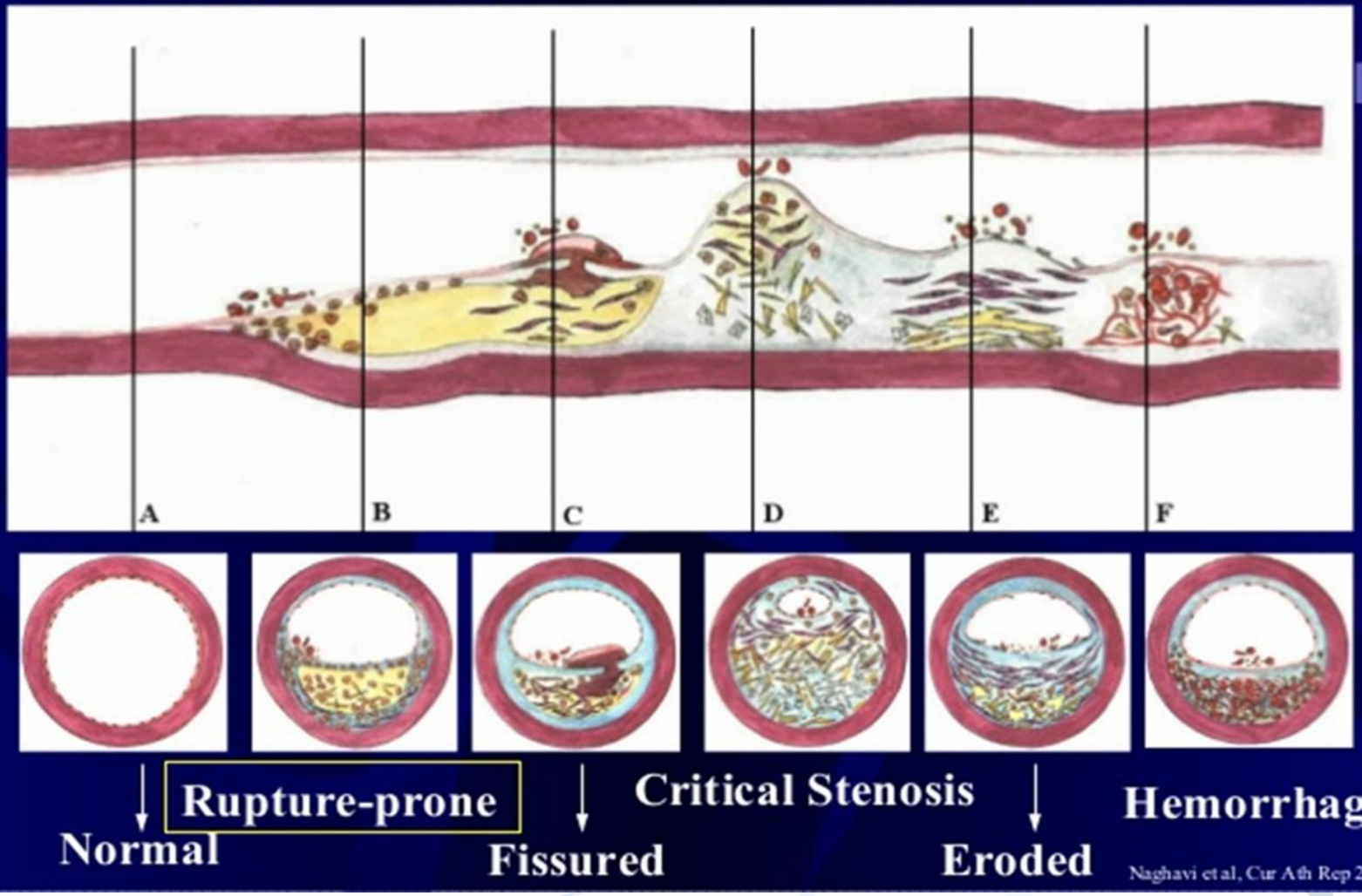
- **The release of MMPs and the apoptosis of SMCs, the fibroatheromas transform into vulnerable plaques** (Mojtahedi, etal.,2015).



Plaque rupture like bridge collapse results from the chance interplay of intrinsic weakness and external force.(Davies MJ Circulation Heart 2000; 83:361-6)

Different Types of Vulnerable Plaques

Major Underlying Cause of Acute Coronary Events

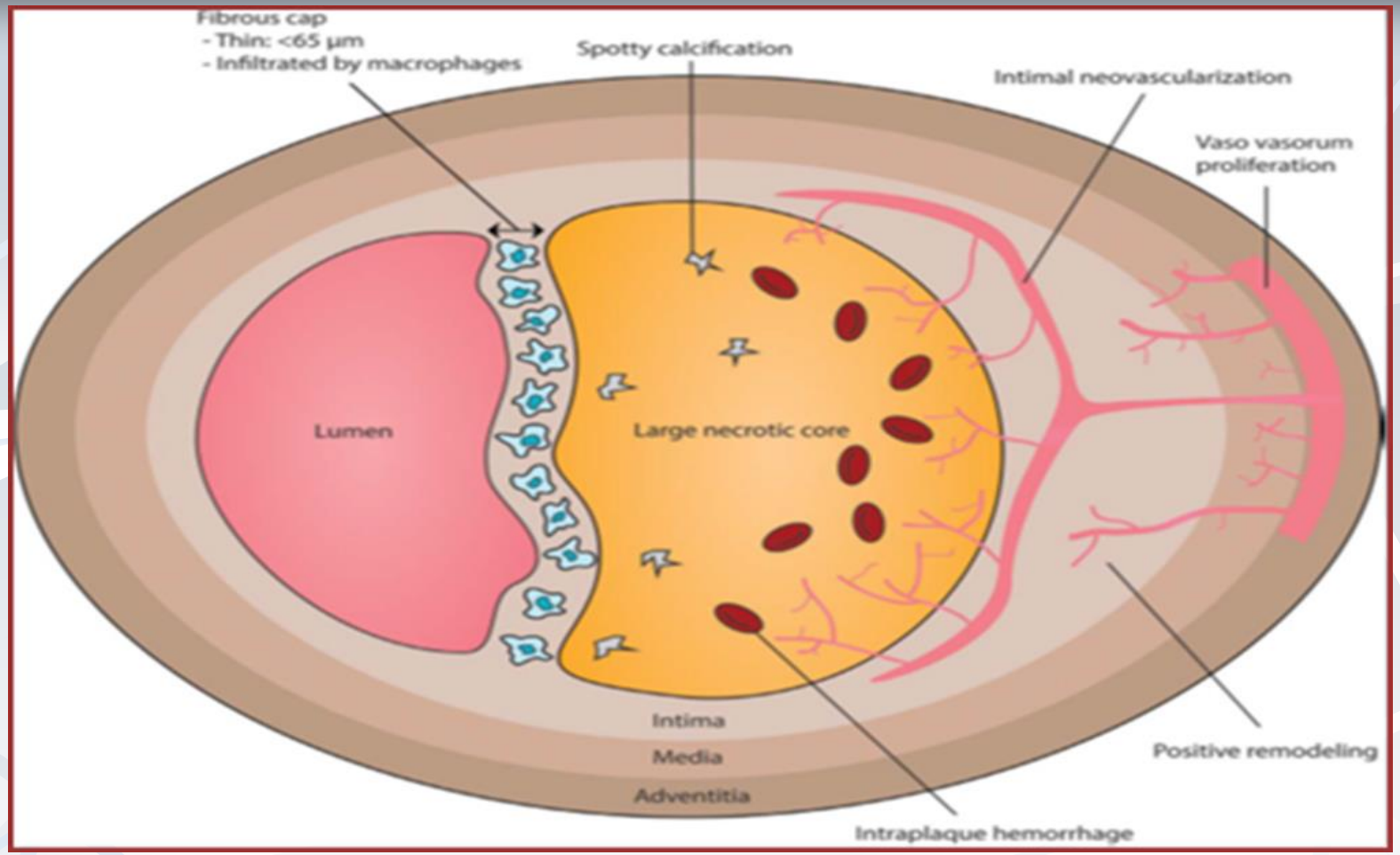


DIAGNOSTIC CRITERIA FOR .V PLAQUE

- **Major criteria :**
- Active inflammation (monocytes/macrophages and sometimes T-cell infiltration).
- Thin cap with large lipid core.
- Endothelial denudation with superficial plaque aggregation.
- Fissured plaque.
- Luminal stenosis > 90%.

DIAGNOSTIC CRITERIA FOR .V PLAQUE

- **Minor criteria:**
- Superficial calcified nodule.
- Glistening yellow.
- Intra plaque hemorrhage.
- Endothelial dysfunction.
- Outward (positive) remodeling.



Schematic representation of a suspected vulnerable plaque. A large necrotic core is separated from the lumen by a thin fibrous cap (<65 µm), infiltrated by macrophages. The proliferation of the vaso vasorum leads to intimal neovascularization. These immature neovessels tend to leak red blood cells and cause intraplaque bleeding. There is positive (outward) remodeling of the vessel and the necrotic core contains spotty calcification.(Stone et al.,2011)

IDEAL METHOD FOR SCREENING VULNERABLE PLAQUE/PATIENT

- Non-invasive.
- Inexpensive.
- Accurate.
- Widely reproducible.

WHY IS NONINVASIVE DETECTION OF.V PLAQUE IMPORTANT ?

- Detection of vulnerable plaque may help avert subsequent acute coronary syndrome by facilitating timely preventive and aggressive medical treatment.
- Noninvasive detection of vulnerable plaque may be clinically relevant especially in very high risk patients.
- Most invasive imaging modalities are novel and therefore require specific training and highly skilled staff, they are expensive to run and consequently are not feasible for routine clinical application.

NONINVASIVE IMAGING OF VULNERABLE PLAQUE

1) Computed Tomography Coronary Angiography (CTCA)
2) Cardiac magnetic resonance (CMR)
    A. High resolution MRI for coronary plaque imaging.
    B. Molecular MR for plaque imaging.
3) Positron emission tomography (PET) imaging

1) Computed Tomography Coronary Angiography (CTCA):

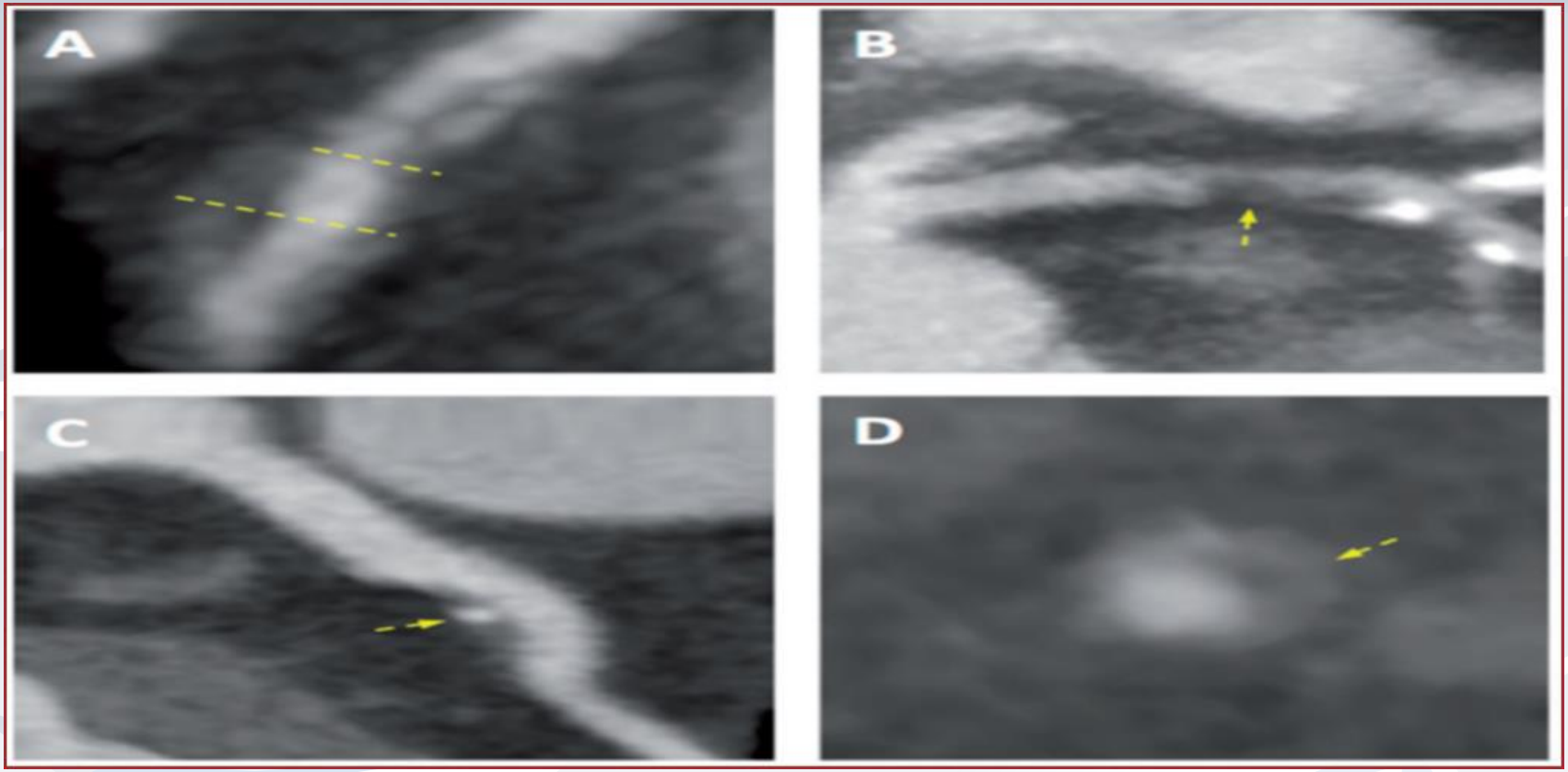
- Its a widely available noninvasive imaging tool with a relatively high spatial resolution that allows visualization of different components of the vulnerable plaque (Leipsic, et al., 2014) .
- The features have been described for non-invasive imaging with CTCA:

(1) Low Attenuation Plaque.

(2) Positive remodeling.

(3) Spotty calcification.

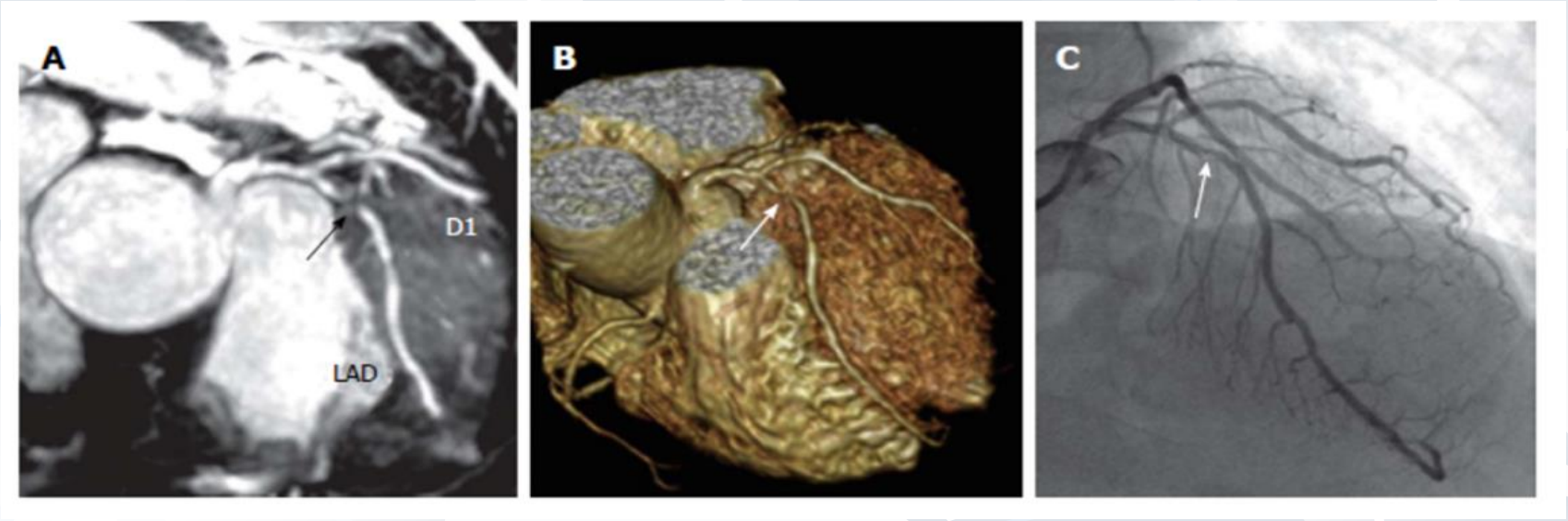
(4) Napkin ring' sign .



plaque features detected using computed tomography coronary angiography including :
(A) positive remodeling—defined as an outer vessel diameter (large yellow line) 10% greater than the mean diameter of the segments immediately proximal (small yellow line) and distal to the plaque; (B) low attenuation plaque—defined as a focal central area of plaque with an attenuation density of <30 Hounsfield Units (yellow arrow);
(C) spotty calcification— defined as focal calcification within the coronary artery wall <3 mm in maximum diameter (yellow arrow); and (D) the 'napkin ring' sign—defined as a central area of low attenuation plaque with a peripheral rim of high attenuation (yellow arrow).).(Motoyama, et al.,2015).

(2) Cardiac magnetic resonance (CMR)

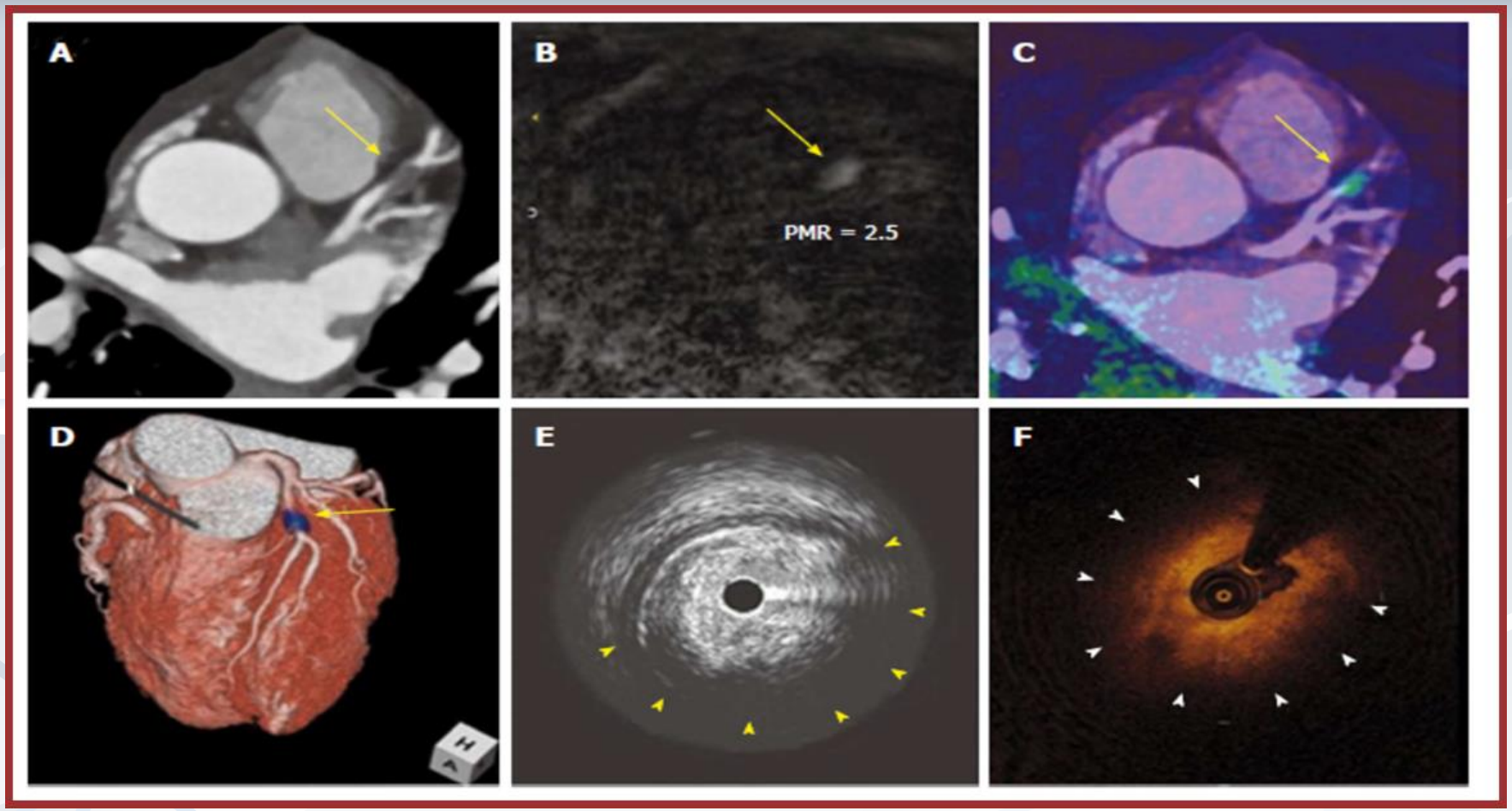
- **CMR not only allows a precise ventricular volume quantification and myocardial tissue characterization but also is able to detect the presence of significant (> 50%) coronary atherosclerosis with similar accuracy than CCT (Sharma, et al., 2014) .**



Correlation of unenhanced whole-heart coronary CMR angiography (A, maximum intensity projection image, and B, volume-rendered image) with invasive coronary angiography (C) in a in a 50-year-old male patient with chest pain on effort. Note the presence of significant stenosis in proximal LAD (arrows). Adapted with permission from (Nagata et al ., 2011

A. High Resolution MRI For Coronary Plaque Imaging:

- High resolution imaging using T1, T2 and proton density weighting allows for identification of calcium which is hypointense on all imaging sequences. (Noguchi, et al., 2014)
- The lipid which is T1- and PD-hyperintense and T2 hypointense, fibrous tissue which produces increased signal intensity on PD-weighted imaging, while it is isointense on T1 and isointense-to-hyperintense on T2-weighted imaging (Noguchi, et al., 2014) .
- T2-weighted sequences have demonstrated their ability to detect coronary vessel wall edema, in probable relation with plaque neovascularization, in initial studies.(Pedersen.,etal 2011)



T1 hyperintense coronary plaques in cardiac magnetic resonance. Noninvasive and invasive coronary imaging of a significant plaque in proximal LAD. CCTA (A) showed a noncalcified plaque in LAD causing significant stenosis. When noncontrast T1-weighted CMR imaging was performed (B) a hyperintense lesion was detected. Afterwards, CMR images were fused with CCTA (C and D) and this lesion was found to correspond with the previously described coronary stenosis. Interestingly, during the subsequent coronary angiography it showed a large lipid component in IVUS (E) as well as OCT (F). Adapted with permission from Asaumi et al., 2015.

B. MOLECULAR MR FOR PLAQUE IMAGING

- **Paramagnetic gadolinium chelates((MNP) are the most commonly used extracellular contrast agent for MRI, these molecular agents have successfully targeted several plaque components:**
  - **Inflammation (Macrophage infiltration).**
  - **Fissured/ Permeable cape.**
  - **Leaking angiogenesis and plaque hemorrhage.**

- **Magnetic iron oxide (MNP) is used as a molecular agent for detection of plaque characteristics.** (Kircher, et al., 2003)

(3) POSITRON EMISSION TOMOGRAPHY (PET) IMAGING

- Besides the detailed morphological characterization provided by CCT and CMR, quantification of inflammation is a key feature in vulnerable coronary plaque evaluation. The nuclear imaging techniques have been extensively used for this purpose in atherosclerosis. (Adamson, et al.,2016)
- PET is the preferred tool, due to its superior spatial resolution and is usually combined with computed tomography for a better anatomical definition. (Wykrzykowska, et al., 2009).

(3) POSITRON EMISSION TOMOGRAPHY (PET) IMAGING

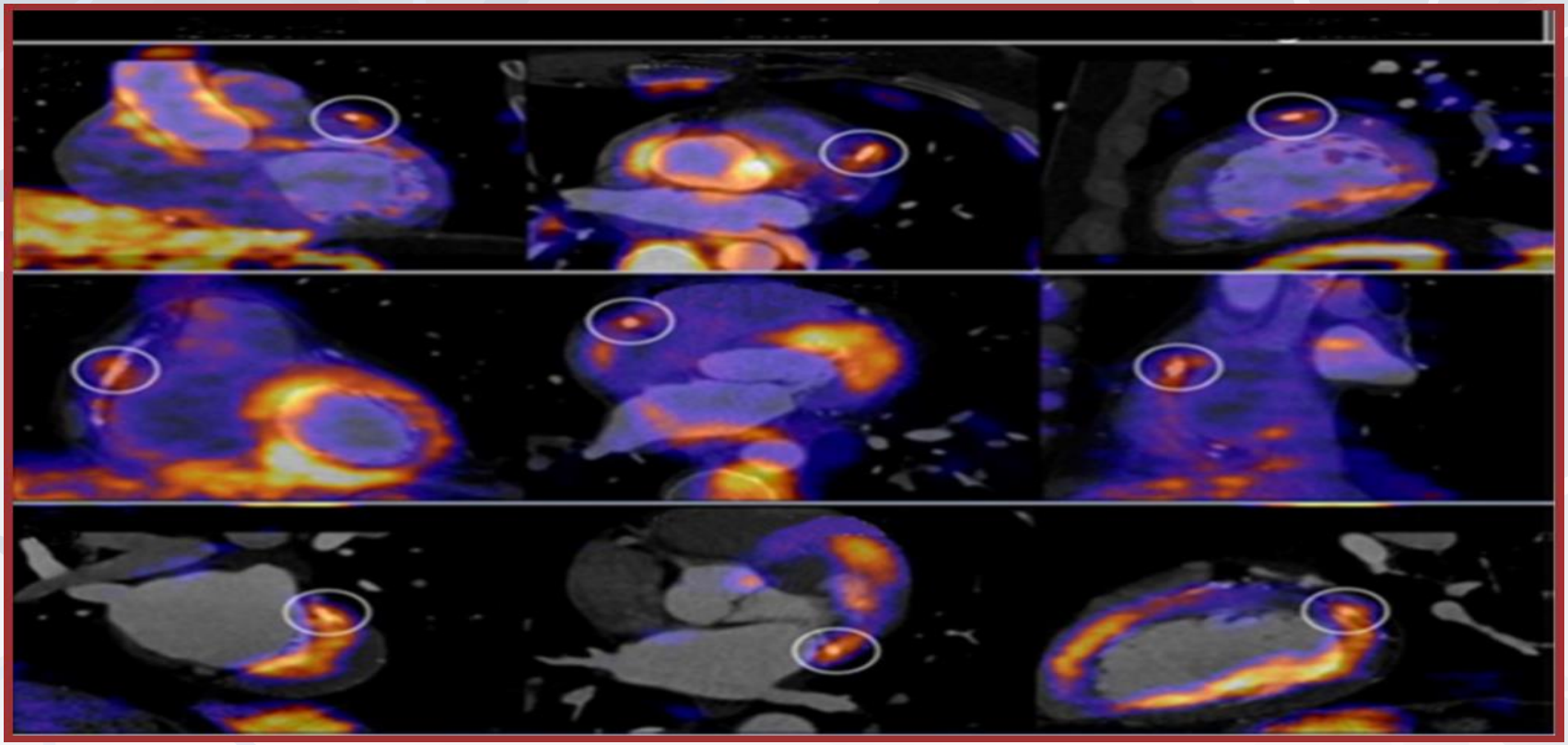
- Positron emission tomography (PET) with F-18-fluorodeoxyglucose (FDG) is a molecular imaging technique that is highly sensitive to metabolically active processes using glucose as a fuel.
- FDG could be considered a marker of inflammation since macrophages, key inflammatory cells in plaque, have higher glucose metabolism than both surrounding plaque cells and healthy artery walls.
- The different distributions of FDG uptake may reflect the different stages of atherosclerosis progression: a higher FDG uptake reveals concurrent extensive and advanced atherosclerosis. (Stolzmann, et al., 2011).

(3) POSITRON EMISSION TOMOGRAPHY (PET) IMAGING

- Several technical issues limit its application: FDG uptake in adjacent structures such as the myocardium, cardiac motion during PET acquisition, and partial volume effect due to small coronary, artifact coronary artery and the size of plaques.

- To override this limitation, free fatty myocardial metabolism was favored with a low-carbohydrate high fat preparation by using the new tracer 18F-sodium fluoride to detect coronary atherosclerosis without the limitation of myocardial metabolism artifact. (Rominger et al., 2010)

FDG positron emission tomography of the coronary arteries. PET CT



Fluorodeoxyglucose positron emission tomography of the coronary arteries. PET CT fusion imaging in three cases of patients with STEMI. An increased 18F-FDG uptake at stent site is shown in different culprit vessels, from A to C: LAD, RCA and LCX. Adapted with permission from Cheng et al., 2012

Diagnostic tests for noninvasive evaluation of coronary vulnerable plaque

	CCT	CMR	PET
Plaque characterization	Plaque morphology	Tissue characterization of plaque	Inflammation (FDG) Macrophage infiltration
Vulnerable features	Positive remodeling Low attenuation Spotty calcification Napkin-ring sign	Positive remodeling T1 hyperintensity Late gadolinium enhancement	(new tracers) Increased tracer uptake
Clinical relevance	Strong association with ACS Prediction of slow-flow after PCI Evaluation of response to statins.	Initial data of association of T1 hyperintense plaques with slow-flow, ACS and response to Statins.	Differentiation between ACS and stable Coronary disease.
Limitations	Radiation exposure Heavy calcification Overlap in attenuation ranges Inability to detect plaque erosion	Direct relation between spatial resolution and acquisition time Susceptibility to motion artifacts.	Low spatial and temporal resolution Myocardial background uptake Expensive and limited availability

Future Perspectives Hybrid Techniques

- Several imaging platforms are currently available for targeted vascular imaging to acquire information on both anatomy and pathophysiology in the same imaging session using hybrid technology, such as PET/CT or PET/MRI.

- PET imaging has relatively low spatial resolution, mandating the use of concurrent structural imaging (CT or MRI) to guide localization of the FDG signal, revealing whether the plaque is actually metabolically active or not. (Wu YW, et al., 2011)

CONCLUSION

- A number of different novel noninvasive imaging modalities have been investigated to define the specific characteristics of vulnerable plaque.
- To date, computed tomography, remains the most clinically applicable technique due to its broad availability and the strength of its evidence base.
- Finally, PET has emerged as a promising molecular imaging technique being able to detect coronary inflammation and even macrophage infiltration.
- At present, MRCA and PET remain largely investigational imaging modalities but landmark trials are now underway that will inform their future clinical role.

Recommendation

- Further research is required to increase the sensitivity and specificity of these modalities to more accurately predict adverse events in the context of high-risk plaque.

- This aspect is of special interest due to the large population that may be the target of a noninvasive imaging strategy for acute coronary events prevention, In this regard, cost-effectiveness should also be evaluated carefully in the future.

- Statin therapy has been shown to induce plaque stabilization and lead to a significant reduction in cardiovascular events.


Thank
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