Best Approaches in the Evaluation of Patients with Coronary Artery Disease

James Sawalla Guseh, M.D.
Program Director, Sports Cardiology Fellowship
Cardiovascular Performance Program
Massachusetts General Hospital
jguseh@mgh.harvard.edu

@JSawallaGusehMD

Cardiovascular Performance Program

Disclosures

No commercial or financial disclosures.

Diagnostics of Stable CAD

J. Sawalla Guseh, M.D.

Therapeutic Approach to CAD

David M. Dudzinski, M.D., J.D.

Approach to ACS

Marc S. Sabatine, M.D., M.P.H.

By the Numbers

- **15.6 million** patients with CAD
- **1.4 million** discharges a year for CAD
- **2.3 million** clinic visits for angina
- **8.2 million** patients with angina

- Death/MI: **3 - 4% per year** in stable CAD on therapy

Mazaffarian 2016, Eisen 2016, Boden 2007, Frye 2009, De Bruyne 2012, Maron 2020.

Audience Question #1

Most stable angina presentations describe chest discomfort of approximately what duration?

a. 30 seconds
b. 3 minutes
c. 30 minutes
d. 3 hours

Answer (B): 3 minutes

Most stable angina presentations last **3-5 minutes** and are usually less than 10 minutes in duration.

Chapter 1:

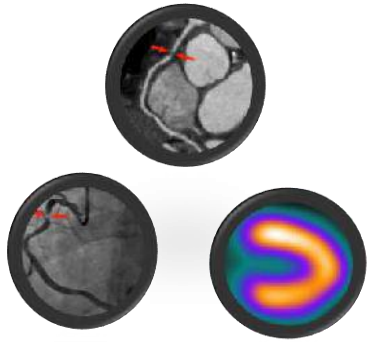
Assess Syndrome Stability

Exclude ACS

Chapter 2:

Estimate CAD probability

(low risk → non-CAD approach)



Chapter 3:

Confirm Disease and Mortality Risk

Select a diagnostic test

Chapter 1:

Is this Stable Angina and what is the syndrome severity?

Strategy: To entrain CAD into your differential diagnosis and exclude an acute coronary syndrome

Stable Ischemic Heart Disease

(Stable CAD; Chronic Coronary Syndrome; Stable Angina)

Chronic Coronary Syndrome / Stable Angina	Angina is stable when the symptom pattern is predictable and unchanged over the course of several weeks. Fluctuation is permitted with emotional stress and changes in ambient temperature. This reflects quiescent progressive coronary plaque.

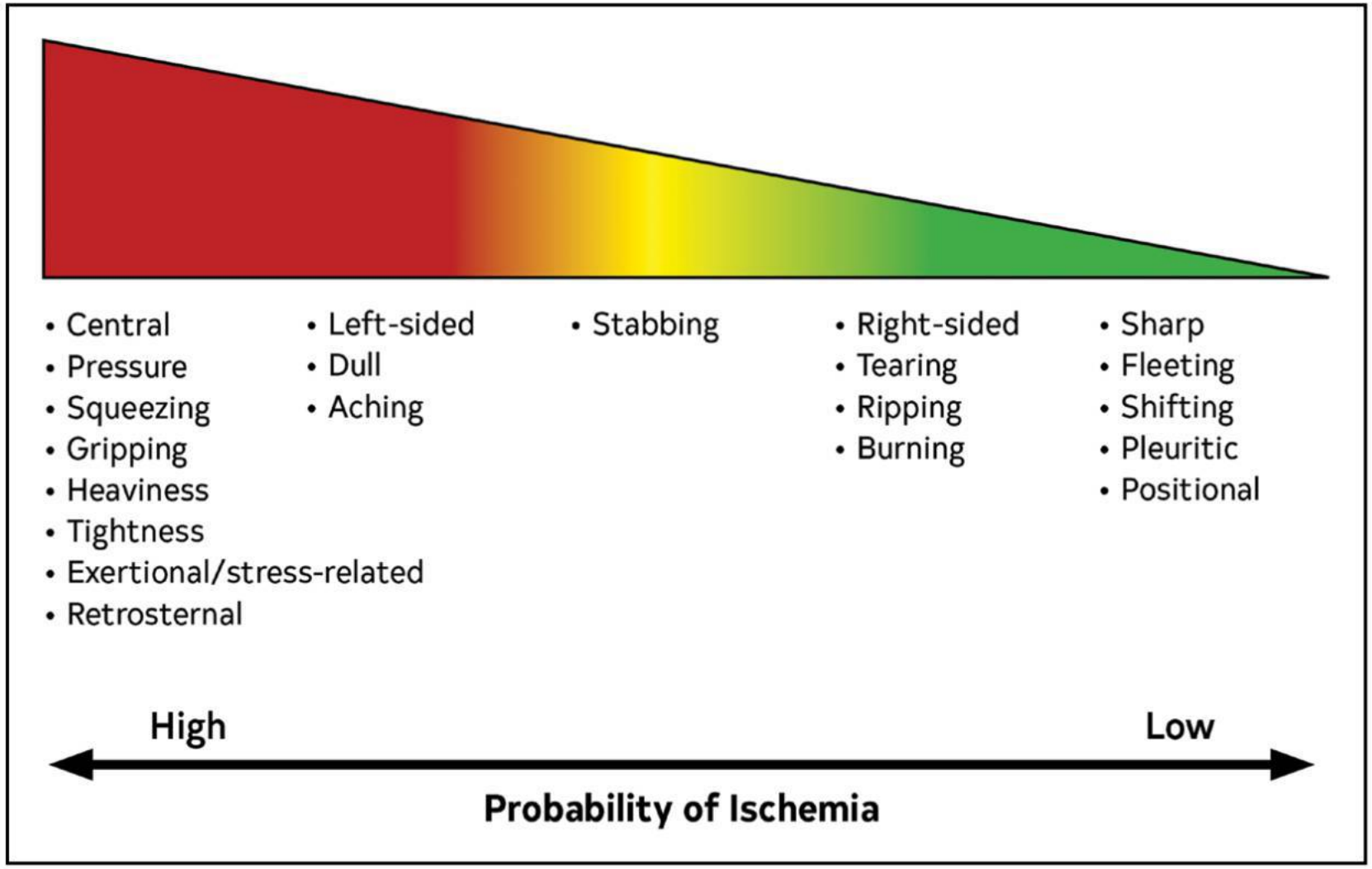
Stable Ischemic Heart Disease

(Stable CAD; Chronic Coronary Syndrome; Stable Angina)

Chronic Coronary Syndrome / Stable Angina	Angina is stable when the symptom pattern is predictable and unchanged over the course of several weeks. Fluctuation is permitted with emotional stress and changes in ambient temperature. **This reflects quiescent progressive coronary plaque.**
Acute Coronary Syndrome/ Unstable Angina	Angina is unstable when the symptom pattern abruptly worsens (frequency or duration) without a cause of increased myocardial oxygen consumption. **This reflects plaque rupture, erosion, and thrombosis.**

Assess for Symptoms and Stability

(Lo …on)



O	
P	P
Q	
R	
S	
T	

…ea

…ional,

…**1.3)**, ill

…ms on a …d?

…etting?

Increasing frequency? Duration?

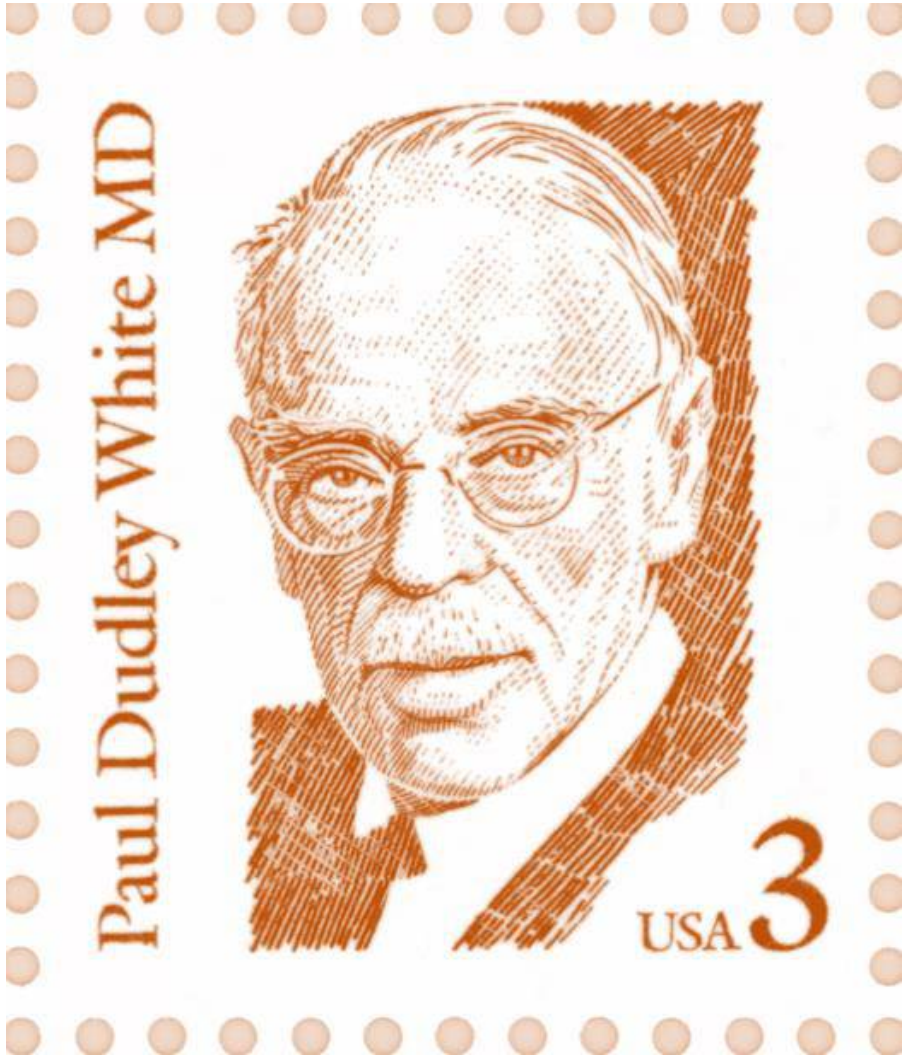
Discomfort Duration is useful

T	**Timing**	Constant vs Intermittent? **Abrupt** or Gradual? Has it happened before and in what setting? **Increasing frequency**? **Duration? Frequency?**

1. Ischemic pain typically lasts 3- 5 minutes (usually less than 10 minutes).
2. It doesn't usually last longer than 30 minutes without causing myocardial infarction.
3. Pain that lasts less than 1 minute is unlikely to be coronary in origin.

Grade Severity

Angina pectoris is often mild, especially at its onset. It does not need to be severe; it may be merely a sensation of slight pressure on some effort that would not normally bring it on. The amount of exercise is more important than the amount of pain. The presence of even mild substernal discomfort on effort is more important than the severity of the pain. The severity of the discomfort or pain is largely dependent on the sensi-



Paul Dudley White's 1942 Lecture in Manchester New Hampshire

Canadian Cardiovascular Society Classification

More Severe

CCS Class	Definition	Comment
I	Angina with strenuous exertion	No angina walking, stairs
II	Angina with moderate exertion	Pain when walking quickly, after a meal, in the cold. **Can walk 2 blocks and climb a flight of stairs without angina.**
III	Angina with mild exertion	Angina when climbing 1 flight of stairs or walking 1-2 blocks.
IV	Rest Angina	Severe limitation. Rest angina or minimal activity.

Exclude Unstable Syndromes

Three Principal Presentations of Unstable Angina	
Rest Angina	Angina Occurring at Rest and usually prolonged > 20 minutes, occurring **within 1 week of presentation**
New Onset Angina	Angina of at least CCS Class III severity with onset **within 2 months of initial presentation**
Increasing Angina	Previously diagnosed angina that is distinctly **more frequent, longer in duration or lower in threshold**. Increasing by 1 or more CCS class within 2 months of initial presentation to at least CCS Class III severity.

E. Braunwald. Unstable angina: A classification. Circulation, 80 (1989).

Who's the Host (Risk Factors)
Smoking (tobacco, cocaine)
Diabetes
Dyslipidemia
Hypertension
Premature Family History

Who's the Host (Risk Factors)	Exacerbating Features
Smoking (tobacco, cocaine)	Hypertension
Diabetes	Valvular Heart Disease
Dyslipidemia	Tachyarrhythmias (e.g. nocturnal angina attributed to nightmares)
Hypertension	Anemia
Premature Family History	

Who's the Host (Risk Factors)	Exacerbating Features	Biochemical Evaluation
Smoking (tobacco, cocaine)	Hypertension	CBC
Diabetes	Valvular Heart Disease	Creatinine
Dyslipidemia	Tachyarrhythmias (e.g. nocturnal angina attributed to nightmares)	Lipid Profile
Hypertension	Anemia	TSH
Premature Family History		HbA1c

*NT-proBNP and high sensitivity troponin

- ❑ History: Pressure, Squeezing, Heavy or Tight?
- ❑ Seconds, minutes, or hours?
- ❑ Happening at rest, new, crescendo?

Chapter 1: Consider Syndrome Stability. Exclude ACS.

ACS
(Dr. Sabatine)

Establish Stability and Severity of the Syndrome

Estimate the Likelihood of CAD

Chapter 2:

What is the pre-test likelihood of obstructive CAD?

Strategy: Identify the patient with a low pretest probability of obstructive coronary artery disease by history and epidemiology

Audience Question #2

What is average LDL cholesterol (mg/dL) in America and median age of first myocardial infarction in men?

a. 130, Age 55

b. 100, Age 60

c. 130, Age 65

d. 160, Age 70

What is average LDL cholesterol (mg/dL) in America and median age of first myocardial infarction in men?

Answer (C): 130, Age 65

The average LDL-C in the US ~ 130 mg/dL

The median age of first MI in men is at age 65.

The median age of first MI in women is age 72.

Historical: Typical or Atypical Classification

Three "Classical" Narrative Features of Angina
Substernal chest discomfort (with a characteristic quality and duration)
Provoked by **exertion** or emotional **stress**
Relieved by **rest** or *nitroglycerin**

Historical: Classify Chest Pain

Features	Classification	
0 - 1	Nonanginal chest pain	Noncardiac
2	Atypical angina	Probable
3	Typical angina	Definite

The typical/atypical and nonanginal paradigm has been used repeatedly to estimate the likelihood of CAD in symptomatic patients.

ANALYSIS OF PROBABILITY AS AN AID IN THE CLINICAL DIAGNOSIS OF CORONARY-ARTERY DISEASE

GEORGE A. DIAMOND, M.D., AND JAMES S. FORRESTER, M.D.

Abstract The diagnosis of coronary-artery disease has become increasingly complex. Many different results, obtained from tests with substantial imperfections, must be integrated into a diagnostic conclusion about the probability of disease in a given patient.

To approach this problem in a practical manner, we reviewed the literature to estimate the pretest likelihood of disease (defined by age, sex and symptoms) and the sensitivity and specificity of four diagnostic tests: stress electrocardiography, cardiokymography, thallium scintigraphy and cardiac fluoroscopy. With this information, test results can be analyzed by use of Bayes' theorem of conditional probability.

This approach has several advantages. It pools the diagnostic experience of many physicians and integrates fundamental pretest clinical descriptors with many varying test results to summarize reproducibly and meaningfully the probability of angiographic coronary-artery disease. This approach also aids, but does not replace, the physician's judgment and may assist in decisions on cost effectiveness of tests. (N Engl J Med 300:1350-1358, 1979)

Table 1. Prevalence of Angiographic Coronary-Artery Disease in Symptomatic Patients.

SYMPTOM	PROPORTION OF PATIENTS AFFECTED	POOLED MEAN ± SEP* (%)
Nonanginal chest pain	146/913	16.0±1.2
Atypical angina	963/1931	49.9±1.1
Typical angina	1874/2108	88.9±0.7

*Standard error of the per cent (see the Appendix). These values establish statistical levels of error but do not include errors due to sampling bias & other factors, which are probably of greater magnitude.

Diamond and Forester. NEJM. 1979

Age, sex, and symptom triangulates pretest likelihood of CAD

Increasing Likelihood

Table 3. Pretest Likelihood of Coronary-Artery Disease in Symptomatic Patients According to Age and Sex.*

AGE	NONANGINAL CHEST PAIN		ATYPICAL ANGINA		TYPICAL ANGINA	
YR	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
30–39	5.2±0.8	0.8±0.3	21.8±2.4	4.2±1.3	69.7±3.2	25.8±6.6
40–49	14.1±1.3	2.8±0.7	46.1±1.8	13.3±2.9	87.3±1.0	55.2±6.5
50–59	21.5±1.7	8.4±1.2	58.9±1.5	32.4±3.0	92.0±0.6	79.4±2.4
60–69	28.1±1.9	18.6±1.9	67.1±1.3	54.4±2.4	94.3±0.4	90.6±1.0

*Each value represents the per cent ±1 standard error of the per cent, calculated from the data in Tables 1 & 2 as described in the Appendix.

12% (1X) 37% (3X) 74% (6X)

Increasing Likelihood

Diamond and Forester. NEJM. 1979

CAD Risk Factors amplify baseline risk

Pretest likelihood of CAD (%)						
	Nonanginal (≤ 1 sx)		Atypical Anginal (2)		Typical Angina (all 3 sx)	
Age	Men	Women	Men	Women	Men	Women
35	3 → 35	1 → 19	8 → 59	2 → 39	30 → 88	10 → 78
45	6 → 47	2 → 22	21 → 70	5 → 43	51 → 92	29 → 79
55	23 → 59	4 → 21	45 → 79	10 → 47	80 → 95	38 → 82
65	49 → 69	9 → 29	71 → 86	20 → 51	93 → 97	56 → 84

Within each cell a → b represents likelihood without risk factors (a) and with all risk factors (b) with include diabetes, smoking, and hypercholesterolemia. Note that there are varying thresholds for intermediate risk (e.g. 10 – 90%, or 20 – 80%).

Pryor et al. Ann Intern Med. 1993.

Pretest likelihood in symptomatic patients (with shortness of breath stratified)

Table 5 **Pre-test probabilities of obstructive coronary artery disease in 15 815 symptomatic patients according to age, sex, and the nature of symptoms in a pooled analysis[64] of contemporary data[7,8,62]**

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

CAD = coronary artery disease; PTP = pre-test probability.

[a]In addition to the classic Diamond and Forrester classes,[59] patients with dyspnoea only or dyspnoea as the primary symptom are included. The regions shaded dark green denote the groups in which non-invasive testing is most beneficial (PTP >15%). The regions shaded light green denote the groups with PTPs of CAD between 5–15%, in which testing for diagnosis may be considered after assessing the overall clinical likelihood based on the modifiers of PTPs presented in *Figure* 3.

Knuuti and others, 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

Low Likelihood Groups Correspond to Premature CAD cutoffs

Table 3. Pretest Likelihood of Coronary-Artery Disease in Symptomatic Patients According to Age and Sex.*

AGE	NONANGINAL CHEST PAIN		ATYPICAL ANGINA		TYPICAL ANGINA	
YR	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
30–39	5.2±0.8	0.8±0.3	21.8±2.4	4.2±1.3	69.7±3.2	25.8±6.6
40–49	14.1±1.3	2.8±0.7	46.1±1.8	13.3±2.9	87.3±1.0	55.2±6.5
50–59	21.5±1.7	8.4±1.2	58.9±1.5	32.4±3.0	92.0±0.6	79.4±2.4

Take Home: Look for <u>non-anginal</u> (or non-cardiac) histories in men < 55 and women < 60.

	Typical		Atypical		Non-anginal		Dyspnoea[a]	
Age	Men	Women	Men	Women	Men	Women	Men	Women
30–39	3%	5%	4%	3%	1%	1%	0%	3%
40–49	22%	10%	10%	6%	3%	2%	12%	3%
50–59	32%	13%	17%	6%	11%	3%	20%	9%
60–69	44%	16%	26%	11%	22%	6%	27%	14%
70+	52%	27%	34%	19%	24%	10%	32%	12%

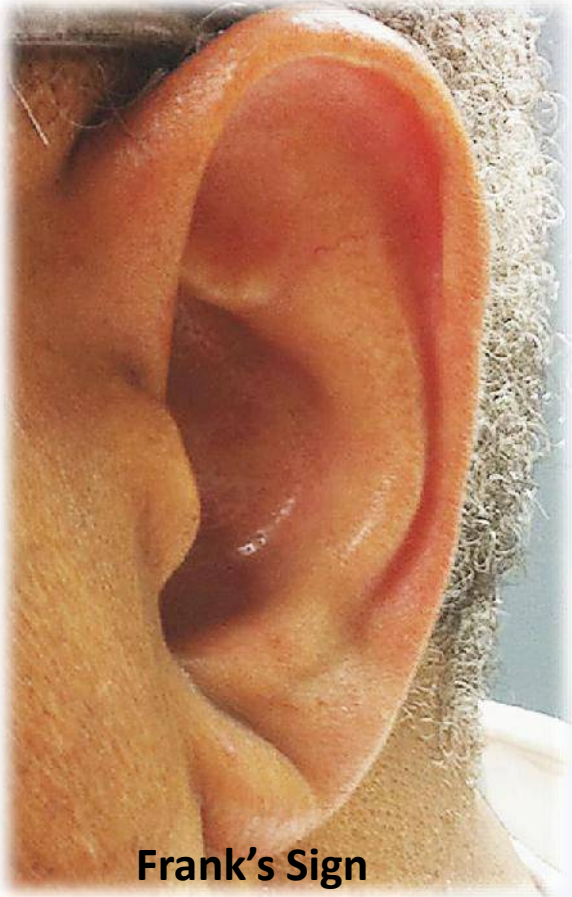
Avoid using and dismissing "atypical chest pain"

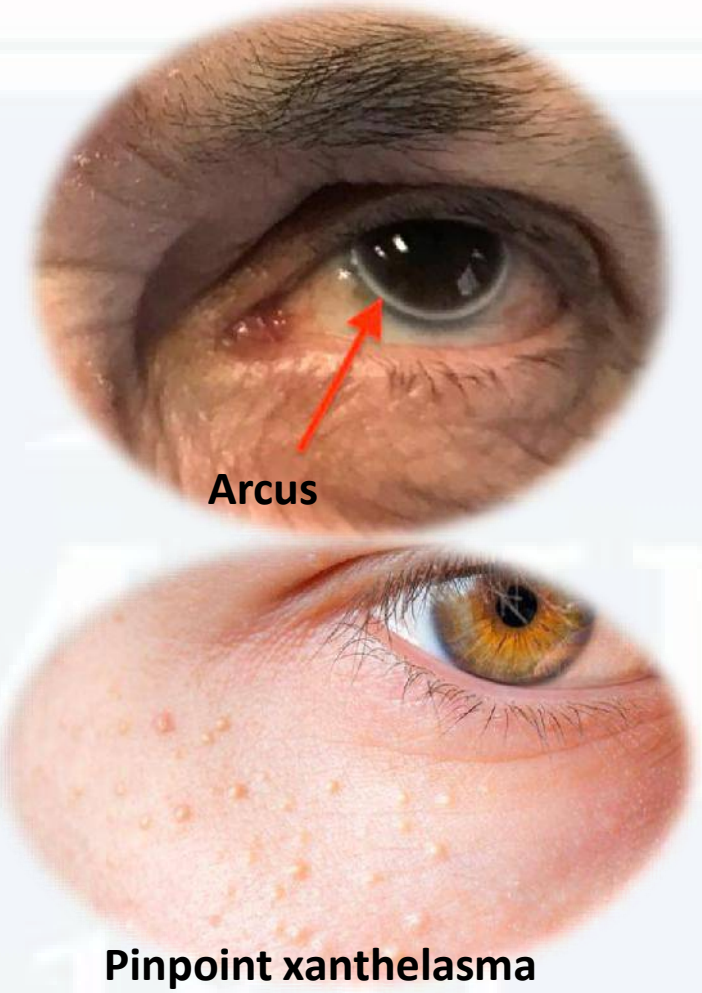
1	C-LD	2. Chest pain should not be described as atypical, because it is not helpful in determining the cause and can be misinterpreted as benign in nature. Instead, chest pain should be described as cardiac, possibly cardiac, or noncardiac because these terms are more specific to the potential underlying diagnosis.

Gulati et al. 2021 ACC/AHA Chest Pain Guidelines.

The examination is rarely rewarding

- Pedal Edema
- Jugular Venous Distension
- S3 gallop, a new murmur
- Orthopnea
- Hypertension
- Corneal Arcus
- Xanthelasma
- Vascular Bruits
- Other Stigmata of CAD


Frank's Sign

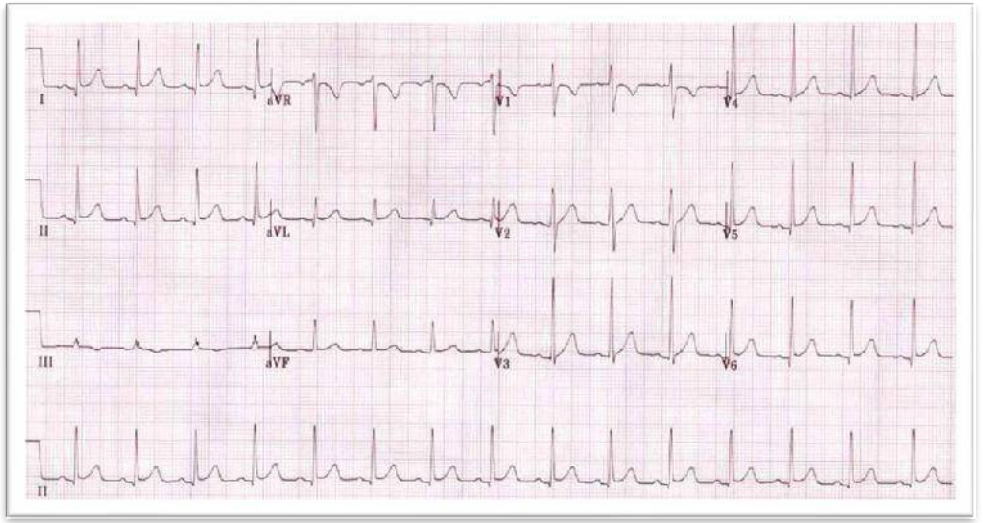

Arcus

Pinpoint xanthelasma

BMJ 2018;360:j5884, Griffing. N Engl J Med 2014; 370:e15

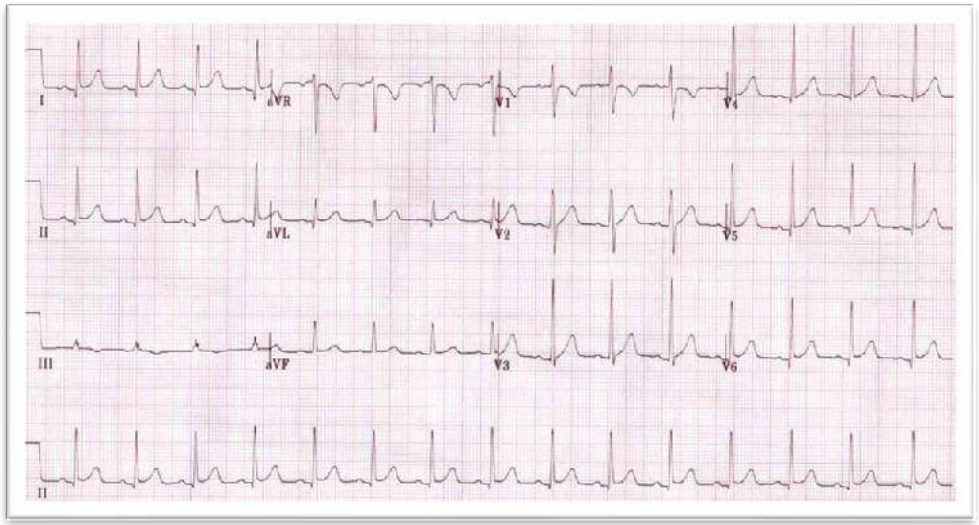
Resting Electrocardiogram (ECG)

- Examine carefully for Infarction (Q-waves)
- Remember Poor R-wave Progression can be a Q-wave equivalent
- Look for territorial fractured QRS complexes
- Look for abundant PVCs
- Note the presence or absence of LVH and ST repolarization abnormalities



~7:50

If your ECG (or exam) is abnormal consider an echocardiogram



Evidence of Infarction
Abundant PVCs or complex arrhythmias
Clinical HF
New murmur

Rest Transthoracic Echocardiogram

If your ECG is abnormal consider an echocardiogram

Recommendations	Class[a]	Level[b]
A resting transthoracic echocardiogram is recommended in all patients for: (1) Exclusion of alternative causes of angina; (2) Identification of regional wall motion abnormalities suggestive of CAD; (3) Measurement of LVEF for risk stratification; and (4) Evaluation of diastolic function.[44,45,52,58]	I	B

Rest Transthoracic Echocardiogram

2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes

After a history, physical, and ECG you should come away with a sense of whether the patient is **low likelihood** of CAD.

		Older with RFs	*Younger without RFs*
		High Likelihood of CAD	**Low Likelihood of CAD**
Good story	**Cardiac or Possibly Cardiac**	High	Intermediate low
Poor story	**Non-Cardiac**	Intermediate high	**Low**

***Typical and Atypical angina are now cardiac and possibly cardiac chest pain.**

The value of estimating the upfront probability of CAD is to identify those with a low probability of SIHD who benefit from an eval focusing on non-CAD causes of chest pain.

Nonischemic Cardiovascular
- Aortic Dissection
- Pericarditis

Pulmonary
- Embolus
- Pneumothorax
- Pneumonia
- Pleuritis

Gastrointestinal
- Esophagitis, Esophageal Spasm, Reflux
- Biliary Colic, Colecystitis, Choledocolithiasis, Cholangitis
- Peptic Ulcer, Pancreatitis

Hematological: Sickle Cell, Polycythemia Vera

Chest Wall
Constochondrosis
Fibrositis
Rib Fracture
Sternoclavicular arthritis
Herpes Zoster (before rash)

Psychiatric
Anxiety disorders
Hyperventilation
Panic Disorder
Primary anxiety
Affective disorders
Somatoform Disorders (e.g. depression)
Thought Disorders (e.g. fixed delusions)

Quick Examples

- **Case 1:** 40M with chest discomfort after eating but not worse with exertion not better with rest. Nonanginal chest pain.

- **Case 2:** 40M with chest discomfort after eating and worse when he takes a walk but not clearly better with rest. Possible Cardiac Chest pain.

- **Case 3:** 40M with chest discomfort after eating, worse when he does hills, better if he stops. High probability cardiac chest pain.

- ❑ Story: Noncardiac, possibly/probably cardiac?
- ❑ Epidemiology. < Men 55. < Women 60.
- ❑ Abnormal Exam? Abnormal ECG?

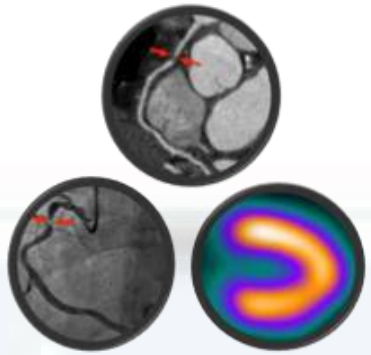
Chapter 2: Likelihood of CAD. Identify the low risk.

Establish Stability and Severity of the Syndrome

ACS
(Dr. Sabatine)

Estimate the Likelihood of CAD

Low Likelihood
(Non-Coronary Testing)



Choose Your Diagnostic Test to Estimate Risk