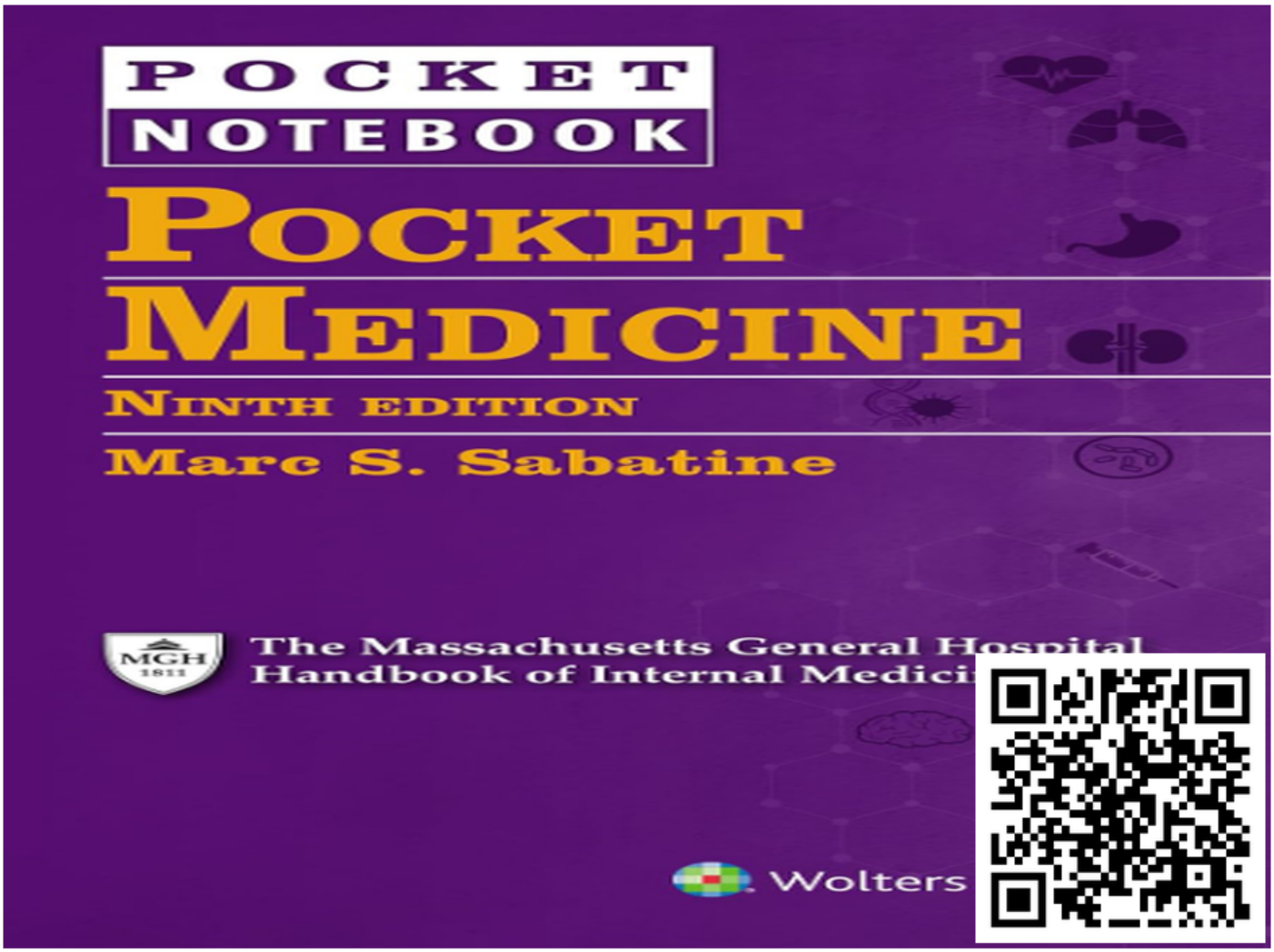

POCKET NOTEBOOK

POCKET MEDICINE

NINTH EDITION

Marc S. Sabatine

The Massachusetts General Hospital Handbook of Internal Medicine

Wolters Kluwer

POCKET NOTEBOOK

MEDICINE

Ninth Edition

Edited by
MARC S. SABATINE, MD, MPH
PROFESSOR OF MEDICINE
HARVARD MEDICAL SCHOOL

A Massachusetts General Hospital Handbook

Wolters Kluwer

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FOREWORD

To the First Edition

It is with the greatest enthusiasm that I introduce *Pocket Medicine.* In an era of information glut, it will logically be asked, “Why another manual for medical house officers?” Yet, despite enormous information readily available in any number of textbooks, or at the push of a key on a computer, it is often that the harried house officer is less helped by the description of differential diagnosis and therapies than one would wish.

Pocket Medicine is the joint venture between house staff and faculty expert in a number of medical specialties. This collaboration is designed to provide a rapid but thoughtful initial approach to medical problems seen by house officers with great frequency. Questions that frequently come from faculty to the house staff on rounds, many hours after the initial interaction between patient and doctor, have been anticipated, and important pathways for arriving at diagnoses and initiating therapies are presented. This approach will facilitate the evidence-based medicine discussion that will follow the workup of the patient. This well-conceived handbook should enhance the ability of every medical house officer to properly evaluate a patient in a timely fashion and to be stimulated to think of the evidence supporting the diagnosis and the likely outcome of therapeutic intervention. *Pocket Medicine* will prove to be a worthy addition to medical education and to the care of our patients.

DENNIS A. AUSIELLO, MD
Physician-in-Chief, Massachusetts General Hospital
Jackson Professor of Clinical Medicine, Harvard Medical School

PREFACE

To my parents, Matt and Lee Sabatine; to their namesake grandchildren, Matteo and Natalie; and to my wife, Jennifer

Written by residents, fellows, and attendings, the mandate for *Pocket Medicine* was to provide, in as concise a manner as possible, the key information a clinician needs for the initial approach to and management of the most common inpatient medical problems.

The tremendous response to the previous editions suggests we were able to help fill an important need for clinicians. With this ninth edition come several major improvements. We have updated every topic thoroughly. In particular, we have included recommendations from the latest guidelines for chronic coronary disease and acute coronary syndromes, data on the newest pharmacotherapies for heart failure, and the latest catheter-based approaches for valvular heart disease and atrial fibrillation. We include data on the latest biologic therapy for IBD and new therapies for MASH and chronic kidney disease. We cover the latest molecularly targeted therapies for liquid tumors as well as breast and lung cancer. We continue to expand the discussion of SGLT2i and GLP-1 RA for diabetes and now have a new section on obesity and weight management. As always, we have incorporated key references to the most recent high-tier reviews and important studies published right up to the time *Pocket Medicine* went to press. We welcome any suggestions for further improvement.

Of course, medicine is far too vast a field to ever summarize in a textbook of any size. Long monographs have been devoted to many of the topics discussed herein. *Pocket Medicine* is meant only as a starting point to guide one during the initial phases of diagnosis and management until one has time to consult more definitive resources. Although the recommendations herein are as evidence-based as possible, medicine is both a science and an art. As always, sound clinical judgment must be applied to every scenario.

I am grateful for the support of the house officers, fellows, and attendings at the Massachusetts General Hospital. It is a privilege to work with such a knowledgeable, dedicated, and compassionate group of physicians. I always look back on my time there as chief resident as one of my best experiences. I am grateful to several outstanding clinical mentors, including Hasan Bazari, Larry Friedman, Nesli Basgoz, Eric Isselbacher, and Mike Fifer, as well as the late Roman DeSanctis, Charlie McCabe, Mort Swartz, and Peter Yurchak.

This edition would not have been possible without the help of Kate Brennan, CMPP, my academic coordinator. She shepherded every aspect of the project from start to finish, with an incredible eye to detail to ensure that each page of this book was the very best it could be. This edition also naturally builds on the work of the many contributors to prior editions of *Pocket Medicine*, whom we thank for creating such an impressive foundation.

Lastly, special thanks to my parents for their perpetual encouragement and love and, of course, to my wife, Jennifer Tseng, who, despite being a surgeon, is my closest advisor, my best friend, and the love of my life.

I hope that you find *Pocket Medicine* useful throughout the arduous but incredibly rewarding journey of practicing medicine.

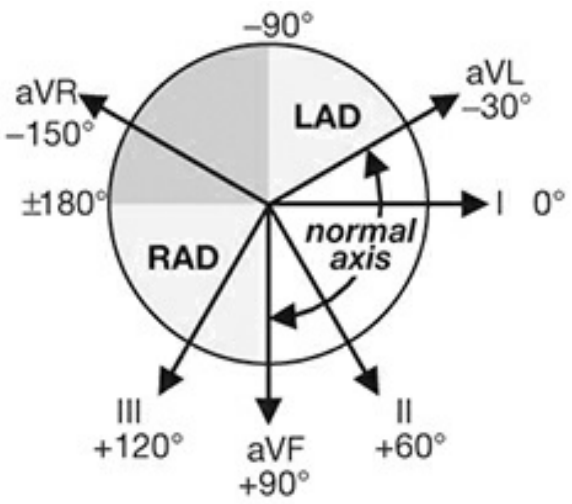
MARC S. SABATINE, MD, MPH

ELECTROCARDIOGRAPHY

Approach (a systematic approach is vital)

- **Rate** (? tachy or brady), **rhythm** (? P waves, regularity, P & QRS relationship)
- **Intervals** (PR, QRS, QT), **axis** (? LAD or RAD), **chamber abnl** (? LAA, RAA, LVH, RVH)
- **QRST changes** (? Q waves, poor R-wave progression V_1–V_6, ST ↑/↓ or T wave Δs)

Figure 1-1 QRS axis

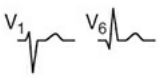


Left axis deviation (LAD)

- **Definition:** axis beyond −30° (S > R in lead II)
- **Etiologies:** LVH, LBBB, inferior MI, WPW
- **Left anterior fascicular block (LAFB):** LAD (–45 to –90°) *and* qR in aVL *and* QRS <120 msec *and* no other cause of LAD (eg, IMI)

Right axis deviation (RAD)

- **Definition:** axis beyond +90° (S > R in lead I)
- **Etiologies:** RVH, PE, COPD (usually not >+110°), septal defects, lateral MI, WPW
- **Left posterior fascicular block (LPFB):** RAD (90–180°) *and* rS in I & aVL *and* qR in III & aVF *and* QRS <120 msec *and* no other cause of RAD

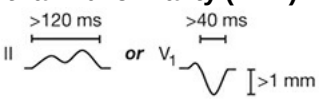
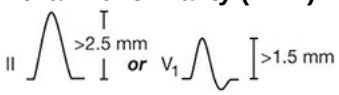
Bundle Branch Blocks (*Circ* 2009;119:e235)		
Normal		Initial depol. left to right across septum (r in V_1 & q in V_6; nb, absent in LBBB) followed by LV & RV free wall, with LV dominating (nb, RV depol. later and visible in RBBB)
RBBB		1. QRS ≥120 msec (110–119 msec = IVCD or “incomplete”)

		2. rSR′ in R precordial leads (V_1, V_2) 3. Wide S wave in I and V_6 4. ± ST↓ or TWI in R precordial leads
LBBB		1. QRS ≥120 msec (110–119 msec = IVCD or "incomplete") 2. Broad, slurred, monophasic R in I, aVL, V_5–V_6 (± RS in V_5–V_6 if cardiomegaly) 3. Absence of Q in I, V_5, and V_6 (may have narrow q in aVL) 4. Displacement of ST & Tw opposite major QRS deflection 5. ± PRWP, LAD, Qw's in inferior leads

Bifascicular block: RBBB + LAFB/LPFB. "Trifascicular block": bifascicular block + 1° AVB.

Prolonged QT interval (*NEJM* 2008;358:169; www.torsades.org)

- Measure QT using threshold method (start of QRS to end of Tw at isoelectric line) or tangent (QRS to where tangent of Tw downslope intersects baseline) when long tail. Use longest QT (often V_2 or V_3) and omit U wave (*Circ* 2018;138:2345).
- QT varies w/ HR → corrected w/ Bazett formula: $QTc = QT/\sqrt{RR}$ (RR = 60/HR, in sec), overcorrects at high HR, undercorrects at low HR (nl QTc <450 msec ♂, <460 msec ♀)
- Fridericia's [$QTc = QT/\sqrt[3]{RR}$] and Framingham [QT_c = QT + 0.154 – (1–RR)] formulae have optimal rate correction
- QT prolongation a/w ↑ risk TdP (espec >500 msec); establish baseline QT and monitor if using QT prolonging meds, no estab guidelines for stopping Rx if QT prolongs
- Etiologies:
  - **Antiarrhythmics:** class Ia (procainamide, disopyramide), class III (amio, sotalol, dofet)
  - **Psych drugs:** antipsychotics (phenothiazines, haloperidol, atypicals), Li, ? SSRI, TCA
  - **Antimicrobials:** macrolides, quinolones, azoles, pentamidine, atazanavir
  - **Other:** antiemetics (droperidol, 5-HT_3 antagonists), alfuzosin, methadone, ranolazine
  - **Electrolyte disturbances:** hypoCa (nb, hyperCa a/w ↓ QT), ± hypoK, ? hypoMg
  - **Autonomic dysfxn:** ICH (deep TWI), Takotsubo, stroke, CEA, neck dissection
  - **Congenital** (long QT syndrome): K, Na, & Ca channelopathies (*Circ* 2013;127:126)
  - **Misc:** CAD, CMP, bradycardia, high-grade AVB, hypothyroidism, hypothermia, BBB

Atrial Abnormalities (*Circ* 2009;119:e251)		
ECG **P-wave criteria**	**Left Atrial Abnormality (LAA)** 	**Right Atrial Abnormality (RAA)** 

Left ventricular hypertrophy (LVH) (*Circ* 2009;119:e251)

- Etiologies: HTN, AS/AI, CMP (HCM, Fabry), coarctation of aorta
- Criteria (all w/ Se <50%, Sp >85%; accuracy affected by age, sex, race, BMI)
  - **Sokolow–Lyon:** S in V_1 + R in V_5 or V_6 ≥35 mm or R in aVL ≥11 mm (↓ Se w/ ↑ BMI)
  - **Cornell:** R in aVL + S in V_3 >28 mm in men or >20 mm in women
  - **Romhilt–Estes point score system** (4 points = probable; 5 points = diagnostic): ↑ volt: limb lead R or S ≥20 mm *or* S in V_1 or V_2 ≥30 mm *or* R in V_5 or V_6 ≥30 mm (3 pts) ST displacement opposite to QRS deflection: w/o dig (3 pts); w/ dig (1 pt) LAA (3 pts); LAD (2 pts); QRS duration ≥90 msec (1 pt) Delayed intrinsicoid deflection (QRS onset to peak of R) in V_5 or V_6 ≥50 msec (1 pt)
  - **If LAD/LAFB:** S in III + max (R+S) in any lead ≥30 mm in men or ≥28 mm in women

Right ventricular hypertrophy (RVH) (*Circ* 2009;119:e251; *JACC* 2014;63:672)

- Etiologies: cor pulmonale, congenital (tetralogy of Fallot, TGA, PS, ASD, VSD), MS, TR
- Criteria [all insensitive, but specific (except in COPD); all w/ poor PPV in general population]
  R > S in V_1 or R in V_1 ≥7 mm, S in V_5 or V_6 ≥7 mm, drop in R/S ratio across precordium
  RAD ≥110° (LVH + RAD *or* prominent S in V_5 or V_6 → consider *biventricular* hypertrophy)

Ddx of dominant R wave in V_1 or V_2

- Ventricular abnl: RVH (RAD, RAA, deep S waves in I, V_5, V_6); HCM; Duchenne's
- Posterior MI: anterior R wave = posterior Q wave; often with inferior or lateral MI
- Abnormal depolarization: RBBB (QRS >120 msec, rSR′); WPW (↓ PR, δ wave, ↑ QRS)
- Other: dextroversion; counterclockwise rotation; lead misplacement; nl variant

Poor R-wave progression (PRWP) (*Am Heart J* 2004;148:80)

- Definition: loss of anterior forces w/o frank Q waves (V_1–V_3); R wave in V_3 ≤3 mm
- Etiologies: old anteroseptal MI (w/ R-wave V_3 ≤1.5 mm, ± persistent ST ↑ or TWI V_2 & V_3)
  LVH (delayed RWP w/ ↑ left precordial voltage); RVH; COPD (may also have RAA, RAD, limb lead QRS amplitude ≤5 mm, $S_I S_{II} S_{III}$ w/ R/S ratio <1 in those leads)
  LAFB/LBBB; WPW; clockwise rotation of the heart; lead misplacement; CMP; PTX

Pathologic Q waves

- Definition: ≥30 msec (≥20 msec V_2–V_3) or >25% height of R wave in that QRS complex
- Small (septal) q waves in I, aVL, V_5 & V_6 are nl, as can be isolated Qw in III, aVR, V_1
- "Pseudoinfarct" pattern may be seen in LBBB, infiltrative dis., HCM, COPD, PTX, WPW

ST elevation (STE) (*NEJM* 2003;349:2128; *Circ* 2009;119:e241 & e262)

- **Acute MI:** upward convexity STE (ie, a "frown") ± TWI (or prior MI w/ persistent STE)
- **Coronary spasm:** Prinzmetal's angina; transient STE in a coronary distribution
- **Pericarditis:** diffuse, upward concavity STE (ie, "smile"); PR ↓; Tw often upright; no Qw
- **HCM, Takotsubo CMP, myocarditis,** LV aneurysm, cardiac contusion
- **Pulmonary embolism:** occ. STE V_1–V_3; classically a/w TWI V_1–V_4, RAD, RBBB, $S_I Q_{III} T_{III}$
- **Repolarization abnormalities:**
  LBBB (↑ QRS duration, STE discordant from QRS complex; see "ACS" for dx MI in LBBB);
  LVH (↑ QRS amplitude); Brugada pattern (rSR′, downsloping STE V_1–V_2); pacing;
  hyperkalemia (↑ QRS duration, tall Ts, no P's); epsilon waves (late afterdepol.) in ACM
- **aVR:** STE >1 mm a/w ↑ mortality in STEMI; STE aVR > V_1 a/w left main disease vs. multivessel disease (LM equivalent)
- **Early repolarization:** most often seen in V_2–V_5 in young adults (*Circ* 2016;133:1520)
  1–4 mm elev of notch peak or start of slurred downstroke of R wave (ie, J point); ± up concavity of ST & large Tw (∴ ratio of STE/T wave <25%; may disappear w/ exercise)
  ? early repol in inf leads may be a/w ↑ risk of VF (*NEJM* 2009;361:2529; *Circ* 2011;124:2208)

ST depression (STD)

- **Myocardial ischemia** (± Tw abnl)
- **Acute true posterior MI:** posterior STE appearing as anterior STD (± ↑ R wave) in V_1–V_3 ✓ posterior ECG leads; manage as a STEMI with rapid reperfusion (see "ACS")
- Repolarization abnl a/w LBBB or LVH (usually in leads V_5, V_6, I, aVL, called "LV strain")
- Digitalis effect (downsloping ST ± Tw abnl, *not* correlated w/ dig levels); hypoK (± U wave)

T-wave inversion (TWI; **≥1** mm; "deep" if **≥**5 mm; normal in III, V_1, aVR) (*Circ* 2009;119:e241)

- Ischemia/MI; *Wellens' sign* (deep, symm precordial TWI) → critical prox LCA lesion; *de Winter's* sign (hyperacute Tw ± upsloping STD V_2–V_6) → acute prox LAD occlusion
- Myopericarditis; CMP (Takotsubo, ARVC, apical HCM); MVP; PE (espec if TWI V_1–V_4)
- Repolarization abnl in a/w LVH/RVH ("strain pattern"); BBB; nl variant if QRS predom. ⊖
- Posttachycardia or postpacing ("memory" T waves)
- Electrolyte, digoxin, P_aO_2, P_aCO_2, pH/core temp Δ's, intracranial bleed ("cerebral Tw")

Low voltage

- QRS amplitude (R + S) <5 mm in all limb leads & <10 mm in all precordial leads
- Etiol: COPD, pericardial/pleural effusion, myxedema, ↑ BMI, infiltrative CMP, diffuse CAD

Electrolyte abnormalities

- ↑ **K:** tented Tw, ↓ QT, ↑ PR, AVB, wide QRS, STE; ↓ **K:** flattened Tw, U waves, ↑ QT
- ↑ **Ca:** ↓ QT, flattened Tw & Pw, J point elevation; ↓ **Ca:** ↑ QT; Tw Δs

ECG in young athletes (*JACC* 2017;69:805)

- Normal patterns may include LVH, RVH, early repolarization
- Evaluate if: arrhythmia, HR <30, ↑ QT, ε/δ waves, LBBB, Brugada pattern, QRS >140 ms, PR >400 ms, Mobitz II, 3° AVB, ST depression, TWI

CHEST PAIN

Disorder	Typical Characteristics & Diagnostic Studies
	Cardiovascular Causes
Angina/ACS (<10% of chest pain in ED)	Substernal "pressure" (⊕ LR 1.3) → neck, jaw, arm (⊕ LR 1.3–1.5) Sharp, pleuritic, positional, or reprod. w/ palp all w/ ⊕ LR ≤0.35 Diaphoresis (⊕ LR 1.4), dyspnea (⊕ LR 1.2), a/w exertion (⊕ LR 1.5–1.8) ≈ prior MI (⊕ LR 2.2); ↓ w/ NTG/rest (but not reliable; *Annals EM* 2005;45:581) ± ECG Δs: STE, STD, TWI, hyperacute Tw, Qw. ± ↑ Troponin.
Pericarditis & myo-pericarditis	Sharp pain → trapezius, ↑ w/ respiration, ↓ w/ sitting forward. ± Pericardial friction rub. ECG Δs (diffuse STE & PR ↓, opposite in aVR) ± pericardial effusion. If myopericarditis, same as above + ↑ Tn and ± s/s HF and ↓ EF.
Aortic dissection	Sudden severe tearing pain (absence ⊖ LR 0.3). ± Asymm (>20 mmHg) BP or pulse (⊕ LR 5.7), focal neuro deficit (⊕ LR >6), AI, widened mediast. on CXR (absence ⊖ LR 0.3); false lumen on imaging.
PE	Sudden pleuritic pain. ↑ RR & HR, ↓ S_aO_2, ECG Δs (sinus tach, RAD, RBBB, $S_IQ_{III}T_{III}$, TWI V_1–V_4, occ STE V_1–V_3), + CTA or V/Q, ± ↑ Tn/BNP.
Pulm HTN	Exertional pressure, DOE. ↓ S_aO_2, loud P_2, RV heave, right S_3 and/or S_4.
	Pulmonary Causes
Pneumonia	Pleuritic; dyspnea, fever, cough, sputum. ↑ RR, crackles. CXR infiltrate.
Pleuritis	Sharp, pleuritic pain. ± Pleuritic friction rub.

PTX	Sudden, sharp pleur pain. Hyperresonance, ↓ breath sounds. Dx w/ CXR.
GI Causes	
Esoph reflux	Substernal burning, acid taste in mouth, ↑ by meals. See "GERD."
Esoph spasm	Intense substernal pain. ↑ w/ swallow, ↓ by NTG/CCB. Dx w/ manometry.
Mallory-Weiss	Esoph tear precipitated by vomiting. ± Hematemesis. Dx w/ EGD.
Boerhaave	Esoph rupture. Severe pain, ↑ w/ swallow. Mediastinal air palpable & on CT.
PUD	Epigastric pain, relieved by antacids. ± GIB. Dx w/ EGD, ± *H. pylori* test.
Biliary dis.	RUQ pain, N/V. ↑ by fatty foods. Dx w/ RUQ U/S, CT, MRCP; ↑ LFTs.
Pancreatitis	Epigastric/back discomfort. Dx w/ ↑ amylase & lipase; abdominal CT.
Musculoskeletal and Miscellaneous Causes	
Costochond	Localized sharp pain. ↑ w/ movement. Reproduced by palpation.
Zoster	Intense unilateral sharp/burning pain. Pain may precede dermatomal rash.
Anxiety	"Tightness," dyspnea, palpitations, other somatic symptoms

(*Braunwald's Heart Disease*, 12th ed, 2022; *JAMA* 2015;314:1955)

Initial diagnostic studies

- **Focused history:** quality, severity, location, radiation; provoking/palliating factors; intensity at onset; duration, freq, & pattern; setting; assoc sx; cardiac hx & risk factors
- **Targeted exam:** VS (incl. BP in both arms); gallops, murmurs, rubs; signs of vascular dis. (carotid/femoral bruits, ↓ pulses) or CHF; lung & abd. exam; chest wall for reproducibility
- **12-lead ECG:** obtain w/in 10 min; comp to priors & obtain serial ECGs; consider *posterior leads* (V_7–V_9) if hx c/w ACS but stnd ECG unrevealing or ST ↓ V_1–V_3 & pain refractory
- **Troponin:** *>99th %ile w/ rise and/or fall in approp. setting is dx of AMI* (*Circ* 2018;138:e618)
  High-sens Tn (hsTn) detectable 1 h after injury, peaks ~24 h, can be elevated for >1 wk
  ✓ at presentation & 1–2 h later; repeat if clinical or ECG Δs; assess absolute level & Δ
  Ddx: *MI* (type 1 [plaque rupture] or 2 [supply–demand mismatch not due to Δ in CAD]), *non-ischemic cardiac* (eg, myocarditis, ADHF, Takotsubo, defibrillation, contusion), *systemic illness* (eg, PE, PHT, stroke, SAH, critical illness)
- **CXR;** other imaging (echo, PE CTA, etc.) as indicated based on H&P and initial testing

Initial approach (*Circ* 2021;144:e368)

- R/o life-threatening causes (ACS, PE, aortic dissection, myopericarditis, etc.)
- If possible ACS, risk-stratify w/ clinician decision pathway (clinical factors + ECG + Tn)
- **Low prob ACS** (eg, H&P unconcerning, ⊖ ECG & Tn): d/c to home; risk factor mgmt
- **Intermed prob ACS** (neither low nor high clinical risk, ± borderline Tn): ✓ TTE and
  If no known CAD → CCTA or stress (former ↓ LOS c/w fxnal testing; *NEJM* 2012;366:1393)
  If recent mildly ⊕ stress or known nonobstructive CAD → CCTA
  If obstructive but not high-risk CAD → stress test
  If recent mod-severely ⊕ stress or high-risk CAD (LM, prox LAD, MVD) → invasive angio
- **High prob ACS** (eg, ECG Δs, ⊕ Tn, new ↓ LVEF): invasive coronary angiography
- Pts w/ acute CP: CCTA vs. stress testing → ↓ time to dx & LOS (less so in era of hsTn), but ↑ probability of cath/PCI (*NEJM* 2012;366:1393 & 367:299; *JACC* 2013;61:880)

NONINVASIVE EVALUATION OF CAD

Stress testing (*J Nucl Cardiol* 2016;23:606; *EHJ* 2020;41:407)

- **Indications:** evaluate possible CAD sx or Δ in clinical status in Pt w/ known CAD, risk-stratify after chest pain, evaluate exercise tolerance, localize ischemia (imaging required)
- **Contraindications** (*Circ* 2002;106:1883 & 2012;126:2465)
  - **Absolute:** AMI w/in 48 h, high-risk UA, acute PE, severe sx AS, uncontrolled HF, uncontrolled arrhythmias, severe HTN (SBP >200), myopericarditis, acute AoD
  - **Relative** (discuss with stress lab): left main CAD, mod symptomatic valvular stenosis, HCM w/ LVOT obstruction, high-degree AVB, severe electrolyte abnl

Exercise tolerance test (w/ ECG alone)

- Generally preferred if Pt can meaningfully exercise; ECG Δs w/ Se ~65%, Sp ~80%
- Typically via treadmill w/ Bruce protocol (modified Bruce or submax if decond. or recent MI)
- Hold anti-isch. meds (eg, nitrates, βB) if dx'ing CAD but give to assess adequacy of meds

Pharmacologic stress test (nb, requires imaging because ECG not interpretable)

- Use if no/low exercise tolerance, recent MI. Se & Sp ≈ exercise. Preferred if LBBB, WPW, or V-paced, because higher prob of false ⊕ imaging with exercise.
- *Coronary vasodilator* (regadenoson [↓ side effects], dipyridamole, adenosine): diffuse arteriolar dilation → relative perfusion defect in vessels w/ fixed epicardial dis. Reveals flow-limiting CAD w/ coronary vasodilation which does not always correlate to ischemia w/ exercise. Side effects: flushing, ↓ HR, AVB, SOB, bronchospasm, ↓ seizure threshold.
- *Chronotropes/inotropes* (dobuta): more physiologic, but longer test; may precip arrhythmia

Imaging for stress test

- Use if uninterp. ECG (V-paced, LBBB, resting ST ↓ >1 mm, digoxin, LVH, WPW), ECG test indeterminate, requires pharm test, or to localize ischemia (eg, prior coronary revasc)
- Radionuclide myocardial perfusion imaging w/ images obtained at rest & w/ stress
  SPECT (eg, ^{99m}Tc-sestamibi): Se ~85%, Sp ~80%
  PET (rubidium-82): Se ~90%, Sp ~85%; requires pharmacologic stress, not exercise
  ECG-gated imaging allows assessment of regional LV fxn (sign of ischemia/infarction)
- **Echo** (exercise or dobuta): Se ~80%, Sp ~85%; no radiation; operator dependent
- **MRI**: Se ~85%, Sp ~90%; requires pharmacologic stress, not exercise

Test results

- **HR** (must achieve ≥85% of max pred HR [220 − age] for *exer.* test to be dx), **BP** response, peak **double product** (HR × BP; nl >20k), HR recovery ($HR_{peak} - HR_{1\ min\ later}$; nl >12)
- **Max exercise capacity** achieved (METS or min); **occurrence of symptoms**
- **ECG Δs:** *downsloping* or *horizontal* ST ↓ (≥1 mm) 60–80 ms after QRS predictive of CAD (but does *not* localize ischemic territory); however, STE highly predictive & localizes
- **Imaging:** radionuclide defects or regional WMA on TTE: reversible defect = ischemia; fixed defect = infarct; transient isch dilation → ? severe 3VD. False ⊖: balanced (3VD) ischemia.
  Coronary flow reserve (PET) →? microvasc dysfxn if ⊖ epicardial CAD (*EHJ* 2020;41:3504).

High-risk test results (PPV ~50% for LM or 3VD, ∴ consider coronary angio)

- ECG: ST ↓ ≥2 mm *or* ≥1 mm in stage 1 *or* in ≥5 leads *or* ≥5 min in recovery; ST ↑; VT

- Physiologic: ↓ or fail to ↑ BP, <4 METS, angina during exercise; ↓ EF
- Radionuclide: ≥1 lg or ≥2 mod. reversible defects, transient LV cavity dilation, ↑ lung uptake

Myocardial viability (*Circ CV Imaging* 2020;13:e53)

- Goal: identify hibernating myocardium that could regain fxn w/ revasc
- Options: **MRI** (Se ~95%, Sp ~50%), **FDG-PET** (Se ~90%, Sp ~65%), **dobutamine stress echo** (Se ~80%, Sp ~80%); **SPECT/rest–redistribution** (Se ~85%, Sp ~65%)
- However, presence of viability has not been shown to predict clinical benefit of revasc.

Coronary CT angiography (*JCCT* 2021;15:192)

- *Gated* CT for contrast enhancement in coronary arteries, NTG given to dilate coronaries. β-blockers commonly used to lower HR.
- CAD–RADS score in stable CP improves risk stratif. of CV events (*JACC Img* 2020;13:1534)
- In stable outPt w/ CP: CCTA added to stnd of care → ↑ early but not overall angio or revasc; ↑ use of preventive med Rx, and ↓ coronary death/MI by 10 y (*Lancet* 2025;405:329). CCTA vs. fxnal testing: no Δ in clinical outcomes overall, but ? ↓ CV death/MI in DM *(NEJM* 2015;372:1291; *JACC* 2019;73:893). In stable CP referred for angio, CCTA vs. invasive with no Δ in CV events (*NEJM* 2022;386:1591).
- CT-FFR: estimates fxnal signif of lesions

Coronary artery calcium (CAC) score

- Quantifies extent of calcium; thus, *estimates* plaque burden (but *not* % coronary stenosis)
- CAC sensitive (91%) but not specific (49%) for presence of CAD; high NPV to r/o CAD
- In intermediate-risk or selected borderline-risk adults (ie, 10-year ASCVD risk of 5–20%), if decision about statin remains uncertain, reasonable to use CAC score to help guide

CORONARY ANGIOGRAPHY & PCI

Precath checklist

- Peripheral arterial exam (radial, fem, DP, PT pulses; bruits); palmar arch eval (eg, w/ pulse oximetry & plethysmography) not routine. ✓ can lie flat × hrs, NPO >6 h, hold metformin and OAC, hold SGLT2i (DKA), preRx w/ steroids + antihist if contrast allergy.
- ✓ CBC, PT-INR (ideally ≤2), Cr; hold ACEI/ARB if renal dysfxn. Blood bank sample.
- ↓ risk of contrast-induced kidney injury: hold ACEI/ARB/ARNI, NSAIDs, diuretics. PreRx w/ isotonic IVF: data mixed but may be helpful if high risk (*Lancet* 2017;389:1312).

Vascular access

- Radial access preferred: ↓ mortality, bleeding, & vascular complications (*Circ* 2022;146:1329)
- Femoral artery commonly used; high puncture ↑ risk of retroperitoneal bleed; low puncture ↑ risk of arterial complic. (eg, AV fistula, superficial femoral artery cannulation)

Periprocedural pharmacotherapy for PCI

- **ASA** 325 mg × 1. **$P2Y_{12}$ inhibitor**: ticagrelor or prasugrel preferred over clopi in ACS. Outside of STEMI, preRx not recommended when anatomy unknown and short time to PCI. Cangrelor (IV $P2Y_{12}$ inhib) ↓ peri-PCI events vs. clopi w/o PreRx (*NEJM* 2013;368:1303).
- GP IIb/IIIa inhibitor: sometimes added if periprocedural thrombotic complication

- **Anticoagulant:** UFH or bivalirudin typically given during case and stopped at end

PCI and peri-PCI interventions

- *Physiology:* fractional flow reserve (FFR): ratio of max flow (induced by adenosine) distal vs. prox to stenosis to ID hemodyn. signif. lesions (≤0.80). Instantaneous wave-free ratio (iFR) similar, doesn't require vasodilator; iFR threshold ≤0.89. Their use ↓ # stents and MACE vs. angio alone (*NEJM* 2009;360:213; 2017;376:1813 & 1824).
- *Advanced imaging:* intravascular U/S (IVUS) or optical coherence tomography (OCT) ↓ MACE (*Lancet* 2024;403:824 & 1855;404:1029)
- Drug-eluting stents (DES): ↓ cardiac death, MI, repeat revasc, & stent thrombosis vs. BMS (*Lancet* 2019;393:2503). Balloon angioplasty alone reserved for lesions too narrow to stent.

Peri-PCI complications

- No or slow reflow, coronary artery spasm: Rx with local delivery of vasodilators
- Coronary artery dissection: treat with stent
- Coronary perforation: immediate balloon tamponade, ✓ for effusion, seal w/ covered stent

Vascular access post-PCI complications

- Postprocedure ✓ vascular access site, distal pulses, ECG, CBC, Cr
- **Bleeding**: reverse/stop anticoag (d/w interventionalist); IV fluids/PRBC/plts as required
  hematoma/overt bleeding: **manual compression**
  retroperitoneal bleed: may p/w ↓ Hct ± flank or back pain. CT abd/pelvis (I^-) or angio if unstable. If does not auto-tamponade, intravascular balloon and/or covered stent.
- **Vascular damage** (~1% of dx angio, ~5% of PCI; *Circ* 2007;115:2666)
  pseudoaneurysm: triad of pain, expansile mass, systolic bruit; diagnose w/ U/S; Rx (if pain or >2 cm): U/S-directed thrombin injection, surgery if former fails
  AV fistula: continuous bruit; Dx: U/S; Rx: surgical repair if large or sx
  limb ischemia (emboli, dissection, clot): cool, mottled extremity, ↓ distal pulses; Dx: loss of pulses, ↓ pulse volume recording, angio; Rx: percutaneous or surgical repair
  radial artery occlusion: if sx, consider 4 weeks LMWH

Other complications (*NEJM* 2017;377:1513)

- **Contrast-induced AKI:** w/in 48 h, peak 3–5 d; pre-hydration reasonable (see "CIAKI")
- **Stroke**: ~0.1–0.4% of cases. Usually ischemic from atheroembolic event during cath. Rx depends on sx/location/timing but includes thrombectomy, tPA, DAPT if ischemic.
- **Cholesterol emboli syndrome**: typically in Pts w/ large burden Ao atheroma; mesenteric ischemia (abd pain, LGIB, pancreatitis); intact distal pulses but livedo and toe necrosis

Stent post-PCI complications

- **Stent thrombosis:** acute clot formation in stent usually in 1st mo but can occur anytime. Typically p/w AMI. Often due to premature d/c antiplt Rx or mech prob. (stent underexpansion or unrecognized dissection, typically presents early).
- **In-stent restenosis:** develops in previously stented segment mos after PCI. Typically p/w gradual ↑ angina. Due to elastic recoil and neointimal hyperplasia; ↓ w/ DES.

Duration of dual antiplatelet therapy (*Circ* 2022;145:e18 & *EHJ* 2018;39:213)

- Determined by presentation (ACS vs. CCD) and ischemic (Pt & procedural) & bleeding risk
- DAPT (ASA 81 + $P2Y_{12}$ inhib) in CCD ideally for ≥3–6 mo. In ACS (qv) default is 1 yr; ASA d/c after 1–3 mos ↓ bleed w/o ↑ MACE. After full course of DAPT, clopi monoRx more efficacious & safer than ASA monoRx (*Lancet* 2025;405:1252).

- If oral anticoag, clopi+DOAC and stop ASA after 1–4 wks to ↓ bleed (*JAMA Cardiol* 2020;5:582). Consider OAC monoRx in low-risk Pts after 12 mos.

CHRONIC CORONARY DISEASE

Definition

- CCD (aka, stable ischemic heart disease) refers to asx and stably sx Pts as well as low-risk new-onset chest pain felt to be due to IHD; excludes rapidly progressive sx or ACS

Noninvasive testing (*Circ* 2021;144:e368 & 2023;148:e20)

- Noninvasive dx testing most valuable when pretest probability is *intermediate* (variably defined as anywhere from 30–70% to 10–90%); typically test if pretest probability >15%
- Several pretest probability scores that take into account age, sex, nature of sx, risk factors
- Exercise ECG testing or CAC reasonable in some low-risk Pts
- In intermediate/high-risk Pts, stress test w/ imaging or CCTA (see "Noninv Eval of CAD")
- If known nonobstructive CAD & stable chest pain: stress testing or CCTA ± FFR
- If obstructive CAD & stable chest pain: stress testing or invasive angio if high-risk CAD

Coronary angiography for CCD (*Circ* 2014;130:1749)

- High-risk noninvasive testing results suggestive of left main or multivessel CAD
- Angina that is refractory to optimal medical therapy
- Uncertain dx after noninvasive testing, occupational need (eg, pilot)
- Unexplained heart failure, ↓ EF, SCD, or life-threatening ventricular arrhythmia

Major risk factor modification (*Circ* 2023;148:e29)

- **LDL-C <70 (or 55) mg/dL**: statin ± EZE, bempedoic acid, PCSK9i (see "Dyslipidemia")
- **BP <130/80** (see "Hypertension"); in CCD may opt for ACEI and βB (if angina)
- **Diabetes** management (qv): GLP1-RA ± SGLT2i; Hb_{A1c} ≤7%
- **Smoking cessation**; influenza vaccine
- **BMI**: 18.5–24.9 kg/m^2; if overweight, GLP-1RA ↓ MACE (*NEJM* 2023;389:2221)
- Diet: ↑ vegetables, fruits, whole grains; ↓ sat. fat, *trans* fatty acids, sweets, red meat, Na; Mediterranean diet ↓ MACE (*Lancet* 2022;399:1876). 150 min/wk mod physical activity.

Optimal medical therapy (OMT) (*Circ* 2023;148:e37)

- **Antiplt Rx:** ASA ~81 mg/d *or* $P2Y_{12}$ inhib (↓ bleeding & ≅ MACE vs. ASA; *JACC* 2023;82:89)
  - DAPT post-PCI & ACS (qv). Prolonged DAPT in CCD w/o MI but w/ DM ↓ MACE but ↑ bleeding (*NEJM* 2019;381:1309).
  - If AF, a/c w/o vs. w/ antiplt ↓ bleeding w/o ↑ MACE (*JACC* 2025;85:1189)
- **βB** if ↓ EF; conflicting data for routine long-term use (*NEJM* 2024;390:1372 & 391:1277)
- **ACEI** (or ARB if intolerant of ACEI) if HTN, DM, CKD, or ↓ EF (*Lancet* 2006;368:581)
- Rivaroxaban 2.5 mg bid + ASA 100 mg/d: 24% ↓ CV events and 18% ↓ death vs. ASA alone, but ↑ major bleeding (*NEJM* 2017;377:1319)
- Colchicine (0.5 mg/d): conflicting data regarding benefit (*NEJM* 2020;383:1838 & 2025;392:633)

Medical therapies for symptomatic relief (*Circ* 2023;148:e59)

- **Beta-blockers** *1st-line therapy*; CCB (except short-acting dihydropyridines)

- **Long-acting nitrates**
- Ranolazine (↓ late inward Na+ current to ↓ myocardial demand): 2nd-line anti-anginal

Revascularization (*JAMA* 2021;325:1765; *Circ* 2022;145:e18 & 2023;148:e61; *Lancet* 2023;401:1611)

- OMT should be initial focus if stable & w/o evidence of critical anatomy & w/ normal EF
- Goal of revasc should be to ↓ risk of CV morbidity & mortality or to relieve refractory sx
- PCI ↓ anginal sx vs. sham procedure for Pts not on anti-anginal Rx (*NEJM* 2023;389:2319)
- *Older studies:* survival benefit w/ revasc (CABG) vs. med Rx (pre-statin) if: LM disease (≥50% stenosis); 3VD (≥70% stenoses) especially if ↓ EF, 2VD w/ critical proximal LAD
- More recent studies have reevaluated benefit of revasc and PCI vs. CABG
- **MVD & LVEF <35%**: CABG vs. med Rx ↓ mortality by 16%, CV mortality by 21%, and hosp for HF by ~20% after median of 10 yrs (*NEJM* 2016;374:1511). In contrast, PCI did *not* ↓ CV mortality or hosp for HF, but did ↓ spont. MI & unplanned revasc (*NEJM* 2022;387:1351).
- **MVD & DM**: CABG (but not PCI) ↓ risk of MACE by ~25% (*NEJM* 2009;360:2503). In head-to-head comparison, CABG vs. PCI ↓ risk of death or MI, but ↑ stroke (*NEJM* 2021;367:2375).
- **MVD or LM**: CABG vs. PCI ↓ risk of MI & repeat revasc; ? ↓ CV death if complex coronary anatomy, but less clear in current era (*Lancet* 2018;391:939; 2021;398:2247; 2025;405:1481)
- In Pts w/o LM disease & nl LVEF, revasc (largely if not exclusively PCI) vs. OMT did not Δ risk of death, ↑ peri-PCI MI, and ↓ spontaneous MI. Magnitude of benefit tended to be greater in those w/ multivessel disease, prox LAD disease, diabetes, and LVEF 35–45% (*NEJM* 2007;356:1503 & 2020;382:1395; *Circ* 2020;142:1725).
- Recs vary by professional societies (*Circ* 2023;148:e61; *EHJ* 2024;45:3415), but generally:
  - Lifestyle-limiting angina after OMT
  - LM (≥50% stenosis): CABG preferred over PCI unless low SYNTAX score
  - MVD w/ EF <35% or DM: CABG (? PCI if very high surgical risk)
  - 3VD: CABG preferred over PCI if intermediate or high SYNTAX score
  - Proximal LAD stenosis: PCI or CABG
  - Heart Team approach recommended if PCI vs. CABG unclear (esp. complex 3VD)

ACUTE CORONARY SYNDROMES

Spectrum of Acute Coronary Syndromes			
Dx	**UA**	**NSTEMI**	**STEMI**
Coronary thrombosis	Subtotal occlusion		Total occlusion
History	Angina that is new-onset, crescendo, or at rest; usually <30 min		Angina at rest
ECG	± ST depression and/or TWI 		ST elevations 
Troponin/CK-MB	⊖	⊕	⊕ ⊕

Ddx (causes of myocardial ischemia/infarction other than atherosclerotic plaque rupture)

- **Ischemia w/o plaque rupture** ("type 2" MI): ↑ demand (eg, ↑ HR), ↓ supply (eg, HoTN). More likely in older, ♀, non-CAD comorbidities (CKD, etc.) (*JACC* 2021;77:848). Distinguishing from ACS is

clinical dx; angiography is gold standard.

- **Nonatherosclerotic coronary artery disease** (*JACC* 2018;72:2231)
  - Spasm: Prinzmetal's variant, cocaine-induced (6% cocaine users w/ chest pain r/i for MI)
  - Dissection: spontaneous (vasculitis, CTD, pregnancy), aortic dissection with retrograde extension (usually involving RCA → IMI) or mechanical (PCI, surgery, trauma)
  - Embolism (*Circ* 2015;132:241): AF, thrombus/myxoma, endocard., prosth. valve thrombosis
  - Vasculitis: Kawasaki syndrome, Takayasu arteritis, PAN, EGPA, SLE, RA
  - Congenital: anomalous origin from aorta or PA, myocardial bridge (intramural segment)
- **Direct myocardial injury:** myocarditis, Takotsubo/stress CMP, toxic CMP, cardiac contusion

Clinical manifestations (*JAMA* 2015;314:1955)

- **Cardiac chest pain ("angina"):** retrosternal pressure/pain/tightness ± radiation to neck, jaw, arms. Precipitated by exertion (physical or emotional), ↓ w/ rest or NTG. In ACS: new-onset, crescendo, or at rest.
- **Associated symptoms:** dyspnea, diaphoresis, N/V, palpitations or light-headedness
- Nonclassic sx (incl N/V & epig pain) may be more common in ♀, elderly, DM, IMI

Physical exam (signs may be seen, but often are not)

- Signs of ischemia: S_4, new MR murmur 2° pap. muscle dysfxn, paradoxical S_2, diaphoresis
- Signs of HF (eg, if large MI or ischemic MR): ↑ JVP, crackles, ⊕ S_3, HoTN, cool extremities
- Signs of other vascular disease: asymmetric BP, carotid or femoral bruits, ↓ distal pulses

Diagnostic studies (*NEJM* 2017;376:2053)

- **ECG:** ST ↓/↑, TWI, new LBBB, hyperacute Tw; Qw/PRWP may suggest prior MI & ∴ CAD
  ✓ ECG w/in 10 min of presentation, with any Δ in sx & at 6–12 h; compare w/ baseline
- STEMI dx challenging w/ old LBBB or ventricular pacing:
  - Sgarbossa: ≥1 mm STE *concordant* w/ QRS (Se 73%, Sp 92%), STD ≥1 mm V_1–V_3 (Se 25%, Sp 96%), STE ≥5 mm *discordant* w/ QRS (Se 31%, Sp 92%)
  - Barcelona: ST deviation ≥1 mm *concordant* w/ QRS in any lead, or ST deviation ≥1 mm *discordant* w/ QRS in leads with max voltage (largest R or S) ≤6 mm (Se 93%, Sp 94%)

Localization of MI		
Anatomic Area	**ECG Leads w/ STE**	**Coronary Artery**
Septal	V_1–V_2	Proximal LAD
Anterior	V_3–V_4	LAD
Apical	V_5–V_6	Distal LAD, LCx, or RCA
Lateral	I, aVL	LCx
Inferior	II, III, aVF	RCA (~85%), LCx (~15%)
RV	V_1–V_2 & V_4R (most Se)	Proximal RCA
Posterior	ST *depression* V_1–V_3 (= STE V_7–V_9 posterior leads, ✓ if clinical suspicion)	RCA or LCx

If ECG non-dx & suspicion high, ✓ leads V_7–V_9 (⊕ if ≥0.5 mm STE) to assess distal LCx/RCA territory. ✓ R-sided precordial leads in IMI to detect RV involvement (STE in V_4R most Se). STE in III > STE in II and lack of STE in I or aVL suggest RCA rather than LCx culprit in IMI. STE in aVR suggests LM, prox LAD, or diffuse ischemia.

- **Cardiac biomarkers:** ✓ Tn (pref. over CK-MB) at presentation & 3–6 h if conventional assay or 1–2 h later if high-sens assay; repeat if clinical or ECG Δs. **Universal def. of MI:** >99th %ile w/ rise and/or fall in appropriate clinical setting (eg, sx, ECG Δs, WMA).
- If low prob, **stress test** or **CCTA** to r/o CAD; new WMA on TTE suggests ACS
- **Invasive coronary angio** gold standard for epicardial CAD

Prinzmetal's (variant) angina

- Coronary spasm → transient STE usually w/o MI (*but* MI, AVB, VT can occur)
- Pts usually young, smokers, ± other vasospastic disorders (eg, migraines, Raynaud's)
- Angiography: nonobstructive CAD (spasm can be provoked during cath but rarely done)
- Treatment: high-dose CCB & standing nitrates (+SL prn), ? α-blockers/statins; d/c smoking. Avoid: high-dose ASA (can inhibit prostacyclin & worsen spasm), nonselect βB, triptans.
- Cocaine-induced vasospasm: CCB, nitrates, ASA; ? avoid βB, but labetalol appears safe

MI in absence of obstructive CAD (MINOCA)

- Definition: MI but w/o coronary stenosis ≥50% in any major epicardial vessel
- More common in younger Pts, women (2× ♀ > ♂), Black/Pacific race or Hispanic
- Advanced coronary imaging (eg, OCT) & cardiac MRI to exclude missed coronary obstruction, other causes of myocyte injury (eg, myocarditis), other causes of ↑ Tn (eg, PE)
- ~75% ischemic (eg, plaque disruption, SCAD, spasm), 25% alternative dx (eg, myocarditis)

Likelihood of ACS (*Circ* 2007;116:e148; *Circ* 1994;90[1]:613-622)			
Feature	**High** (any of below)	**Intermediate** (no high features, any of below)	**Low** (no high/inter. features, may have below)
History	Chest or L arm pain like prior angina, h/o CAD (incl MI)	Chest or arm pain, age >70 y, male, diabetes	Atypical sx (eg, pleuritic, sharp, or positional pain)
Exam	HoTN, diaphoresis, HF, transient MR	PAD or cerebrovascular disease	Pain reproduced on palp.
ECG	New STD (≥1 mm) TWI in mult leads	Old Qw, STD (0.5–0.9 mm), TWI (>1 mm)	TWF/TWI (<1 mm) in leads w/ dominant R wave
Biomarkers	⊕ Tn or CK-MB	Normal	Normal

Acute Anti-Ischemic and Analgesic Treatment for All ACS Types	
Nitrates (SL or IV) 0.3–0.4 mg SL q5min ×3, then consider IV if still sx	Use for sx, control HTN or Rx of HF. No clear ↓ in mortality. *Caution* if preload-sensitive (eg, HoTN, AS, sx RV infarct); contraindic. if marked brady/tachy or recent PDE5i use.
β-Blockers eg, metop 25–50 mg PO q6h titrate slowly to HR 50–60 *may* consider IV (5 mg q2–5′ × 3) if planning 1° PCI or HTN and no contraindic.	↓ ischemia & progression of UA to MI (*JAMA* 1988;260:2259) STEMI: ↓ arrhythmic death & reMI, but high doses can ↑ cardiogenic shock (espec if signs of HF), & ∴ no Δ overall mortality (*Lancet* 2005;366:1622) *Contraindicated* if PR >0.24 sec, HR <60, 2°/3° AVB, severe bronchospasm, s/s HF or low output, risk factors for shock (eg, >70 y, HR >110, SBP <120, late presentation STEMI)
Morphine	Relieves pain/anxiety; venodilation ↓ preload. Do not mask refractory sx. May delay antiplt effect of $P2Y_{12}$ inhibitor.
Oxygen	Use if needed to keep S_aO_2 >90% (*NEJM* 2017;377:1240)
Transfusion	Data mixed (favoring restrictive in 1 trial, liberal in another, w/ no

	benefit in most anemic in the latter). Hb goal of ≥8 g/dL, can consider ≥10 g/dL (*JAMA* 2021;325:552; *NEJM* 2023;389:2446).

Other early adjunctive therapy for all ACS types

- **Intensive lipid-lowering therapy** High-intensity statin (eg, atorva 80 mg qd) ↓ ischemic events (PROVE-IT TIMI 22, *NEJM* 2004;350:1495) w/ benefit emerging w/in wks (*JAMA* 2001;285:1711 & *JACC* 2005;46:1405); ↓ peri-PCI MI (*JACC* 2010;56:1099); ? ↓ contrast-induced nephropathy (*NEJM* 2019;380:2156)
  - Ezetimibe: ↓ CV events when added to statin (IMPROVE-IT, *NEJM* 2015;372:2387)
  - PCSK9i: being studied in ACS, but favorable effects on plaque & ↓ MACE longterm
- **RASi & MRA:** start once hemodynamics and renal fxn stable (hold RASi if anticipate CABG). See "Long-Term Post-ACS Mgmt" section for details.
- IABP: can be used for refractory angina as bridge to definitive revascularization

NSTE-ACS (*EHJ* 2021;42:1289; *Circ* 2025;151:e771)

Antiplatelet Therapy	
Aspirin: 162–325 mg × 1, then 81 mg qd (non-enteric-coated, chewable)	50–70% ↓ D/MI (*NEJM* 1988;319:1105) If allergy, use clopi and/or desensitize to ASA
P2Y$_{12}$ inhibitor (choose one in addition to ASA). Timing (on presentation or at angio) controversial, but consider upstream clopidogrel or ticagrelor if anticipate >24 hrs to angio.	
• **Ticagrelor** (preferred over clopi) 180 mg × 1 → 90 mg bid Reversible, but wait 3–5 d prior to surg. Antidote being developed (*NEJM* 2019;380:1825).	More rapid and potent plt inhib c/w clopi 16% ↓ CVD/MI/stroke & 21% ↓ CV death c/w clopi; ↑ non-CABG bleeding (*NEJM* 2009;361:1045) Given upstream or at time of PCI Dyspnea (but S_aO_2 & PFTs nl) & ventricular pauses
• **Prasugrel** (preferred over clopi) 60 mg × 1 at PCI → 10 mg qd (consider 5 mg/d if <60 kg) Wait 7 d prior to surgery Contraindicated if h/o TIA/CVA; caution if ≥75 y	More rapid and potent plt inhib c/w clopi 19% ↓ CVD/MI/stroke in ACS w/ planned PCI vs. clopi, but ↑ bleeding (*NEJM* 2007;359:2001) In NSTE-ACS, should be given at time of PCI (not upstream) due to ↑ bleeding (*NEJM* 2013;369:999) ? ↓ MACE vs. ticagrelor (*NEJM* 2019;381:1524)
• **Clopidogrel** 300–600 mg × 1 → 75 mg qd Wait 5 d prior to surgery	ASA+clopi → 20% ↓ CVD/MI/stroke vs. ASA alone ~30% of population has ↓ fxn CYP2C19 → ↑ CV events if PCI on clopi (*NEJM* 2009;360:354)
• **Cangrelor*** Only IV P2Y$_{12}$ inhibitor Rapid onset/offset; t½ 3–5	22% ↓ CV events (mostly peri-PCI MI and stent thrombosis) vs. clopi 300 mg at time of PCI; no significant ↑ bleeding (*NEJM* 2013;368:1303)

min	
GP IIb/IIIa inhibitors (GPI): abciximab; eptifibatide; tirofiban Given ≤24 h peri- & post-PCI	No clear benefit for routinely starting prior to PCI and ↑ bleeding (*NEJM* 2009;360:2176) Consider if large clot burden, no reflow or slow flow

*Transition from cangrelor to oral $P2Y_{12}$ inhib.: ticagrelor loading dose during infusion or immediately after d/c of infusion; prasugrel or clopidogrel loading dose only immediately *after* d/c of infusion

Anticoagulant Therapy (choose one)	
UFH: 60 U/kg IVB (max 4000 U) then 12 U/kg/h (max 1000 U/h initially) × 48 h or until end of PCI	24% ↓ D/MI (*JAMA* 1996;276:811) Titrate to aPTT 1.5–2× control (~50–70 sec) Hold until INR <2 if already on warfarin
Enoxaparin (low-molec-wt heparin) 1 mg/kg SC bid (± 30 mg IVB) (qd if CrCl <30) × 2–8 d or until PCI	~10% ↓ D/MI vs. UFH (*JAMA* 2004;292:45,89). Can perform PCI on enox (*Circ* 2001;103:658), but ↑ bleeding if switch b/w enox and UFH.
Bivalirudin (direct thrombin inhibitor) 0.75 mg/kg IVB at PCI → 1.75 mg/kg/h	No diff in bleeding, MI, or death c/w UFH (*NEJM* 2017;377:1132). Use instead of UFH if HIT.
Fondaparinux (Xa inh) 2.5 mg SC qd	Rarely used; must supplement w/ UFH if PCI

Coronary angiography (*Circ* 2025;141:e00; *EHJ* 2023;44:3720)

- **Immediate/urgent coronary angiography** (w/in 2 h) if refractory/recurrent angina, hemodynamic or electrical instability, s/s HF or cardiogenic shock
- **Invasive strategy**
  - *Routine = coronary angiography for all*
  - *Selective = invasive angio only if recurrent sx or ⊕ noninvasive test (stress or CCTA)*
  - Routine strategy → 32% ↓ rehosp for ACS, nonsignif 16% ↓ MI, no Δ in mort. c/w select angio (*JAMA* 2008;300:71). ↑ peri-PCI MI counterbalanced by ↓↓ in spont. MI.
  - ∴ Routine invasive recommended if high or intermediate risk (eg, based on TIMI or GRACE risk score). If lower risk (TIMI Risk Score <2, GRACE <109, sx resolved, Tn ⊖, no ST Δs) either strategy acceptable.
  - Elderly (≥75): no clear benefit, but 25% ↓ MI; proc. complic. <1% (*NEJM* 2024;391:1673)
- **Timing of angiography** (*NEJM* 2009;360:2165; *Circ* 2018;138:2741)
  - *Early (w/in 24 h) if:* steeply rising Tn, ongoing dynamic ST Δ, GRACE risk score >140
  - *Delayed (ie, w/in 48–72 h) acceptable if:* GRACE 109–140, stable or ↓ Tn, sx resolved
- PCI of all significant non-culprit lesions (either at time of procedure or later during hosp.) ↓ CV death & recurrent MI (*NEJM* 2023;389:889; *JACC* 2024;84:276)

TIMI Risk Score (TRS) for UA/NSTEMI (*JAMA* 2000;284:835)			
Calculation of Risk Score		**Application of Risk Score**	
Characteristic	**Point**	**Score**	**D/MI/UR by 14 d**
Historical		0–1	5%
Age ≥65 y	1	2	8%
≥3 risk factors for CAD	1	3	13%
Known CAD (stenosis ≥50%)	1	4	20%
ASA use in past 7 d	1	5	26%

Presentation		6–7	41%
Severe angina (≥2 episodes w/in 24 h)	1	Higher risk Pts (TRS ≥3) derive ↑ benefit from LMWH, GP IIb/IIIa inhibitors, and early angiography (*JACC* 2003;41:89S)	
ST deviation ≥0.5 mm	1		
⊕ cardiac marker (troponin, CK-MB)	1		
RISK SCORE = Total points	**(0–7)**		

STEMI (*EHJ* 2023;44:3720; *Circ* 2025;151:e771)

Requisite ECG changes

- STE at J point in ≥2 contiguous leads w/ ≥1 mm (except for V_2–V_3: ≥2.5 mm in ♂ <40 yrs, ≥2 mm in ♂ ≥40 yrs, and ≥1.5 mm in ♀ regardless of age), *or*
- New or presumed new LBBB w/ compelling H&P, *or*
- True posterior MI: ST depression V_1–V_3 ± tall Rw w/ STE on posterior leads (V_7–V_9)

Reperfusion ("time is muscle")

- In PCI-capable hospital, goal should be **primary PCI w/in 90 min** of 1st medical contact
- In non–PCI-capable hospital, consider *transfer* to PCI-capable hospital (if PCI w/in 120 min of 1st medical contact), otherwise **fibrinolytic therapy** w/in 30 min of hospital presentation
- Do not let decision regarding *method* of reperfusion delay *time* to reperfusion

Primary PCI (*JACC* 2013;61:e78 & 2016;67:1235)

- Definition: immediate PCI upon arrival to hospital or transfer for immediate PCI
- Indications: **STE** + sx onset w/in <12 h; ongoing ischemia 12–24 h after sx onset; shock
- Superior to lysis: 27% ↓ death, 65% ↓ reMI, 54% ↓ stroke, 95% ↓ ICH (*Lancet* 2003;361:13)
- Transfer to center for 1° PCI superior to lysis (*NEJM* 2003;349:733), vide infra

Fibrinolysis (TNK-tPA, tPA, rPA)

- Indic: STE/LBBB + sx <12 h (& >120 min before PCI can be done); benefit if sx >12 h less clear; reasonable if persist. sx & STE, hemodynamic instability or large territory at risk
- Mortality ↓ ~20% in anterior MI or LBBB and ~10% in IMI c/w Ø reperfusion Rx
- Prehospital lysis (ie, ambulance): further 17% ↓ in mortality (*JAMA* 2000;283:2686)
- ~1% risk of ICH; high risk incl elderly (~2% if >75 y), ♀, low wt. ? PCI more attractive
- **Absolute contraindications**: prior ICH, intracranial neoplasm/aneurysm/AVM, ischemic stroke or closed head trauma w/in 3 mo, head/spinal surg w/in 2 mo, active internal bleed, bleeding diathesis, suspected Ao dissection, severe uncontrolled HTN
- **Relative contraindication**: h/o severe HTN or SBP >180 or DBP >110 on presentation, ischemic stroke >3 mo prior, CPR >10 mins, major surg/trauma w/in 3 wk, internal bleed w/in 2–4 wk, active PUD, pregnancy, current a/c Rx, non-compressible vascular puncture

Nonprimary PCI

- Rescue PCI if shock, unstable, failed reperfusion, or persistent sx (*NEJM* 2005;353:2758)
- Routine angio ± PCI w/in 24 h of successful lysis: ↓ D/MI/revasc (*Lancet* 2004;364:1045) and w/in 6 h ↓ reMI, recurrent ischemia, & HF compared to w/in 2 wk (*NEJM* 2009;360:2705);

∴ *if lysed at hosp. w/o PCI, transfer to PCI-capable hosp. ASAP espec. if high risk (eg, ant. MI, IMI w/ ↓ EF or RV infarct, extensive STE/LBBB, HF, ↓ BP or ↑ HR)*

- Late PCI (median day 8) of occluded infarct-related artery: no benefit (*NEJM* 2006;355:2395)

Antiplatelet Therapy	
Aspirin 162–325 mg × 1 (crushed/chewed) then 81 mg qd	23% ↓ in death (*Lancet* 1988;ii:349) Should not be stopped if CABG required
$P2Y_{12}$ inhibitor *Give ASAP (do not wait for angio)* Ticagrelor or prasugrel (if PCI) as detailed above Clopidogrel: 600 mg pre-PCI; 300 mg if lysis (no LD if >75 y) → 75 mg qd	*PCI:* prasugrel and ticagrelor ↓ CV events c/w clopi (*Lancet* 2009;373:723 & *Circ* 2010;122:2131) Prehospital ticagrelor may be safe & ? ↓ rate of stent thrombosis (*NEJM* 2014;371:1016) *Lysis:* clopidogrel 41% ↑ in patency, 7% ↓ mort, no Δ major bleed or ICH (*NEJM* 2005;352:1179; *Lancet* 2005;366:1607); no data for pras or ticag w/ lytic
GP IIb/IIIa inhibitors abciximab, eptifibatide, tirofiban	*Peri-PCI:* consider if lg thrombus, no/slow reflow *Lysis:* no indication (*Lancet* 2001;357:1905)

(*NEJM* 2021;384:452; *JAMA* 2021;325:1545)

Anticoagulant Therapy (choose one)	
UFH *PCI:* 70–100 U/kg IVB (if w/o GP inhib) *Lysis:* 60 U/kg IVB (max 4000 U) → 12 U/kg/h (max 1000 U/h initially)	No demonstrated mortality benefit ↑ patency with fibrin-specific lytics Titrate to ACT for PCI or to aPTT 1.5–2× control (~50–70 sec) for lysis
Bivalirudin 0.75 mg/kg IVB → 1.75 mg/kg/hr IV extending 2–4 hrs post-PCI	*PCI:* ↓ bleeding, and w/ post-PCI infusion, no excess in ischemic events, ↓ stent thrombosis, and 25% ↓ mortality vs. UFH (*Lancet* 2022;400:1847)
Enoxaparin *PCI:* 0.5 mg/kg IVB *Lysis:* 30 mg IVB → 1 mg/kg SC bid (adjust for age >75 & CrCl)	*PCI:* ↓ D/MI/revasc and ≈ bleeding vs. UFH (*Lancet* 2011;378:693) *Lysis:* 17% ↓ D/MI w/ ENOX × 7 d vs. UFH × 2 d (*NEJM* 2006;354:1477)

Management of non-culprit arteries (*JACC* 2025;85:19)

- Primary PCI refers to revascularization of infarct-related or “culprit” artery in STEMI
- Pts w/ STEMI often have coexisting atherosclerotic lesions in non–infarct-related coronary arteries. Inflammatory milieu post-STEMI may ↑ risk of further plaque rupture.
- PCI of non-culprit arteries (stenoses ≥70% or FFR ≤0.80 if 50–69%) early after STEMI (during initial PCI, prior to or early after d/c) ↓ recurrent MACE, primarily recurrent MI (COMPLETE, *NEJM* 2019;381:1411 & FIRE, *NEJM* 2023;389:889). For unclear reasons, purely FFR-guided revasc of non-culprit lesions did not show a benefit (*NEJM* 2024;390:1481).
- Comparison of immediate vs. staged (19–45 d later) non-culprit PCI showed immediate ↓ ischemia-driven revasc & periprocedural MI (as hard to dx in setting of STEMI), but no clear effect on spont. MI or cardiac death (MULTISTARS AMI, *NEJM* 2023;389:1368). PCI of non-culprit arteries during same hosp. reasonable (espec. if severe proximal stenosis).
- Risks outweigh benefits (↑ death and renal replacement Rx) in Pts with cardiogenic shock at presentation (CvLPRIT-SHOCK, *NEJM* 2017;377:2419)

CABG in STEMI

- Urgent CABG if coronary anatomy not amenable to PCI, particularly if (1) ongoing ischemia or large area of jeopardized myocardium, or (2) cardiogenic shock or severe HF
- Timing based on hemodynamic stability, ongoing ischemia, and myocardium at risk
- Do not hold ASA, but, if possible, wait several days after last dose of $P2Y_{12}$ inhibitor

LV failure (occurs in ~25%)

- Diurese to achieve PCWP ~14 mmHg → ↓ pulmonary edema, ↓ myocardial O_2 demand
- ↓ Afterload → ↑ stroke volume & CO, ↓ myocardial O_2 demand. Can use IV NTG or nitroprusside (although risk of coronary steal) → short-acting ACEI.
- Inotropes if HF despite diuresis & ↓ afterload; use dobutamine, milrinone or dopamine
- **Cardiogenic shock** (~7%) SBP <90, CI <2.2 L/min/m^2, PCWP >18 mmHg, e/o end-organ dysfunction (eg, ↑ lactate)
  - If not done already, coronary revasc (*NEJM* 1999;341:625)
  - Support w/ inotropes or mechanical circulatory support to keep CI >2.2
    - **Intra-aortic balloon pump (IABP)** counterpulsation offers ~0.5 L/min CO and ↑ coronary perfusion, but no 30-day survival benefit if early revasc or long-term survival benefit (*NEJM* 2012;367:1287; *Circ* 2018;139:395)
    - **Axial flow pumps (eg, Impella)** offer up to 3.7–5.5 L/min CO, ↓ death by 26%, but approximately doubled risk of major bleeding, sepsis, and renal replacement therapy, and ~6% risk of limb ischemia (*NEJM* 2024;390:1382)

IMI complications (*Circ* 1990;81:401; *NEJM* 1994;330:1211; *JACC* 2003;41:1273)

- **Heart block:** ~20%, occurs in part because RCA typically supplies AV node; 40% on present., 20% w/in 24 h, rest by 72 h; high-grade AVB can develop abruptly; Rx: atropine, epi, aminophylline (100 mg/min × 2.5 min), temp pacing wire
- **RV infarct:** proximal RCA occlusion → ↓ flow to RV marginals
  - Angiographically present in 30–50% of cases, but only ~½ clinically significant
  - HoTN, ↑ JVP, ⊕ Kussmaul's; ≥1 mm STE in V_4R; RA/PCWP ≥0.8; RV dysfxn on TTE
  - Rx: optimize preload (RA goal 10–14 mmHg; *BHJ* 1990;63:98); ↑ contractility (dobutamine); maintain AV synchrony (pacing as necessary); reperfusion (*NEJM* 1998;338:933); mechanical support (eg, RVAD); pulmonary vasodilators (eg, inhaled NO)

Mechanical complications (incid. **<1%** for each; typically occur a few days post-MI)

- **Free wall rupture:** ↑ risk w/ lysis, large MI, ↑ age, ♀, HTN; p/w PEA or hypoTN, pericardial sx, tamponade; Rx: volume resusc., ? pericardiocentesis, inotropes, **surgery**
- **VSD:** large MI; AMI → apical VSD, IMI → basal septum; 90% w/ harsh murmur ± thrill (*NEJM* 2002;347:1426); Rx: diuretics, vasodil., inotropes, IABP/MCS, **surgery**, perc. closure
- **Papillary muscle rupture:** more common after IMI (PM pap m. supplied by PDA alone) than AMI (AL pap m. supplied by OMs & diags); 50% w/ new murmur; ↑ *v* wave in PCWP tracing; asymmetric pulm edema. Rx: diuretics, vasodilators, IABP/MCS, **surgery.**

Arrhythmias post-MI (treat all per ACLS protocols if unstable or symptomatic)

- **AF** (10–16% incidence): βB or amio, ± digoxin (particularly if HF), heparin
- **VT/VF:** lido or amio × 6–24 h, then reassess; ↑ βB as tol., replete K & Mg, r/o ischemia; MMVT <48 h post-MI does *not* worsen prognosis; >48 h, consider ICD (vide infra)
- Accelerated idioventricular rhythm (AIVR): "slow VT" (<110 bpm), often after reperfusion; typically asx, gradual onset/offset, and does not require treatment
- Backup transcutaneous *or* transvenous pacing if: 2° AVB type II; BBB + AVB
- **Transvenous pacing** if: 3° AVB; new BBB + 2° AVB type II; alternating LBBB/RBBB

Other Post-MI Complications (*JACC* 2024;83:1886, 1902, 1917)		
Complication	**Clinical Features**	**Treatment**
LV thrombus	~30% incid. (espec lg anteroapical MI)	AC × 3–6 mo (VKA or DOAC)
Ventricular aneurysm	Noncontractile outpouching of LV; 8–15% incid. (espec ant); persist STE	Surgery or perc repair if HF, thromboemboli, arrhythmia
Ventricular pseudoaneurysm	Rupture (narrow neck) → sealed by thrombus and pericardium (esp in inf).	Urgent surgery (or percutaneous repair)
Pericarditis	10–20% incid.; 1–4 d post-MI ⊕ pericardial rub; ECG Δs rare	High-dose ASA, colchicine, Ø NSAIDs; minimize anticoag
Dressler's syndrome	<4% incid.; 2–10 wk post-MI fever, pericarditis, pleuritis	High-dose aspirin, colchicine

Checklist and Long-Term Post-ACS Management

Risk stratification

- Stress test if anatomy undefined
- If significant residual CAD (beyond revascularized culprit lesion) consider revascularization during index hospitalization (vide supra)
- Assess LVEF prior to d/c; EF ↑ ~6% after STEMI over 6 mo (*JACC* 2007;50:149)

Antiplatelet therapy

- **Aspirin:** 81 mg daily (no clear benefit to higher doses)
- **$P2Y_{12}$ inhibitor:** ticagrelor or prasugrel preferred over clopi. In landmark analyses, benefit over clopidogrel both early & late. De-escalation (ticag → clopi or pras 10 → 5 mg) after 1 mo ↓ bleeding w/o clear ↑ MACE, but wide CIs (*Lancet* 2020;396:1079 & 2021;398:1305).
- Duration controversial. Traditionally ASA lifelong and $P2Y_{12}$ inhib for 12 mos. *d/c ASA* after 1–3 mos and continue $P2Y_{12}$ inhib monoRx (pref. ticagrelor, not clopi) ↓ bleeding ~40% w/o ↑ MACE (*Circ* 2020;142:538; *JAMA Cardiol* 2022;7:407; *Lancet* 2024;404:937) *prolonged $P2Y_{12}$ inhib* >12 mos → ↓ MACE but ↑ bleeding (*NEJM* 2014;371:2155 & 2015;372:1791). Consider if high ischemic and low bleeding risk.
- PPI should be started w/ DAPT or AC if high GI bleeding risk

Anticoagulation

- If need a/c (eg, AF), use DOAC + DAPT (typically clopi + ASA) then d/c ASA after 1–4 wks
- Consider dropping $P2Y_{12}$ inhibitor after 6–12 mos depending on bleeding & ischemic risk

Other CV drugs

- **β-blocker:** in older trials, 23% ↓ mortality after MI. Recent open-label trial w/ relatively high crossover did not show benefit of post-discharge βB in AMI s/p revasc w/ nl LVEF (although possible benefit in STEMI) (*NEJM* 2024;390:1372).
- **ACEI/ARB:** if HF, ↓ EF, HTN, DM, anterior STEMI. Trend toward ARNI better than ACEI in post-MI Pts w/ ↓ EF (*NEJM* 2021;385:1845). ? long-term benefit of ACEI/ARB in CAD w/o HF (*NEJM* 2000;342:145 & 2004;351:2058).
- **Aldosterone antag:** 15% ↓ mort. if EF <40% & either s/s of HF or DM (*NEJM* 2003;348:1309); in STEMI Rx'd w/ PPCI, no Δ in mort., but nonsignif. 23% ↓ HF hosp (*NEJM* 2025;392:643)
- Nitrates: standing long-acting agents if symptomatic; SL NTG prn for all
- Mixed data for low-dose colchicine (*NEJM* 2019;381:2497; 2025;392:633)

Risk factors and lifestyle modifications (*Circ* 2019;139:e1082 & 2025;151:e771; *EHJ* 2020;41:111)

- **LDL-C**: goal <55 mg/dL or even <40 mg/dL if recurrent events
  - *Statin*: high-intensity ↓ LDL-C by ~50% & ↓ MACE (PROVE-IT TIMI 22, *NEJM* 2004;350:1495)
  - *Ezetimibe*: ↓ LDL-C by ~20–24% & ↓ MACE when added to statin (IMPROVE-IT, *NEJM* 2015;372:1500)
  - *PCSK9 inhibitor*: ↓ LDL-C by ~60% & ↓ MACE when added to statin (*NEJM* 2017;376:1713; 2018;379:2097)
  - *Bempedoic acid* ↓ LDL-C by ~18% & ↓ MACE in Pts not on statin (*NEJM* 2019;380:3022)
- **BP** <130–140/80–90, ? SBP 120s espec. if DM (*NEJM* 2021;384:1921 & 2025;392:1155)
- DM: GLP-1RA ↓ MACE. SGLT2i ↓ CV death/HF hosp, w/ possible ↓ MI (*Lancet D&E* 2019;7:776; *Circ* 2024;149:1789); further tailor Hb_{A1c} goal based on Pt (avoid TZDs and saxa if HF)
- BMI ≥27: GLP-1RA ~20% ↓ MACE (*NEJM* 2023;389:2221)
- Quit smoking; exercise (30–60′ 5–7×/wk) 1–2 wk after revasc; cardiac rehab (center or home based) ↓ MI and CV mortality (*NEJM* 2024;390:830)
- Influenza vaccine (*Circ* 2021;144:14764; *NEJM* 2018;378:345); ✓ for depression

ICD (*Circ* 2018;138:e272)

- Sustained VT/VF >2 d post-MI w/o reversible ischemia
- 1° prevention if EF 31–40% w/ NYHA II–III or induc. VT or ≤30% w/ NYHA I–III; wait ideally 40 d after MI and 90 d after revasc. ? *Wearable* defib as bridge (*NEJM* 2018;379:1205).

PA CATHETER AND TAILORED THERAPY

Rationale

- Cardiac output (CO) = SV × HR; optimize SV (and thereby CO) by manipulating preload/ LVEDV (w/ IVF, diuretics), contractility (w/ inotropes), & afterload (w/ vasodilators)
- Balloon at catheter tip inflated → floats into "wedge" position. Column of blood extends from tip of catheter, through pulm venous circulation to a point just prox to LA. Under conditions of no flow, PCWP ≈ LA pressure ≈ LVEDP, which is proportional to LVEDV.
- Situations in which these basic assumptions fail:
  1. Catheter tip not in West lung zone 3 (and ∴ PCWP = alveolar pressure ≠ LA pressure); clues include lack of *a* & *v* waves and if PA diastolic pressure < PCWP
  2. PCWP > LA pressure (eg, mediastinal fibrosis, pulmonary VOD, PV stenosis)
  3. Mean LA pressure > LVEDP (eg, MR, MS)
  4. Poor compliance: "nl" LVEDP may not translate to adequate LVEDV

Indications (*NEJM* 2013;369:e35; *Circ* 2017;136:e268)

- **Diagnosis and evaluation**
  - Ddx of shock (cardiogenic vs. distributive; espec if trial of IVF failed or is high risk) and of pulmonary edema (cardiogenic vs. not; espec if trial of diuretic failed or is high risk)
  - Evaluation of CO, intracardiac shunt, pulm HTN, MR, tamponade, cardiorenal syndrome
  - Evaluation of unexplained dyspnea (PAC during provocation w/ exercise, vasodilator)
- **Therapeutics** (*Circ* 2017;136:e232)
  - Tailored therapy to optimize PCWP, SV, $S_{MV}O_2$, RAP, PVR in heart failure or shock
  - Guide to vasodilator therapy (eg, inhaled NO, nifedipine) in PHT, RV infarction
  - Guide peri-op mgmt in some high-risk Pts, candidacy for mech circ support & transplant
- **Contraindications**

Absolute: right-sided endocarditis, thrombus/mass or mechanical valve; proximal PE
Relative: coagulopathy (reverse), recent PPM or ICD (place under fluoroscopy), LBBB (~5% risk of RBBB → CHB, place under fluoro), bioprosthetic R-sided valve

Efficacy concerns (*NEJM* 2006;354:2213; *JAMA* 2005;294:1664)

- No benefit to routine PAC use in high-risk surgery (*JACC* 2014;62:e77), sepsis, ARDS
- No benefit in decompensated HF (*JAMA* 2005;294:1625); untested in cardiogenic shock
- But: ~½ of *clinical* CO & PCWP estimates incorrect; CVP & PCWP not well correl.; ∴ use PAC to (a) answer hemodynamic ? and then remove, or (b) manage cardiogenic shock

Placement (*NEJM* 2013;369:e35)

- Insertion site: **R IJ** or **L subclavian veins** preferred for "anatomic" flotation into PA
- **Inf late** balloon (max 1.5 mL, mindful of resistance) when **advancing** and to ✓ **PCWP**
- **Deflate** the balloon when **withdrawing** and at all other times
- CXR should be obtained after placement to assess for catheter position and PTX
- If catheter cannot be floated (ie, severe TR, RV dilatation), consider fluoroscopic guidance

Complications

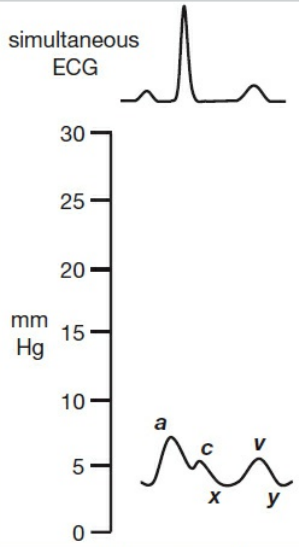
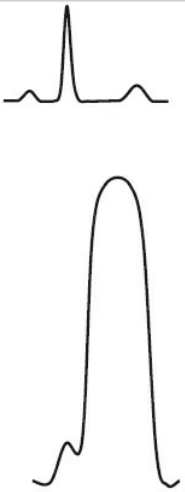
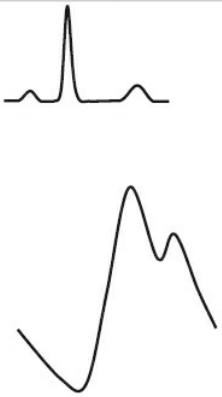
- **Central venous access:** pneumo/hemothorax (~1%), arterial puncture (if inadvertent cannulation w/ dilation → surgical/endovasc eval), air embolism, thoracic duct injury
- **Advancement:** atrial or ventricular arrhythmias (20% NSVT; 3% VT), RBBB (5%), catheter knotting, cardiac perforation/tamponade, PA rupture
- **Maintenance:** infection (espec if catheter >3 d old), thrombus, pulm infarction (≤1%), valve/chordae damage, PA rupture/pseudoaneurysm (espec w/ PHT), balloon rupture

Intracardiac pressures

- Transmural pressure (≈ preload) = measured intracardiac pressure – intrathoracic pressure
- Intrathoracic pressure (usually slightly ⊖) is transmitted to vessels and heart
- **Always measure intracardiac pressure at end-expiration**, when intrathoracic pressure closest to 0 ("high point" in spont. breathing Pts; "low point" in Pts on ⊕ pressure vent.)
- If ↑ intrathoracic pressure (eg, PEEP), measured PCWP *overestimates* true transmural pressures. Can approx by subtracting ~½ PEEP (× ¾ to convert cm H_2O to mmHg).
- PCWP: LV preload best estimated at *a* wave; risk of pulm edema driven by avg PCWP

Cardiac output

- **Thermodilution:** saline injected in RA or intermittent heating of prox thermal filament in some PA lines ("continuous CO"). Δ in temp over time measured at thermistor (in PA) used to calc CO. Inaccurate if ↓ CO, severe TR, or shunt.
- **Fick method:** O_2 consumption (L/min) = CO (L/min) × Δ arteriovenous O_2 content ∴ **CO=$\dot{V}O_2$/C(a–v)O_2**
  - $\dot{V}O_2$ ideally measured (esp. if ↑ metab demands), but freq estimated (125 mL/min/m^2)
  - $C(a\text{-}v)O_2$ = [10 × 1.36 mL O_2/g of Hb × Hb g/dL × (S_aO_2 – $S_{MV}O_2$)]. *$S_{MV}O_2$ is key var that* Δ*s.*
  - If $S_{MV}O_2$ >80%, consider if PAC is "wedged" (ie, pulm vein sat), L→R shunt, impaired O_2 utilization (severe sepsis, cyanide, carbon monoxide), ↑↑ CO or FiO_2

PA Catheter Waveforms				
Location	**RA**	**RV**	**PA**	**PCWP**
Distance	~20 cm	~30 cm	~40 cm	~50 cm
Normal pressure (mmHg)	mean ≤6	syst 15–30 diast 1–8	syst 15–30 mean 9–18 diast 6–12	mean ≥12
Waves				
Comment	*a* = atrial contraction, occurs in PR interval *c* = bulging TV back into RA at start of systole *x* = atrial relax and descent of base of heart *v* = blood entering RA, occurs mid T wave *y* = blood exiting RA after TV opens at start of diastole	RVEDP occurs right before upstroke and ≥ mean RA pressure unless there is TS or TR	Waveform should contain notch (closure of PV). Peak *during* Tw. PA systolic = RV systolic unless there is PS. PA diastolic ≈ PCWP unless ↑ trans-pulm ∇ (eg, ↑ PVR).	Similar to RA except *dampened* and *delayed*. *a* wave *after* QRS, ± distinct *c* wave, *v* wave *after* Tw (helps distinguish PCWP w/ large *v* waves 2° MR from PA).

- PCWP waveform abnormalities: large *a* wave → ? mitral stenosis; large *v* wave → ? mitral regurgitation; blunted *y* descent → ? tamponade; steep *x* & *y* descents → ? constriction

Other calculated metrics

- **SVR & PVR:** calculated by applying Ohm's law (V = IR, or voltage = current × resistance) to circulation. SVR = (MAP – RAP) / CO. PVR = (mean PA pressure – PCWP) / CO.
- Pulmonary artery pulsatility index (PAPi): measure of RV f**x**n based on ratio of R-sided pulse pressure to filling pressure where PAPi = [PA systolic – PA diastolic] / RA pressure

Hemodynamic Profiles of Various Forms of Shock (*NEJM* 2013;369:1726)				
Type of Shock	**RA**	**PCWP**	**CO**	**SVR**
Hypovolemic	↓	↓	↓	↑
Cardiogenic	nl or ↑	↑	↓	↑

RV infarct/massive PE	↑	nl or ↓	↓	↑
Tamponade	↑	↑	↓	↑
Distributive	variable	variable	usually ↑ (can be ↓ in sepsis)	↓

Surrogates: RA ≈ JVP (1 mmHg = 1.36 cm H_2O); pulmonary edema on CXR implies ↑ PCWP; UOP ∝ CO (barring AKI); delayed capillary refill (ie, >2–3 sec) implies ↑ SVR

Tailored therapy in cardiogenic shock (*Circ* 2009;119:e391)

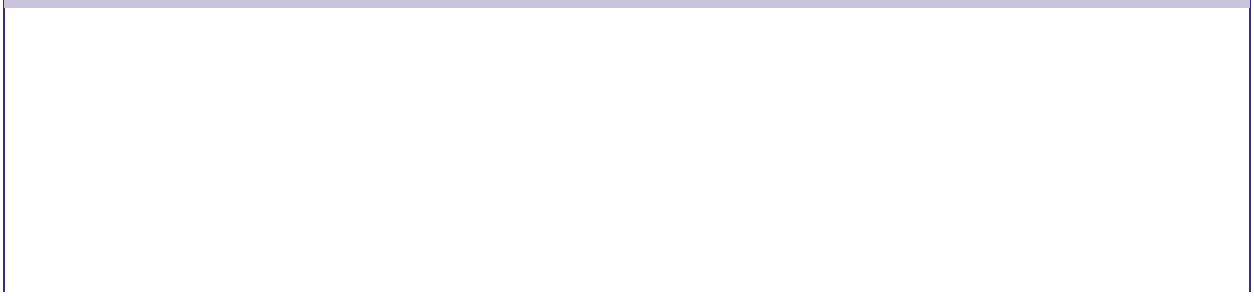
- **Goals:** optimize both MAP and CO while ↓ risk of pulmonary edema
  MAP = CO × SVR; CO = HR × SV (which depends on preload, afterload, and contractility)
  pulmonary edema when PCWP >20–25 (↑ levels may be tolerated in chronic HF/MS)
  hepatic and renal congestion (↓ GFR) occur when CVP/RAP >15 mmHg
- **Optimize preload** = LVEDV ≈ LVEDP ≈ LAP ≈ PCWP (*NEJM* 1973;289:1263)
  goal **PCWP ~14–18 in acute MI, ≤14 in acute decompensated HF**
  optimize in individual Pt by measuring SV w/ different PCWP to create Starling curve
  ↑ by giving crystalloid (albumin w/o clinical benefit over NS; PRBC if significant anemia)
  ↓ by diuresis (qv), continuous hemofiltration if refractory to diuretics or ESRD
- **Optimize afterload** ≈ wall stress during LV ejection = [(~SBP × radius) / (2 × wall thick.)] and **∴** ∝ MAP and ∝ SVR; goals: **MAP** >**60**, **SVR 800–1200**
  MAP >60 (& **∴** SVR ↑): vasodilators (eg, nitroprusside, NTG, ACEI, hydral.) or wean pressors
  MAP <60 (& **∴** SVR low/nl, ie, inappropriate vasoplegia): start with inopressor
- **Optimize contractility** ∝ CO for given preload & afterload; **goal CI** = **(CO / BSA)** >**2.2** if too low despite optimal preload & vasodilators (as MAP permits):
  ⊕ *inotropes:* eg, dobutamine (mod inotrope & mild vasodilator) or milrinone (strong inotrope & vasodilator, incl pulm), both proarrhythmic, or epi (strong inotrope & pressor)
  mech circulatory support: Impella (↓ death in STEMI); IABP; VA ECMO

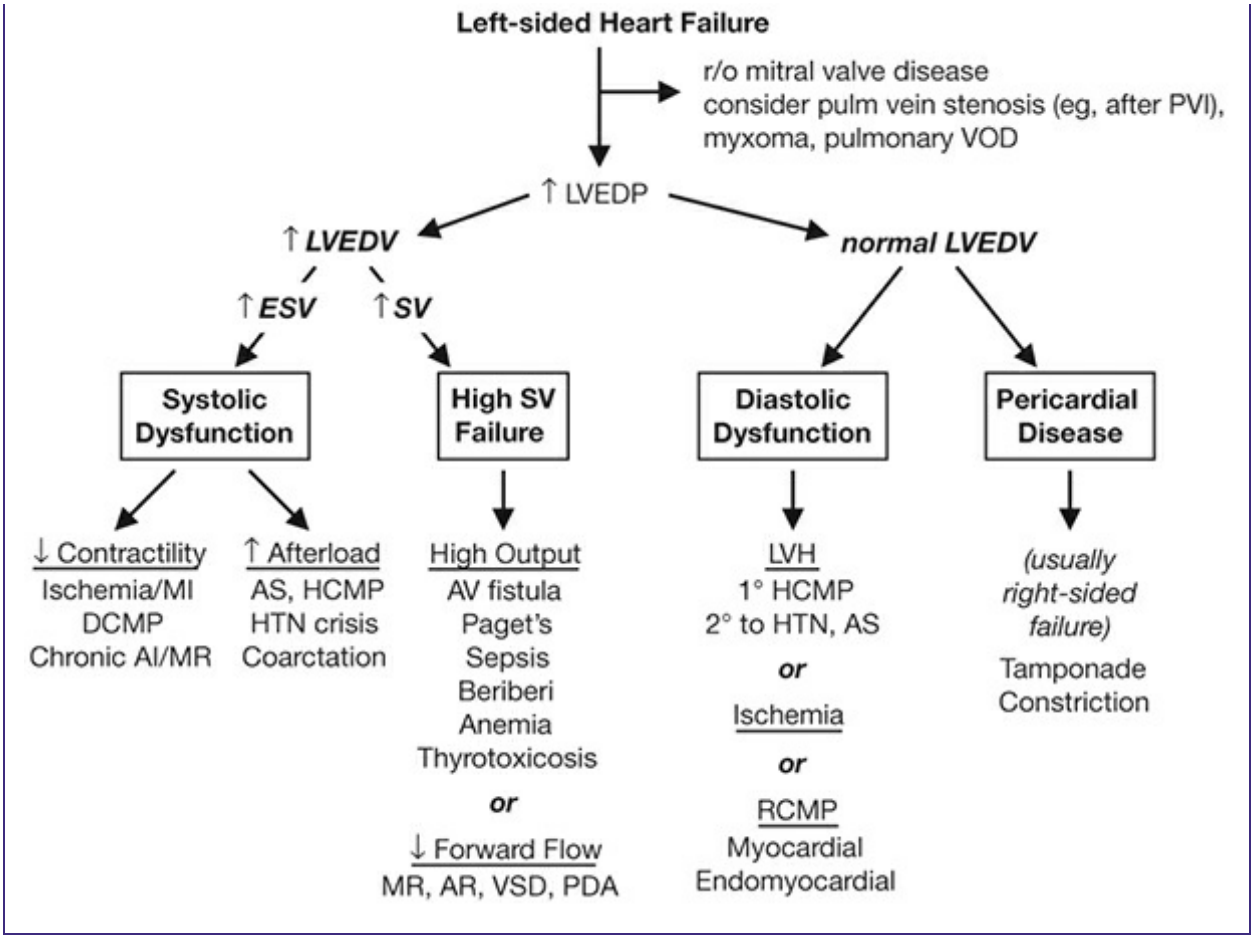
HEART FAILURE

Definitions (*Braunwald's Heart Disease*, 12th ed, 2022; *Circ* 2022;145:e895)

- Failure of heart to pump blood forward at rate sufficient to meet metabolic demands of peripheral tissues, or ability to do so only at abnormally high cardiac filling pressures
- Low output (↓ cardiac output) vs. high output (↑ stroke volume ± ↑ cardiac output)
- Left-sided (pulmonary edema) vs. right-sided (↑ JVP, hepatomegaly, peripheral edema)
- Backward (↑ filling pressures, congestion) vs. forward (impaired systemic perfusion)
- Systolic (inability to expel sufficient blood) vs. diastolic (failure to relax and fill normally)
- Reduced (HFrEF, EF <40%), mildly reduced (HFmrEF, EF 40–49%), preserved (HFpEF, EF >50%), improved (HFimpEF, baseline ≤40%, follow-up >40% & 10% ↑ from baseline)

Figure 1-2 Approach to left-sided heart failure





History

- Low output: fatigue, weakness, exercise intolerance, Δ MS, anorexia, nausea, vomiting
- Congestive: left-sided → dyspnea, orthopnea, paroxysmal nocturnal dyspnea
  right-sided → peripheral edema, RUQ discomfort, bloating, satiety

Functional classification (New York Heart Association class)

- Class I: no sx w/ ordinary activity; class II: sx w/ ordinary activity; class III: sx w/ minimal activity; class IV: sx at rest

Physical exam ("2-minute" hemodynamic profile; *JAMA* 1996;275:630 & 2002;287:628)

- **Congestion ("dry" vs. "wet"):** ↑ JVP (~80% of the time JVP >10 → PCWP >22)
  ⊕ hepatojugular reflux: ≥3 cm ↑ in JVP for ≥10–15 sec w/ abdominal pressure Se/Sp 73/87% for RA >8 and Se/Sp 55/83% for PCWP >15 (*AJC* 1990;66:1002)
  S_3 (in Pts w/ HF → ~40% ↑ risk of HF hosp. or pump failure death; *NEJM* 2001;345:574)
  Rales, dullness at base 2° pleural effus. (*often absent* in chronic HF due to lymphatic compensation) ± hepatomegaly, ascites and jaundice, peripheral edema
- **Perfusion ("warm" vs. "cold")**
  narrow pulse pressure (<25% of SBP) → CI <2.2 (91% Se, 83% Sp; *JAMA* 1989;261:884);
  soft S_1 (↓ dP/dt), pulsus alternans, cool & pale extremities, ↓ UOP, muscle atrophy
- ± Other: Cheyne-Stokes resp., abnl PMI (diffuse, sustained or lifting depending on cause of HF), S_4 (diast. dysfxn), murmur (valvular dis., ↑ MV annulus, displaced papillary muscles)

Evaluation for the presence of heart failure

- CXR (see Radiology insert): pulm edema, pleural effusions ± cardiomegaly, cephalization, Kerley B-lines; lung U/S better than CXR (PPV & NPV 92% vs. 77%; *Chest* 2015;148:202)
- BNP/NT-proBNP can help exclude HF; levels ↑ w/ age, renal dysfxn, AF; ↓ w/ obesity (∴ can be less helpful in HFpEF, which has high rates of obesity); Se ≥95%, Sp: ~50%, PPV ~65%, NPV ≥ 94% for HF in Pts p/w SOB (*BMJ* 2015;350:h910)
- Evidence of ↓ organ perfusion: ↑ Cr, ↓ Na, abnl LFTs, ↑ lactate
- Echo (see inserts): ↓ EF & ↑ chamber size → systolic dysfxn; hypertrophy, abnl MV inflow, abnl tissue Doppler → ? diastolic dysfxn; abnl valves or pericardium; ↑ estimated RVSP
- PA catheterization: ↑ PCWP, ↑ CVP, ↓ CO, and ↑ SVR (in low-output failure)

Evaluation for the potential causes of heart failure

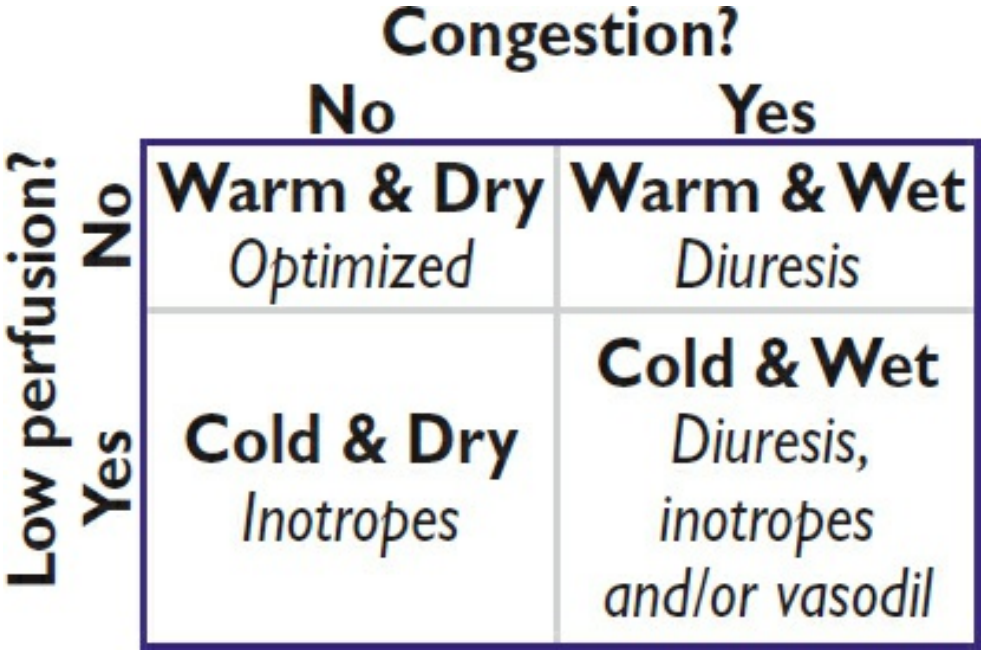
- **ECG:** e/o CAD, LVH, LAE, arrhythmia, heart block, or low voltage (? infiltrative CMP/DCM)
- **TTE:** LV & RV size & fxn, valve abnl (cause or consequence?), infiltrative or pericardial dis.
- **Cardiac MRI:** distinguishes ischemic vs. nonischemic and can help determine etiol. of latter
- **Coronary angio** (or noninv. imaging, eg, CT angio, or stress); if no CAD, w/u for NICM

Precipitants of acute heart failure

- **Dietary indiscretion or medical nonadherence** (~40% of cases)
- **Myocardial ischemia or infarction** (~10–15% of cases); **myocarditis**
- **Renal failure** (acute, progression of CKD, or insufficient dialysis) → ↑ preload
- **Hypertensive crisis (incl. from RAS), worsening AS** → ↑ left-sided afterload
- **Drugs** (βB, CCB, NSAIDs, TZDs), **chemo** (anthracyclines, trastuzumab), or **toxins** (EtOH)
- **Arrhythmias; acute valvular dysfxn** (eg, endocarditis), espec mitral or aortic regurgitation
- COPD/PE → ↑ right-sided afterload; extreme stress; anemia; systemic infxn; thyroid dis.

Rx of acute decompensated HF

- Assess congestion & adequacy of perfusion
- For **congestion:** IV loop diuretics (1–2.5× usual total PO dose) ± thiazides or acetazolamide (*NEJM* 2022;387:1185); no clear Δ between gtt vs. IVB q12h; oral bioavailability ~50% for furosemide (so IV 2× as potent as PO), 80–100% for torsemide. Consider nitrates, especially if HTN.
- "LMNOP": **L**asix, **M**orphine (↓ sx & preload), **N**itrates (↓ preload), **O**xygen (± NIV), **P**osition (sitting up & legs dangling → ↓ preload)
- For **low perfusion**, vide infra
- **Home meds:** prefer to continue, except:
  RASi: hold/↓ dose if HoTN; Δ to hydral/nitrates w/ AKI
  βB: hold if hypoperfusion or HoTN



Treatment of acute advanced heart failure (*Circ* 2013;128:e240)

- Consider PAC if not resp to Rx, unsure re: vol status, HoTN, hypoperfusion, need inotropes
- Tailored Rx w/ PAC (qv); goals of MAP >60, CI >2.2 (MVO2 >60%), SVR ~1000, PCWP <18
- **IV vasodilators:** nitroprusside (preferred due to potent ↓ in SVR; risk of coronary steal if CAD), NTG (venodilation > arterial dilation; eventual tachyphylaxis)
- **Inotropes** (properties in addition to ↑ inotropy and arrhythmogenicity listed below)
  dobutamine: vasodilation at ≤5 µg/kg/min; mild ↓ PVR; desensitization; lasts mins
  dopamine: splanchnic vasodil. → ↑ GFR & natriuresis; vasoconstrictor at ≥5 µg/kg/min
  milrinone: ↑↑ systemic/pulmonary vasodilation; ↓ dose by 50% in renal dysfxn; lasts hours
- **Mechanical circulatory support** (also see "Tailored Therapy" *JACC* 2015;65:e7 & 2542)
  Temporary: bridge to recovery, transplant, or durable MCS; periprocedural support Intra-aortic balloon pump (IABP): inflates in diastole & deflates in systole to ↓ impedance to LV ejection, ↓ myocardial O_2 demand & ↑ coronary perfusion; +0.5 L/min CO Axial flow pumps (eg, Impella): Archimedes screw principle in LV; +3.7–5.5 L/min Extracorporeal centrifugal pumps: CentriMag (10 L/min, but typically 5–7; surgical) Extracorporeal membrane oxygenation (ECMO): 6 L/min (*JACC HF* 2018;6:503)
  Durable: surgically placed LVAD ± RVAD as bridge to sufficient recovery (in 5–50% of niCMP; *JACC* 2017;69:1924), to transplant or as destination Rx (>50% ↓ 1-y mort. vs. med Rx; *NEJM* 2001;345:1435 & 2009;361:2241). Most common option is fully magnetically levitated centrifugal flow pump (HeartMate 3), axial flow models and HeartWare devices taken off the market (*NEJM* 2019;380:1618; *JAMA* 2022;328:1233).
- Cardiac transplantation: ~4500/yr in U.S. <10% mort. in 1st y, median survival >12 y

Recommended Chronic Therapy by HF Stage (*JACC* 2021;77:772)		
Stage (not NYHA Class)		**Therapy**
A	At risk for HF (eg, HTN); but asx & w/o struct. dis.	Rx HTN, lipids, DM; stop smoking, EtOH; ↑ exercise ACEI/ARB if HTN/DM/CAD/PAD
B	⊕ Struct. heart dis. (eg, CMP, LVH), but asx	As per stage A + ACEI/ARB + βB if MI/CAD or ↓ EF. ? ICD.
C	⊕ Struct. heart dis.	As per stage A + diuretics, ↓ Na

	⊕ Any h/o sx of HF	If rEF: RASi (ARNI > ACEI/ARB); βB; MRA; SGLT2i; ICD; ? CRT; ± nitrate/hydral; ± dig If pEF: ?ARNI; MRA; SGLT2i; GLP-1RA if BMI >30
D	Refractory HF requiring specialized interventions	All measures for stages A–C. Consider IV inotropes, VAD, transplant, end-of-life care (4-y mortality >50%).

- Implantable PA pressure sensor in sx Pts: ~30% ↓ risk of hosp (*Lancet* 2016;387:453; 2021;398:991; 2023;401:2113); possibly ↓ mortality in HFrEF w/ prior HF hosp (JACC 2024;83:682)

Treatment of Chronic HF with Reduced EF (*EHJ* 2021;42:3599; *Circ* 2022;145:e895)	
Diuretics	Loop ± thiazides diuretics (sx relief; no mortality benefit)
RASi: ARNI (ARB + neprilysin inhib), **ACEI,** or **ARB** 36-hr washout if transition ACEI to ARNI; N/A for ARB	*ARNI preferred*. Neprilysin degrades natriuretic peptides, bradykinin & ATII. Valsartan + sacubitril ↓ CV mort & HF hosp by 20% vs. ARB; ↑ HoTN, AKI (*NEJM* 2014;371:993). ∅ if h/o angioedema. *ACEI or ARB:* if unable to tolerate/afford ARNI. ↓ mortality vs. pbo. High-dose more effective. Watch for ↑ Cr, ↑ K (Rx: low-K diet, diuretics, K binders), cough (ACEI), angioedema.
β-blocker (data for carvedilol, metoprolol, bisoprolol)	*Add in concert w/ RASi* 35–40% ↓ mort. and in HF hosp in NYHA II–IV (*JAMA* 2002;287:883) EF will transiently ↓, then ↑. Contraindicated in ADHF.
Mineralocorticoid receptor antagonists	*Add after RASi and βB if adeq. renal fxn and w/o hyperkalemia* 30–35% ↓ CV mortality & HF hosp in NYHA II–IV (*Lancet* 2024;404:1119) Watch for ↑ K. Do not use if GFR <30 or K ≥5.
SGLT2i	~25% ↓ death or HF hosp in NYHA II–IV *(NEJM* 2019;381:1995; 2020;383:1413; 2021;385:1451). Limited data in eGFR <20. Risk of GU infection, euglycemic DKA.
Hydralazine + nitrates	*Consider if cannot tolerate ACEI/ARB or in Black Pts w/ class III/IV* 25% ↓ mort. but inferior to ACEI (*NEJM* 1991;325:303) 40% ↓ mort. in Blacks on standard Rx (A-HEFT, *NEJM* 2004;351:2049)
Ivabradine (I_f blocker)	*Reasonable if EF ≤35%, NYHA II–III, HR ≥70, NSR on max βB*. ↓ HR w/o ⊖ inotropy. 18% ↓ CV mort or HF hosp (*Lancet* 2010;376:875).
Digoxin	23% ↓ HF hosp., no Δ mort. Optimal levels 0.5–0.8 ng/mL.
Vericiguat	10% ↓ CV mort or HF hosp in NYHA II–IV (*NEJM* 2020;382:1883)
Cardiac resynch therapy (CRT, qv)	*Consider if EF ≤35%, LBBB or IVCD ≥150 ms, and sx HF.* ~40% ↓ mort. & HF hosp (*NEJM* 2005;352:1539 & 2014;370:1694). No clear e/o benefit if QRS <150 ms or RBBB (*Circ* 2023;147:812)
ICD (qv)	*For 1° prevention if EF ≤30–35% or 2° prevention; not if NYHA IV* ↓ mort. in ischemic CMP but perhaps only SCD in modern era in niCMP (*NEJM* 2005;352:225 & 2016;375:1221)
Revasc.	↓ CV mortality w/ CABG but not PCI (*NEJM* 2016;374:1511 & 2022;387:135)
mTEER	*If mod–severe fxnal MR & LVEF ≤30–35% on GDMT* 25–30% ↓ death or HF hosp (*NEJM* 2018;379:2297 & 2307; 2024;391:1799)
Heart rhythm	If AF & NYHA II–IV w/ EF <35%, catheter ablation ↓ D/HF hosp and need for advanced Rx vs. med Rx (*NEJM* 2018;378:417; 2023;389:1380)
Iron supplementation	*IV (not PO) if NYHA II/III, EF ≤40%, Fe-defic* (ferritin <100 or 100–300 & TSAT <20%). ~20% ↓ HF hosp. or CV mortality (*Nature Med* 2025;epub).

Diet, exercise	? Na <2 g/d, ? fluid restriction, exercise training in ambulatory Pts
Meds to avoid	NSAIDs, nondihydropyridine CCB, TZDs

Heart Failure with Preserved EF (HFpEF) (*NEJM* 2025;392:173)

Definition, epidemiology, pathophysiology

- HF iso LVEF ≥50% w/o alternate cause such as 1° myocardial, valvular or pericardial dis. if very thick walls → HCMP or infilt. CMP; if thin walls → ischemia or constriction
- ~½ of Pts w/ HF. Typically a/w HTN, diabetes, advanced age, AF, CKD, obesity.
- Pathophysiology: confluence of ventricular stiffness, ventricular–vascular uncoupling, ↓ fxn reserve, ↓ chronotropy, pulmonary vascular & endothelial dysfunction
- Precipitants of CHF: volume overload, ischemia, tachycardia/AF, HTN

Diagnosis

- Echo: impaired relaxation (eg, e′ <9 cm/s), ↑ filling pressures (eg, E/e′ ≥15), large LA
- Exercise-induced ↑ PCWP ± inadequate ↑ stroke volume, HR, CO (stress echo or CPET)

Treatment (*JACC* 2023;81:1835)

- **Diuresis**: sx control; as poorly compliant LV, small volume Δs → large filling pressure Δs
- Rx HTN, tachycardia, ischemia
- **SGLT2i:** ~20% ↓ CV death or HF hosp (*NEJM* 2021;385:1451; 2022;387:1029)
- **RASi:** nonsignif trend ↓ D/HF w/ ARB vs. pbo & w/ ARNI vs. ARB; ∴ ARNI reasonable
- **MRA**: ~18% ↓ HF hosp, but only nonsignificant ~8% reduction in CV death (*NEJM* 2014;370:1383 & 2024;391:1475; *Lancet* 2024;404:1119)
- **GLP-1RA**: if BMI ≥30 kg/m^2, improve sx & ~35% ↓ CVD or HF hosp (*Lancet* 2024;404:949; *NEJM* 2025;392:427)

CARDIOMYOPATHIES

Diseases with mechanical and/or electrical dysfunction of the myocardium

Dilated Cardiomyopathy (DCM)

Definition and epidemiology (*EHJ* 2023;44:3503)

- **LV or biventricular dilatation and global ↓ contractility** ± ↓ wall thickness in absence of ischemia/infarct or abnl loading conditions (eg, primary valvular disease or HTN). Pts w/ prior MI complicated by LV dilation and ↓ EF are often termed “ischemic CMP. ”

Etiologies (*JACC* 2021;77:2551)

- **Familial/genetic** (>35%): Pt & ≥2 1st- or 2nd-degree family members w/ unexplained DCM; >60 genes identified to date, encoding structural & nuclear proteins (eg, titin)
- **Idiopathic** (<20%): ? undx infectious, EtOH, or genetic cause; ¼ w/ e/o DCM in relative
- **Toxic:** alcohol (~20%) typ. 5 drinks/d × >5 y, but variable; cocaine; XRT (usu RCMP); anthracyclines (risk ↑ >550 mg/m^2, may manifest late), CYC, trastuzumab, TKIs
- **Infectious** (10–15%): most common = viral myocarditis; other: HIV, Chagas, Lyme

- **Infiltrative** (5%): amyloid typically RCMP (qv), but can be DCM with thickened walls; sarcoidosis (usually dilated); hemochromatosis (RCMP → end-stage dilates)
- **Peripartum** (onset 3rd trimester → 5 mo postpartum; *NEJM* 2024;390:154): ~1:2000; ↑ risk w/ multip, ↑ age, Black, 15–20% w/ mutation in DCM gene; stnd HF Rx (if preg, no RASi, spironolact., SGLT2i); ~30% recur w/ next preg → refer to cardio-OB
- **Stress-induced** (Takotsubo = apical ballooning; *JACC* 2018;72:1955): typically postmenopausal ♀; mimics MI (chest pain, ± STE & ↑ Tn; deep TWI & ↑ QT); mid/apex dyskinesis; ? Rx w/ βB, ACEI; usu. improves in wks. In-hosp morb/mort similar to ACS.
- **Tachycardia**: likelihood ∝ rate/duration; usu. resolves w/ rate/rhythm cntl
- **CTD/vasculitis** (<5%): typically assoc. w/ myopericarditis; SLE, SS, PAN, RA, EGPA
- **Arrhythmogenic right ventricular cardiomyopathy** (ACM/ARVC): fibrofatty replacement of RV → dilation (dx w/ MRI); ECG: ± RBBB, TWI V_1–V_3, ε wave; VT risk (*JACC* 2024;83:2214)
- **LV noncompaction** (*Lancet* 2015;386:813): prominent trabeculae, arrhythmias, cardioemboli
- **Metab/other:** hypothyroid, acromegaly, pheo, cirrhosis, vit B_1, selenium or carnitine defic.

Clinical manifestations

- **Heart failure:** both congestive & poor forward flow sx; signs of L- & R-sided HF **diffuse**, **laterally displaced PMI**, **S3**, ± MR or TR (annular dilat., displaced pap. muscle)
- Embolic events (~10%), supraventricular/ventricular arrhythmias, & palpitations

Diagnostic studies and workup (*Circ* 2022;145:e876; *EHJ* 2023;44:3503)

- ECG: may see PRWP, Q waves, or BBB; low voltage; AF (20%); AVB; may be normal
- Echocardiogram: LV dilatation, ↓ EF, *regional or global* LV HK ± RV HK, ± mural thrombi
- Cardiac MRI: high Se for myocarditis or infiltration; extent of scar correlated w/ mortality
- Labs: TFTs, Fe panel, HIV, SPEP, ANA; viral sero *not* recommended; others per suspicion
- Family hx (20–35% w/ familial dis.), genetic counseling & testing (*JAMA* 2009;302:2471)
- Coronary CT angiography (or invasive) to r/o CAD if risk factors, h/o angina, Qw MI
- Endomyocardial biopsy: consider if fulminant myocarditis or suspect infiltrative disease

Treatment (see “Heart Failure” for standard HF Rx)

- Possibility of reversibility of CMP may temper implantation of devices
- Prognosis differs by etiology: postpartum (best), ischemic/GCM (worst)

Myocarditis (*NEJM* 2022;387:1488; *JACC* 2025;85:391)

Etiologies

- **Infectious** (*Lancet* 2012;379:738; *JACC* 2012;59:779)
  - Viruses (parvo B19, Coxsackie, adeno, HIV, SARS-CoV-2/vaccine, etc.)
  - Bacterial, fungal, rickettsial, TB, Lyme (mild myocarditis, often with AVB)
  - Chagas: apical aneurysm ± thrombus, RBBB, megaesophagus/colon (*Lancet* 2018;391:82)
- **Autoimmune**
  - Idiopathic giant cell myocarditis (GCM): avg age 42, fulminant, AVB/VT (*Circ HF* 2013;6:15)
  - Eosinophilic (variable peripheral eos): hypersensitivity (mild HF but at risk for SCD) or acute necrotizing eosinophilic myocarditis (ANEM; STE, effusion, severe HF)
  - Collagen vasc. dis. (pericarditis > myocarditis): PM, SLE, scleroderma, PAN, RA, EGPA
- **Immune checkpoint inhibitors (ICI):** due to molecular mimicry, stop ICI if concern

Clinical manifestations

- Highly variable, ranging from incidental dx based on labs/imaging to fulminant HF w/ shock
- Can present like ACS (chest pain, ECG Δs, ↑ Tn but w/o rapid fall), ADHF, arrhythmias

Diagnostic studies and workup

- Echo: ± systolic dysfxn (typically global but can be regional); ± ↑ LV wall thickness due to edema; LV size may be small in fulminant and dilated in chronic; ± pericardial effusion
- Cardiac MRI: can show hyperemia, edema, and scar (*JACC* 2009;53:1475)
- Endomyocardial biopsy: useful in GCM & eosinophilic; ∴ consider if rapidly progressive HF, high-grade AVB or sustained VT, suspected allergic rxn or eosinophilia

Treatment

- Standard HF Rx if LV dysfxn (but do not start if e/o shock); temporary MCS as needed
- Immunosuppression: for GCM (high-dose steroids + [CsA or tacrolimus] ± AZA), collagen vascular disease, peripartum (? IVIg), ICI & eosinophilic; no proven benefit if viral

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Hypertrophic Cardiomyopathy (HCM) (Circ 2024;149:e1239)

Definition, epidemiology, pathology

- LV (usually ≥15 mm) and/or RV hypertrophy disproportionate to hemodynamic load
- Due to gene mutations affecting proteins of or related to sarcomere; prev.: ~1/200–500
- Myocardial fiber disarray with hypertrophy, which creates arrhythmogenic substrate
- Many morphologic hypertrophy variants: asymmetric septal; concentric; midcavity; apical
- Ddx LVH: HTN, AS, elite athletes (wall usu. <13 mm, symmetric & nl diastology; *Circ* 2011;123:2723), infiltrative CMP (amyloid), non-sarcomeric genetic syndromes (eg, Fabry's)

Pathophysiology

- Dynamic LV outflow tract obstruction (LVOTO) in ≥70%: narrowed tract 2° hypertrophied septum + systolic anterior motion (SAM) of ant. MV leaflet (variable) and papillary muscle displacement. Pressure gradient (∇) across LVOT worse w/ ↑ contractility (digoxin, β-agonists, exercise, PVCs), ↓ preload (eg, Valsalva maneuver) or ↓ afterload.
- Mitral regurgitation: due to SAM (mid-to-late, post.-directed regurg. jet) and/or abnl mitral leaflets & papillary muscles (pansystolic, ant.-directed regurg. jet)
- Diastolic dysfunction: ↑ chamber stiffness + impaired relaxation
- Ischemia: small vessel dis., perforating artery compression (bridging), ↓ coronary perfusion

Clinical manifestations (70% are asymptomatic at dx)

- **Dyspnea** (90%): due to ↑ LVEDP, MR, and diastolic dysfunction
- **Angina** (25%) even w/o epicardial CAD; microvasc. dysfxn (*NEJM* 2003;349:1027)
- **Arrhythmias** (AF in 20–25%; VT/VF): palpitations, syncope, sudden cardiac death

Physical exam

- Sustained PMI, S_2 paradoxically split if severe outflow obstruction, ⊕ S_4 (occ. palpable)
- **Systolic murmur:** crescendo–decrescendo; LLSB; ↑ **w/ Valsalva** & standing (↓ preload)
- ± mid-to-late or holosystolic murmur of MR at apex
- Bifid (biphasic) carotid pulse (brisk rise, decline, then 2nd rise); JVP w/ prominent *a* wave
- Contrast to AS, which has murmur that ↓ w/ Valsalva and ↓ carotid pulses

Diagnostic studies

- ECG: LVH, anterolateral TWI and inferior pseudo-Qw, ± apical giant TWI (apical variant)
- **Echo:** any LV wall segment ≥15 mm (13–14 mm if ⊕ FHx), often involving septum; ± dynamic outflow obstruction, SAM, or MR; exercise echo may provoke ↑ LVOT ∇

- MRI: hypertrophy + patchy delayed enhancement (useful for dx & prog) (*Circ* 2015;132:292)
- Cardiac cath: subaortic pressure ∇; *Brockenbrough sign* = ↓ pulse pressure post-PVC (in contrast to AS, in which pulse pressure ↑ post-PVC); spike & dome Ao pressure pattern
- Consider genotyping for family screening; pathogenic variant ID'd in <½ (*Circ* 2020;142:e558)

Treatment

- Heart failure
  - ⊖ **inotropes/chronotropes:** β-blockers, CCB (verapamil), disopyramide
    Careful w/ diuretics, b/c ↓ preload. If LVOTO, *avoid vasodilators* and digoxin.
    If sx refractory to drug Rx + *obstructive* physio. (∇ ≥30 mmHg at rest or w/ provocation):
    (a) **Cardiac myosin inhibitors**: mavacamten & aficamten (invest.) ↓ LVOTO & sx and ↑ fxnl capacity (*Lancet* 2020;396:750; *JACC HF* 2023;7:735; *NEJM* 2024;390:1849). LVEF must be ≥55% and requires monitoring as can ↓ by ~4%, greater in some.
    (b) Surgical myectomy: long-term ↓ symptoms in 90% Pts (*Circ* 2014;130:1617)
    (c) Alcohol septal ablation (*JACC* 2018;72:3095): ∇ ↓ by ~80% & 5–20% w/ residual NYHA III–IV sx; 14% req. repeat procedure. Good alt for older Pts w/ comorbidities. Complic: transient (& occ. delayed) 3° AVB w/ 10–20% req. PPM; VT due to new scar
    (d) Transcatheter myotomy: under investigation (*JACC* 2024;83:1257)
    If refractory to drug therapy and there is *nonobstructive* pathophysiology: transplant
- Acute HF: can be precip. by dehydration or tachycardia; Rx w/ fluids, βB, phenylephrine
- AF: rate control w/ βB/non-DHP CCB, maintain SR w/ DCCV, disopyramide or amio; a/c indicated regardless of CHA_2DS_2-VASc score given high stroke risk
- ICD if VT/VF. Reasonable for 1° prevention if ≥1 risk factor: ⊕ FHx SCD, unexplained syncope, LV wall ≥30 mm, LV aneurysm or EF <50%; consider if NSVT, failure of SBP to ↑ or fall from peak ≥20 mmHg w/ exercise, extensive MRI delayed enhancement. EPS *not* useful. AHA HCM Risk-SCD Score online.
- Avoid dehydration, extreme exertion. Vigorous exercise may be okay (*JAMA Card* 2023;8:595).
- 1st-degree relatives: screen w/ TTE q12–18m as teen or athlete then q5y as adult, ECG (because timing of HCMP onset variable). Genetic testing if known mutation.

Restrictive & Infiltrative CMP

Definition (*JACC* 2018;71:1130 & 1149)

- Restrictive CMP: ↓ ventricular filling due to ↓ compliance in nonhypertrophied, nondilated ventricles; nl/↓ diastolic volumes, nl or near-nl EF; must r/o pericardial disease
- Infiltrative CMP: myocardial deposition; ± ↑ wall thickness; may present as RCM or DCM

Etiologies (*JACC* 2018;71:1130 & 1149)

- **Amyloidosis** (*JAMA* 2024;331:778): age at presentation ~60 y; ♂:♀ = 3:2
  AL (eg, MM); familial (transthyretin, ATTR-m); ATTR-wt; AA (produced by liver)
  ECG: ↓ QRS amplitude (50%), pseudoinfarct pattern (Qw), AVB (10–20%), hemiblock (20%), BBB (5–20%)
  Echo: ↑ LV/RV wall thickness (*yet w/ low voltage on ECG*), granular sparkling (30%), biatrial enlargement (40%), valve thickening, small effusions
  Normal ECG voltage & septal thickness has NPV ~90%
  Cardiac MRI: distinct late gadolinium enhancement pattern (*JACC* 2008;51:1022)
- **Sarcoidosis** (*Circ* 2024;149:e1197): presents at age ~30 y; ↑ in Blacks, N. Europe, ♀
  Cardiac involvement in 25–58% of sarcoid, many not overt; cardiac w/o systemic in 10%
  ECG: AVB (75%), RBBB (20–60%), VT; PET: ↑ FDG uptake in affected area
  Echo: regional WMA (particularly basal septum) w/ thinning or mild hypertrophy or DCM
  Cardiac MRI: T2 early gad (edema); fibrosis/scar in basal septum; LGE prognostic
- **Other myocardial processes**

Hemochromatosis: often middle-aged men (espec N. European); 15% w/ cardiac sx
Diabetes; radiation (also accelerated athero, valvular disease, constrictive pericarditis)
Autoimmune (scleroderma, polymyositis–dermatomyositis)

- **Endomyocardial diseases**: carcinoid heart disease (R-sided HF w/ TR/TS, PR/PS, left-sided valves with PFO); Löffler's endocarditis (↑ eos; mural thrombi that can embolize; fibrosis); endomyocardial fibrosis (tropical climates; resembles Löffler's but w/o eos)
- **Storage diseases**: Fabry (glycosphingolipids); Gaucher (glucocerebrosidase)

Pathophysiology & clinical manifestations (*JACC* 2018;71:1130 & 1149)

- ↓ myocardial compliance → ↑ filling pressures; ↓ ventricular cavity size → ↓ SV and ↓ CO
- Both **L & R HF** w/ periph. edema ± ascites & pulm edema; DOE & poor exercise tolerance
- **Diuretic "refractoriness"** w/ AKI; thromboemboli
- Poorly tolerated atrial/ventricular tachyarrhythmias; infiltrative → VT → syncope/SCD

Physical exam

- ↑ JVP, ± Kussmaul's sign (JVP not ↓ w/ inspir., classically seen in *constrict. pericarditis*)
- Cardiac: ± S_3 and S_4, ± murmurs of MR and TR
- Peripheral & pulmonary edema; congestive hepatomegaly ± ascites & jaundice

Diagnostic studies (*JACC* 2022;79:372)

- ECG: low voltage, pseudoinfarction pattern (Qw), ± arrhythmias
- Echo: ± symmetric wall thickening, biatrial enlarge., ± mural thrombi, ± cavity oblit. w/ diast dysfxn: ↑ early diast (E) and ↓ late atrial (A) filling, ↑ E/A ratio (restrictive pattern); ↓ mitral annular velocity (e′) on tissue Doppler, ↑ E/e′ ratio; ↑ TR velocity
- Labs: NT-proBNP, serum & urine immunofixation electrophoresis (IFE), serum free light chains (SFLC), Fe ± HFE mutation
- Cardiac MRI/PET: may reveal inflammation or evidence of infiltration (but nonspecific)
- Amyloid (qv) eval: ✓ for plasma cell dyscrasia (IFE & SFLC). If ⊕ → fat pad bx. If ⊖ → PYP SPECT for TTR eval → if ⊕ → TTR gene sequencing.
- Endomyocardial biopsy if suspect amyloid (Se ~100%) & noninvasive tests non-dx. Se low for sarcoidosis b/c patchy disease infiltrative process.
- Cardiac catheterization (see "Pericardial Disease" for restrictive vs. constrictive processes)
  Atria: **M's** or **W's** (prominent *x* and *y* descents)
  Ventricles: **dip & plateau** (rapid ↓ pressure at onset of diastole, rapid ↑ to early plateau)
  Concordance of LV–RV pressure peaks w/ respiration (vs. discordance in constriction)

Treatment (*JACC* 2022;79:372; in addition to Rx'ing underlying disease)

- Gentle diuresis (goal ⊖ ≤1 L/d). May not tolerate CCB or other vasodilators.
- Control HR (but can ↓ CO); maintain SR (helps filling). Digoxin ↑ arrhythmias in amyloid.
- Anticoagulation (if AF regardless of CHA_2DS_2-VASc; ? if ↓↓ CO); ? transplant if refractory
- AL amyloid: Rx targeted at plasma cell dyscrasia
- ATTR amyloid: TTR stabilizers (eg, tafamidis & acoramidis) improve sx & fxnal capacity and ↓ death & CV hosp (*NEJM* 2018;379:1007 & 2024;390:132); TTR siRNA (eg, patisiran & vutrisiran) preserve fxnal capacity and ↓ death & CV hosp (*NEJM* 2023;389:1553 & 2025;392:33)
- Sarcoid: consider steroids/immunomodulators if FDG-PET ⊕ for inflammation + AVB, VT or LV dysfxn; ↑ risk for VT; unique indications for ICD placement (*Circ* 2018;138:e272)

VALVULAR HEART DISEASE

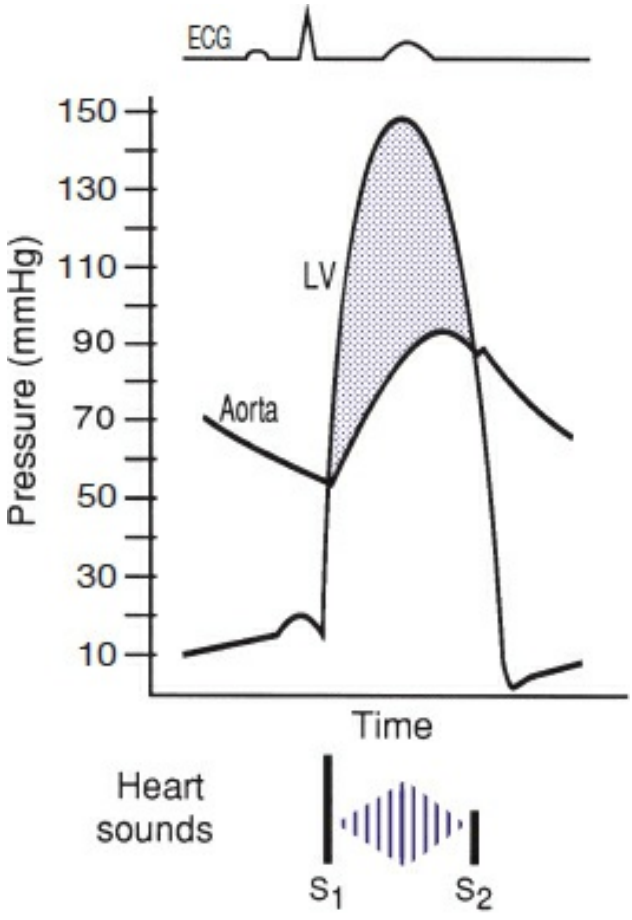
Aortic Stenosis (AS) (*JAMA* 2024;332:2014)

Etiology

- **Calcific:** predominant cause in Pts >70 y; risk factors: HTN, ↑ LDL-C, ↑ Lp(a), ESRD
- **Congenital** (ie, bicuspid AoV w/ premature calcification): cause in 50% of Pts <70 y
- **Rheumatic heart disease** (AS usually accompanied by AR and MV disease)
- AS mimickers: subvalvular (HCMP, subaortic membrane) or supravalvular stenosis

Clinical manifestations (usually indicates AVA **<1** cm^2 or concomitant CAD)

- **Angina:** ↑ O_2 demand (hypertrophy) + ↓ O_2 supply (↓ cor perfusion pressure) ± CAD
- **Syncope** (*exertional*): peripheral vasodil. w/ fixed CO → ↓ MAP → ↓ cerebral perfusion
- **Heart failure:** outflow obstruct + diastolic dysfxn → pulm. edema, esp. if ↑ HR/AF (↓ LV fill.)
- Acquired vWF disease (~20% of sev. AS): destruction of vWF; GI angiodysplasia
- Natural hx: usually slowly progressive (AVA ↓ ~0.15 cm^2/y, but varies; *Circ* 1997;95:2262), until sx develop; mean survival based on sx: angina = 5 y; syncope = 3 y; CHF = 2 y



Pathophys Heart Disease, 7th ed, 2021, for this et al.

Physical exam

- **Midsystolic crescendo–decrescendo** murmur at **RUSB**, harsh, high-pitched, radiates to carotids, apex (holosystolic = Gallavardin effect), ↑ w/ passive leg raise, ↓ w/ standing & Valsalva. Dynamic outflow obstruction (HCM) is the reverse.

- Ejection click after S_1 sometimes heard with *bicuspid* AoV
- Signs of severity: *late-peaking* murmur, paradoxically split S_2 or inaudible A_2, small and delayed carotid pulse ("*pulsus parvus et tardus*"), LV heave, ⊕ S_4 (occasionally palpable)

Diagnostic studies

- ECG: may see LVH, LAE, LBBB, AF (in late disease)
- CXR: cardiomegaly, AoV calcification, post-stenotic dilation of ascending Ao, pulmonary congestion
- **Echo:** valve morph., jet velocity → estimate pressure gradient (∇) & calculate AVA, dimensionless index (DI); LVEF
- **Cardiac cath:** usually to *r/o CAD* (in ~½ of calcific AS); for hemodyn. if disparity between exam & echo: ✓ pressure gradient (∇) across AoV, calc AVA (underestim. if mod/sev AR)
- **Low-flow, low-gradient (LFLG) severe AS:** AVA ≤1, but mean ∇ <40. "Classical" due to LVEF <50% due to afterload mismatch from AS or myocardial process. "Paradoxical" iso nl LVEF but small LV (eg, HTN or amyloid).
- **Dobutamine challenge** (echo or cath) can be used in potential LFLG to differentiate *afterload mismatch* (20% ↑ SV & ∇, no Δ AVA; implies good contractile reserve) vs. *pseudostenosis* (20% ↑ SV, no Δ in ∇, ↑ AVA; implies low AVA *artefact* of LV dysfxn)
- **Cardiac CT:** AoV calcium score can be used in LFLG to assess AS severity

Classification of Aortic Stenosis (*Circ* 2021;143:e72)

Stage	Sx	Severity	Max Jet Vel ($^m/_s$)	Mean ∇ (mmHg)	AVA (cm^2)[a]	LVEF	DI
n/a	N	Normal	1	0	3–4	nl	n/a
A	N	At risk	<2	<10	3–4	nl	n/a
B	N	Mild	2–2.9	<20	>1.5	nl	>0.5
		Moderate	3–3.9	20–39	1–1.5	nl	0.25–0.5
C1	N	Severe	≥4	≥40	≤1.0	nl	<0.25
		Very severe	≥5	≥60	≤0.8	nl	
C2		Severe + ↓ EF	≥4	≥40	≤1.0	↓	
D1	Y	Severe	≥4	≥40	≤1.0	nl	<0.25
D2		Severe + low flow/∇ + ↓ EF[b]	<4	<40	≤1.0	↓	
D3		Severe + low flow/∇ + nl EF[c]	<4	<40	≤1.0	nl	

[a]AVA indexed to BSA <0.6 cm^2/m^2 also severe (use for smaller Pts); [b]DSE → max jet vel ≥4 & AVA ≤1.0; [c]Small LV w/ ↓ stroke vol (LVSVi <35 mL/m^2), severe LVH with marked diastolic dysfunction, consider cardiac amyloid

Valve replacement (*Circ* 2021;143:e72)

- Based on *symptoms:* once they develop → AVR needed
- *Indicated in:* **sx severe** (stage D1; D2; D3 if AS felt to be cause of sx); **asx severe** + **EF <50%** (stage C2); or severe (stage C1) *and* undergoing other cardiac surgery
- *Reasonable if:* **asx severe** (C1) *but* either ↓ **BP or sx w/ exercise** (can *carefully* exercise asx AS to uncover sx; do *not* exercise sx AS), **very severe,** ↑ BNP, rapid progression

- Asx severe AS: ↓ hosp, ? death (if nearly very severe) (*EHJ* 2024;45:4526; *NEJM* 2025;392:217)

Valve selection

- **Mechanical** (more durable, but done surgically and requires lifelong a/c) vs. **bioprosthetic**
- Pt <50 y: SAVR. Pt 50–65 y: either. Pt >65 y or ⌀ a/c: bioprosthetic (by TAVI or SAVR)

TAVI (transcatheter AoV implantation) (*JAMA* 2021;325:2480; *Circ* 2021;143:e72)

- Balloon-expandable or self-expanding. Usually transfemoral access (best outcomes).
- TAVI noninferior to SAVR in terms of risk of death or disabling stroke for Pts of any surgical risk (*NEJM* 2014;370:1790; 2020;382:799; *NEJM* 2023;389:1949 & 2024;390:1572; *JACC* 2023;82:2163)
- In *nonoperative Pts* (ie, vs. med Rx): ↓ mortality but still ~72% at 5 y (*Lancet* 2015;385:2485)
- Complications: CHB ~15% at 30 d, more common if preexisting RBBB (*JACC* 2020;76:2391); annular rupture or coronary occlusion (both rare); stroke; local vascular; paravalvular leaks; "suicide" left ventricle due to dynamic intraventricular pressure ∇ (Rx like HCM)
- Postprocedural antithrombotic Rx: ASA 75–100 mg/d (*NEJM* 2020;383:1447). In Pts *with indication for OAC*: OAC alone superior to OAC + $P2Y_{12}$ (*NEJM* 2020;382:1696); apixaban & edoxaban appear comparable to warfarin (*NEJM* 2021;385:2150; *EHJ* 2022;42:2783).

Other therapy

- If not AVR candidate or to temporize: careful diuresis prn (preload-dependent physiology)
- Control HTN. Maintain SR; digoxin if ↓ EF & HF or if AF. *Avoid* venodilators (nitrates) & ⊖ inotropes (βB/CCB) if severe AS. Avoid vigorous physical exertion once AS mod–severe.
- If cardiogenic shock: inotropes; IABP (especially if CAD) vs. Impella
- Afterload reduction (eg, SNP) w/ PAC if HF w/ sev. AS, ↑↑ SVR & BP nl (*Circ* 2013;128:1349)

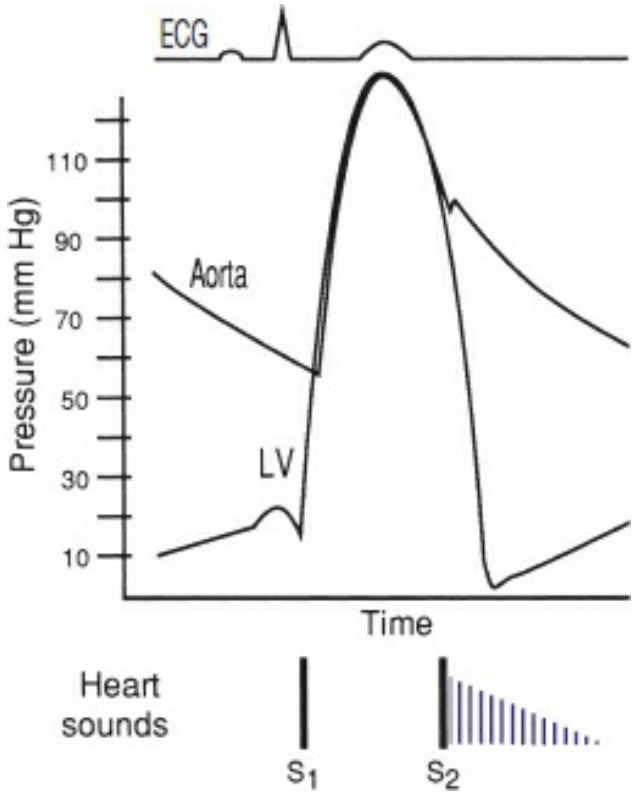
Aortic Regurgitation (AR)

Etiology (*Circ* 2006;114:422)

- **Valve disease** (~45%): **rheumatic** (usually mixed AS/AR + MV disease); **bicuspid AoV** (natural hx: 1⁄3 → normal, 1⁄3 → AS, E 1⁄6 → AR, 1⁄6 → endocarditis → AR); **infective endocarditis;** valvulitis (RA, SLE, certain anorectics & serotonergics, XRT)
- **Root disease** (~55%): **HTN**, aortic aneurysm/dissection, annuloaortic ectasia (ie, Marfan), **aortic inflammation** (GCA, Takayasu's, ankylosing spond., reactive arthritis, syphilis)

Clinical manifestations

- **Acute**: sudden ↓ forward SV and ↑ LVEDP (noncompliant ventricle) → pulmonary edema ± hypotension and cardiogenic shock
- **Chronic**: clinically silent while LV dilates (to ↑ compliance to keep LVEDP low) more than it hypertrophies → chronic volume overload → LV decompensation → CHF
- **Natural hx**: *variable* progression (unlike AS, can be fast or slow); once decompensation begins, prognosis poor w/o AVR (mortality ~10%/y)



Physical exam

- **Early diastolic decrescendo murmur at LSB** (RSB if dilated Ao root); ↑ w/ sitting forward, expir, handgrip; severity of AR ∝ duration of murmur (except in acute and severe late); *Austin Flint murmur:* mid-to-late diastolic rumble at apex (AR jet interfering w/ mitral inflow)
- **Wide pulse pressure** + **low DBP** due to ↑ stroke volume; hyperdynamic pulse; pulse pressure narrows in late AR with ↓ LV fxn; bisferiens (twice-beating) arterial pulse
- PMI diffuse and laterally displaced; soft S_1 (early closure of MV); ± S_3 (≠ ↓ EF but rather just volume overload in AR)

Classic Eponymous Signs in Chronic AR (*South Med J* 1981;74:459)	
Sign	**Description**
Corrigan's pulse	"water hammer" pulse (ie, rapid rise/fall or distention/collapse)
Hill's sign	(popliteal SBP – brachial SBP) >60 mmHg
Duroziez's sign	to-and-fro murmur heard over femoral artery w/ light compression
Pistol shot sounds	pistol shot sound heard over femoral artery
Traube's sound	double sound heard over femoral artery when compressed distally
de Musset's sign	head-bobbing with each heartbeat (low Se)
Müller's sign	systolic pulsations of the uvula
Quincke's pulses	subungual capillary pulsations (low Sp)

Diagnostic studies

- ECG: can see LVH, LAD, abnl repol; CXR: cardiomegaly ± ascending Ao dilatation

- **Echo:** severity of AR (severe = regurg jet width ≥65% LVOT, regurg fraction ≥50%, effective regurg orifice ≥0.3 cm^2, holodiastolic flow reversal in prox abd Ao; moderate = jet width 25–64%, regurg fraction 30–49%, regurg orifice 0.1–0.29 cm^2); LV size & fxn

Treatment (*Lancet* 2016;387:1312; *Circ* 2021;143:e72)

- Acute decompensation (consider endocarditis as possible acute precipitant): *surgery* usually urgently needed for acute severe AR, which is poorly tolerated by LV IV afterload reduction (eg, nitroprusside) & inotropic support (dobutamine) ± chronotropic support (↑ HR → ↓ diastole → ↓ time for regurg.) pure vasoconstrictors, βB & IABP contraindicated
- Chronic AR: management decisions based on *LV size and fxn* (and before sx occur); low diastolic BP and high resting HR associated with mortality (*JACC* 2020;75:29)
- **Surgery** (AVR, replacement or repair if possible):
  Severe and **sx** (if equivocal, consider stress test)
  Asx *and* either **EF ≤55%**, **LV dilation** [LVESD >50 mm or LVESDi (indexed to BSA) ≥ 25 mm/m^2 (*JACC* 2019;73:1741)], or **undergoing cardiac surg**
- TAVI not approved for pure AR, under investigation (*Lancet* 2024;403:1451)
- Medical therapy: **vasodilators** (nifedipine, ACEI/ARB, hydralazine) if severe AR w/ sx or LV dysfxn & not operative candidate or to improve hemodynamics before AVR

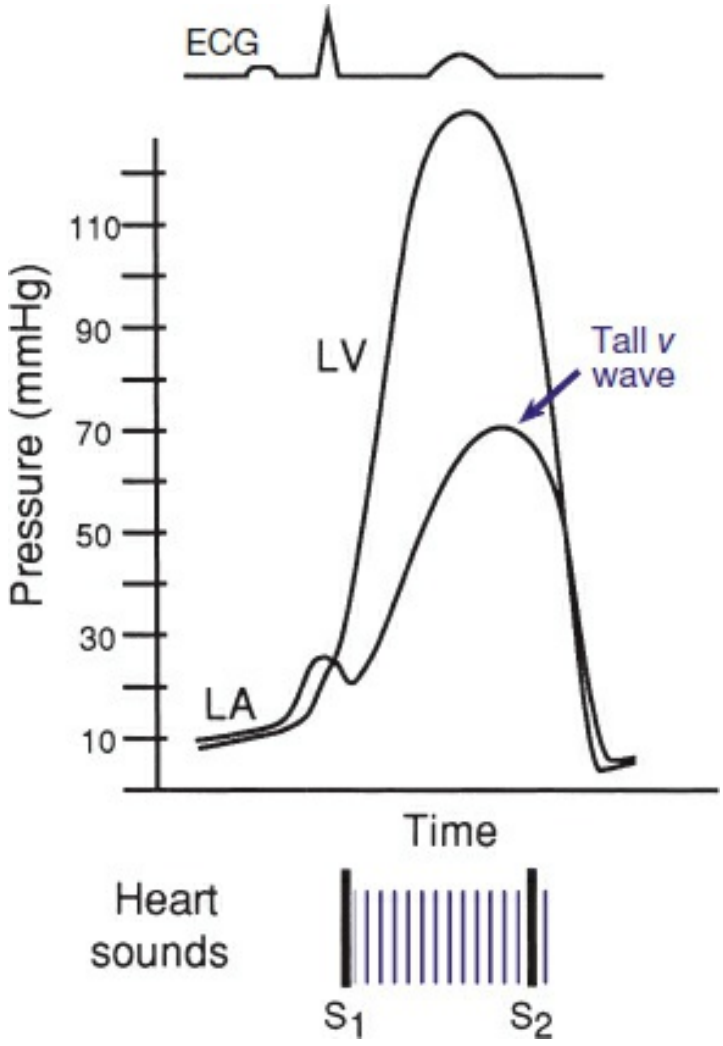
Mitral Regurgitation (MR)

Etiology (*NEJM* 2010;363:156 & 2020;383:1458)

- **Primary** (~2/3; degeneration of valve apparatus)
  Leaflet abnl: myxomatous (MVP), endocarditis, calcific, RHD, valvulitis (collagen vascular disease), congenital (eg, cleft), anorectic drugs (phen-fen), XRT
  Chordae tendineae rupture: myxomatous, endocarditis, spontaneous, trauma
  Papillary muscle dysfxn b/c of ischemia or *rupture* during MI [usu. posteromedial papillary m. (supplied predominantly by PDA) vs. anterolateral (suppl. by diags & OMs)]
- **Secondary** (~1/3; functional): inferoapical papillary muscle displacement due to ischemic LV remodeling or DCM; HCM (*JACC* 2015;65:1231); atrial remodeling (lack of coaptation)
- In 1° MR, leaflet prolapsing into LA; jet directed to opposite side of prolapsing leaflet
- In 2° MR, leaflet tethering, jet directed centrally or to same side as tethered leaflet

Clinical manifestations

- Acute: **pulmonary edema**, hypoxia, hypotension, cardiogenic shock (*NEJM* 2004;351:1627)
- Chronic: typically asx for yrs, then as LV fails → progressive DOE, fatigue, AF, PHT
- Prognosis. In 1°: 5-yr survival w/ meds is ~70% if asx, ~15% if NYHA Class III–IV (*NEJM* 1996;335:1417). In 2°: 2-yr survival ~20–30% (*JACC* 2015;65:1231).



Physical exam

- **High-pitched, blowing, holosystolic murmur at apex;** radiates to axilla; ± thrill; ↑ w/ handgrip (Se 68%, Sp 92%), ↓ w/ Valsalva (Se 93%)
  - ant. jets heard at sternum & base of heart
  - post. jets heard at axilla, infrascap, & spine
- ± diastolic rumble b/c ↑ flow across valve
- Lat. displ. hyperdynamic PMI, obscured S_1, widely split S_2 (A_2 early b/c ↓ LV afterload, P_2 late if PHT); ± S_3
- Carotid upstroke brisk (vs. diminished and delayed in AS)

Diagnostic studies (*Circ* 2021;143:e72)

- ECG: may see LAE, LVH, ± atrial fibrillation
- CXR: dilated LA, dilated LV, ± pulmonary congestion
- **Echo:** MV anatomy (ie, etiol); MR severity: jet area, jet width at origin (vena contracta) or effective regurgitant orifice (ERO; predicts survival); LV fxn (EF should be *supranormal*, ∴ EF <60% w/ sev. MR = LV dysfxn). W/ exercise if suspect exertional ↑ in MR severity.
- TEE or cardiac MR if TTE not sufficiently informative or being considered for intervention
- Cardiac cath: prominent PCWP *c-v* waves (not spec. for MR), LVgram for MR severity & EF

INDEX

A