# *What is the Definition of Moderate to Heavy Calcification? Based on Fluoroscopy or Intravascular Imaging*

**Gary S. Mintz, MD**

***Cardiovascular Research Foundation***

# Definition of Calcified Lesions – Angiography/Fluoroscopy

Patterns of Calcification in Coronary Artery Disease

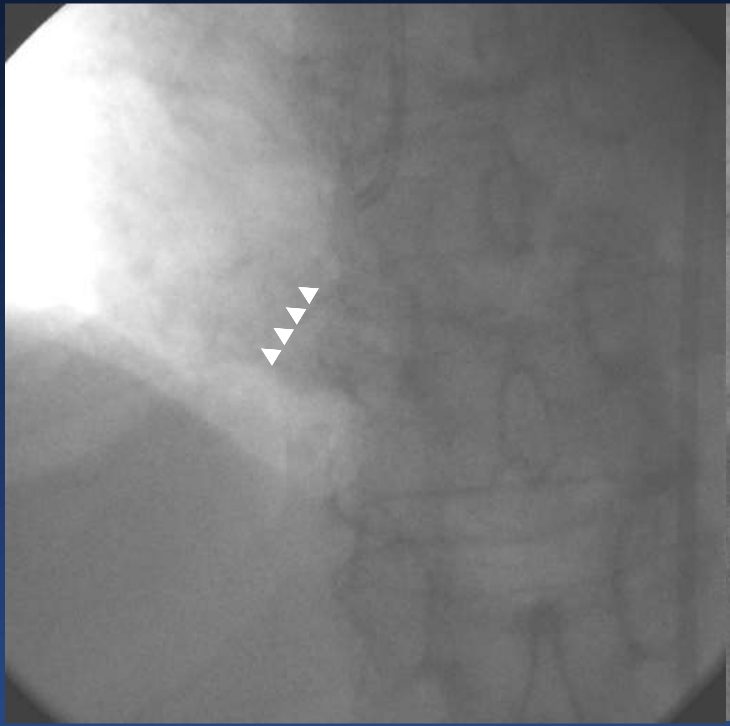
A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions

Gary S. Mintz, MD; Jeffrey J. Popma, MD; Augusto D. Pichard, MD; Kenneth M. Kent, MD, PhD; Lowell F. Satler, MD; Ya Chien Chuang, PhD; Christine J. Ditrano, BS; Martin B. Leon, MD

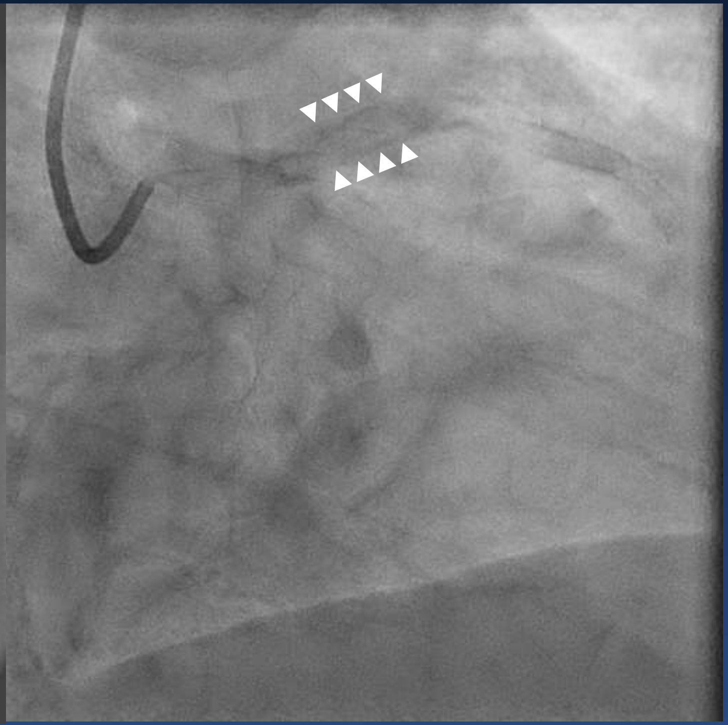
- Readily apparent densities noted within the vascular wall at the site of the stenosis
  - **Moderate:** *Densities seen prior to contrast injection, but only during cardiac motion*
  - **Severe:** *Densities seen prior to contrast injection, but w/o cardiac motion and usually involve both sides of the arterial wall*

*Mintz et al. Circulation 1995;91:1959-65.*

# Definition of Calcified Lesions – Angiography/Fluoroscopy



**Moderate:**
*Seen only during cardiac motion on one side of vessel*



**Severe:**
*Seen without cardiac motion on both sides of vessel*

# Meta-analysis of 13 studies and 66,361 pts assessing the association between angiographic arget lesion calcification and adverse outcomes in pts undergoing DES implantation

| Endpoint | # of studies | HR |
|---|---|---|
| All cause mortality | 4 | 1.41 (1.27-1.56) |
| Cardiac mortality | 5 | 1.97 (1.68-2.31) |
| Myocardial infarction | 6 | 1.33 (1.13-1.57) |
| MACE | 5 | 1.37 (1.19-1.58) |
| TLR | 8 | 1.47 (1.18-1.83) |
| Early TLR (<1 year) | 7 | 1.63 (1.43-1.85) |
| Stent thrombosis | 12 | 1.63 (1.36-1.96) |
| Early ST (<30 days) | 5 | 1.69 (1.16-2.45) |

*10/13 studies compared moderate/severe calcium vs no/mild calcium*

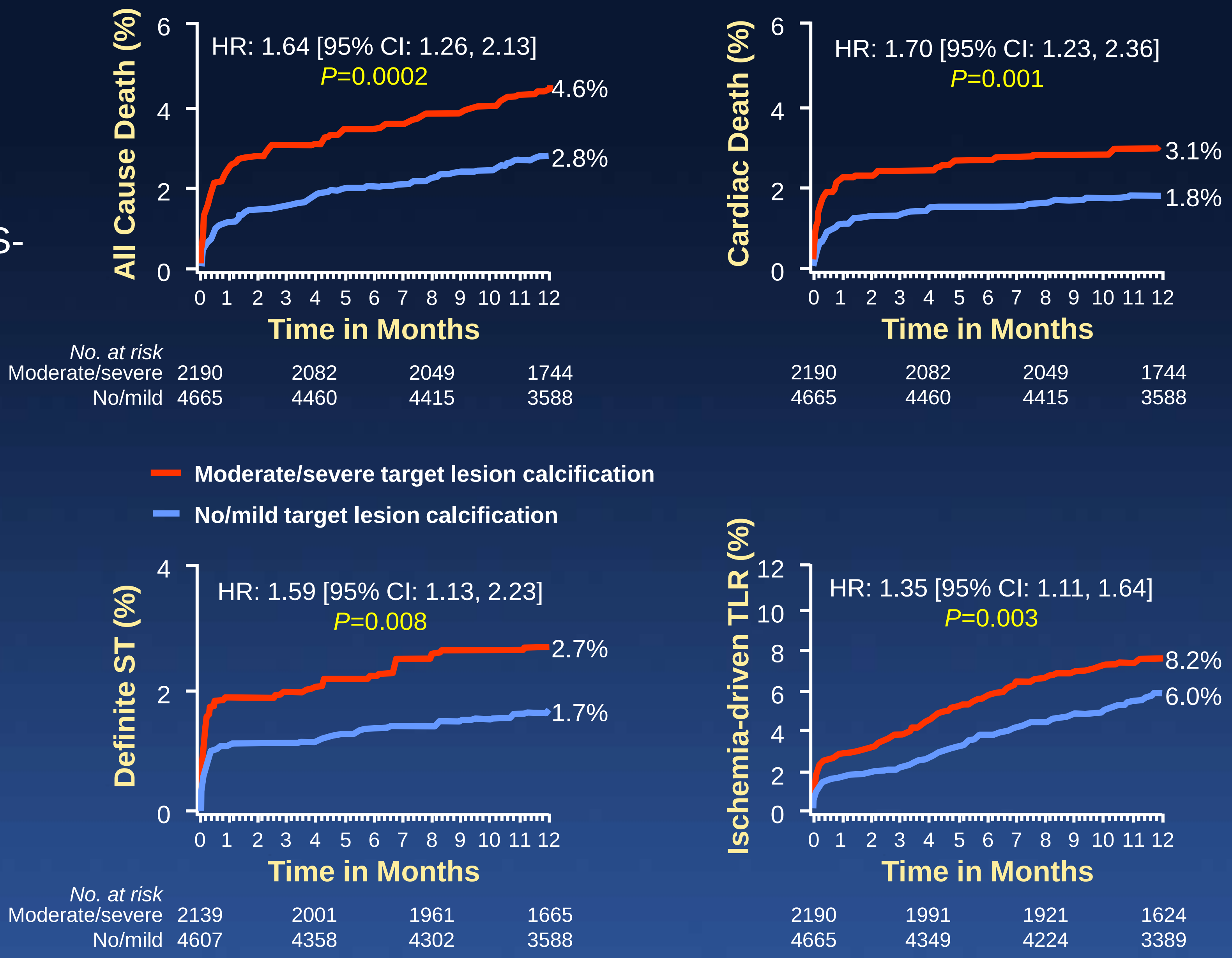


Huang et al. Herz 2015;40:1097-106

# Ischemic Outcomes After PCI of Calcified Vessels in ACS Pts

Pooled Analysis from the HORIZONS-AMI and ACUITY Trials

*The presence of moderate/severe target lesion calcification was an independent predictor of 1-year definite ST (hazard ratio [HR]: 1.62; 95% confidence interval [CI]: 1.14 to 2.30; p=0.007) and ischemic TLR (HR: 1.44; 95% CI: 1.17 to 1.78; p=0.0007)*

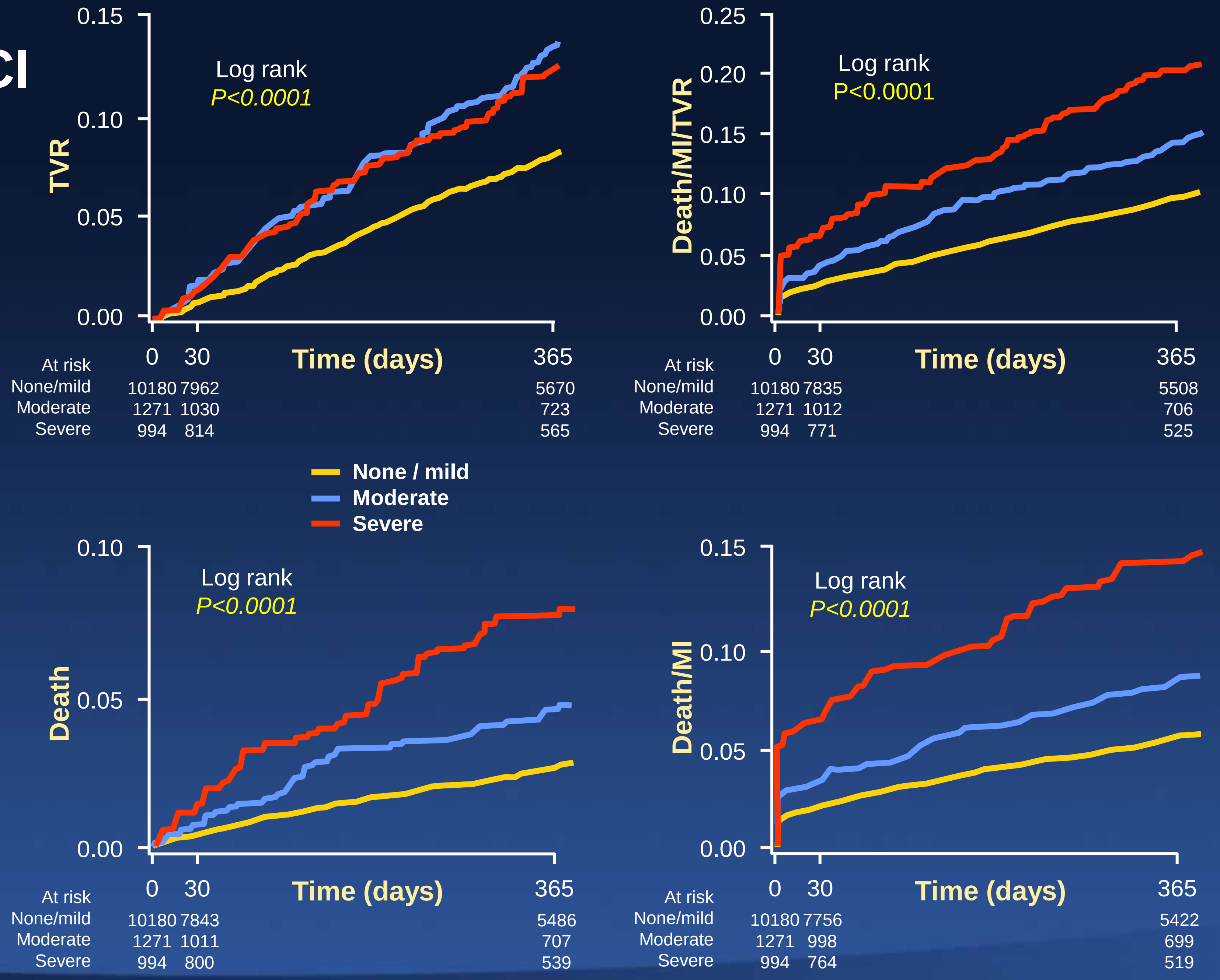



*Genereux et al. J Am Coll Cardiol 2014;63:1845-54*

# Adverse Events Post-PCI And Calcification

Findings from a large multiethnic registry

*The three strongest independent predictors of moderate to severe coronary calcification were lesion length, pt age, and LM location (c-statistic 0.73). After adjusting for age, race, BMI, CKD, hypertension, smoking, prior MI or CABG, PAD, anemia, and lesion length, location, and angiographic characteristics, moderate or severe calcification remained associated with MACE (HR 1.63 [1.42, 1.86], P<0.001) and mortality (HR 1.64 [1.26, 2.15], P<0.001).*

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*Copeland-Halperin et al. Cathet Cardiovasc Interv 2018;91:859-66*

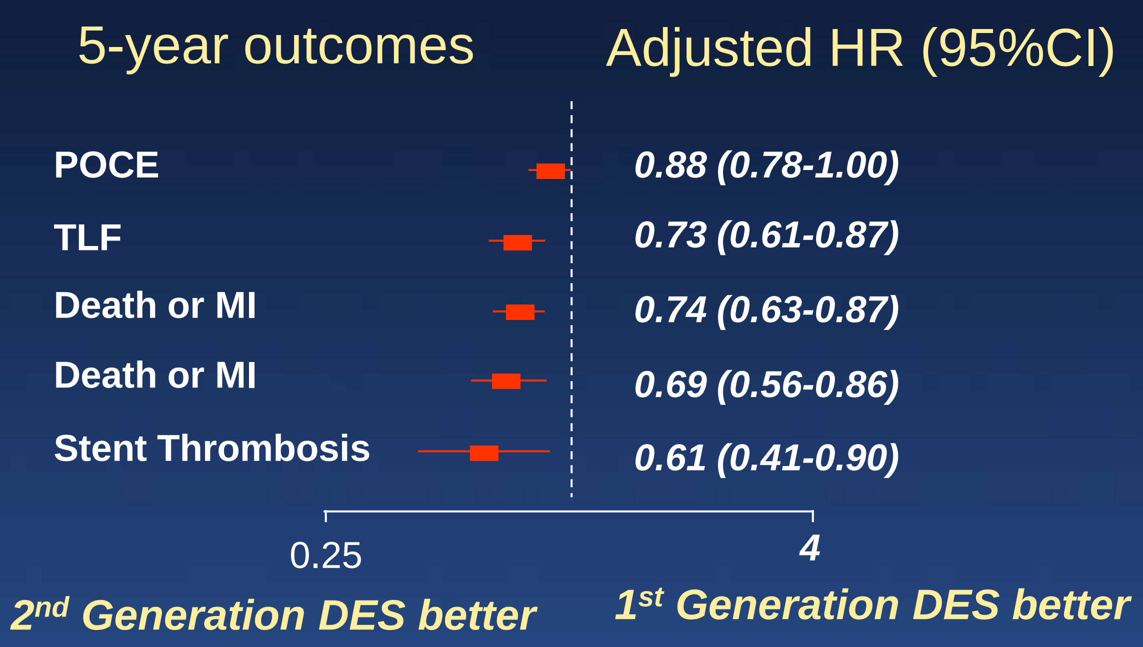
# 10-yr clinical outcomes: Pooled analysis of the ISAR-TEST 4 and 5 randomized trials

| | No calcium | Mild calcium | Moderate calcium | Severe calcium | P-value |
|---|---|---|---|---|---|
| # | 1212 | 2069 | 1276 | 396 | |
| All cause mortality | 25.3% | 32.1% | 41.7% | 46.5% | 0.004 |
| TLR | 17.4% | 16.5% | 19.8% | 28.7% | 0.001 |
| MI | 4.9% | 5.9% | 6.0% | 10.5% | 0.02 |
| Definite/probable ST | 1.3% | 1.4% | 1.8% | 3.6% | 0.6 |



*Rheude et al. EuroIntervention. 2022 ;18:1188-96*

# Moderate/Severe Angiographic Coronary Calcification and Long-Term Outcomes According to DES Generation




- Individual pt data were pooled from 18 RCT evaluating DES, categorized according to the presence of angiography core laboratory-confirmed moderate or severe coronary artery calcium.
- A total of 19,833 patients were included. Moderate or severe calcium was present in 1 or more target lesions in 6,211 patients (31.3%).
- Major endpoints were the patient-oriented composite endpoint (POCE; death, MI, or any revascularization) and the device-oriented composite endpoint of target lesion failure (cardiac death, target vessel MI, or ischemia-driven TLR).

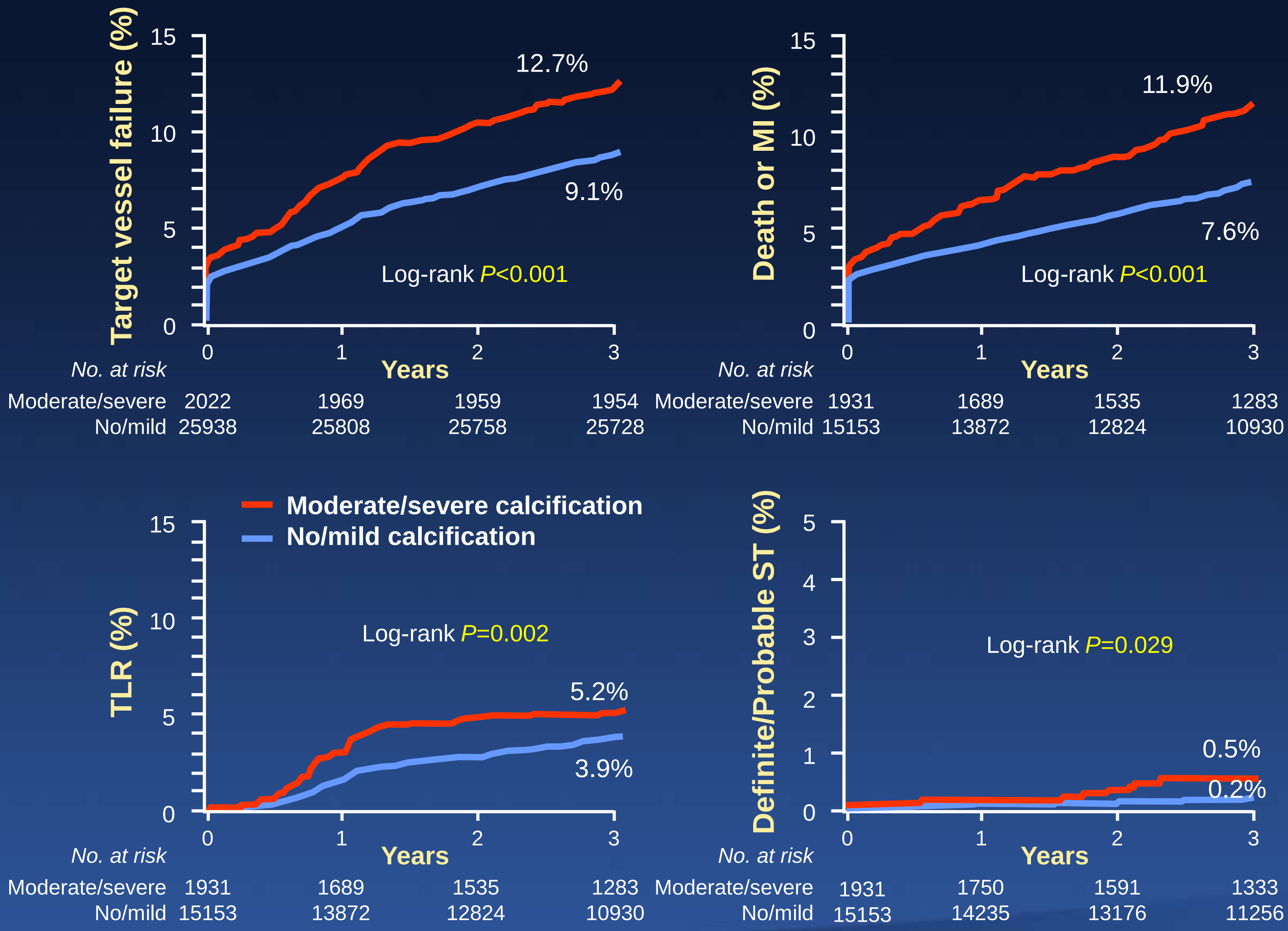


*Guedeney et al. JACC Cardiovasc Interv. 2020;22:1417-28.*

# IRIS-DES Registries (n=17,084 pts with 27,739 lesions)

The presence of moderate/severe coronary artery calcium was significantly associated with an adjusted risk of TVF at 3 yrs [hazard ratio, 1.37; 95% confidence interval (CI), 1.19-1.58; P < 0.001].

*For severe calcium, optimal lesion preparation was associated with a lower 3-year rate of TVF (22.3vs. 12.8%) in the late F-U period of 1–3yrs (HR, 0.28; 95% CI, 0.12–0.69; P=0.003), but not in the early F-U period <1yr (HR, 1.16; 95% CI, 0.37–3.71; P=0.80). However, post-dilation with a high-pressure noncompliant balloon had no effect on the outcome. There was no impact of technique on lesser amounts of calcium.*

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*Lee et al. Coron Artery Dis 2021;32:42-50*

# Randomized clinical trials using the fluoroscopic definition of moderate/severe calcium


High-Speed Rotational Atherectomy Before Paclitaxel-Eluting Stent Implantation in Complex Calcified Coronary Lesions

The Randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) Trial

Abdel-Wahab *et al.* JACC Cardiovasc Interv 2013;6:10-9


CORONARY INTERVENTIONS

Super high-pressure balloon versus scoring balloon to prepare severely calcified coronary lesions: the ISAR-CALC randomised trial

Rheude et al. EuroIntervention. 2021;17:481-488.


Circulation: Cardiovascular Interventions

ORIGINAL ARTICLE

High-Speed Rotational Atherectomy Versus Modified Balloons Prior to Drug-Eluting Stent Implantation in Severely Calcified Coronary Lesions

The Randomized PREPARE-CALC Trial

*Abdel-Wahab et al.* Circ Cardiovasc Interv. 2018;11:e007415


Cardiovascular Revascularization Medicine

Randomized Comparison of Strategies to PrepAre SeveRely CALCified Coronary Lesions 2: Design and Rationale of the ISAR-CALC 2 Trial

Scalamogna et al. Cardiovasc Revasc Med 2023;49:22-27

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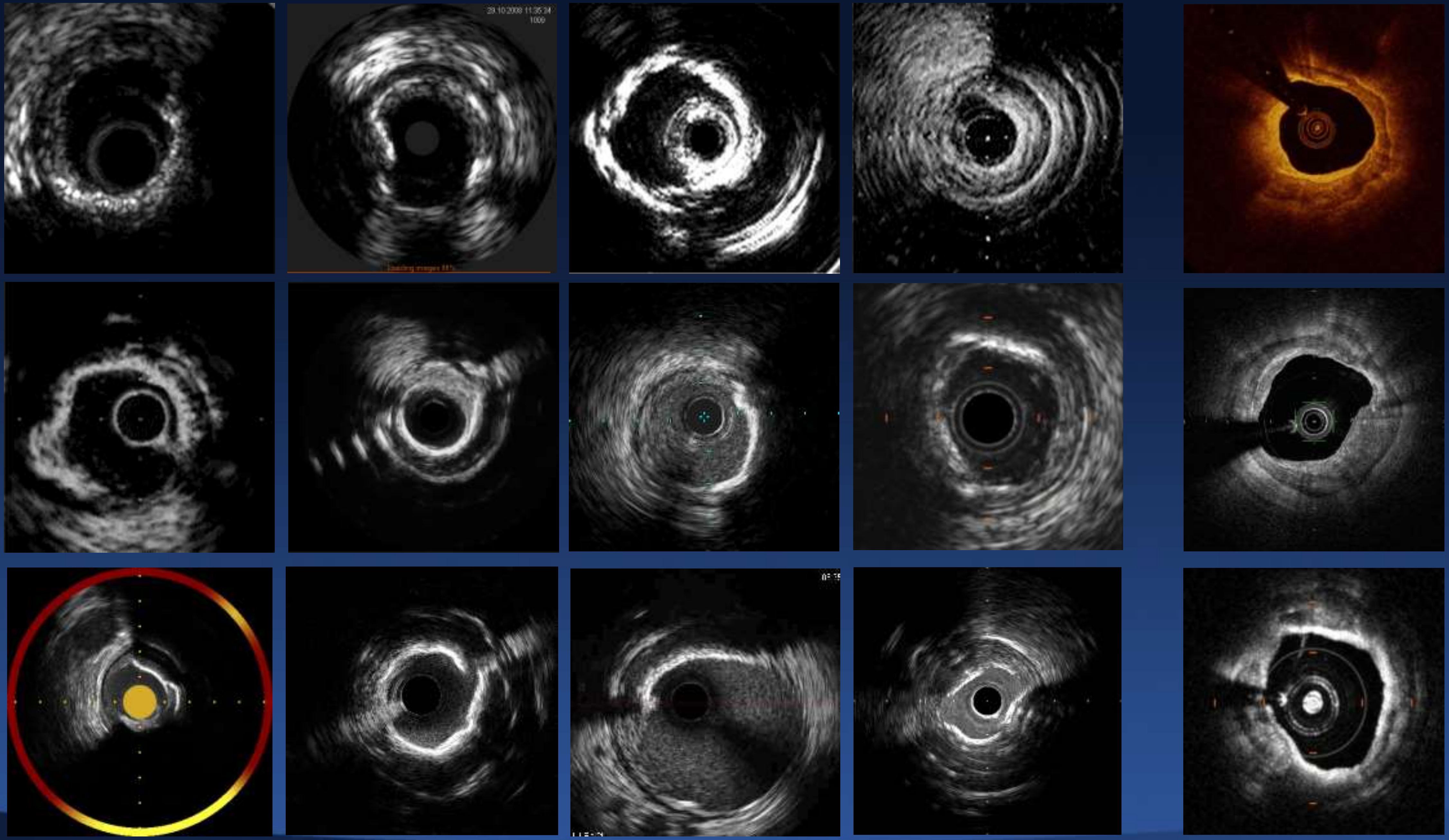

# Angiography is only moderately sensitive for detection of extensive lesion calcium (sensitivity 60% and 85% for 3- and 4-quadrant calcium, n=1155)

Patterns of Calcification in Coronary Artery Disease

A Statistical Analysis of Intravascular Ultrasound and Coronary Angiography in 1155 Lesions

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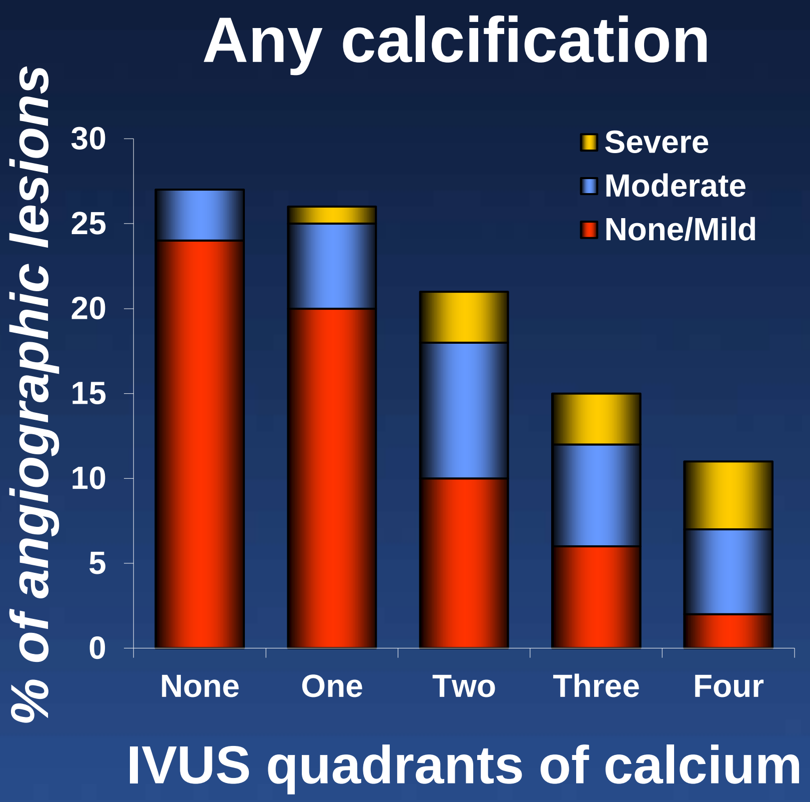


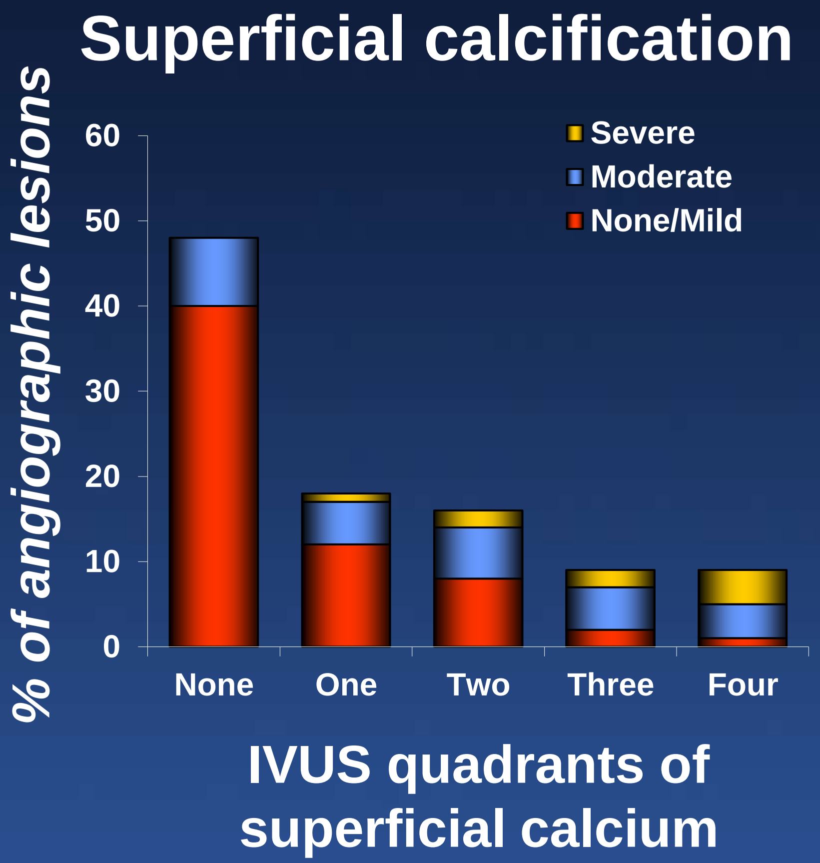


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*Mintz et al. Circulation 1995;91:1959-65.*

| | Angiographic Calcification | | |
|---|---|---|---|
| IVUS | None/Mild | Moderate | Severe |
| # | 715 | 306 | 134 |
| Target lesion $Ca^{++}$ | 61% | 90% | 98% |
| Arc of lesion $Ca^{++}$ (°) | 71±83 | 165±106 | 238±104 |
| Superficial lesion $Ca^{++}$ | 37% | 72% | 92% |
| Arc of Superficial lesion $Ca^{++}$ (°) | 44±74 | 124±110 | 215±119 |
| Arc of reference $Ca^{++}$ (°) | 25±63 | 61±93 | 87±98 |
| Total length of $Ca^{++}$ (mm) | 3.6±4.4 | 7.2±6.4 | 9.7±6.4 |

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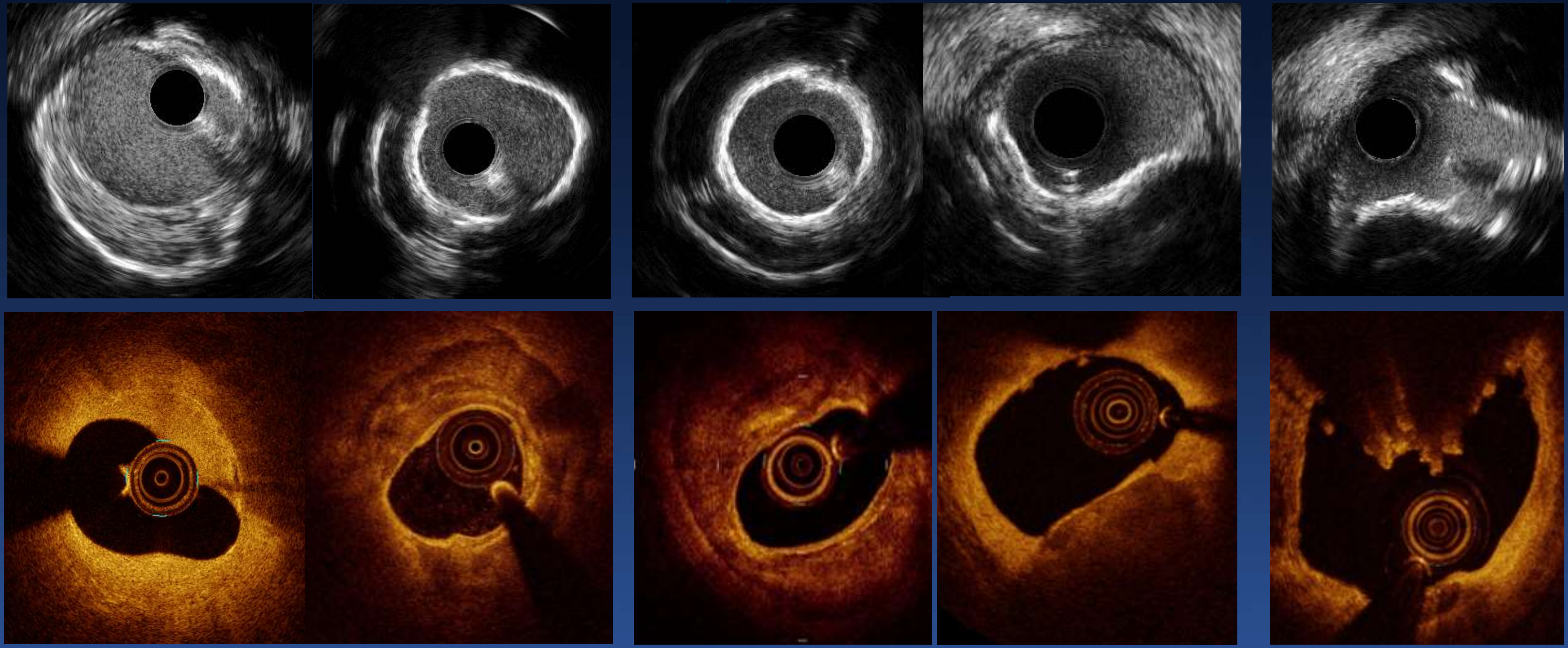
*Mintz et al. Circulation 1995;91:1959-65.*

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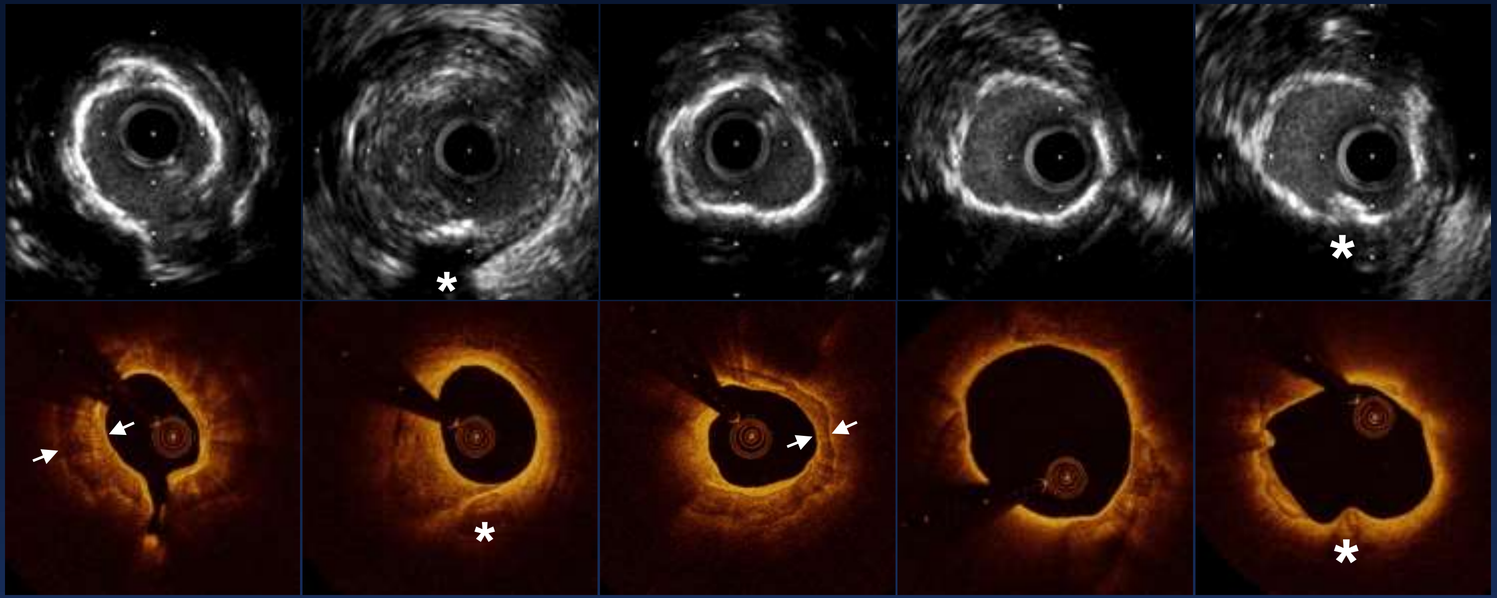
Jeremias et al. Circ Cardiovasc Interv. 2020;13:e008686. doi: 10.1161/CIRCINTERVENTIONS.120.008686

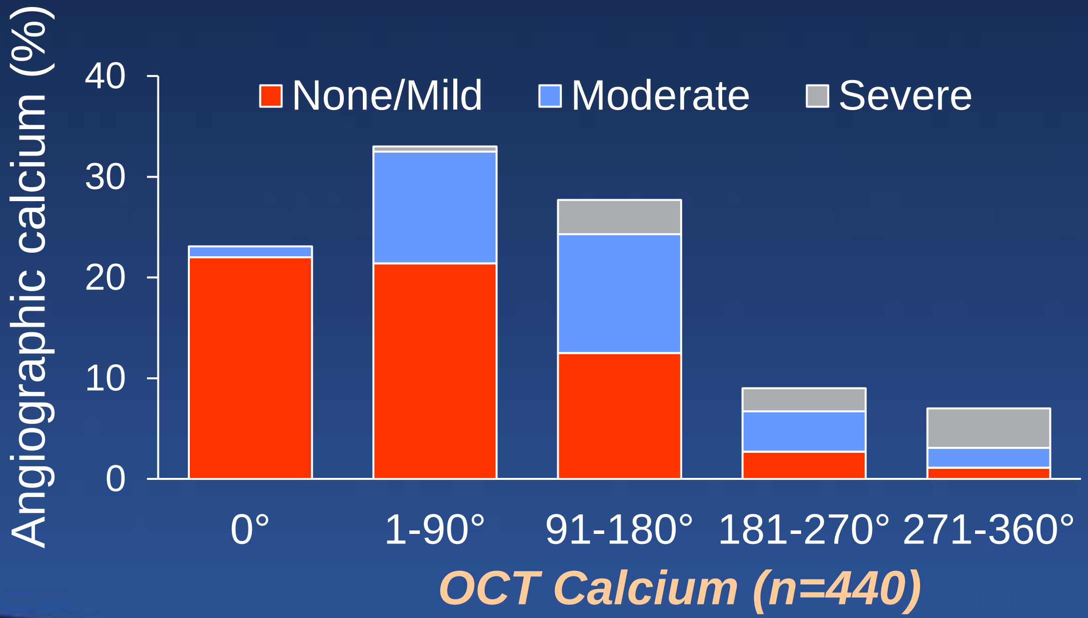
IVUS

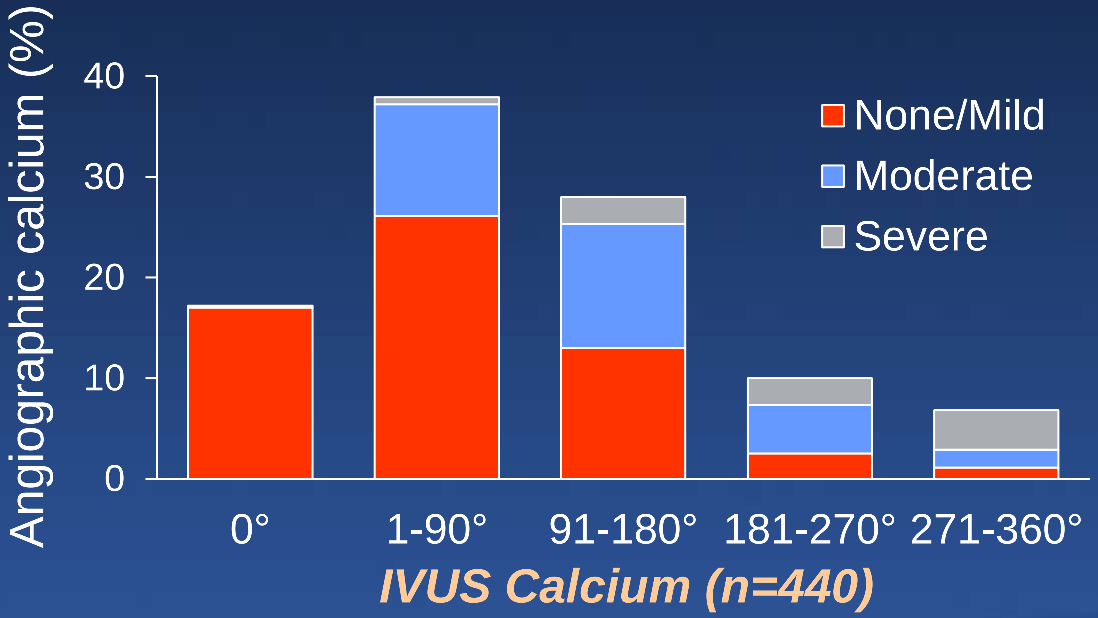
OCT



Arc
Length

Arc
Length
Thickness
Area
Volume



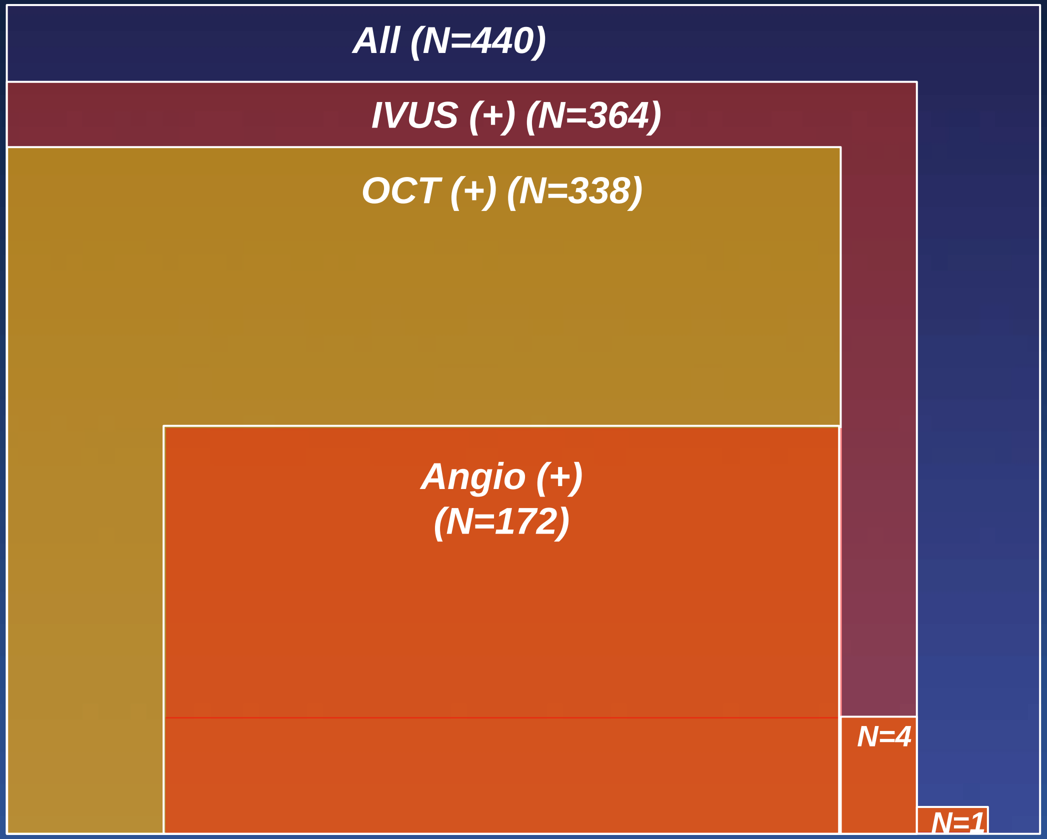




*Wang et al. JACC Cardiovasc Imaging 2017;10:869-79*
*Mintz and Guagliumi. Lancet 2017;390:793-809*

| | IVUS (+) | IVUS (-) |
|---|---|---|
| Angio (+) | 176 | 1 |
| Angio (-) | 188 | 75 |

| | OCT (+) | OCT (-) |
|---|---|---|
| Angio (+) | 172 | 5 |
| Angio (-) | 166 | 97 |

| | OCT (+) | OCT (-) |
|---|---|---|
| IVUS (+) | 338 | 26 |
| IVUS (-) | 0 | 76 |






*Wang et al. JACC Cardiovasc Imaging 2017;10:869-79*

# Pre and post-OCT calcium scoring system predicting stent expansion

## Test cohort of 128 pts

| | Regression Coefficient | 95% CI | P-value | Calcium Score | | |
|---|---|---|---|---|---|---|
| Maximum calcium angle (per 180°) | -7.43 | -12.6 to -2.21 | <0.01 | Maximum calcium angle | ≤180° | 0 |
| | | | | | >180° | 2 |
| Maximum calcium thickness (per 0.5 mm) | -3.40 | -6.35 to -0.45 | 0.02 | Maximum calcium thickness | ≤0.5mm | 0 |
| | | | | | >0.5mm | 1 |
| Calcium length (per 5 mm) | -3.32 | -4.09 to -0.55 | 0.01 | Calcium length | ≤5mm | 0 |
| | | | | | >5mm | 1 |

## Validation cohort of 133 pts

| Score | 0 (n=27) | 1 (n=45) | 2 (n=34) | 3 (n=3) | **4 (n=24)** | P-value |
|---|---|---|---|---|---|---|
| MSA, $mm^2$ | 7.2 (5.4, 9.2) | 6.3 (5.2, 8.4) | 5.9 (4.8, 8.0) | 6.7 (5.8, 7.1) | **5.7 (4.4, 7.4)** | 0.21 |
| Stent expansion at target lesion calcium, % | 99 (93, 108) | 98 (86, 109) | 86 (77, 100) | 98 (83, 104) | **78 (70, 86)** | <0.01 |
| Stent expansion at MSA, % | 91 (84, 95) | 85 (78, 93) | 80 (73, 93) | 80 (73, 85) | **69 (60, 77)** | <0.01 |

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*Fujino et al. EuroIntervention 2018;13(18):e2182-e2189*

# IVUS calcium score predicting stent expansion (as a continuous variable) in lesions with calcium >270°

## Test cohort of 97 pts

| | Regression Coeff | 95% CI | P-value | Cut-off | Calcium Score | |
|---|---|---|---|---|---|---|
| Length of calcium >270° (per 5mm) | -5.5 | -9.7, -1.2 | 0.01 | 5.0 | ≤5mm | 0 |
| | | | | | >5mm | 1 |
| Calcium Nodule | -10.2 | -16.3 to -4.2 | 0.0009 | | absent | 0 |
| | | | | | present | 1 |
| Vessel diameter (per 1mm) | 8.6 | 2.7 to 14.4 | 0.004 | 3.5 | >3.5mm | 0 |
| | | | | | ≤3.5mm | 1 |
| Circumferential calcium | -14.3 | -25.0 to -3.5 | 0.009 | | absent | 0 |
| | | | | | present | 1 |

## Stent underexpansion (<70%) in the validation cohort of 97 pts

| | Cut-off | C-statistics | Sensitivity | Specificity | PPV | NPV |
|---|---|---|---|---|---|---|
| Score | ≥2 | 0.85 [0.77, 0.93] | 89% | 63% | 48% | 94% |

***In 67 lesions without angiographically visible calcium, but with a maximum IVUS angle of superficial calcium >270°, there were none with a calcium score of 4 and only 1 with stent underexpansion.***

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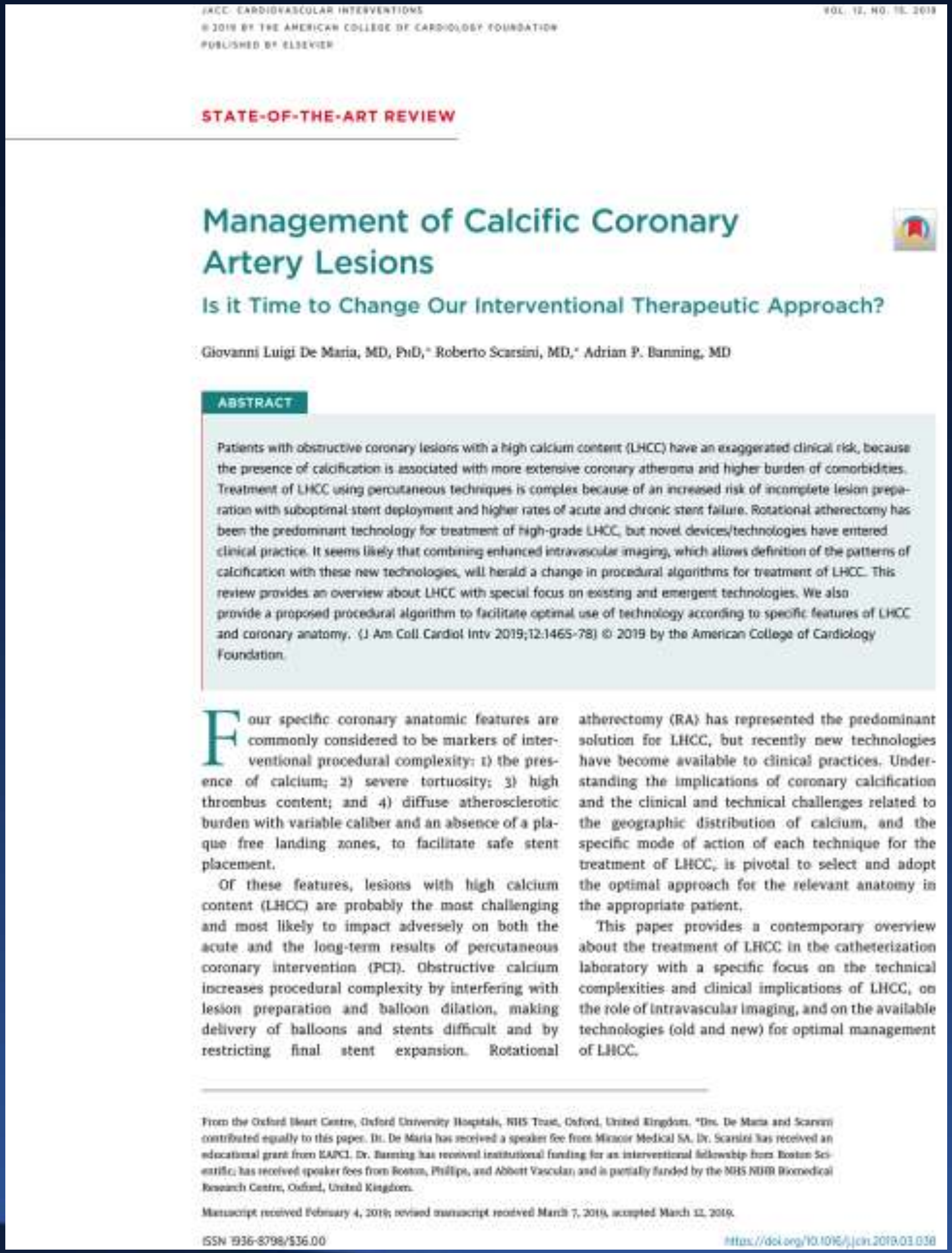
Zhang et al. Circ Cardiovasc Interv. 2021;14:e010296. doi: 10.1161/CIRCINTERVENTIONS.120.010296



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STATE-OF-THE-ART REVIEW

# Management of Calcific Coronary Artery Lesions

## Is it Time to Change Our Interventional Therapeutic Approach?

Giovanni Luigi De Maria, MD, PhD,* Roberto Scarsini, MD,* Adrian P. Banning, MD

ABSTRACT

Patients with obstructive coronary lesions with a high calcium content (LHCC) have an exaggerated clinical risk, because the presence of calcification is associated with more extensive coronary atheroma and higher burden of comorbidities. Treatment of LHCC using percutaneous techniques is complex because of an increased risk of incomplete lesion preparation with suboptimal stent deployment and higher rates of acute and chronic stent failure. Rotational atherectomy has been the predominant technology for treatment of high-grade LHCC, but novel devices/technologies have entered clinical practice. It seems likely that combining enhanced intravascular imaging, which allows definition of the patterns of calcification with these new technologies, will herald a change in procedural algorithms for treatment of LHCC. This review provides an overview about LHCC with special focus on existing and emergent technologies. We also provide a proposed procedural algorithm to facilitate optimal use of technology according to specific features of LHCC and coronary anatomy. (J Am Coll Cardiol Intv 2019;12:1465-78) © 2019 by the American College of Cardiology Foundation.

Four specific coronary anatomic features are commonly considered to be markers of interventional procedural complexity: 1) the presence of calcium; 2) severe tortuosity; 3) high thrombus content; and 4) diffuse atherosclerotic burden with variable caliber and an absence of a plaque free landing zones, to facilitate safe stent placement.

Of these features, lesions with high calcium content (LHCC) are probably the most challenging and most likely to impact adversely on both the acute and the long-term results of percutaneous coronary intervention (PCI). Obstructive calcium increases procedural complexity by interfering with lesion preparation and balloon dilation, making delivery of balloons and stents difficult and by restricting final stent expansion. Rotational atherectomy (RA) has represented the predominant solution for LHCC, but recently new technologies have become available to clinical practices. Understanding the implications of coronary calcification and the clinical and technical challenges related to the geographic distribution of calcium, and the specific mode of action of each technique for the treatment of LHCC, is pivotal to select and adopt the optimal approach for the relevant anatomy in the appropriate patient.

This paper provides a contemporary overview about the treatment of LHCC in the catheterization laboratory with a specific focus on the technical complexities and clinical implications of LHCC, on the role of intravascular imaging, and on the available technologies (old and new) for optimal management of LHCC.

From the Oxford Heart Centre, Oxford University Hospitals, NHS Trust, Oxford, United Kingdom. *Drs. De Maria and Scarsini contributed equally to this paper. Dr. De Maria has received a speaker fee from Miracor Medical SA. Dr. Scarsini has received an educational grant from EAPCI. Dr. Banning has received institutional funding for an interventional fellowship from Boston Scientific; has received speaker fees from Boston, Phillips, and Abbott Vascular; and is partially funded by the NHS NIHR Biomedical Research Centre, Oxford, United Kingdom.

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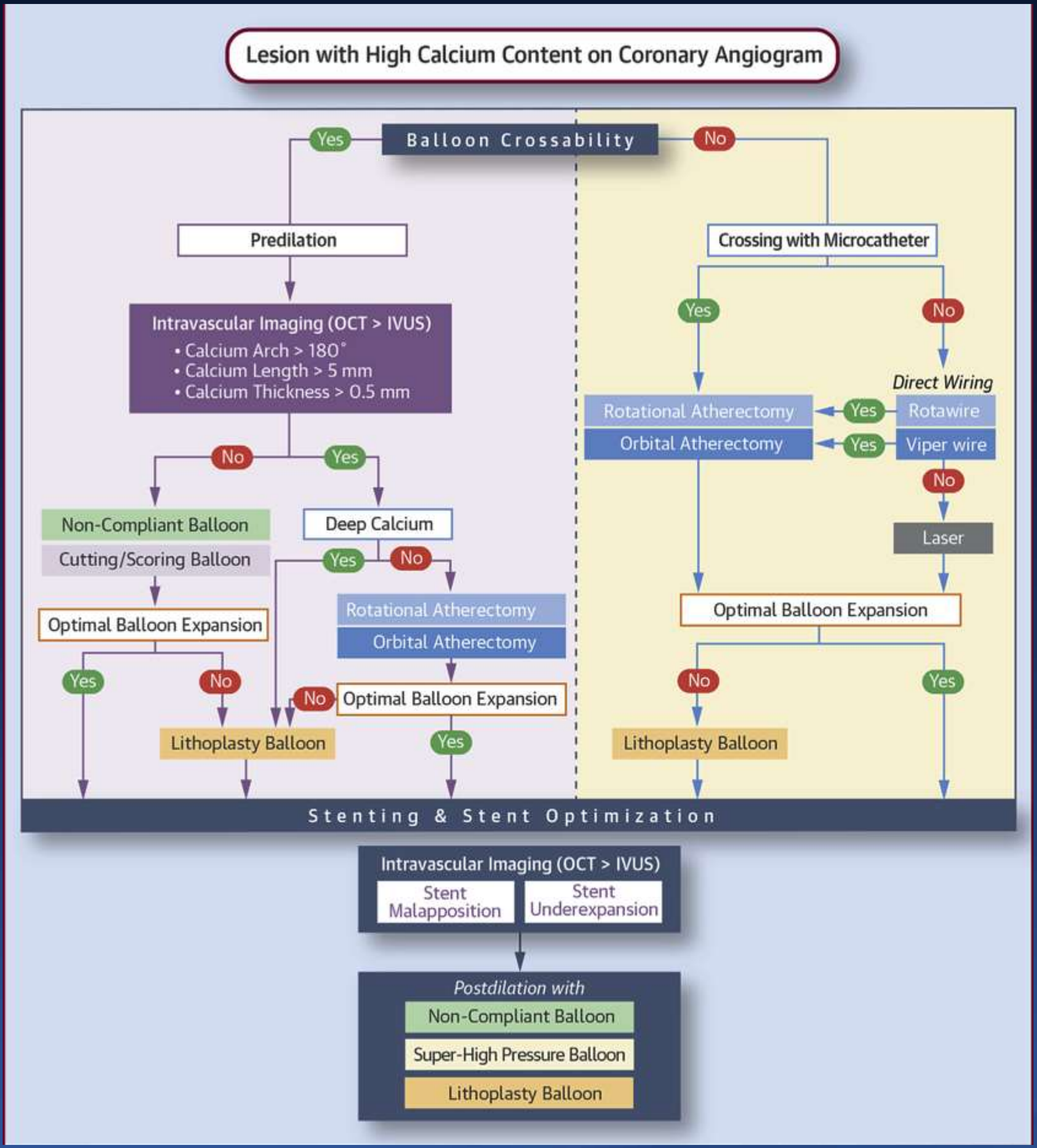
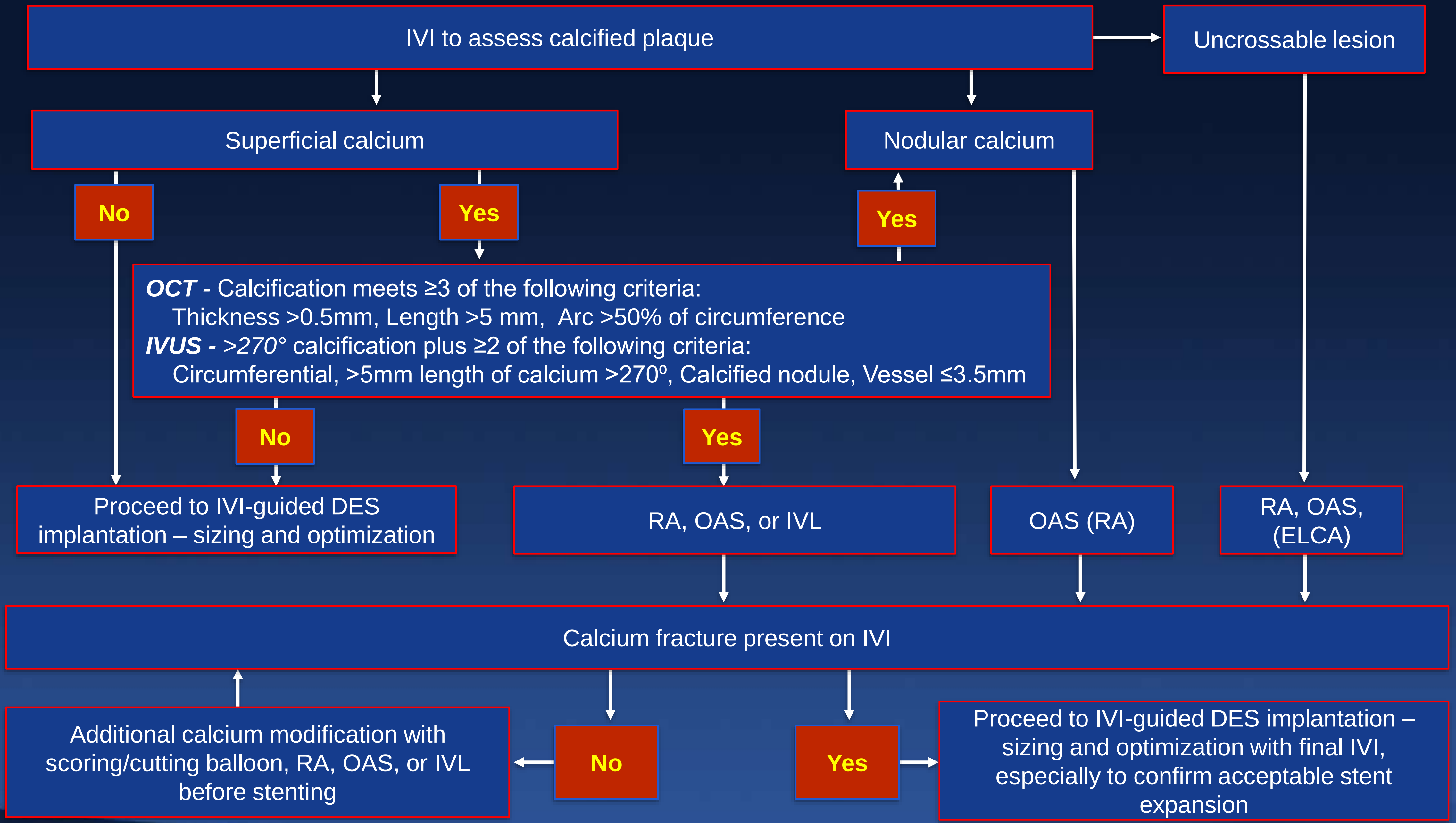



DeMaria et al. J Am Coll Cardiol Intv 2019;12:1465–78




*Mintz et al. Heart* 2021;107:755-64

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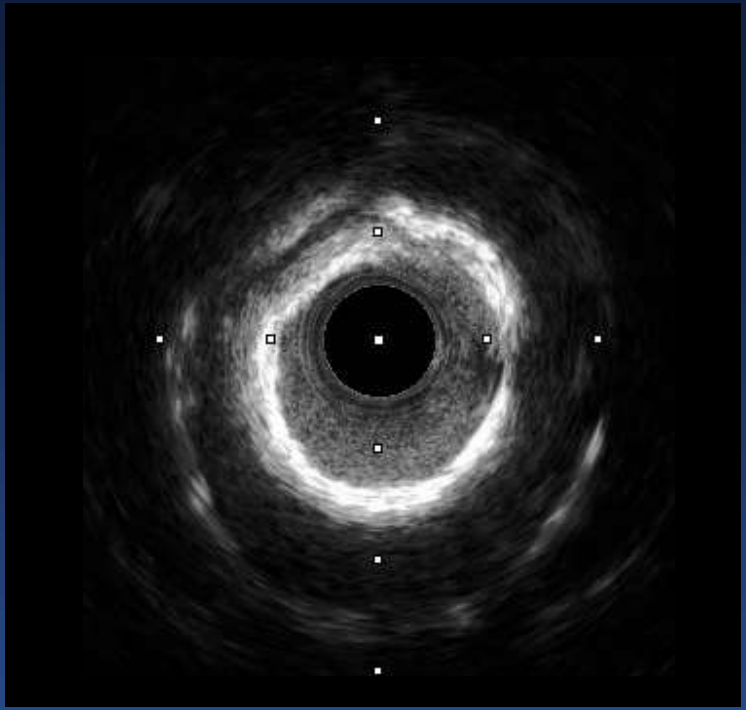
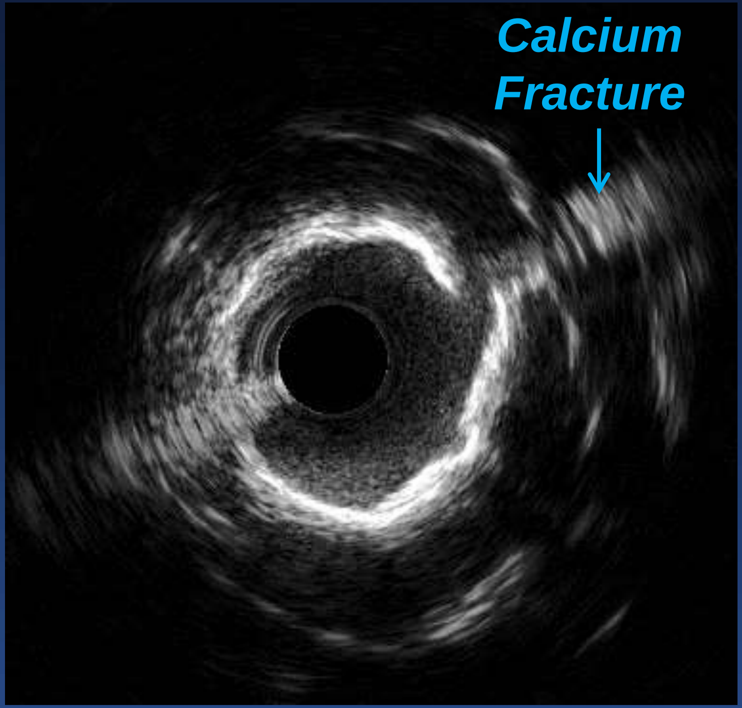
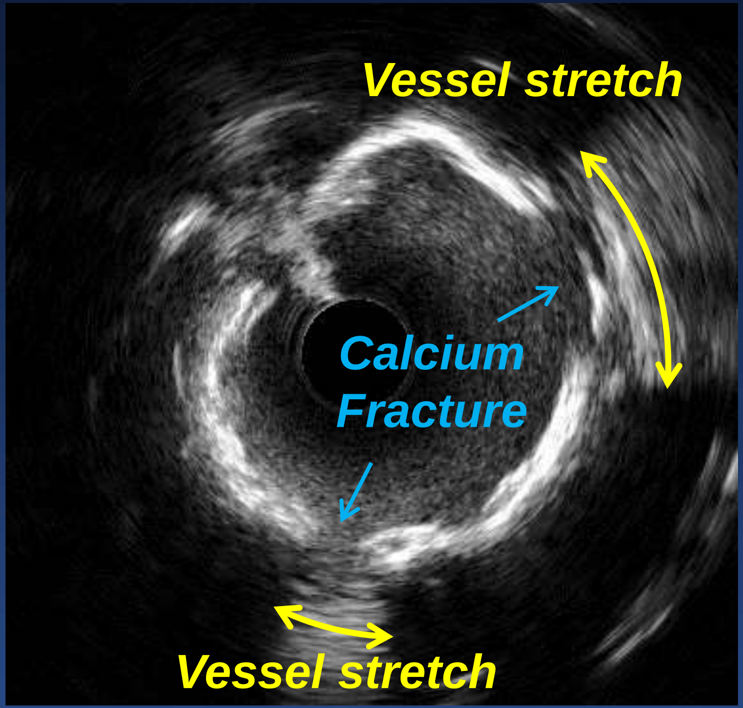
# Detection of Calcium Fracture



*Post-Balloon*




*Post-Stent Final*



# Question

Is the definition of Moderate to Heavy Calcification based on fluoroscopy or intravascular imaging

# Answer

Both. It depends on the situation.