

Role of Coronary Artery Calcium Score, Advanced Lipid Panel, Lipoprotein A and APO Lipoprotein B in CV Incremental Risk Stratification: A Preventive Cardiology Update for Primary Care

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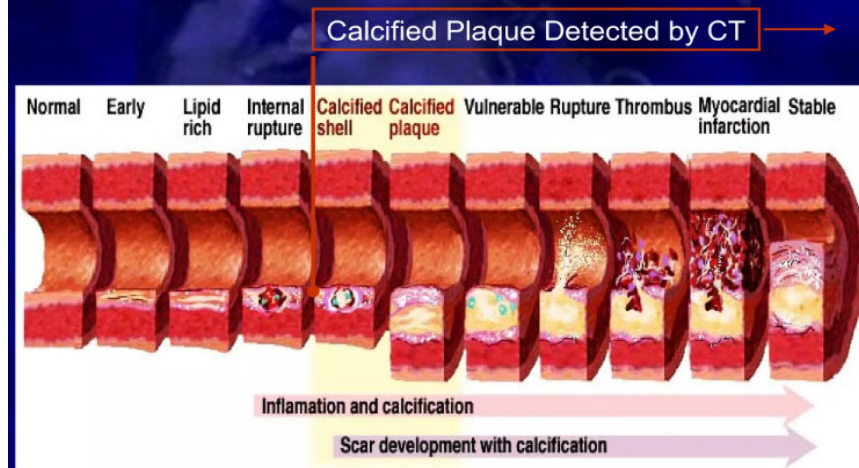
Activity Purpose/Professional Practice Gap

- UF Health St. Johns physicians, clinical advanced practice practitioners, and other healthcare professionals require an update on cardiovascular risk stratification.

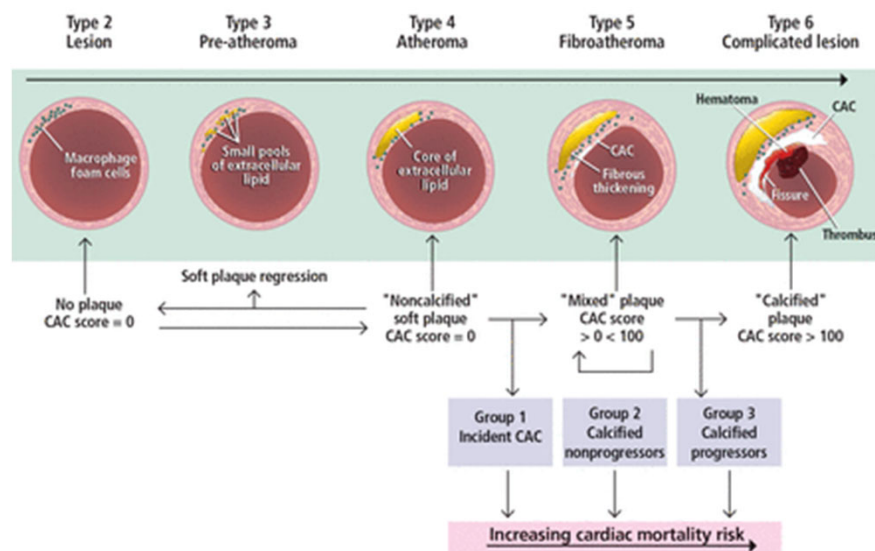
Objectives

1. Discuss when it is appropriate to order a CT calcium test
2. How to interpret Lipoprotein A results.
3. Explain how CV risk is modified with CT calcium score and Lipoprotein A results.
4. Define the American College of Cardiology lipid LDL guidelines.
5. Discuss new FDA approved alternatives to Statins.

Coronary Disease Progression



Akifab93. CT calcium score.pptx Slideshare 2023 Nov. 3. Retrieved from <https://www.slideshare.net/slideshow/ct-calcium-scorepptx-dc66/263002058#1>

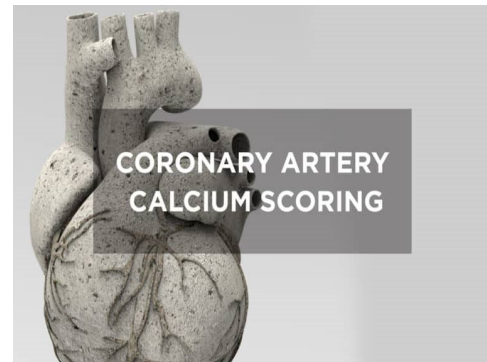


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Vascular calcification was shown independently to predict cardiovascular morbidity and mortality.¹

These associations, combined with the radio-opaque appearance of calcium hydroxyapatite on CT images, have led to extensive investigation of the quantification, or scoring, of coronary artery calcium (CAC).¹

CAC scoring has emerged as a widely available and powerful tool for stratifying cardiovascular risk, predicting patient outcomes, and guiding preventive therapy.¹



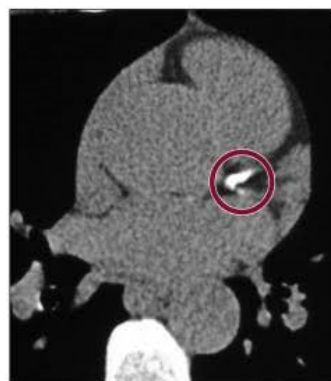
1. Akifab93. *CT calcium score.pptx* Slideshare 2023 Nov. 3. Retrieved from <https://www.slideshare.net/slideshow/ct-calcium-scorepptx-dc66/263002058#1> August 5, 2021

2. Role of the Coronary Artery Calcium Score for Lipid-Lowering Therapy Decisions Harlan M. Krumholz, MD, SM, reviewing Patel J et al. *JAMA Cardiol* 2021;Jul 14

Calculation of the Agatston Score

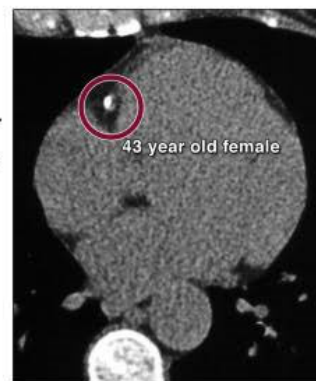
$$\text{Agatston Lesion Score} = \text{Lesion Area} \times \text{Density Weighting Factor}$$

$$\text{Total Agatston Score} = \sum \text{Lesion Scores}$$



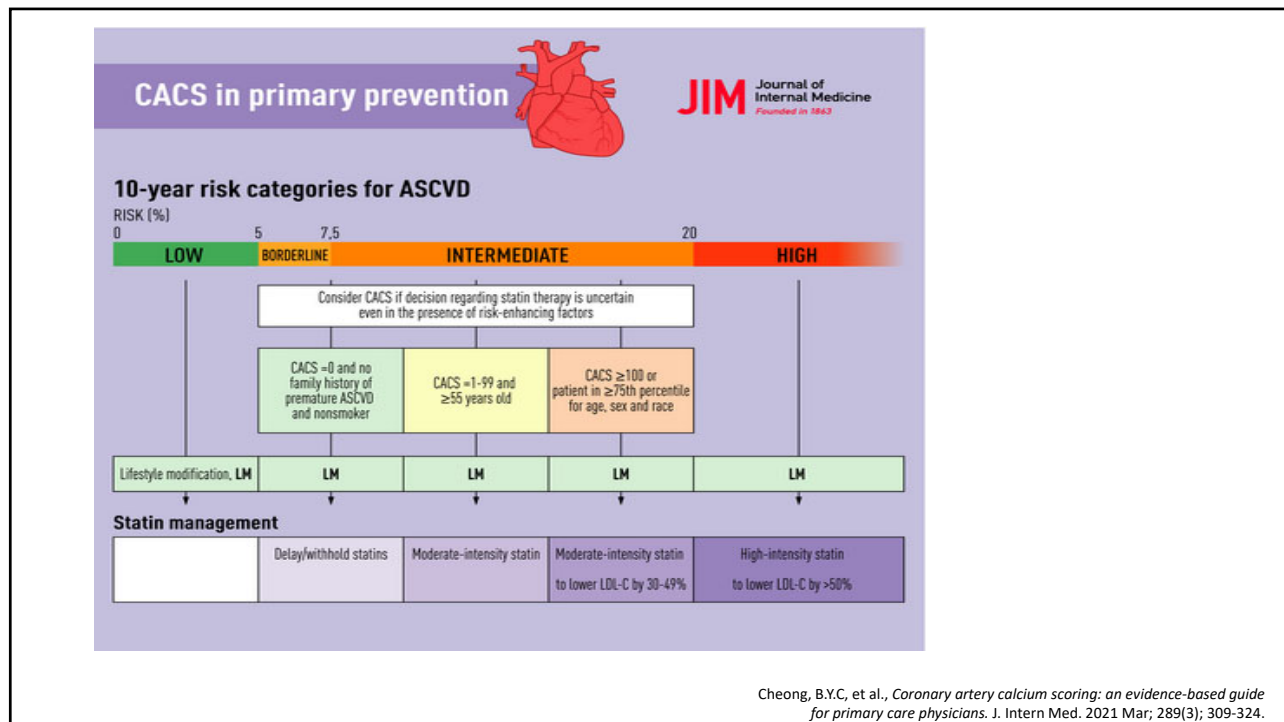
Left Coronary Descending
Area = 15 mm², Peak = HU = 450
Lesion Score = 15 x 4 = 60

Peak Attenuation Weighting Factor	
Hounsfield Units	
130** - 199	1
200 - 299	2
300 - 399	3
>400	4



Right Coronary Descending
Area = 8 mm², Peak = HU = 290
Lesion Score = 8 x 2 = 16

Blaha, M.J., et al. *Coronary artery calcium scoring: Is it time for a change in methodology?*. *JACC Cardiovascular Imaging*. 2017 Aug; 10(8):923-937



MESA The Multi-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification [Back to CAC Tools](#)

1. Gender Male ☒ Female ☐

2. Age (45-85 years) 80 Years

3. Coronary Artery Calcification 0 Agatston

4. Race/Ethnicity Choose One

Caucasian ☐

Chinese ☐

African American ☐

Hispanic ☒

5. Diabetes Yes ☐ No ☒

6. Currently Smoke Yes ☐ No ☒

7. Family History of Heart Attack (History in parents, siblings, or children) Yes ☐ No ☒

8. Total Cholesterol 180 mg/dL or 4.7 mmol/L

9. HDL Cholesterol 50 mg/dL or 1.3 mmol/L

10. Systolic Blood Pressure 130 mmHg or 17.3 kPa

11. Lipid Lowering Medication Yes ☐ No ☒

12. Hypertension Medication Yes ☒ No ☐

Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 3.5%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 12.7%.

Gupta, A. et al. *Coronary artery calcium scoring: current status and future directions*. RadioGraphics. 2022 Jun 3; 42(4). Retrieved from <https://pubs.rsna.org/doi/full/10.1148/rg.210122>

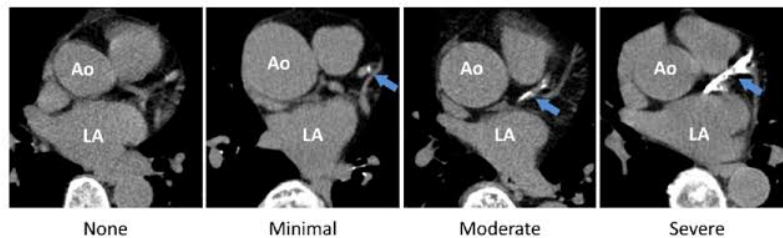
For people with risk on the borderline for treatment, the guidelines recommend evaluation of risk-enhancing factors (e.g., family history of premature ASCVD).

Chronic kidney disease; metabolic syndrome; premature menopause; elevated inflammatory and lipid biomarkers; low ankle-brachial index [ABI]), with consideration of coronary artery calcium (CAC) testing to further refine risk.

Investigators from the Multi-Ethnic Study of Atherosclerosis assessed the association between the CAC score and other factors and risk for ASCVD in people at intermediate risk (10-year risk, 7.5%–20%).

August 5, 2021
Role of the Coronary Artery Calcium Score for Lipid-Lowering Therapy Decisions
Harlan M. Krumholz, MD, SM, reviewing Patel J et al. *JAMA Cardiol* 2021;Jul 14

A) CT images of coronary arteries:



B) Calculation of CAC score (Agatston Method):

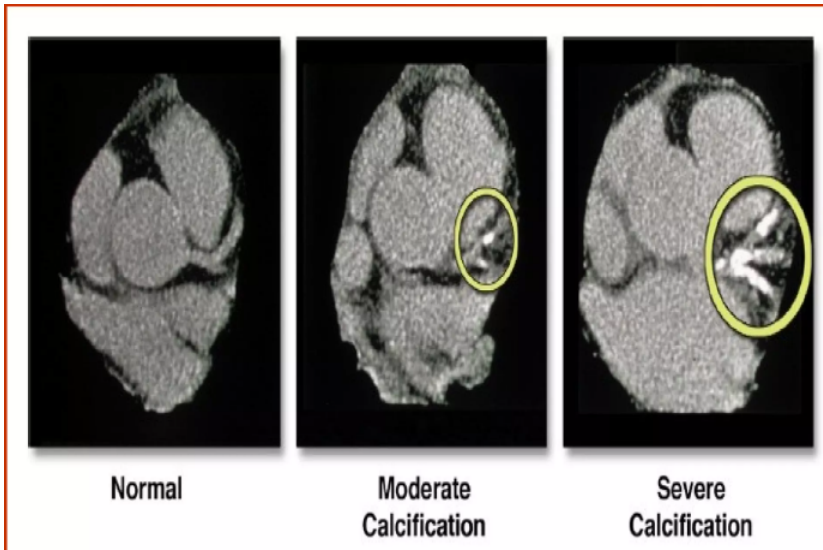
Definition of calcified lesion: (1) ≥ 130 Hounsfield Unit (HU) density
(2) $\geq 1\text{mm}^2$ Area of lesion

Weights assigned to lesion density:

Lesion density	Weight	Lesion Score
130 to <200 HU	1	= Weight \times Area of lesion (mm^2)
200 to <300 HU	2	
300 to <400 HU	3	
≥ 400 HU	4	

Total CAC Score: Sum of all lesion scores for all coronary CT slices (3mm)

Ziad, M., et al. *Coronary artery calcium and carotid artery intima media thickness and plaque: clinical use in need of clarification.* *J. Artheroscler Thromb.* 2017 Mar 1; 24(3):227-239.



Yamada, G.M. 2023 May 1. *Calcium score (heart scan): what you need to know*. Retrieved from <https://www.greggyamada.com/post/calcium-score-heart-scan-what-you-need-to-know>

CAC is typically quantified using the Agatston score

The Agatston score can be reported as an absolute score (in Agatston units) or as an age-, sex-, and race-specific percentile that is derived using the MESA risk score calculator

The absolute score is the best predictor of the **total risk** of a CHD event for an individual in the near to midterm (in the next 5 to 10 years)

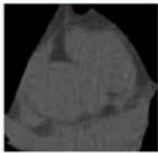
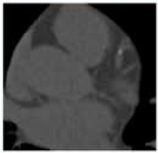
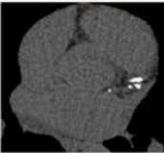
In contrast, the percentile score best represents **relative risk** of CHD event for the individual compared with other individuals of the same age, race, and sex

In this way, the percentile score is the better predictor of **lifetime risk** of developing CHD.

Akifab93. *CT calcium score.pptx* Slideshare 2023 Nov. 3. Retrieved from <https://www.slideshare.net/slideshow/ct-calcium-scorepptx-dc66/263002058#1>

CCS (Agaston)	Risk	Description
0	Non-identified	Negative test. Findings are consistent with a low risk of having a cardiovascular event in the next 5 years.
1-10	Minimal	Minimal atherosclerosis is present. Findings are consistent with a low risk of having a cardiovascular event in the next 5 years.
11-100	Mild	Mild coronary atherosclerosis is present. There is likely mild or minimal coronary stenosis. A mild risk of having CAD exists.
101-400	Moderate	Moderate calcium is detected in the coronary arteries and confirms the presence of atherosclerotic plaque. A moderate risk of having a cardiovascular event exists.
>400	High	A high calcium score may be consistent with significant risk of having a cardiovascular event within the next 5 years

Akifab93. CT calcium score.pptx Slideshare. 2023 Nov. 3. Retrieved from <https://www.slideshare.net/slideshow/ct-calcium-scorepptx-dc66/263002058#1>

				
		CAC = 0	CAC 1-100	CAC > 100
Population (% patients) ³²		56%	26%	18%
Annual CHD Event Rate ³³		0.1%	0.5%	1.9%
Annual CVD Event Rate ³²		0.4%	0.8%	2.4%
Number Needed to Treat (NNT) to Prevent One CHD Event Over 5-Years				
NNT Aspirin ³²	FRS <10%	2036	571 [^]	173
	FRS ≥10%	808	146 [^]	92
NNT Statin ³³		549	94	24
		↓	↓	↓
		Reassure	Individualize Statin + Aspirin	Treat with Statin + Aspirin
All Patients: Lifestyle Management + Control CVD Risk Factors				

Thomas, D.M., et al. *Management of coronary artery calcium and coronary CTA findings.* Curr Cardiovasc Imaging Rep. 2015; 8(6): 18. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/25960825/>

FIGURE 8 The ACC/AHA Recommendations for Aspirin Use

COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk. ^{54,6-1-54,6-8}
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age. ^{54,6-9}
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. ^{54,6-10}

Golub, I.S., et al. *Major global coronary artery calcium guidelines*. JACC Cardiovascular Imaging. 2023 Jan; 16(1):98-117. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/36599573/>

CAC score of (0) is associated with a low risk of future ASCVD events over the next 10 years

In addition, despite an increased risk of short-term ACSVD events among those with vs without risk-enhancing factors, data suggest that certain risk-enhancing factors (family history of premature ASCVD, dyslipidemia, diabetes, and metabolic syndrome) are frequently associated with low short-term rates of ASCVD events (ie, <7.5 events per 1000 person-years) among those with CAC scores of 0.

Patel, J. et al. *Assessment of coronary artery calcium scoring to guide statin therapy allocation according to risk-enhancing factors*. JAMA Cardiol. 2021 Jul 14;6(10):1-10. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC8281019/>

The initial finding of a CAC score of 0 may encourage the patient to continue to maintain a healthy lifestyle.

Clinicians can continue to review lifestyle-associated factors (such as diet, physical activity, weight or body mass index, tobacco use, and blood glucose level) and assess risk factor burden over time following appropriate guidelines.

If clinically indicated, repeated CAC scanning among those with CAC scores of 0 can be considered 5 years after the initial CAC scan to assess the progression of CAC. Given that previous studies have reported that CAC progression is associated with a higher risk of ASCVD events over medium- to long-term follow-up, individuals with CAC progression could be considered for treatment with statin therapy to mitigate the risk of ASCVD.

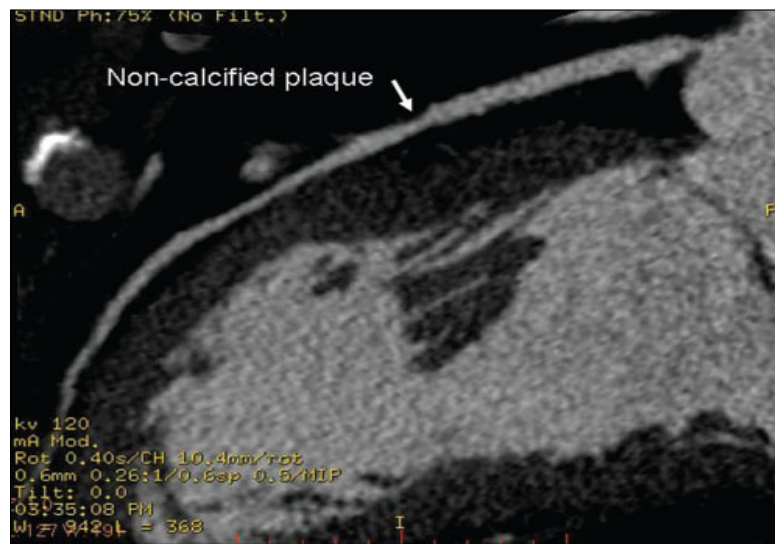
Patel, J. et al. *Assessment of coronary artery calcium scoring to guide statin therapy allocation according to risk-enhancing factors*. JAMA Cardiol. 2021 Jul 14;6(10):1-10. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC8281019/>

TREAT THE RISK

The presence of a CAC score of 0 does not indicate lifetime low-risk status.

The natural history of atherosclerosis is dynamic, with a tendency to progress over time. Therefore, a CAC score of 0 is likely to convert to a CAC score higher than 0, especially in the presence of traditional cardiovascular risk factors or risk-enhancing factors

Patel, J. et al. *Assessment of coronary artery calcium scoring to guide statin therapy allocation according to risk-enhancing factors*. JAMA Cardiol. 2021 Jul 14;6(10):1-10. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC8281019/>



Sun, A., Choo, G.H., Ng, K.H. *Coronary CT angiography: current status and continuing challenges.* Br J Radiol. 2012 May;85(1013):495-510. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/22253353/>

CORONARY CT ANGIOGRAPHY OF CALCIFIED PLAQUES



1

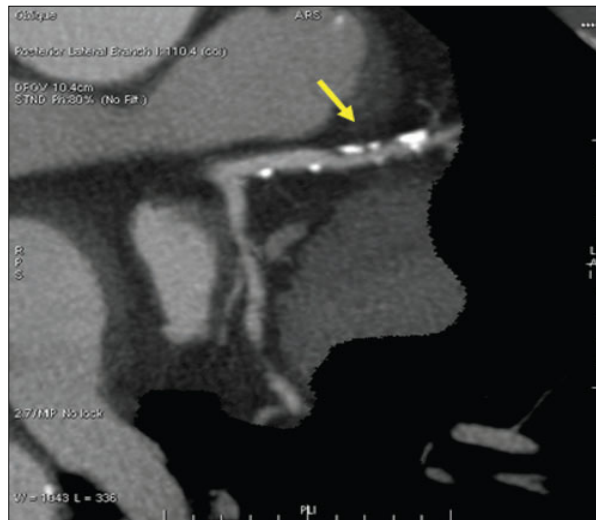


2



3

1. Nakano, Y., & Sadamatsu, K. *Successful intravascular ultrasound-guided transradial coronary intervention with a 4FR guiding catheter.* Case Rep Cardiol 2016 Sep 8;2016:6369812.
2. Perez-Riera, A. R. et al. *Transient left septal fascicular block and left anterior fascicular block as a consequence of proximal subocclusion of the left anterior descending coronary artery.* Ann Noninvasive Electrocardiol. 2019 May;24(3): e12546
3. Machida, H. et al. *Current and Novel Imaging Techniques in Coronary CT.* Radiographics. 2015 Jul-Aug; 35(4):991-1010



Al-Khatib, S. et al. *Radiologic assessment of native renal vasculature: a multimodality review.* Radiographics. 2017 Jan 11. 37(1): 136-156

CT Calcium score test DOES NOT Check for Non calcified Plaque, Based on CV risk , co morbid risk factors, and results of Testing /Stress test and Echo , Consider Cardiac CTA for further eval .

We do not use CAC scoring as a primary diagnostic tool in patients with symptoms concerning for myocardial ischemia

Serial CAC scoring in patients with established CAC (>0), particularly those with CAC >100 is not recommended, as repeated measurement will rarely alter management.

Statin therapy known to get CT calcium score higher in serial reports.

Crawford, M. *Utility of serial coronary calcium scores*. Clinical Cardiology Alert. 2017, Feb 1. Relias Media. Retrieved from <https://www.reliasmedia.com/articles/139983-utility-of-serial-coronary-calcium-scores>

Do not offer Calcium CT Score in
Pregnancy

Prior MI/ PCI/ CABG

Cardiac implants including mechanical valves,
pacemaker wires or stents

Advantages

Rapid

Doesn't require contrast

Reproducible

Prognostic significance

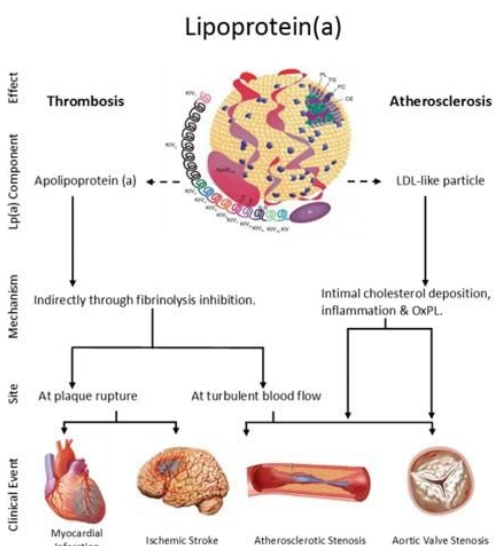
Table 5: Incidental Findings at Routine CAC Scoring CT

Incidental Finding	Clinical Significance	Best Next Step in Management
Solitary pulmonary nodules	Wide differential, including benign and malignant causes	Dedicated chest CT scan follow-up per Fleischner Society recommendations
Myocardial findings related to fat deposition, calcification, or aneurysm	Indicates sequela of old myocardial infarction	Coronary CTA or catheter angiography for management as warranted Cardiac MRI may be performed for viability assessment
Pericardial effusion or thickening	Pericardial tamponade physiologic features if there is large pericardial effusion Pericardial thickening with possible constrictive physiologic features	Echocardiography or cardiac MRI to assess tamponade or constrictive physiologic features
Cardiac chamber enlargement	Sign of underlying cardiac disease (eg, right heart failure, valvular dysfunction, cardiomyopathy)	Echocardiography or cardiac MRI for chamber and valvular function assessment, if clinically appropriate
Aortic valve and mitral annular calcifications	Association with aortic or mitral stenosis Mitral annulus correlation with coronary disease; associated with worse cardiovascular outcome	Echocardiography for valve function, if clinically appropriate Cardiovascular risk assessment for mitral annular calcifications
Thoracic aorta dilatation	Increased risk of rupture with increasing aorta size	CTA or MRA at 6–12 months, or referral for surgical repair, depending on aorta size
Pulmonary artery enlargement	Marker of pulmonary artery hypertension Size >30 mm at CT	Echocardiography to estimate pulmonary artery pressures and assess for pulmonary valvular disease and right heart dysfunction
Mediastinal lesion or mass	Benign lesions, such as pericardial cyst and calcified lymph nodes Malignant masses such as lymphoma, teratoma, and germ-cell tumors	For benign lesions, no further workup; MRI may be needed to confirm the cystic nature or benignity of the mediastinal lesion. For malignant or suspicious lesions, consider further dedicated imaging evaluation or staging with CT, MRI, and/or PET/CT
Hiatal hernia and other upper abdominal pathologic entities	Majority are asymptomatic; however, symptoms can include epigastric or chest pain, nausea, and vomiting Neoplastic lesions of esophagus and upper abdominal viscera	Further evaluation with a modified barium swallow; symptomatic hiatal hernias should be managed surgically Further evaluation with dedicated abdominopelvic CT or PET/CT
Osseous and chest wall disease	Fractures Osseous metastases Chest wall deformity (pectus excavatum or carinatum) Chest wall and breast masses	Fracture fixation, if needed MRI and/or bone biopsy as deemed necessary Assessment for need of surgical correction Further dedicated imaging and staging, as needed

Note.—CTA = CT angiography, MRA = MR angiography.

Gupta, A. et al. Coronary artery calcium scoring: current status and future directions. RadioGraphics. 2022 Jun 3; 42(4). Retrieved from <https://pubs.rsna.org/doi/full/10.1148/rg.210122>

Use of Lipoprotein(a) in Clinical Practice: A Biomarker Whose Time Has Come



Structurally, it is a variant of low-density lipoprotein and features apolipoprotein(a), or apo(a), which is bound to apolipoprotein B-100, or apoB100. These 2 structures are assembled in the hepatocyte cell membranes and are bound by 1 disulfide bridge.

Wilson, D.P. et al. Use of Lipoprotein(a) in clinical practice: a biomarker whose time has come. A scientific statement from the National Lipid Association. J. Clin Lipidol. 2019 May-June; 13(3): 374-392.

Lipids, such as cholesterol and triglycerides, are insoluble in plasma.

Circulating lipid is carried in lipoproteins that transport the lipid to various tissues for energy utilization, lipid deposition, steroid hormone production, and bile acid formation.

The lipoprotein consists of esterified and unesterified cholesterol, triglycerides, phospholipids, and protein. The protein components of the lipoprotein are known as apolipoproteins (apo) or apoproteins. The different apolipoproteins serve as cofactors for enzymes and ligands for receptors.

Lipoprotein (a), also known as Lp(a), is a variant of low-density lipoprotein (LDL) that contains a protein called apolipoprotein (a), or apo(a)

Lipoproteins are particles made of protein and fats (lipids) that transport cholesterol through the bloodstream to cells in the body

Genetic and epidemiological studies have identified Lp(a) as a risk factor for atherosclerosis and related diseases, such as coronary heart disease

Lp(a) promotes inflammation, which increases the likelihood of plaque rupture and can lead to the narrowing of the aortic valve, known as aortic stenosis.

This is due to the role of Lp(a) in inflammation, causing chronic inflammation that leads to calcium buildup on the valve and resulting stiffness [Lp(a) is considered an independent risk factor for cardiovascular disease, and its level in a person's blood is entirely genetically predetermined.

... an independent risk marker for ASCVD.

- What are the causal links between increased circulating concentrations of Lp(a) and 1) ASCVD and 2) valvular aortic stenosis?
- How should we measure and report Lp(a)?
- Who should have Lp(a) measured and when?
- How does the level of Lp(a) affect treatment.

Risk enhancing

Lipid/biomarkers: Associated with increased ASCVD risk o

Persistently* elevated, primary hypertriglyceridemia (≥ 175 mg/dL);

A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL or ≥ 125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).

Elevated apoB ≥ 130 mg/dL: A relative indication for its measurement would be triglyceride ≥ 200 mg/dL.

II. Lipoprotein(a) Testing in Clinical Practice 1. Adults (> 20 years of age)
Measurement of Lp(a) is reasonable to refine risk assessment for ASCVD events in: 1) Individuals with a family history of 1 st degree relatives with premature ASCVD (<55 years of age in men; <65 years of age in women)

2) Individuals with premature ASCVD (<55 years of age in men and <65 years of age in women), particularly in the absence of traditional risk factors.

3) Individuals with primary severe hypercholesterolemia (LDL \geq 190mg/dL) or suspected familial hypercholesterolemia.

4) Individuals at very high** ASCVD risk to better define those who are more likely to benefit from PCSK9 inhibitor therapy.

Rallidis, 2018 Ila Ila Ila Ila C-LD B NR B-NR Erqou, 2009; Kamstrup

Coronary artery disease • ACS: Risk in those with Lp(a) >50 is tripled in those age<45 and doubled age 45-60

Does Drug Therapy Affect Risk in ASCVD patients with \uparrow Lp(a)?

Khera A.V. et al. Circulation.2014 Feb 11;129(6)

Lp(a) and Secondary Prevention: Summary

Be aware of Lp(a)-associated increased risk for recurrent events

Continue to follow Guideline based therapies, as most lipid-related risk is still attributable to LDL-C

Consider more aggressive LDL-C lowering for ASCVD patients with increased Lp(a)

Consider earlier use of PCSK9 inhibitors in ASCVD patients with elevated Lp(a)

Statins have shown mixed results and, in some cases, have been shown to increase Lp(a).

Nonetheless, statins are a primary treatment option for patients with hyperlipidemia.

High Lp(a) levels may indicate the need for more intensive statin therapy to optimize a patient's low-density lipoprotein level and reduce their risk for coronary artery disease.

PCSK9 inhibitors are also an option for lowering Lp(a). A meta-analysis showed PCSK9 inhibitors lowered Lp(a) by 26%, in addition to improved cardiac outcomes..

Testosterone replacement therapy has been shown to lower Lp(a) levels.

Current Treatment Strategies

- STATIN
- Ezetimibe
- Niacin
- PCSK9 ANTIBODY OR siRNA
- LPA
- In an exploratory analysis from the FOURIER trial, which randomly assigned statin-treated cardiovascular disease patients to Evolocumab or placebo, Evolocumab reduced the risk of coronary heart disease death, myocardial infarction, or urgent coronary revascularization

Key Points

- CT CAC>100
- Treat the Risk
- Consider ASA, Ezetimibe, Statin
- Keep LDL <55 mg/dl in high risk population
- Consider Alternatives of statins- Evolocumab, Inclisiran as FDA approved, current strategies to lower Lpa, and LDL , ESPECIALLY FOR 55 mg/dl
- Bempedoic acid with Ezetimibe is an alternative to statins, when intolerant