



A SYSTEMATIC APPROACH TO MEDICALLY  
UNEXPLAINED SYMPTOMS

---

# Chronic Non-Cardiac Chest Pain & Palpitations

Jeffrey B. Geske, MD  
Professor of Medicine

August 17-20, 2022  
*The Ritz-Carlton, Half Moon Bay*

**@MayoClinicGIM**  
**@jeffreygeske**



# Disclosure

## Relevant Financial Relationships

None

## Off-Label/Investigational Uses

None

# Acknowledgement

**Michael W. Cullen, MD**

**Coronary vasospasm**

**Angina**

**Congestive  
heart failure**

**Gastroesophageal  
reflux**

**Pleurisy**

**COPD**

**Atrial  
fibrillation**

**Atrial  
flutter**

**Chronic chest  
pain and  
palpitations**

**Pericarditis**

**Depression**

**Costochondritis**

**Anxiety**

**Cardiomyopathies**

**Obstructive  
sleep apnea**

**Supraventricular  
tachycardia**

**Ventricular  
tachycardia**

# Learning objectives

1. Differentiate important clinical diagnoses that might be dismissed as medically unexplained chest pain or palpitations.
2. Review the evaluation and management of patients with specific conditions that frequently present as chronic chest pain or palpitations.
3. Manage patients with otherwise undiagnosed chronic chest pain or palpitations.

# Case #1

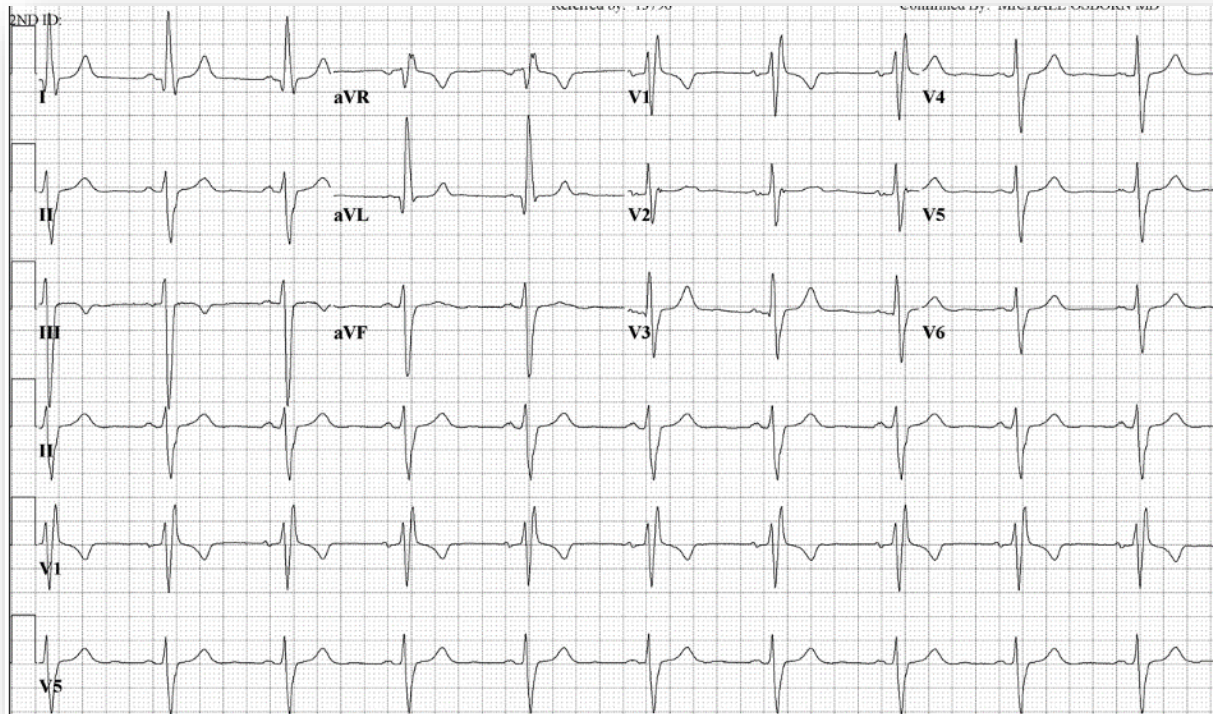
# 59-year-old female

- 4-6 months of progressive “tightening” in chest radiating to jaw
- Worse with stress or physical activity
- Better with rest
- Associated with exertional dyspnea
- Cardiac risk factors
  - Diabetes mellitus
  - Hypertension
  - Prior smoking
  - Hyperlipidemia

# 59-year-old female

## Exertional chest tightness

- Atenolol 100 mg daily





# Assessment of chest pain

Sub-sternal chest pain or discomfort	Typical angina = all 3
Provoked by exertion or emotional stress	Atypical angina = 2 of 3
Relieved by rest and / or nitroglycerin	Non-anginal chest pain = 0-1 of 3

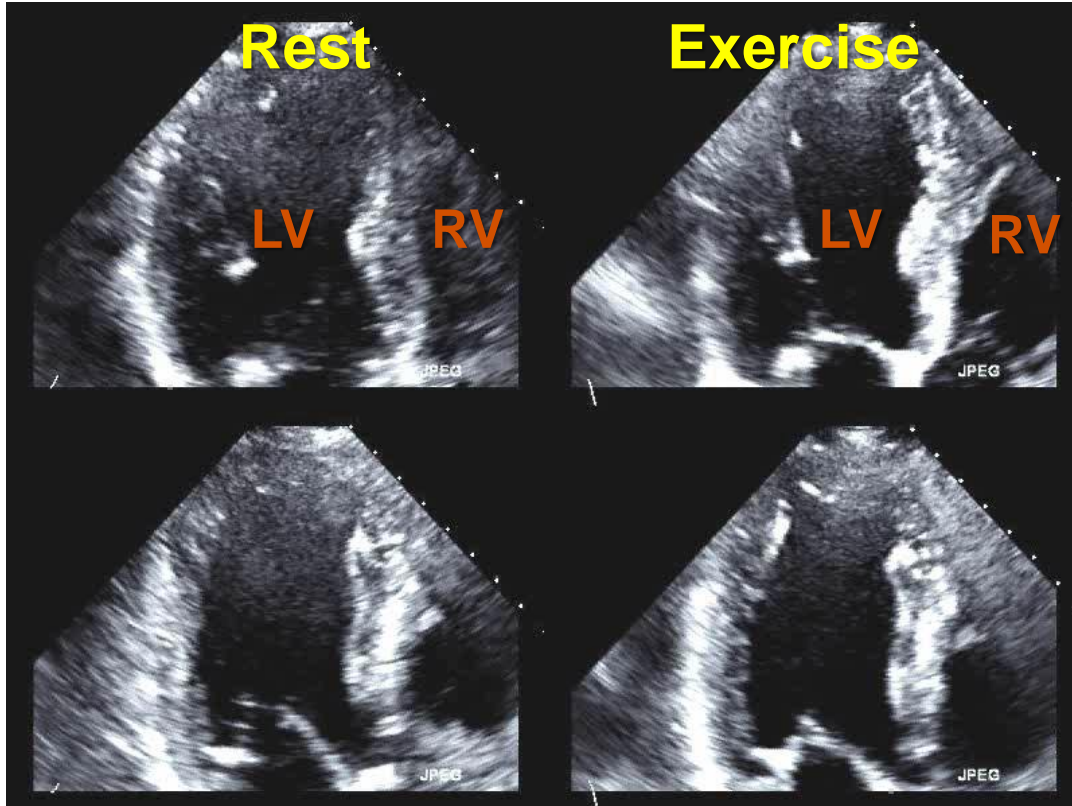
Age	Sex	Typical angina	Atypical angina	Non-anginal chest pain
≤39	Male	Intermediate	Intermediate	Low
	Female	Intermediate	Very low	Very low
40-49	Male	High	Intermediate	Intermediate
	Female	Intermediate	Low	Very low
50-59	Male	High	Intermediate	Intermediate
	Female	Intermediate	Intermediate	Low
≥60	Male	High	Intermediate	Intermediate
	Female	High	Intermediate	Intermediate

Category	Pre-test probability
High	≥90%
Intermediate	10-90%
Low	5-10%
Very low	≤5%

# Exercise echocardiogram

- Remained in Stage 1 of Bruce protocol
- Chest pain with exercise
- Peak heart rate → 111 bpm (69% predicted)
- Peak double product → 19,092 bpm x mmHg
- No ischemic ECG changes

# Exercise echocardiogram



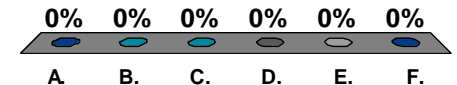
@MayoClinicGIM

# Exercise echocardiogram

- Negative for ischemia at the workload achieved
- Limited exercise capacity
- Ejection fraction 65% → 70%
- No stress-induced regional wall motion abnormalities

# What is your next step?

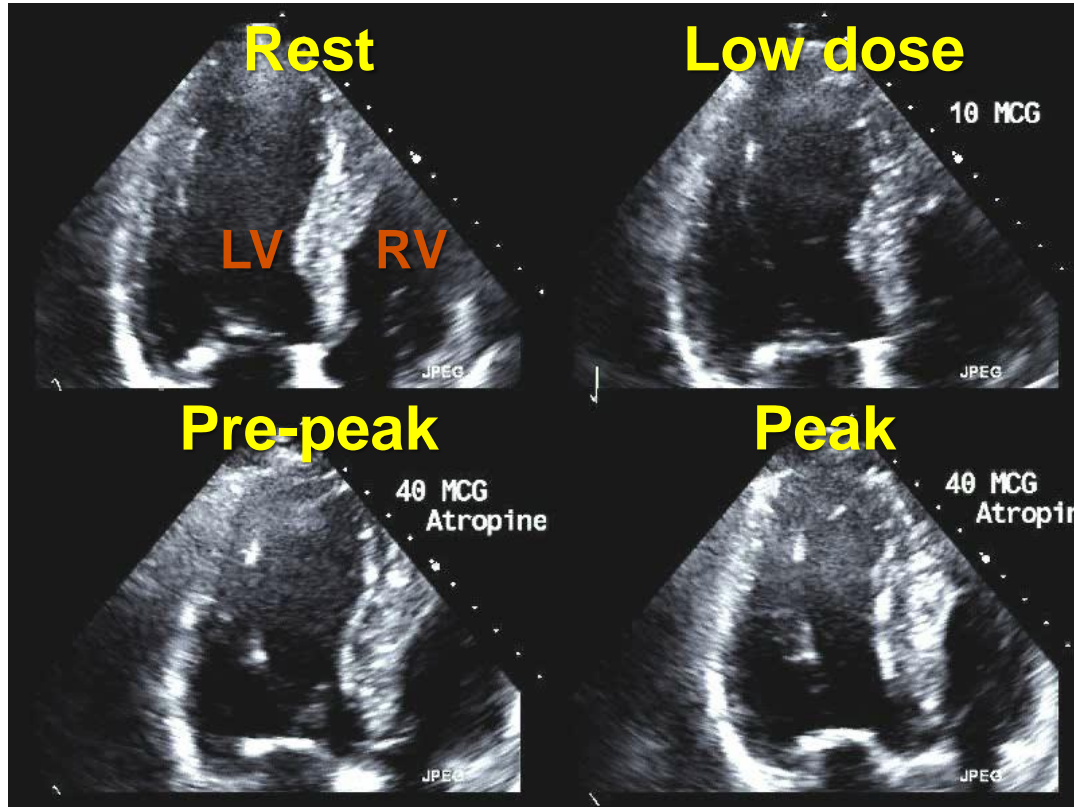
- A. Observation
- B. Exercise sestamibi test
- C. Regadenoson sestamibi test
- D. Dobutamine stress echo
- E. CT coronary angiogram
- F. Invasive coronary angiogram



# Dobutamine echocardiogram

- Dobutamine: 5 → 40 mcg/kg/min
- Atropine 2 mg
- Peak heart rate → 125 bpm (78% age-predicted maximum)
- No ECG changes

# Dobutamine echocardiogram



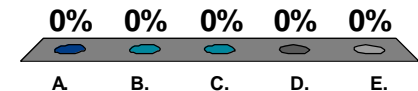
# Dobutamine echocardiogram

- Negative for ischemia
- Ejection fraction 65% → 75%
- No stress-induced regional wall motion abnormalities



# What is your next step?

- A. Observation
- B. Regadenoson sestamibi test
- C. Dobutamine stress MRI
- D. CT coronary angiogram
- E. Invasive coronary angiogram



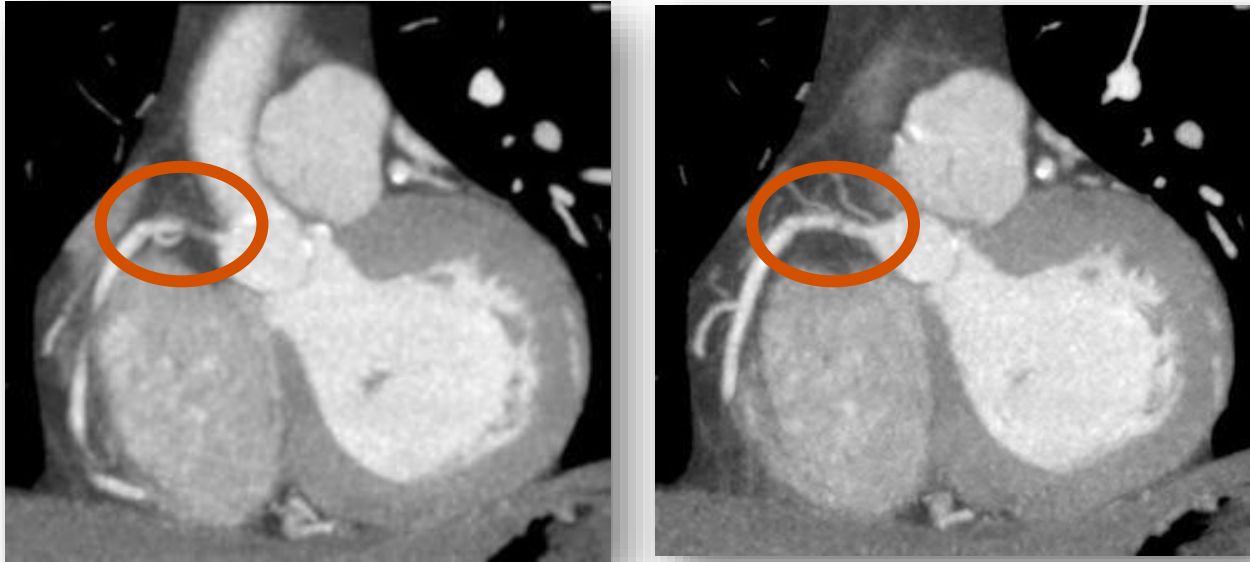
# Patient had symptoms very typical for angina...

Category	Pre-test probability
High	$\geq 90\%$
Intermediate	10-90%
Low	5-10%
Very low	$\leq 5\%$

**Symptoms were progressing**

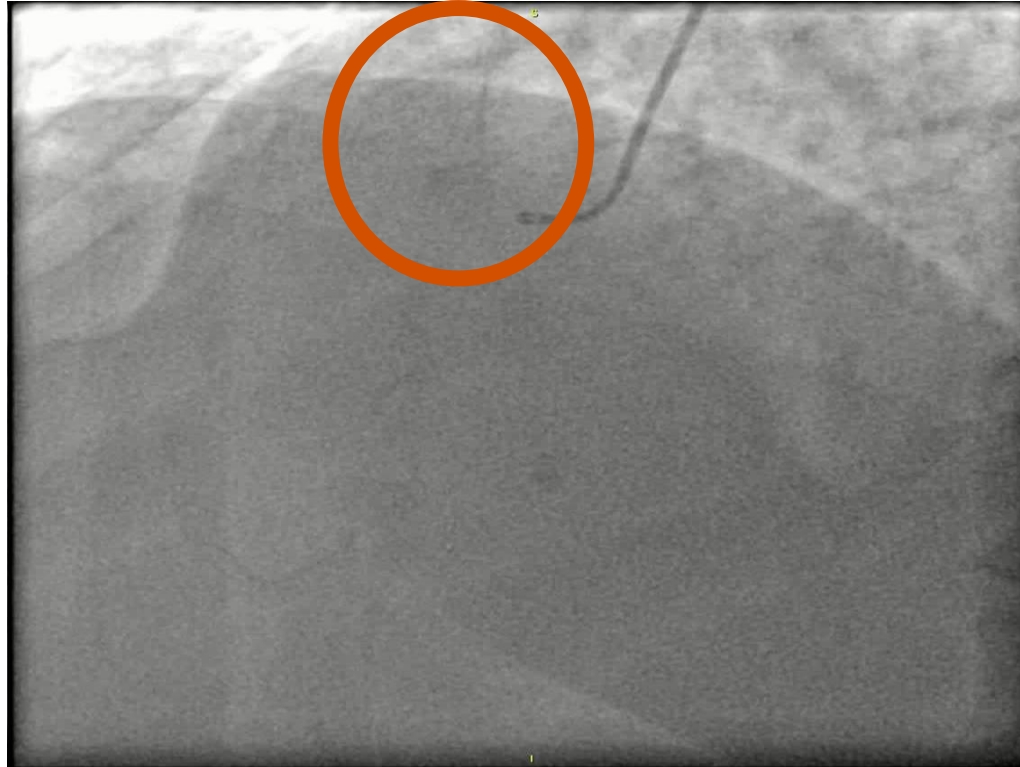
**Low workload on treadmill test**

# CT coronary angiogram



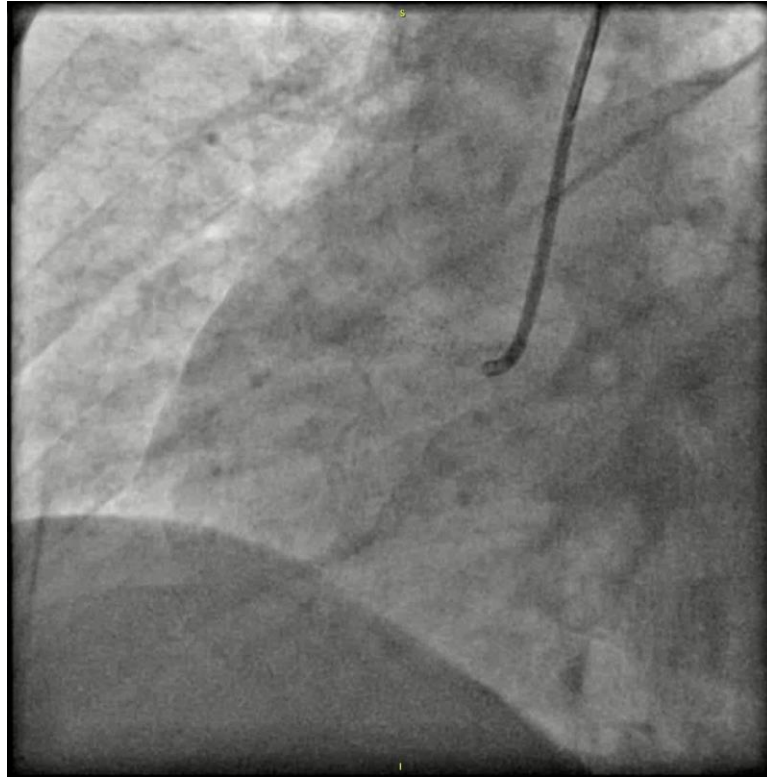
**Focal stenosis in proximal RCA due to non-calcified plaque**

# Invasive coronary angiogram



@MayoClinicGIM

# Drug eluting stent to RCA



@MayoClinicGIM

# Why the negative stress echoes?

## Myocardial oxygen demand

- Heart rate
- Afterload
- Wall tension
- Contractility

### Surrogates

Heart rate  
Blood pressure  
Double product

Atenolol 100 mg daily

↓ exercise capacity

↓ HR and BP response

↓ myocardial O<sub>2</sub> demand

↓ sensitivity of test

**If the pre-test probability is high and the stress test results don't fit, keep looking!**

# How can you keep looking?

## CT coronary angiography

- Anatomic assessment of coronaries in patients with chest pain
- NOT same as a coronary calcium score!
  - Uses contrast
  - Requires ECG gating
  - Can be done with a coronary calcium score
- High negative predictive value
- Less accurate in calcified vessels

# CT coronary angiography

## What do the guidelines say?

**Class IIa**

**CT coronary angiography is reasonable for the diagnosis of CAD in intermediate risk patients with...**

 **Symptoms despite prior normal testing**

**Inconclusive results from prior testing**

**Inability to undergo traditional stress testing**



# 59-year-old female

## Exertional chest tightening



**Recognize symptoms of typical angina in patients with chronic chest pain**

**Sub-sternal chest pain or discomfort**

**Provoked by exertion or emotional stress**

**Relieved by rest and / or nitroglycerin**

**If the stress test is negative and the pre-test probability is high, coronary CTA is an appropriate next step**

# **A quick word on other causes of chronic anginal pain...**

**Vasospastic angina  
“Prinzmetal angina”  
“Variant angina”**

**Nitrate responsive angina  
Frequently nocturnal**

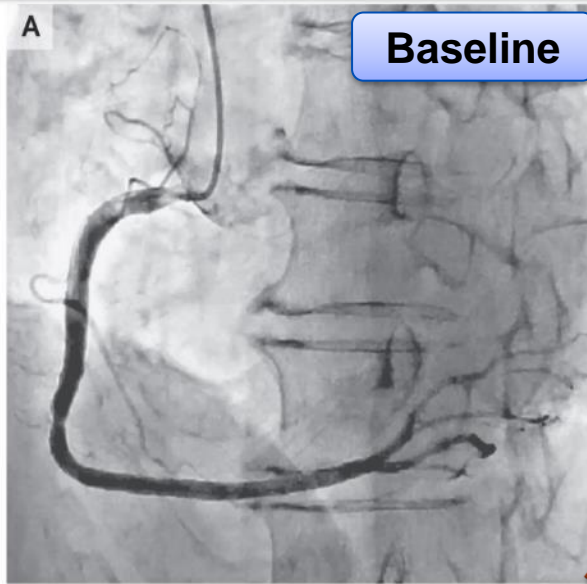
**Ischemic ECG changes  
associated with pain**

**Coronary artery spasm on  
provocative testing**

**Microvascular angina  
“Cardiac syndrome X”**

# Coronary artery vasospasm

52-year-old man with 1 month of nightly chest pain, responsive to nitroglycerin



**Vasospastic angina  
“Prinzmetal angina”  
“Variant angina”**

**Nitrate responsive angina  
Frequently nocturnal**

**Ischemic ECG changes  
associated with pain**

**Coronary artery spasm on  
provocative testing**

**Smoking cessation and lifestyle  
are critical!**

**CCB's (i.e. diltiazem) are 1<sup>st</sup> line  
therapy**

**Microvascular angina  
“Cardiac syndrome X”**

**Exertional angina  
Ischemic stress tests**

**Normal epicardial coronaries**

**No epicardial coronary artery  
vasospasm with provocation**

**Abnormal coronary  
microvascular function**

**Sublingual nitroglycerin is 1<sup>st</sup>  
line therapy**

# Case #2

# 26-year-old female

- 1-2 years of palpitations
- <1-minute, multiple times per day
- Worse with stress or exercise
- Associated fleeting, sharp chest pain
- No pre-syncope or syncope
- No regular medications
- No other cardiac risk factors

# 26-year-old female

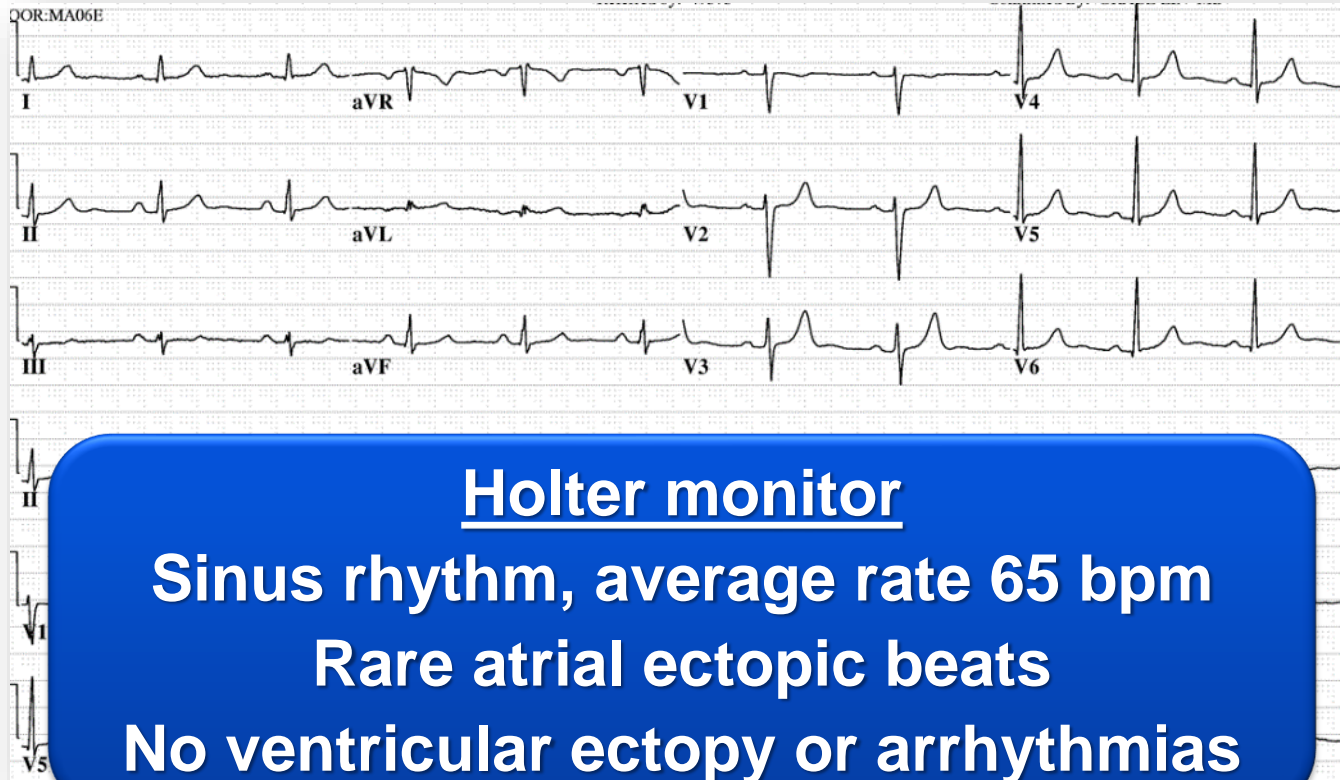
## Palpitations and chest pain

- Normal vital signs
- Normal S1 and S2
- Mid-systolic click at apex
- 2/6 late systolic murmur at apex
- Prolongation of murmur with squat to stand



# 26-year-old female

## Palpitations and chest pain



# 26-year-old female

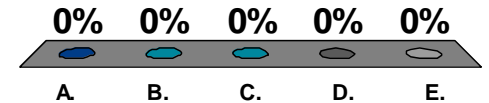
## Palpitations and chest pain



**Normal LV size, EF 65%**  
**Myxomatous mitral valve leaflets**  
**Bileaflet mitral valve prolapse**  
**Mild mitral regurgitation**

# What is your next step?

- A. Exercise stress echocardiogram
- B. 30-day event monitor
- C. Transesophageal echocardiogram
- D. Electrophysiology referral for ICD implantation
- E. Reassurance & repeat echocardiogram in 3 years



# Mitral valve prolapse syndrome

## Mild mitral regurgitation and the mitral prolapse fiasco

Aubrey Leatham\*  
Wallace Brigden\*\*  
London, England

*American Heart Journal*  
May, 1980, Vol. 99, No. 5

## *Editorial Comment*

---

## **Prolapse Paranoia\***

KENNETH M. KESSLER, MD, FACC

*Miami, Florida*

**JACC Vol. 11, No. 1  
January 1988:48-9**

# BRITISH MEDICAL JOURNAL

LONDON, SATURDAY 23 JUNE 1984

---

**Mitral valve prolapse: harbinger of death or variant of normal?**

# Malignant mitral valve prolapse

Small portion of patients with MVP have  $\uparrow$  risk of sudden cardiac death

Pre-syncope or syncope

T-wave inversion

QTc prolongation

Polymorphic PVCs or ventricular tachycardia

Mitral annular dysjunction

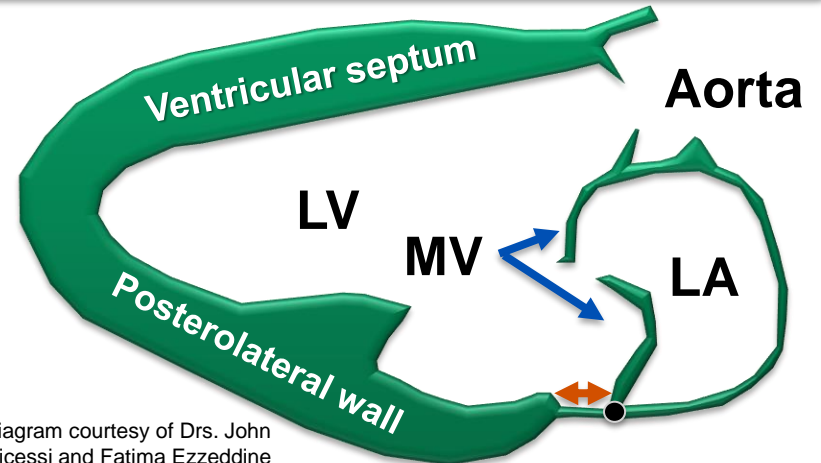


Diagram courtesy of Drs. John Giudicessi and Fatima Ezzeddine

# Mitral valve prolapse syndrome

**3488 patients  
Framingham Study**

Clinical finding	Mitral valve prolapse (n=84)	No mitral valve prolapse (n=3407)
	no. (%)	
Congestive heart failure	0	25 (0.7)
Atrial fibrillation	1 (1.2)	58 (1.7)
Cerebrovascular disease	1 (1.2)	52 (1.5)
Syncope	3 (3.6)	103 (3.0)

**No difference in clinical findings**

**No difference in coronary disease or coronary risk factors**

**Patients with mitral valve prolapse more likely to have mitral regurgitation**

**Degree of mitral regurgitation associated with risk of arrhythmias**

# Mitral valve prolapse syndrome

**“Indeed, mitral valve prolapse is evolving into an interesting cause of mitral regurgitation rather than into a unique syndrome.”**

# Monitoring mitral valve prolapse

Frequency of echocardiograms in mitral regurgitation and normal left ventricular function

Symptoms	Severity	Frequency
No	Mild	3-5 years
No	Moderate	1-2 years
No	Severe	6-12 months
Yes	Severe	Operate!



# What is your next step?

- A. Exercise stress echocardiogram
- B. 30-day event monitor
- C. Transesophageal echocardiogram
- D. Electrophysiology referral for ICD implantation
- E. Reassurance & repeat echocardiogram in 3 years

**No risk factors for CAD**

**Benign Holter monitor, no risk factors for arrhythmias**

**Not additive to TTE in this case**

**No malignant features**

**Reassurance that palpitations are benign, chest pain non-cardiac. Monitor for mitral regurgitation**

# 26-year-old female

## Palpitations and chest pain



**Mitral valve prolapse is a primary valvular abnormality, not a clinical syndrome.**

**Evaluate chronic chest pain and palpitations in patients with mitral valve prolapse like you would any other patient.**

**Understand the intervals for surveillance echocardiography in patients with mitral regurgitation.**

# Case #3

# 42-year-old male

- 4 months of sharp chest discomfort
- Worse with deep breathing, laying supine
- Better sitting upright
- Otherwise, healthy, no cardiac risk factors
- Training for a marathon
  - No symptoms during exertion
  - Symptoms worse after exertion

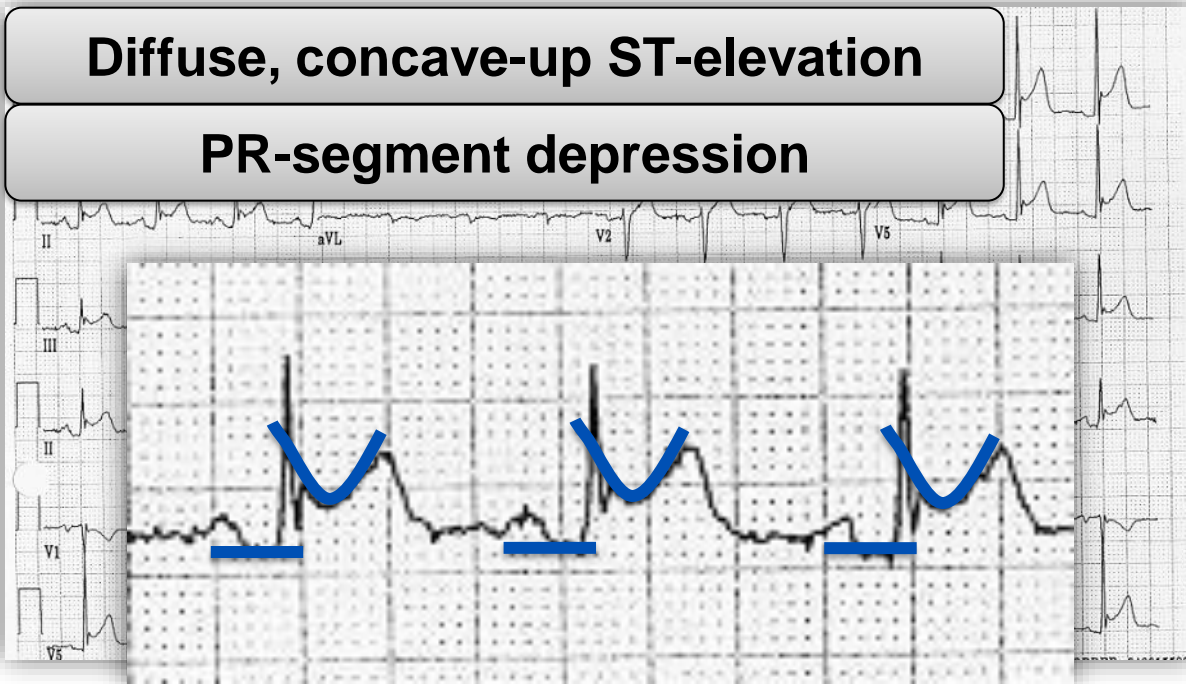
# 42-year-old male

## Sharp chest discomfort

**Presented to ED 4 months ago**

**Diffuse, concave-up ST-elevation**

**PR-segment depression**



**Diagnosed with acute pericarditis**

**Treated with NSAIDs x2 weeks**

**Symptoms initially improved**

**Returned after ~3 weeks, now less severe**

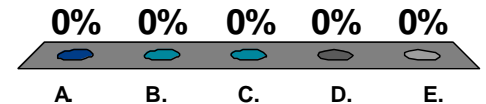
# 42-year-old male

## Sharp chest discomfort

- Vitals, physical exam normal
- ESR 22, CBC and electrolytes normal
- ECG
  - Sinus rhythm at 52 bpm
  - ST-segment changes resolved
- Echocardiogram
  - Ejection fraction 55%, valves normal
  - No effusion, no constrictive pericarditis

# What is your next management step?

- A. Exercise stress echocardiogram
- B. Cardiac MRI
- C. Oral prednisone x 3 months
- D. Ibuprofen 800 mg tid, taper over 6 weeks
- E. Ibuprofen 800 mg tid, taper over 6 weeks + colchicine 0.6 mg bid x 3 months
- F. Reassurance



# Acute pericarditis

## Presentation

**History and physical**

**Sharp, positional chest pain**

**± Fever, recent infection**

**Pericardial friction rub**

**Pericardial rub heard best at end-expiration  
Pleural rub heard best with respiration**

**Most cases**

**Idiopathic  
Autoimmune  
Viral**

**Other causes**

**Malignancy, uremia  
Trauma, radiation  
Meds (hydralazine)**



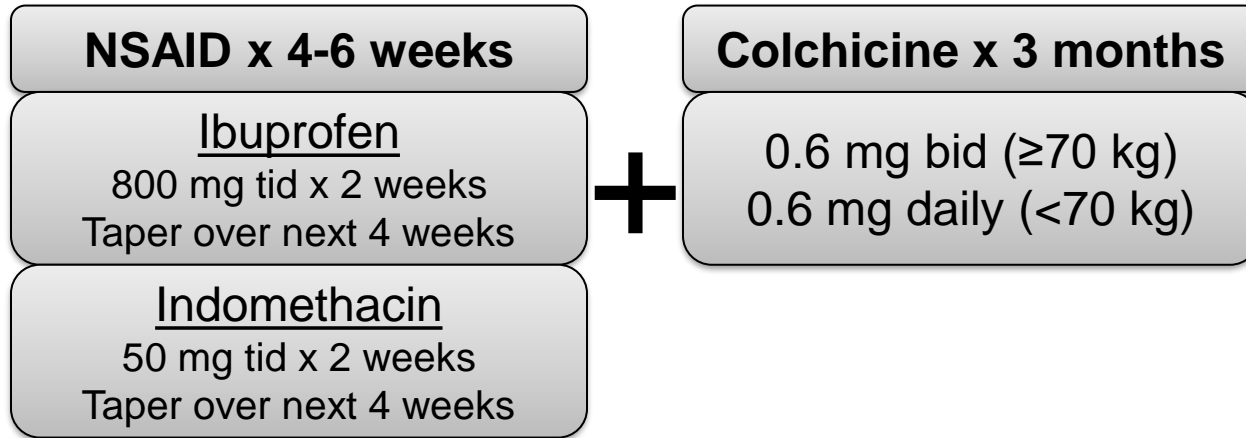
# Chronic pericarditis

## Presentation

- Symptoms of acute pericarditis for >3 months
- Symptom-free period after acute treatment
- Ongoing symptoms usually less severe
- Common etiologies
  - Idiopathic, autoimmune, viral
  - **Suboptimal treatment of acute pericarditis!**

# Acute pericarditis

## Treatment

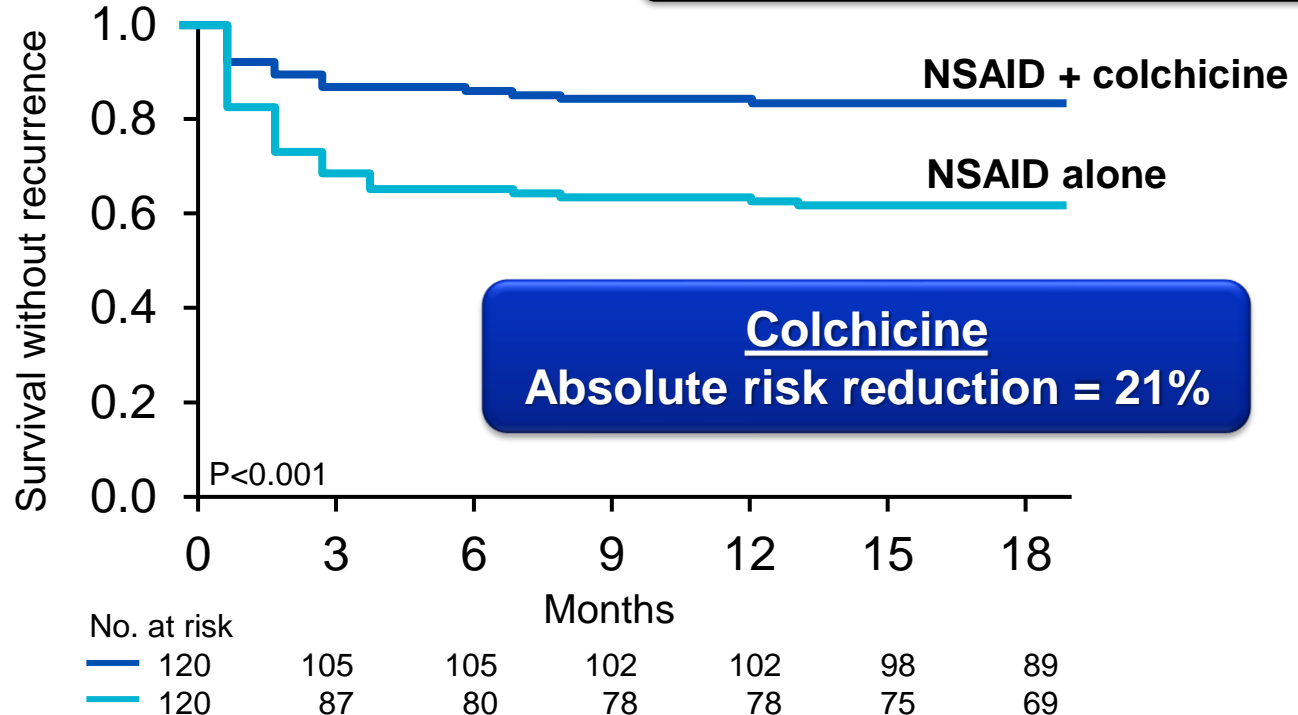


# Acute pericarditis

## Colchicine

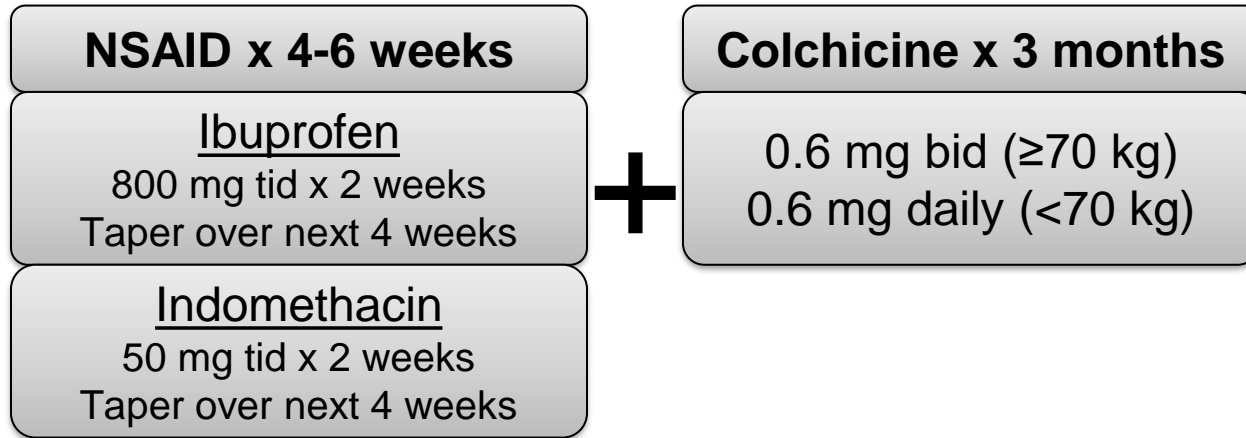
240 patients with acute pericarditis

NSAID vs. NSAID + colchicine



# Acute pericarditis

## Treatment



**Avoid glucocorticoids as first line therapy!**

**Early therapy with steroids increases recurrence risk!**

# Chronic pericarditis

## Treatment

- Proper treatment for acute pericarditis
  - NSAIDs x 6 weeks, tapering every 2 weeks
  - Colchicine x 3-6 months
- Avoid intense physical activity
- Assess after completion of therapy
  - Resolution of symptoms
  - Normalization of inflammatory markers

# What is your management step?

- A. Exercise stress echocardiogram
- B. Cardiac MRI
- C. Oral prednisone x 3 months
- D. Ibuprofen 800 mg tid, taper over 6 weeks
- E. Ibuprofen 800 mg tid, taper over 6 weeks + colchicine 0.6 mg bid x 3 months
- F. Reassurance

**No indication, avoid exercise**

**Obtain if diagnosis uncertain**

**Avoid early Rx with steroids**

**Use NSAIDs + colchicine**

**Completely treat acute episode!**

**Not yet!**

@MayoClinicGIM

# 42-year-old male

## Chronic pericarditis



**Incomplete treatment of acute pericarditis is a common cause for chronic pericarditis.**

**Initial treatment for acute (and chronic) pericarditis includes NSAIDs x 6 weeks + colchicine x 3-6 months.**

**Avoid glucocorticoids as initial treatment for pericarditis. Avoid intense physical activity during treatment.**

**A quick word on another  
cause of sharp pleuritic  
chest pain...**



# Costochondritis

**Sharp chest discomfort, can be positional/pleuritic**

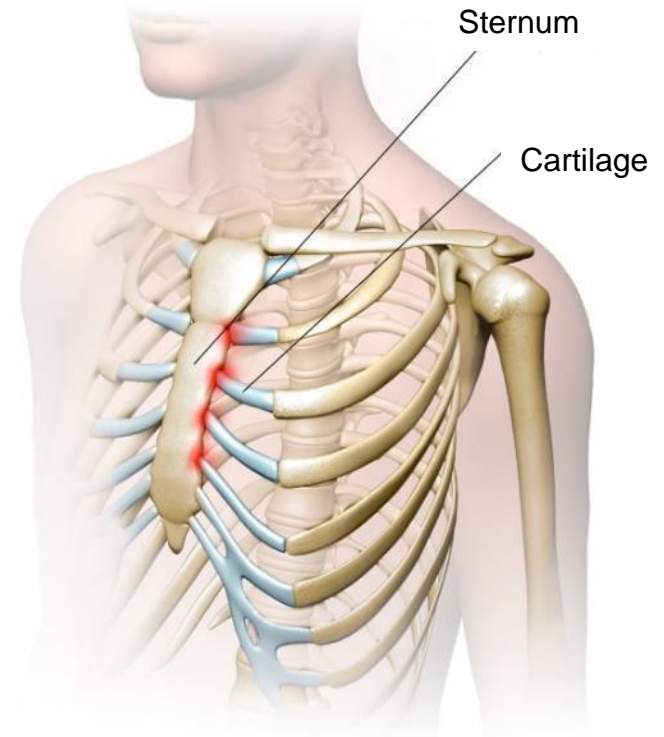
**Inflammation of costochondral joint, upper>lower joints, typically absent swelling, but can occur (Tietze syndrome)**

**Diagnosis = reproducible with palpation**

**Treatment = reassurance, acetaminophen and/or NSAIDs, heat/cold, avoidance of aggravating activities**

**Stretching activities – doorway stretch, rolled towel stretch**

## Sharp chest pain Pericarditis mimic



© MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH. ALL RIGHTS RESERVED.

**@MayoClinicGIM**

# Case #4

# 32-year-old female

- 6 months of sporadic palpitations
- “Flip-flopping” in chest
- Multiple times daily, last seconds
- Random, no provoking factors
- Associated with mild dyspnea
- No syncope or chest pain

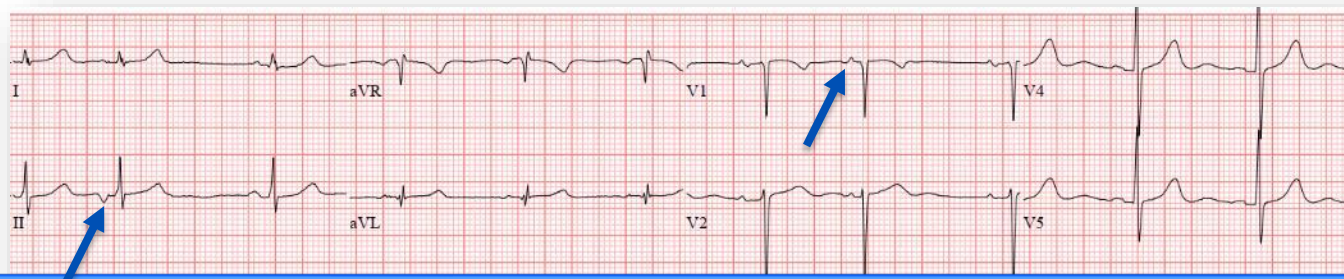
# 32-year-old female

## “Flip-flopping” in chest

- Non-smoker, rare alcohol & caffeine
- Heart rate 65 bpm
- Blood pressure 115/75 mmHg
- Occasional ectopic beats on exam
- Otherwise normal physical exam
- CBC, electrolytes, TSH normal

# 32-year-old female

## “Flip-flopping” in chest



### Holter monitor

Sinus rhythm with sinus arrhythmia, average 72 bpm

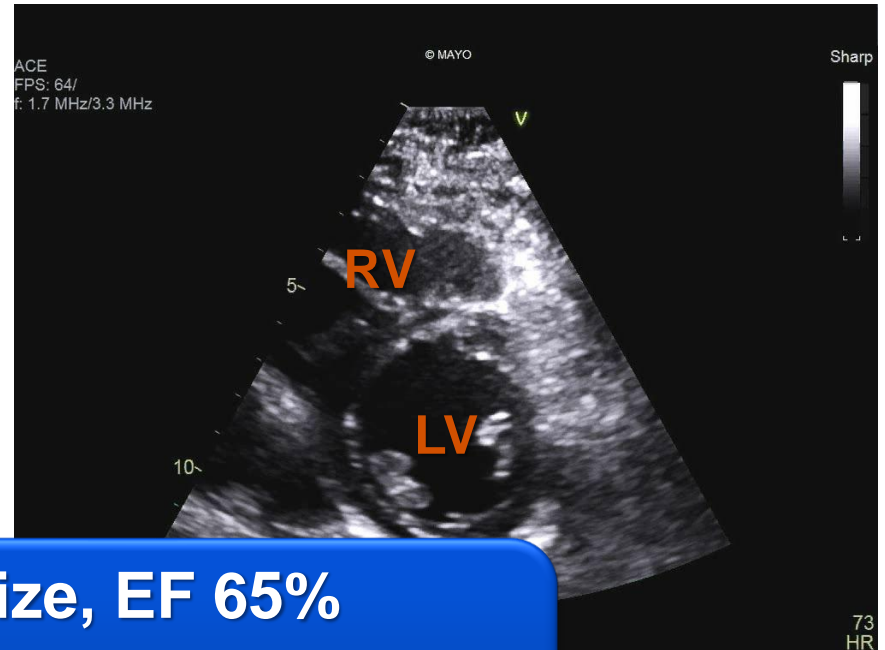
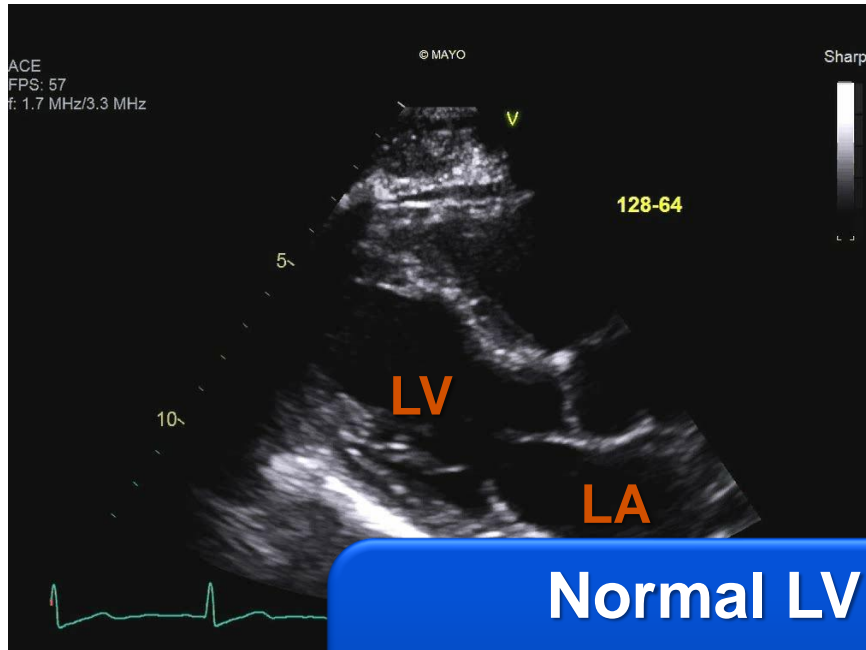
Frequent supraventricular ectopic beats

500 single PVC's in a 24-hour period

Post-ectopic pauses, longest 2.2 seconds

“Flip-flops” associated with supraventricular ectopy

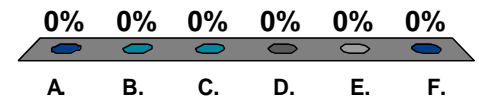
# 32-year-old female “Flip-flopping” in chest



**Normal LV size, EF 65%**  
**Normal RV size and function**  
**Normal valves, no effusion**

# What is your next step?

- A. Exercise stress test
- B. Atenolol 25 mg twice daily
- C. Metoprolol succinate 200 mg once daily
- D. Flecainide 100 mg 2x daily
- E. Refer for pacemaker implantation due to sinus node dysfunction
- F. Refer for invasive electrophysiology testing and potential ablation

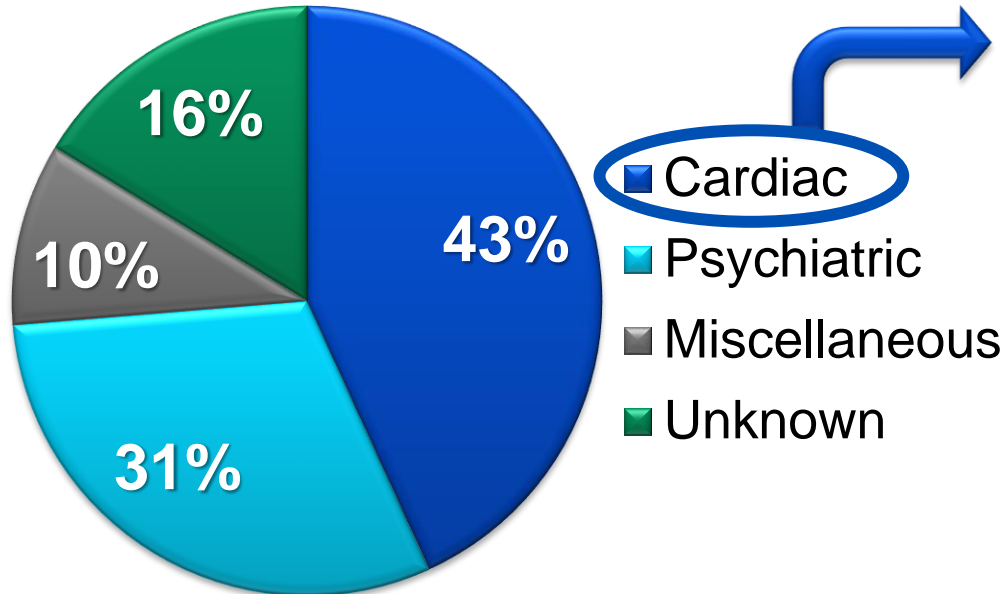


# Spectrum of palpitations

## General medicine patients

190 patients with palpitations

### Etiology of palpitations



A-fib / flutter	15.8%
SVT	9.5%
PVC's	7.9%
PAC's	3.2%



# Spectrum of palpitations

## General medicine patients

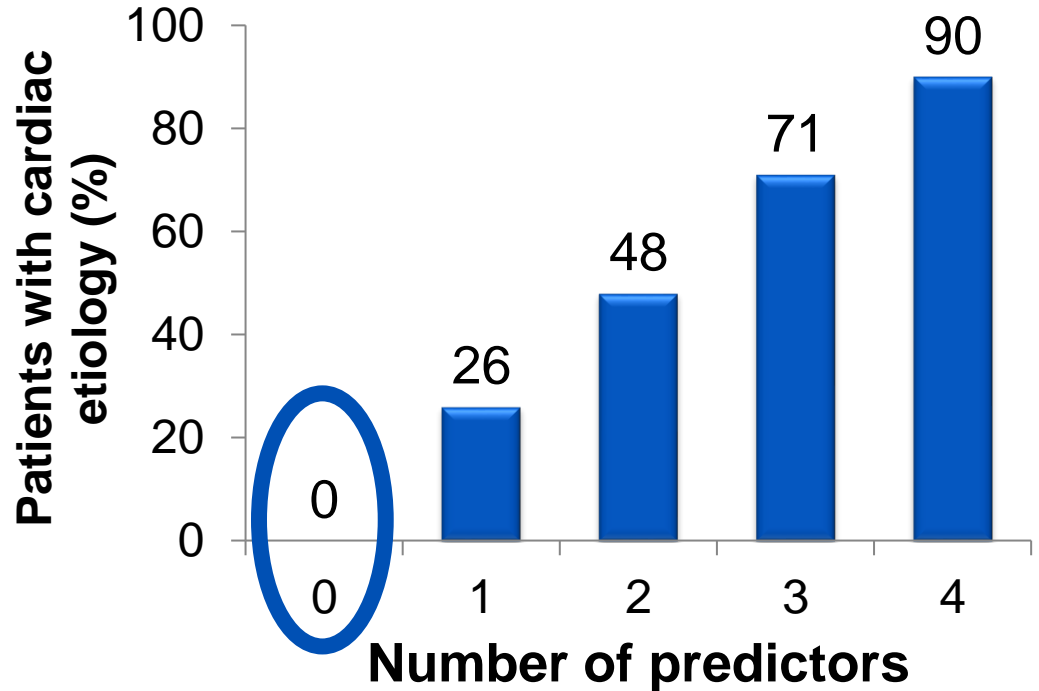
### Predictors of cardiac etiology

Male sex

Description of “irregular heartbeat”

History of heart disease

Event duration >5 min



# Evaluation of palpitations

## Ambulatory monitoring

### Common findings on Holter reports

Finding	Significance
Sinus arrhythmia	Common, usually normal More frequent in young & healthy
Supraventricular ectopy	Includes junctional and atrial premature beats Usually benign and asymptomatic
Ventricular ectopy	>20,000 PVC's necessary to cause cardiomyopathy Look for secondary causes
Pauses	≥3 seconds in sinus rhythm or ≥5 seconds in a-fib is concerning

# Evaluation of palpitations

## Ambulatory monitoring

### Alternative monitoring: Two questions

How frequent are the spells?

How symptomatic is the patient?

Scenario	Monitor
Daily	24- or 48-hour Holter monitor
1-2x weekly, prolonged symptoms	Patient-triggered event (i.e. loop) monitor OR patch monitor
1-2x weekly, minimal symptoms	Auto-triggered event (i.e. loop) monitor OR patch monitor
Monthly or less, $\pm$ high risk features	Implantable loop recorder
Possible high-risk arrhythmia	Mobile cardiac outpatient telemetry

# Evaluation of palpitations

## Wearable monitors



**Improve patient engagement**

**Increase detection of atrial fibrillation**

**More frequent use of anticoagulation**

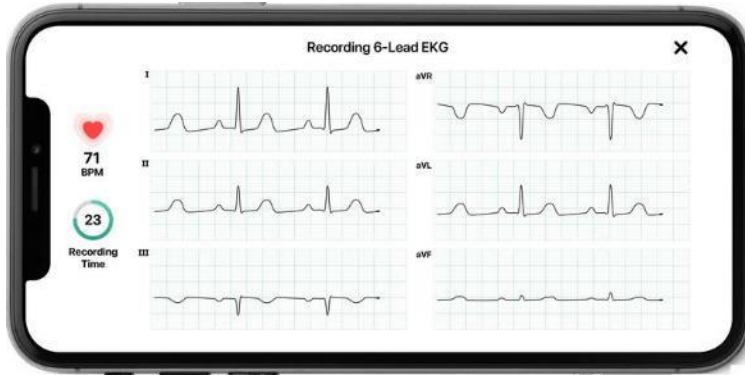
**Limited impact on patient outcomes (yet)**

@MayoClinicGIM

Images licensed by Mayo Clinic, Shutterstock  
©2021 Mayo Foundation for Medical Education and Research | slide-68

# Evaluation of palpitations

## Commercial devices



**AliveCor KardiaMobile 6L**

**Currently \$129**

**6 lead device, may help with interpreting artifact vs real arrhythmia**

**Take device diagnoses with a grain of salt**

**Balance risks/benefit on patient's stress level**

# Supraventricular ectopy

## Treatment

- Exclude structural heart disease
- If asymptomatic → Observe
- Limit exacerbating factors → OSA, alcohol, stress
- $\beta$ -blockers
  - 1<sup>st</sup> line medical therapy
  - Start low dose (metoprolol succinate 25 mg daily)
- 2<sup>nd</sup> line therapy
  - Calcium channel blockers
  - Anti-arrhythmics, digoxin

# What is your next step?

- A. Exercise stress test
- B. Atenolol 25 mg twice daily
- C. Metoprolol succinate  
200 mg once daily
- D. Flecainide 100 mg 2x daily
- E. Refer for pacemaker  
implantation due to sinus  
node dysfunction
- F. Refer for invasive  
electrophysiology testing  
and potential ablation

**No indication!**

**Low dose  $\beta$ -blocker best choice**

**Dose too high!**

**Rarely use antiarrhythmic meds**

**Pauses not worrisome**

**Not yet, and it shouldn't be  
necessary!**

# 32-year-old female “Flip-flopping” in chest



**Remember the predictors for a cardiac etiology of palpitations** (male sex, duration >5 minutes, “irregular” heartbeat, known heart disease)!

**Pauses <3 seconds and sporadic PVCs are usually not severe enough to cause trouble.**

**Low dose  $\beta$ -blockers are first line medical treatment for symptomatic supraventricular ectopy.**



# Summary

- Case #1 → 59-year-old female with exertional chest tightening
- Case #2 → 26-year-old female with palpitations, chest pain, and mitral valve prolapse
- Case #3 → 42-year-old male with chronic pericardial pain
- Case #4 → 32-year-old female with “flip flopping” in chest

**Some closing thoughts...**

# What do you do when all the tests are negative?

## 1. Reassurance

- No more cardiac tests
- No invasive procedures
- No life-altering heart disease

**“Your heart is pretty healthy.”**

**“Let’s keep it that way!”**

## 2. Lifestyle modification

- Smoking cessation, alcohol limitation
- Healthy weight, diet, exercise

## 3. Basic primary cardiovascular prevention

# Take home points



1. Always consider the pre-test probability for coronary disease when evaluating a patient with chronic chest pain
2. Mitral valve prolapse is a cause of mitral regurgitation rather than a unique clinical syndrome or an explanation for chronic chest pain or palpitations
3. Ensure patients with chronic pericarditis have been appropriately treated for acute pericarditis
4. Supraventricular ectopy is usually benign and responds to  $\beta$ -blocker therapy, if necessary

# QUESTIONS & ANSWERS



[geske.jeffrey@mayo.edu](mailto:geske.jeffrey@mayo.edu)  
@jeffreygeske

**@MayoClinicGIM**