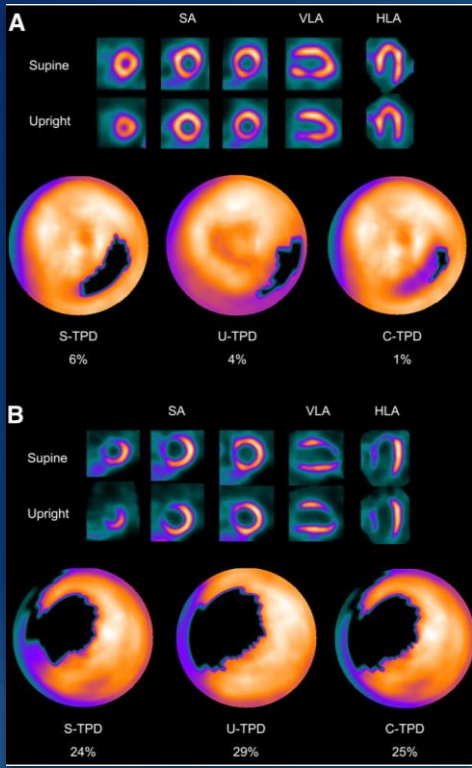
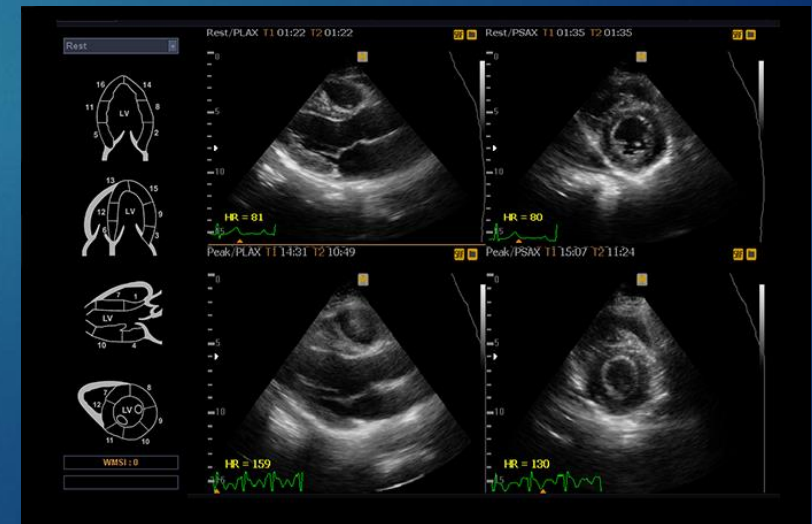


Non-Invasive Cardiac Testing: When should I order this test?



NATHANIEL J. DITTOE MD, FACC



Presentation Goals


- ▶ To give an overview and discuss various types of noninvasive testing including imaging studies and lab tests in outpatient and inpatient settings.
- ▶ Review the indications for each type of noninvasive cardiac test and their utility.
- ▶ Discuss appropriate indications and situations for each test.
- ▶ Give an overview of pretest probability and how it relates to ordering tests.
- ▶ Review how testing for inappropriate reasons can lead to potential bad, inefficient and/or harmful outcomes.

Presentation Goals

- ▶ We will cover several different non-invasive modalities
 - ▶ Cardiac stress tests
 - ▶ Coronary calcium scores
 - ▶ Coronary artery CT angiography (CTA)
 - ▶ Echocardiograms

Presentation Goals

- ▶ We will also cover laboratory testing
 - ▶ Troponin I (My favorite test)
 - ▶ Advanced lipoprotein testing including lipid particle size testing
 - ▶ High sensitivity CRP



“Medicine is a science of uncertainty and
an art of probability.”

Sir William Osler

“Equation Testing”

a) $y = 2x^2 + 3x - 1$
x-axis: $(-y) = 2x^2 + 3x - 1$
 $y = -2x^2 - 3x + 1$ No
y-axis: $y = 2(-x)^2 + 3(-x) - 1$
 $y = 2x^2 - 3x - 1$ No
origin: $-y = 2(-x)^2 + 3(-x) - 1$

“Equation Testing”

- ▶ Refers to ordering tests and making management decisions based on a simple symptom
- ▶ Chest Pain= (ECG x2) + CXR + CBC+ CMP+(troponin x 2)+ CTA of chest+ CDU admission + Stress test+ Cardiology consult
- ▶ Dyspnea = (ECG x2)+ CXR + CBC+ CMP + D-dimer + BNP+ (troponin x 2) + CTA of chest + 2D echocardiogram

a) $y = 2x^2 + 3x - 1$

x-axis: $(-y) = 2x^2 + 3x - 1$ No

y-axis: $y = 2(-x)^2 + 3(-x) - 1$ No

origin: $-y = 2(-x)$

The image shows a person's hands writing on graph paper. The original equation is $y = 2x^2 + 3x - 1$. For the x-axis test, the person writes $(-y) = 2x^2 + 3x - 1$, which is not equal to the original equation. For the y-axis test, the person writes $y = 2(-x)^2 + 3(-x) - 1$, which simplifies to $y = 2x^2 - 3x - 1$, also not equal to the original equation. For the origin test, the person writes $-y = 2(-x)$.

“Equation Testing”

- ▶ Can lead to missed diagnosis
- ▶ Costly
- ▶ Inefficient
- ▶ Can lead to patient harm
- ▶ Save the equations for the mathematicians (and nephrologists)

a) $y = 2x^2 + 3x - 1$
x-axis: $(-y) = 2x^2 + 3x - 1$
 $y = -2x^2 - 3x + 1$ No
y-axis: $y = 2(-x)^2 + 3(-x) - 1$
 $y = 2x^2 - 3x - 1$ No
origin: $-y = 2(-x)$

“Locked On”



“Locked On”

Refers to the phenomenon of focusing on one diagnosis without appropriate consideration to other possible diagnoses despite equivocal or negative testing that does not support it.



“Locked On”

- ▶ Can lead to missed or delay of diagnosis
- ▶ Costly
- ▶ Inefficient
- ▶ Can lead to patient harm



Case 1

A 54-year-old white male presented to the Emergency Department with complaints of progressive dyspnea and chest pain that had started simultaneously with acute onset 10 h before arrival. He stated the chest pain started while going from a seated to standing position. The pain was substernal and sharp with epigastric radiation initially. The pain was also noted to be worse with movement, and although it was still present, it had subsequently waned since the initial symptom onset. His dyspnea started immediately after the onset of chest pain and was worse with exertion. At presentation, he had progressed to the point of breathlessness, prompting his ED visit. Review of systems revealed no nausea, vomiting, diarrhea, fevers, or recent cough or congestion, as well as no similar episodes of pain or history of coronary artery disease, heart failure, chronic obstructive pulmonary disease, gastroesophageal reflux disease, or GI bleeding episodes.

Case 1

His past medical history was significant for osteoarthritis and benign prostatic hypertrophy, and he denied any prior surgery. His medications included ibuprofen (800 mg three times a day with meals), which he has taken routinely over the past month. Of note, he had smoked a pack of cigarettes per day for the past 40 years and claimed only occasional alcohol usage.

[Int J Emerg Med.](#) 2011; 4: 34.

Case 1

Physical examination revealed an obese, ashen colored male in obvious respiratory distress. Vital signs were temperature of 36.4°C (97.5°F), heart rate 118, respiratory rate 36, oxygen saturation 77% on room air, and blood pressure 151/88 mmHg. The patient was alert, oriented and in obvious discomfort. His cardiovascular examination was remarkable for tachycardia, with regular and strong distal pulses in all four extremities. Pulmonary evaluation demonstrated clear breath sounds in the upper and lower lung fields, with diminished volume in the bases. His abdomen was soft and mildly distended with slight but **diffuse tenderness to soft touch and percussion without tympany or guarding. Stool was positive for occult blood.** A bedside abdominal ultrasound was performed and was negative for free fluid or abdominal aortic aneurysm. The ultrasound was difficult to perform because the patient became increasingly dyspneic and anxious while laying supine and was unable to lay still. His skin was ashen and diaphoretic without petechiae, purpura, or stigmata of liver disease.

[Int J Emerg Med.](#) 2011; 4: 34.

Case 1

Initial diagnostics ordered included an electrocardiogram revealing sinus tachycardia and no ischemic changes, and an upright portable chest x-ray that was unremarkable for acute cardiopulmonary processes or free air in the abdomen. Laboratory analysis showed an elevated i-stat troponin-I of 0.74 ng/ml (normal <0.034 ng/ml), D-dimer was 5.73 mcg/ml (normal <0.48 mcg/ml), and a white blood cell count of 18.8 ($\times 1,000/\mu\text{l}$) with a left shift. Electrolytes, renal function, and coagulation studies were normal, and his lactate was 1.4 mmol/l (normal <2.2 mmol/l).

[Int J Emerg Med.](#) 2011; 4: 34.

Case 1

He was immediately started on oxygen using a non-rebreather with immediate improvement in his dyspnea and oxygen saturation. His pain was addressed using morphine. **Given his positive troponin, 162 mg of aspirin was given; heparin was withheld because the patient was guaiac positive.** Shortly after his improved chest pain and respiratory distress, the patient stated that the abdominal pain was more prominent.

Cardiology consultation was considered because of the troponin elevation, but because of the increased abdominal pain, a non-contrasted CT of the abdomen was obtained, which revealed free air in the abdomen and a perforated duodenal ulcer.

Troponin Trumps Common Sense

“My concern, shared by many cardiologists, is that troponin testing has gotten out of hand. Most cardiologists have been asked to see a patient (often urgently) found to have a mildly elevated troponin when the test was ordered reflexively—regardless of the patient’s presenting complaints or past history. Cardiologists on hospital services are tripping over troponin every day. The most challenging situation is when a patient presents with a serious (even life-threatening) noncardiac condition, and one or more doctors involved in their care gets distracted by an incidental mild troponin elevation. **Occasionally, this leads to a sudden obsession over one test result, a phenomenon I call “troponin trumps common sense”**”

W. Bruce Fye, MD, MA, MACC

Troponin

- Troponin is a very sensitive marker of myocardial necrosis.
 - Useful when applied to correct clinical circumstances.
 - NOT USEFUL ACUTELY if applied indiscriminately.

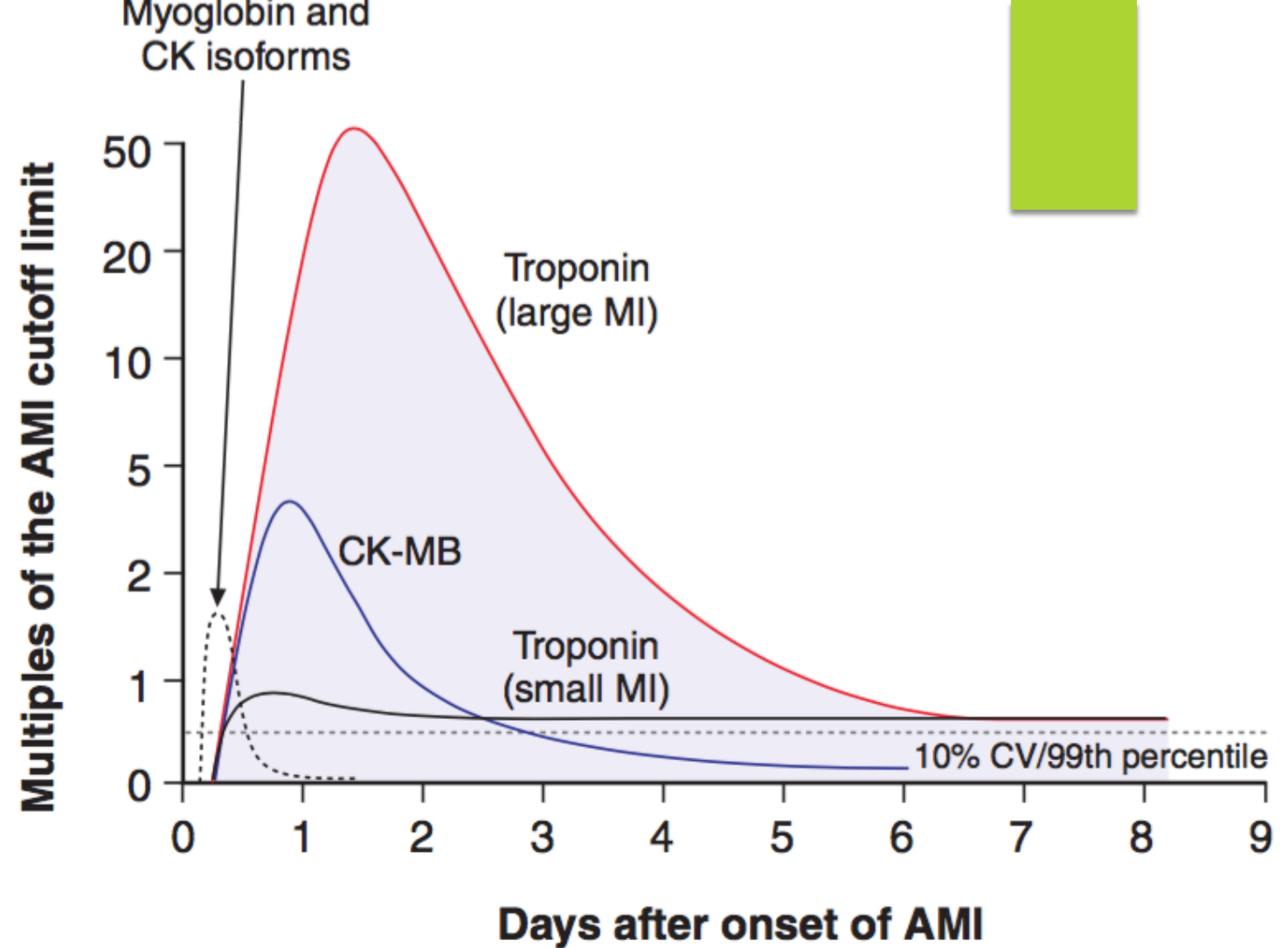
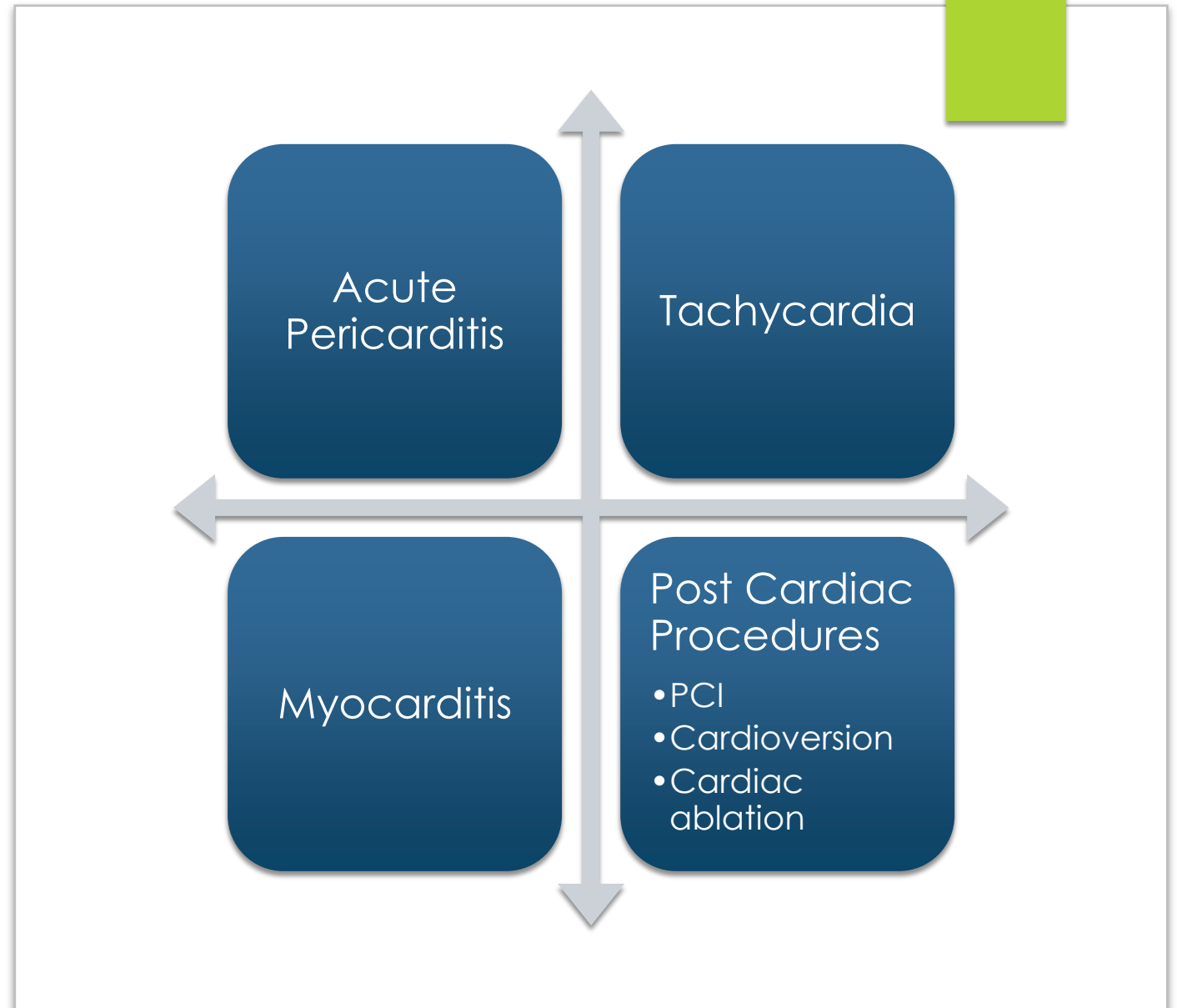


FIGURE 1-5 Time course of the appearance of various markers in the blood after acute myocardial infarction. (Reprinted from Jaffe AS, Babuin L, Apple FS. Biomarkers in acute cardiac disease—The present and the future. *J Am Coll Cardiol* 2006;48:4. Copyright © 2006, with permission from Elsevier.)

Non-Cardiac Causes of Troponin Elevation

- Chronic Renal Failure
- Advanced Heart Failure
- Subarachnoid Hemorrhage
- Ischemic Stroke
- Pulmonary Embolism
- Chronic Obstructive Pulmonary Disease
- **Acute non-cardiac illness**
- Strenuous Exercise
- Direct Myocardial Trauma

Non-Myocardial Infarction Cardiac Causes of Troponin Elevation



A Cardiologist's Nightmare

“Hi Doctor Hart, it's Doctor Stitch down in ER. We have a patient that came in with explosive diarrhea, we think it's gastroenteritis, but just to be sure what got an ECG and this new super ultra sensitive Troponin on him.

It's .0000000000016 and the normal is $<.0000000000015$. Do you want to admit?”





Stress Testing

Stress Testing

- ▶ There is no such thing as an urgent stress test.
- ▶ Inpatient stress testing is an outpatient test that we do to reassure ourselves and make patients feel better.
- ▶ Patients should not be admitted to the hospital just for a stress test, hospital admission for chest pain is appropriate if there is a concern for active ischemia or impending myocardial infarction for serial cardiac enzymes and ECGs.
- ▶ There is no role for stress testing in suspected unstable angina as it should not be used to rule in or out ACUTE coronary conditions.
- ▶ A normal stress test has a good prognosis for risk of cardiac events over the next year 1-3%.

Pre-Test Probability

- ▶ Patients with intermediate probability for CAD are appropriate for stress testing (25-75%.)
- ▶ Low probability (<25%) should not be tested.
- ▶ High probability(>75%) should go on to further invasive testing such as coronary angiography if clinically appropriate.
- ▶ Multitudes of cardiac risk calculators and chest pain indices exist.



My Bucket List

37. Climb Mount Everest

38. Run the Honolulu marathon

~~39. Incorporate an 80's videogame retromercial into a grand rounds~~

Pitfalls of Stress Testing



- ▶ Epicardial disease versus microcirculatory disease.
 - ▶ Microvascular disease can cause angina and stress test abnormalities including wall motion abnormalities and abnormal nuclear imaging.
- ▶ Post test referral(verification) bias.
 - ▶ Patients are generally referred to angiography for abnormal test results.
 - ▶ Artificially increases sensitivity and decreases specificity.
- ▶ Treadmill stress testing in women has had a traditionally lower predictive accuracy in women due to:
 - ▶ Lower prevalence of CAD than men.
 - ▶ Higher prevalence of non-obstructive CAD.
 - ▶ Higher incidence of false positive ST segment depression during exercise.

Exercise Physiology

Comparative Effectiveness of Exercise Electrocardiography With or Without Myocardial Perfusion Single Photon Emission Computed Tomography in Women With Suspected Coronary Artery Disease

Results From the What Is the Optimal Method for Ischemia Evaluation in Women (WOMEN) Trial

Leslee J. Shaw, PhD; Jennifer H. Mieres, MD; Robert H. Hendel, MD; William E. Boden, MD;
Martha Gulati, MD; Emir Veledar, PhD; Rory Hachamovitch, MD; James A. Arrighi, MD;
C. Noel Bairey Merz, MD; Raymond J. Gibbons, MD;
Nanette K. Wenger, MD; Gary V. Heller, MD, PhD; for the WOMEN Trial Investigators

- WOMEN trial randomized 824 women with intermediate risk of CAD to ECG exercise vs myocardial perfusion imaging.
- Found that treadmill ECG testing in women lead to more downstream testing, but was less costly overall. Clinical outcomes were similar.

Pre-Operative Stress Tests



On her 4th
cup of coffee



Training for her 15th
marathon

NAME THAT FISH



The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

DECEMBER 30, 2004

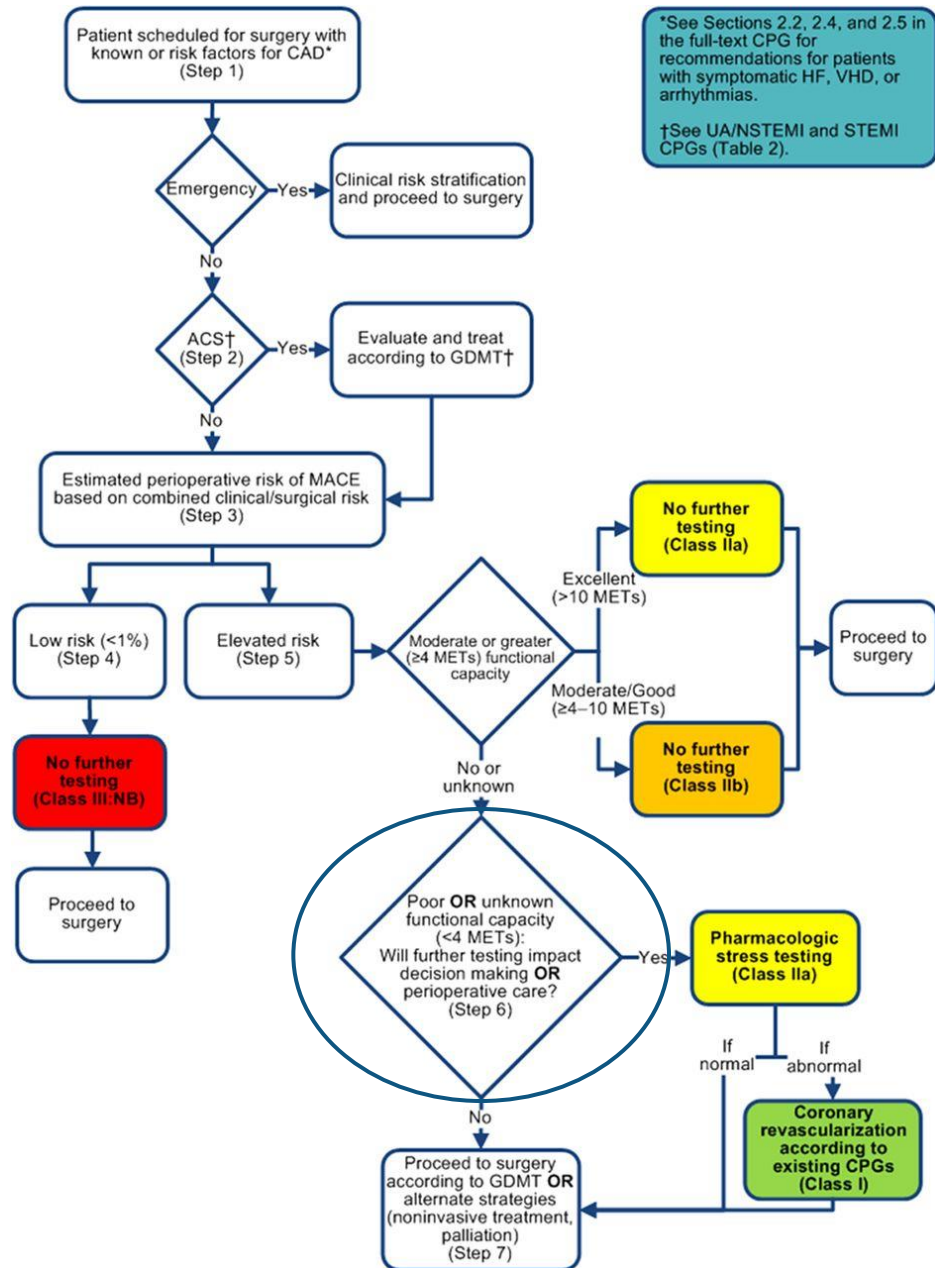
VOL. 351 NO. 27

Coronary-Artery Revascularization before Elective Major Vascular Surgery

Edward O. McFalls, M.D., Ph.D., Herbert B. Ward, M.D., Ph.D., Thomas E. Moritz, M.S., Steven Goldman, M.D., William C. Krupski, M.D.,* Fred Littooy, M.D., Gordon Pierpont, M.D., Steve Santilli, M.D., Joseph Rapp, M.D., Brack Hattler, M.D., Kendrick Shunk, M.D., Ph.D., Connie Jaenicke, R.N., B.S.N., Lizy Thottapurathu, M.S., Nancy Ellis, M.S., Domenic J. Reda, Ph.D., and William G. Henderson, Ph.D.

CONCLUSIONS

Coronary-artery revascularization before elective vascular surgery does not significantly alter the long-term outcome. On the basis of these data, a strategy of coronary-artery revascularization before elective vascular surgery among patients with stable cardiac symptoms cannot be recommended.



Pre-Operative Stress Testing

Pre-Operative Stress Tests

- ▶ Rarely appropriate.
- ▶ Costly
- ▶ Can lead to testing that may delay surgery, sometimes to the detriment of the patient.



Coronary Artery Calcium Score

Coronary Artery Calcium Score

- ▶ Uses low dose CT scan to quantify calcium burden in coronary arteries (Does not detect soft plaque.)
- ▶ Takes about 5 minutes
- ▶ One of the few studies that has no false positives.



Coronary Artery Calcium Score

- ▶ A score of zero has great prediction for low coronary heart event risk.
- ▶ In comparison to a score of zero, hazard ratios for coronary events at higher calcium scores:

1-100 **1.28**

101-1000 **3.04**

>1000 **7.77**

Journal of Cardiovascular Computed Tomography (2016) 1e11



Coronary Artery Calcium Score

- ▶ So when should we order this test?
- ▶ In moderate risk individuals in **whom the results will change your management.**
 - ▶ Very few people will fall into this category.



Coronary Artery Calcium Score

- ▶ CT calcium scores will be offered for very low prices by hospitals because they know it increases downstream testing.
- ▶ Asymptomatic patients end up getting stress tests and even cardiac catheterizations!



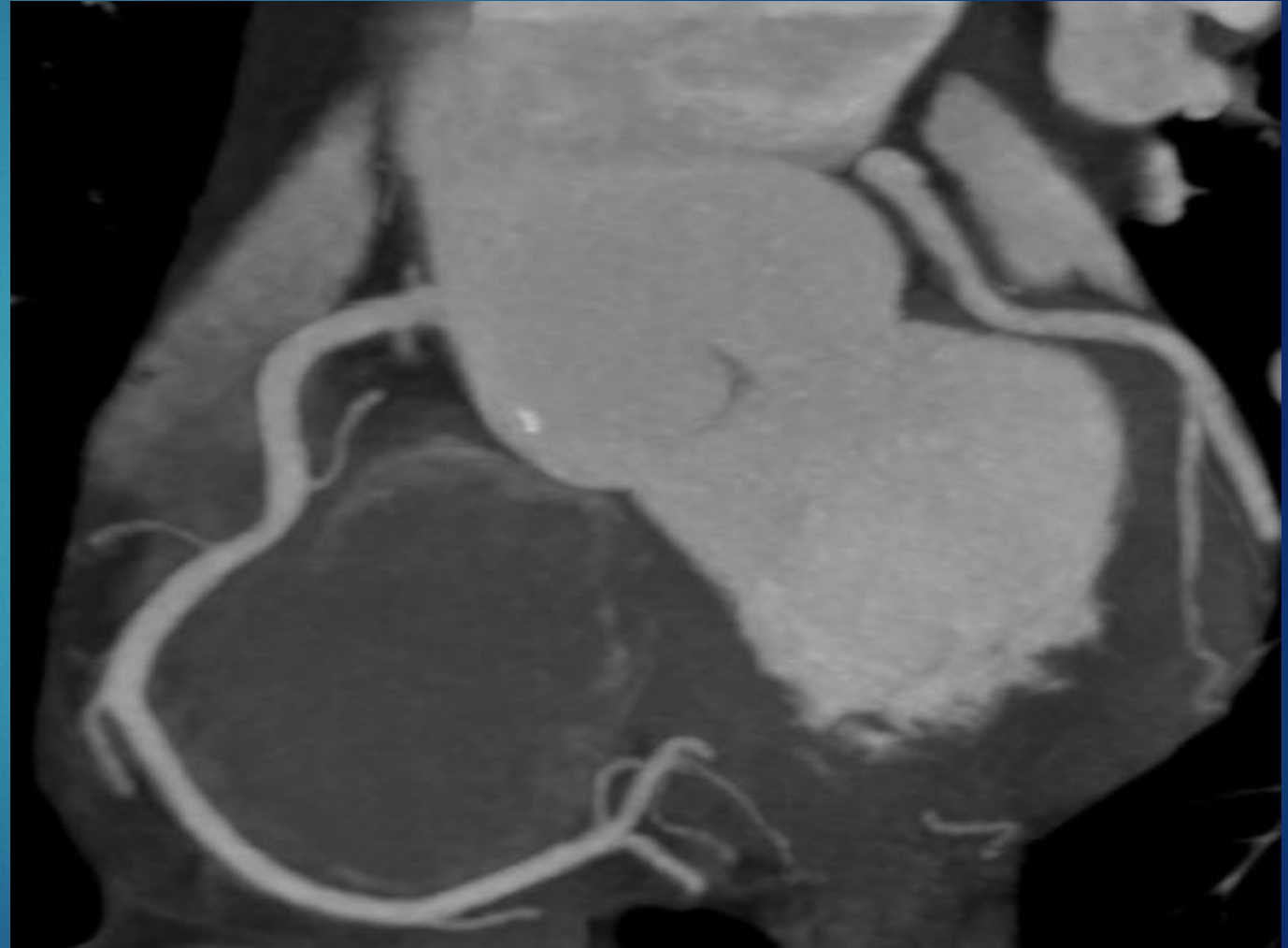
Coronary Computed Tomography Angiography

- ▶ High resolution non-invasive angiography of the coronaries.
- ▶ Rapid, readily available, in theory can be offered 24 hours a day (as long as readers are on call.)
- ▶ Can be used in a triple rule out protocol (PE, Aortic dissection and CAD.)
- ▶ Less risk than invasive coronary angiography.



Coronary Computed Tomography Angiography

- ▶ Not useful if a lot of calcium is present as there can be “blooming” artifact making lesions appear worse than they are.
- ▶ Can be difficult to get insurance approval as an outpatient.
 - ▶ Likely due to increased downstream testing.



Coronary Computed Tomography Angiography

- ▶ Radiation doses have been a concern in the past, but new techniques are lowering the dose.



Coronary Computed Tomography Angiography

- ▶ Who should we order this test in?
- ▶ Low-intermediate risk symptomatic patients for a “rapid rule” out in ER.
- ▶ Avoid using in higher CAD risk individuals, or those with known elevated coronary calcium score.



Comparison of the 2006 and 2010 Cardiac CT Appropriateness Criteria in a Real-World Setting

Sula Mazimba, MD, MPH^a, Nakash Grant, MD^a, Analkumar Parikh, MD^a,
Trupti Patel, MD^b, Bhakti Dahale, MD^b, Zurisadai Franco, MD^c,
Nathaniel Dittoe, MD^d, Tushar Shah, MD^e, Harvey S. Hahn, MD^a

Background: Coronary CT angiography (CCTA) is a relatively new technique whose role has yet to be fully defined. The initial appropriateness criteria (AC) guidelines published in 2006 have already been revised. There is paucity of data on the effect of the AC on the use of CCTA at academic centers and none for the private sector.

Methods: All CCTA studies ordered at one institution (a large community hospital with internal medicine and cardiovascular training programs) from 2006 to 2008 were retrospectively evaluated, and the ordering indications were categorized per the published AC for both 2006 and 2010.

Results: There were 384 studies, of which 243 were included in this study. The majority of the studies were ordered for chest pain (67.1% of patients). A significant proportion of studies (43.2%) were classified as inappropriate on the basis of the 2006 published criteria. Uncertain indications made up 39.1%, and appropriate indications were a minority. There was a significant regrading of appropriateness using the 2010 guidelines. Inappropriate testing remained similar at 48.1%, but uncertain cases decreased to only 2.8%, while appropriateness increased to 49.0% ($P = .0001$ for trend).

Conclusions: The updated 2010 AC guidelines for CCTA resulted in a significant reclassification of the indications for ordering CCTA from the previous 2006 guidelines. This shift in the AC reflects increased familiarity and confidence with this new technology across the imaging community. A large proportion of CCTA studies were ordered for inappropriate indications using both sets of criteria. Further research and enhanced education are needed to disseminate the appropriate role of CCTA in cardiovascular imaging.

Key Words: Cardiac CT, appropriate use criteria, coronary artery disease

J Am Coll Radiol 2012;9:630-634. Copyright © 2012 American College of Radiology

Echocardiography



Echocardiography

- Non-invasive.
- Readily available.
- Can give a lot of cardiac structural and hemodynamic information.
- Safe.
- Makes it a very attractive test.
- Very easy to “just order an echo”
- A lot of echos ordered are not needed though.



Echocardiography

- Who needs an echo?
- How often does someone need an echo?
- Inappropriate uses of echocardiography



Echocardiography Inappropriate Uses

- Routine evaluation in the setting of mild chest trauma with no electrocardiographic changes or biomarker elevation.
- Transient fever without evidence of bacteremia or a new murmur.
- Transient bacteremia with a pathogen not typically associated with infective endocarditis and/or a documented nonendovascular source of infection.
- Routine surveillance of uncomplicated infective endocarditis when no change in management is contemplated.



Echocardiography Inappropriate Uses

- Routine surveillance (<1 y) of HF (systolic or diastolic) when there is no change in clinical status or cardiac exam.
- Routine surveillance (<1 y) of known cardiomyopathy without a change in clinical status or cardiac exam.



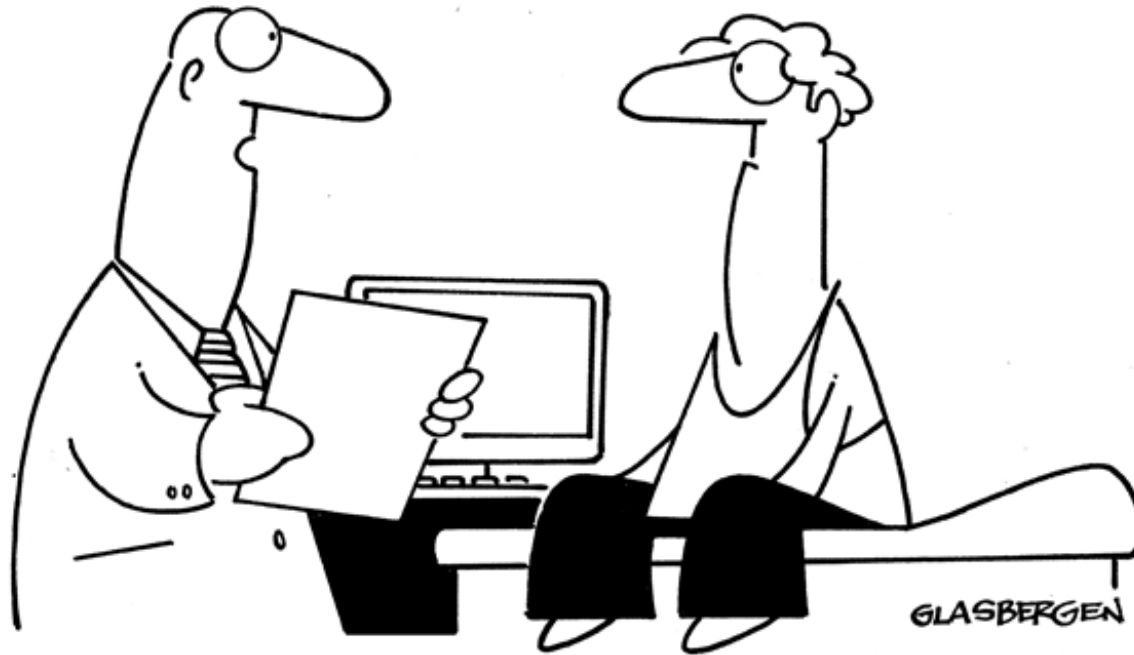
Echocardiography

- Always ask “How will this change my management?”
- I would argue that an 89 year old patient with know frequent exacerbations of systolic HF and an EF of 20% since 2014 on optimal medical therapy with a Biventricular ICD who presented 3 months ago with a similar CHF exacerbation and has had an echocardiogram 6 months ago gets absolutely NO benefit from an echocardiogram.



Advanced Lipid Particle Testing

© Randy Glasbergen
glasbergen.com



“Your good cholesterol is fine, but your bad cholesterol is plotting to hack into your computer, empty your bank account and steal your wife.”

Lipid Equations

$$\text{LDL} = \text{Total cholesterol} - \text{HDL} - (\text{TG}/5)$$

$$\text{Non-HDL cholesterol} = \text{Total cholesterol} - \text{HDL}$$

Advanced Lipid Particle Testing

- ▶ Multiple advanced lipid profile panels exists.
- ▶ Often offered as a part of a screening test.
- ▶ More in depth than traditional panels (LDL HDL TG)

LDL Size

- ▶ Size of LDL particles has been thought to be associated with how atherogenic they are.
- ▶ Multiple studies have shown correlation between small dense LDL particles and higher risk of CAD.
- ▶ Large LDL particles are still atherogenic though.
- ▶ Further studies have shown correlation of small LDL particles with CAD is weaker than once thought.
- ▶ Unclear how LDL size would change patient management.

HDL Size

- ▶ These particles varies in size as well.
- ▶ The metabolism and function of these particles is not well understood.
- ▶ Very little data supporting hypothesis that HDL subfractions provide additional risk prediction over total HDL and other traditional risk factors.

Apolipoprotein B (Apo-B)

- ▶ All of the pro atherogenic lipoproteins carry one Apo-B on their surface.
 - ▶ Represents total number of atherogenic particles.
- ▶ Better than LDL for prediction of CAD.
- ▶ May be minimally better than non-HDL cholesterol.
- ▶ Amount of benefit that this additional information can give us is still up for debate, likely does not justify routine testing.

LDL Particle Number

- ▶ Number of LDL particles can vary and don't always correlate with LDL levels.
- ▶ Number of LDL particles are strongly associated with CAD.
- ▶ Again, not much better than non-HDL cholesterol.

Lipoprotein A Lp(a)

- ▶ Lp(a) is a LDL particle with apoprotein (a) particle on it.
- ▶ Levels can vary in people substantially.
- ▶ Does not correlate with LDL, non-HDL, Apo(B) or LDL particle number.
- ▶ Strongly associated with CAD, and calcific aortic stenosis.
- ▶ Patients with high Lp(a) may have statin “resistance” meaning their LDL does not drop as much as expected.
 - ▶ Statins do not decrease Lp(a.)
- ▶ No specific therapy for high Lp(a.)

Lipoprotein A Lp(a)

- ▶ May be useful in screening some patients:
 - ▶ Statin resistant.
 - ▶ Strong family history of premature CAD.
 - ▶ Unexplained progression of atherosclerosis.
 - ▶ Familial hypercholesterolemia.

Advanced Lipid Particle Testing

- ▶ For the most part do not offer much more useful information.
- ▶ Some rare exception with Lp(a).
- ▶ In full disclosure I've never ordered a panel.

High Sensitivity CRP



High Sensitivity CRP

- ▶ Has been evaluated as a marker for risk of cardiac events for years.
- ▶ In the past it's utility has been questioned.
- ▶ Specifically how will this change management?
- ▶ There have been no proven anti-inflammatory drugs other than statins that reduce risk of CAD...until now.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

SEPTEMBER 21, 2017

VOL. 377 NO. 12

Antiinflammatory Therapy with Canakinumab for Atherosclerotic Disease

P.M. Ridker, B.M. Everett, T. Thuren, J.G. MacFadyen, W.H. Chang, C. Ballantyne, F. Fonseca, J. Nicolau, W. Koenig, S.D. Anker, J.J.P. Kastelein, J.H. Cornel, P. Pais, D. Pella, J. Genest, R. Cifkova, A. Lorenzatti, T. Forster, Z. Kobalava, L. Vida-Simiti, M. Flather, H. Shimokawa, H. Ogawa, M. Dellborg, P.R.F. Rossi, R.P.T. Troquay, P. Libby, and R.J. Glynn, for the CANTOS Trial Group*

ABSTRACT

BACKGROUND

Experimental and clinical data suggest that reducing inflammation without affecting lipid levels may reduce the risk of cardiovascular disease. Yet, the inflammatory hypothesis of atherothrombosis has remained unproved.

METHODS

We conducted a randomized, double-blind trial of canakinumab, a therapeutic monoclonal antibody targeting interleukin-1 β , involving 10,061 patients with previous myocardial infarction and a high-sensitivity C-reactive protein level of 2 mg or more per liter. The trial compared three doses of canakinumab (50 mg, 150 mg, and 300 mg, administered subcutaneously every 3 months) with placebo. The primary efficacy end point was nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death.

RESULTS

At 48 months, the median reduction from baseline in the high-sensitivity C-reactive protein level was 26 percentage points greater in the group that received the 50-mg dose of canakinumab, 37 percentage points greater in the 150-mg group, and 41 percentage points greater in the 300-mg group than in the placebo group. Canakinumab did not reduce lipid levels from baseline.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Ridker at the Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital, 900 Commonwealth Ave., Boston, MA 02215, or at pridker@partners.org.

*A complete list of members of the Canakinumab Antiinflammatory Thrombosis Outcome Study (CANTOS) Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Libby and Glynn contributed equally to this article.

This article was published on August 27, 2017, at NEJM.org.

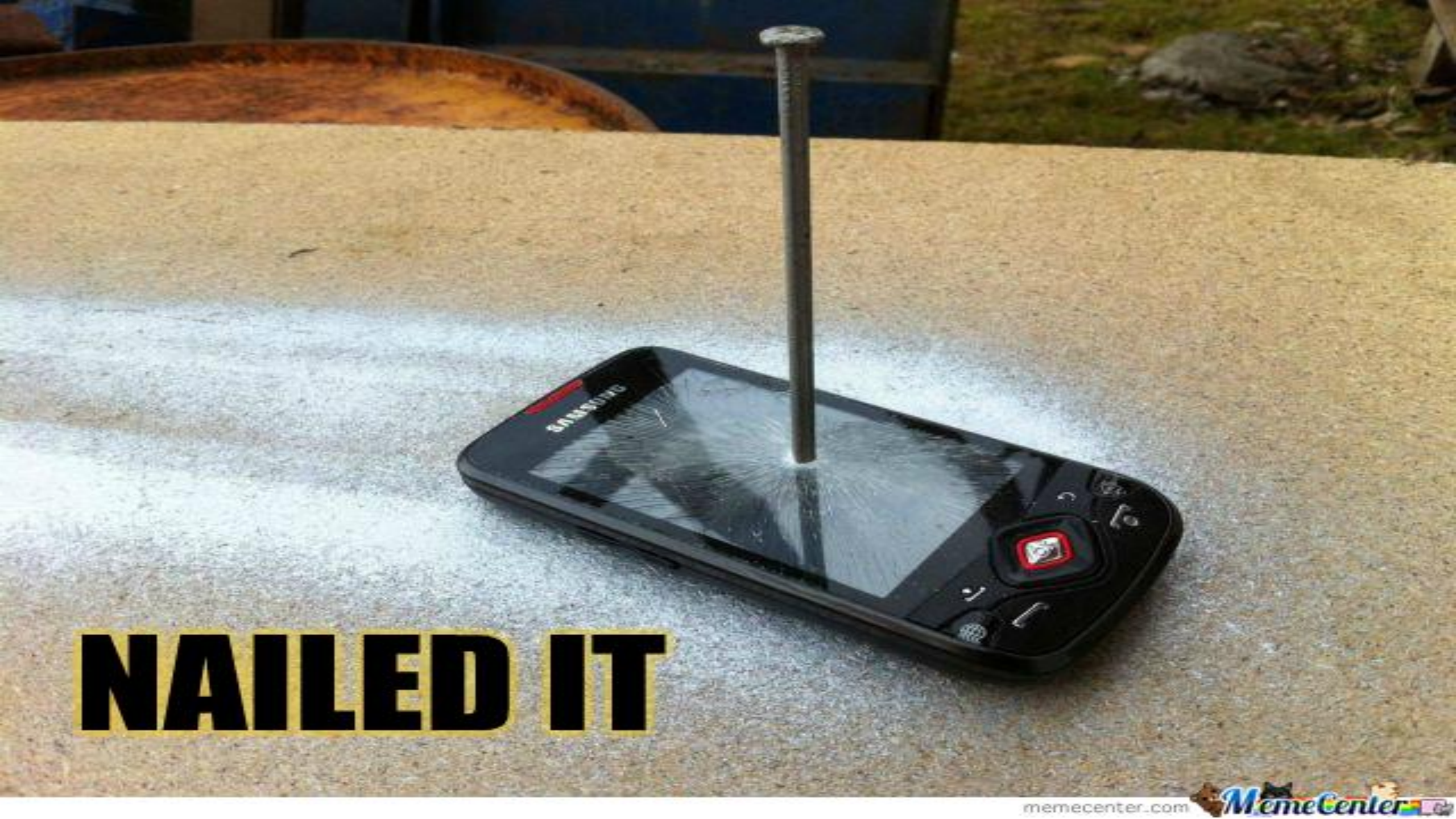
N Engl J Med 2017;377:1119-31.
DOI: 10.1056/NEJMoa1707914

CONCLUSIONS

Antiinflammatory therapy targeting the interleukin-1 β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo, independent of lipid-level lowering. (Funded by Novartis; CANTOS ClinicalTrials.gov number, NCT01327846.)

High Sensitivity CRP

- ▶ This will likely change the way we approach some patients.
- ▶ Up to 50% of people have myocardial infarctions do not have abnormal cholesterol profiles.
- ▶ Further analysis of data are forthcoming.



NAILED IT

QUESTIONS?

