CORONARY ARTERY DISEASE

Background

- **Definitions:** Coronary artery disease (CAD) refers to atherosclerotic deposition in the coronary vasculature and its complications
- **Varying presentations:** May manifest as angina, acute coronary syndromes, sudden cardiac death, or heart failure
  - **Silent MI/ischemia:** Asx disruption in coronary circulation detectable by ambulatory ECG or stress testing (ECG, TTE, or nuclear imaging); new Q-wave on ECG (*Ann Intern Med* 2001;135:801); risk of silent ischemia ↑ in DM & hypothyroid pts
  - **Ischemic cardiomyopathy (CMP):** EF ≤40% due to CAD
  - **Cardiac syndrome X/Microvascular angina:** Angina + ST depression on ETT w/ nl angio (*NEJM* 2007;356:830); due to microvascular CAD or hypersensitivity to cardiac pain (*Circulation* 2004;109:568); treated w/ βB, CCB, nitrates, reassurance
  - **Variant/Prinzmetal angina:** Angina + ST elevations 2/2 to coronary vasospasm w/o significant coronary artery stenosis; typically, attacks occur at rest in younger pts
- **Pathophysiology:** Endothelial + intimal dysfunction, cholesterol deposition, Mϕ foam cell accumulation → fatty streak; + inflammation → atheroma → fibrous cap formation & remodeling → calcification & plaque formation → stenosis (angina) or plaque rupture + thrombosis (MI ± HF or SCD) (*Nature* 2011;473:317; *NEJM* 2013;368:2004)
- **Epidemiology:** 1 in 2 ♂ & 1 in 3 ♀ will develop CAD (*Lancet* 1999;353:89); CAD is the leading cause of death in US, responsible for 1 in 6 deaths (*Circulation* 2010;121:948)
- **Women and CAD:** Less likely than ♂ to have typical angina, & typically present at a later age than ♂ (*Am Heart J* 2006;151:813; *Eur Heart J* 2008;29:707)
- **Risk factors: ↑ risk:** Smoking (2.9 OR), HLD, HTN (1.9 OR), DM (2.4 OR), obesity (1.1 OR), ↑ age, rheumatoid arthritis (RA) (3.1 ↑ RR), SLE, FHx of CAD, ♂ gender, HIV, XRT exposure, metabolic syndrome; **↓ risk:** Daily fruits & vegetables (0.7 OR), regular EtOH consumption (0.91 OR), ASA, regular exercise (0.86 OR) (*Circulation* 2003;107:103; *Lancet* 2004;364:937; *NEJM* 2012;366:321)

Genetics: Inheritance of CAD is complex & assoc w/ multiple genetic loci (*Nat Genet* 2012;45:25)

CAD risk equivalents: Carotid artery disease, PAD, AAA, DM, CKD

Definition of ⊕ FHx: MI or CAD death in 1° relative <50 y for ♂, <60 y for ♀

CKD: ↓ GFR & ↑ proteinuria assoc w/ ↑ risk of CV events (*Circulation* 2003;108:2154; *Lancet* 2010;375:2073)

Estrogen supplementation in ♀: USPSTF recommends against use of HRT to prevent CAD in postmenopausal ♀ or s/p hysterectomy (*AFP* 2005;72:311)

Evaluation

- **History:** Assess for presence/quality of chest discomfort (see *"Chest Pain"*), presence of risk factors (above), activity level, DOE, diet, exercise, tob/EtOH use, FHx, depression & ED (often comorbid w/ CAD) (*Circulation* 2008;118:1768)
- **Risk estimation: Framingham risk model** most commonly used in US; version for non-DM pts at http://hp2010.nhlbihin.net/atpIII/calculator.asp (*Circulation* 2008;117:743)
- **Workup:** Waist circumference, BMI, lipids, & DM2 screening (see *"Screening"*); Framingham risk should be calculated at least q5y; ambulatory ECG monitoring useful in dx of silent ischemia, variant angina; may consider use of CRP & LpA for further risk stratification (*Circulation* 2003;107:363;499; *Arch Intern Med* 1997;157:1170)

PREVENTION

	Primary (1°) Prevention	Secondary (2°) Prevention
Goal	**Prevent Disease**	**Prevent Harm From Disease**
Exercise, healthy diet	**X**	**X**
Quit tob, mod EtOH	**X**	**X**
BMI 18.5–24.9, waist <40″ ♂, 35″ ♀	**X**	**X**
Lipids at goal	**X**	**X**
DM well controlled	**X**	**X**
BP at goal (<140/90)	**X**	**X**
ASA	See below	**X** (unless contraindicated)
ACEI/ARBs		DM2, HTN, MI, EF <40%, CKD
βB		Hx MI or CHF

(*AFP* 2010;82:289; 2011;83:819; *Circulation* 2002;106:388; *JACC* 2006;47:2130)

- **Diet:** Rich in fruits, vegetables, fiber; low in red meat, trans fatty acid, saturated fats, high-fructose corn syrup; stepwise implementation of 1–2 dietary improvements q3–6mos may ↑ compliance (*AFP* 2009;79:571)
  - **Mediterranean diet:** ↓ CV events by ~30% in pts at high CV risk (*NEJM* 2013;368:1279); rich in vegetables, locally sourced, minimal consumption of processed foods, low in red meat, <4 eggs/wk, moderate intake dairy products, olive oil as main source of fat, moderate red wine, fresh fruit for dessert (*AFP* 2009;79:571)
  - **Vitamin supplementation:** RCT do not demonstrate benefit of β-carotene, Vit C, or Vit E (*Arch Intern Med* 1998;158:668; *JAMA* 2005;294:56; 2008;300:2123; *Lancet* 2001;357:89; *NEJM* 1996;334:1145;1150); USPSTF does not recommend vitamin supplementation in prevention (*Ann Intern Med* 2003;139:51)
- **Aspirin:** Established role in 2° prevention (*NEJM* 2005;353:2373; 2013;368:204); role in 1° prevention depends on pt risk for CV events (*JAMA* 2012;307:2318); *Dose recommendations:* 75–325 mg QD (FDA), 75–162 mg QD (ACC, AHA), 75–100 mg QD (ACCP) (*Chest* 2012;141:e637s; *JACC* 2006;47:2130); in pts anticoagulated w/ warfarin, addition of ASA does not significantly ↓ risk of CV death, MI, & stroke (*JACC* 2003;41:62S)
  - **1° prevention:** In meta-analysis of pts w/o hx CAD, ASA ↓ risk of nonfatal MI (NNT = 162) w/o mortality benefit & w/ significant ↑ in bleeding (NNH = 73) (*Arch Intern Med* 2012;172:209); benefit of ASA must be weighed against risk of bleeding & incorporate pt preference (*Ann Intern Med* 2009;150:396; 405); risk of bleeding likely to outweigh benefits in pts w/ Framingham 10 y risk score < 10%; consider in pts w/ DM2 who have a 10 y CVD risk > 5%, & in pts w/ CKD (*Diabetes Care* 2010;33:1395)
  - **USPSTF recommendations:** In ♂ 45–79 y ASA encouraged when CV benefit (MIs avoided) > risk of GIB; in ♀ 55–79 y ASA encouraged when CV benefit (stroke prevented) > risk of GIB; ASA for MI prevention not recommended in ♂ <45 y & not recommended for stroke prevention in ♀ <55 y (*AFP* 2011;83:1464)
  - **2° prevention:** In pts w/ hx vascular disease (i.e., MI, stroke, PAD), ASA ↓ risk of MI/stroke/vascular death by ~20% w/o difference btw 75–325 mg QD dose (*BMJ* 2002;324:71)
  - **Bleeding risk:** While ASA for CV protection assoc w/ ↑ risk of major GI (2.1 RR) & intracranial (1.7 RR) bleeds, absolute risk of bleeding is low (add'l 1.3 bleeds/1000 ASA treated pts compared to placebo) (*Am J Med* 2006;119:624); No difference btw 75–325 mg/d in bleeding risk; in pts w/ hx GIB who must be on ASA, *H. pylori* eradication + a PPI ↓ risk of rebleed (*NEJM* 2002;346:2033); ASA + esomeprazole superior to clopidogrel at ↓ risk of rebleed (*NEJM* 2005;352:238)
  - **Enteric-coated ASA:** Variable absorption may ↓ effectiveness (*Circulation* 2013;127:377)
- **Patient information:** *AFP* 2010;82:275 (MI risk); *JAMA* 2013;309:1645 (ASA use)

Treatment

Medical Management
All pts: 1° & 2° prevention (see above); screening for depression **Cardiac rehab:** Exercise-based tx programs ↓ risk of reinfarction, cardiac, & all cause mortality (*Am Heart J* 2011;162:571); recommended by Medicare for pts w/ stable angina or who are s/p MI or CABG
After CABG: (*NEJM* 2003;348:1456) **ACEI:** Quinapril & ramipril evaluated in pts s/p CABG **βB:** Atenolol or metoprolol validated
After STEMI: (*Circulation* 2013;127:529) **ACEI:** For pts w/ anterior STEMI, CHF, EF < 40%; consider for all STEMI survivors; use ARB in pts intolerant of ACEI **Aldosterone antagonist:** For pts already on an ACEI + βB & w/ EF < 40%, sx CHF, or DM **βB:** Continue for at least 3 y & consider indefinitely (*Circulation* 2011;124:2458)
After NSTEMI: (*JACC* 2011;57:e215) **ACEI:** For pts w/ DM2, CHF, EF < 40%; use ARB in pts intolerant of ACEI **Aldosterone antagonist:** Same as after STEMI (above) **βB:** Metoprolol or atenolol; continue for 3 y & consider indefinitely **CCB:** Useful if βB contraindicated or ischemia/pain persists despite βB and/or nitrates **NTG:** Pts should be instructed on PRN use & when to seek medical attention

Antiplatelet Therapy (*Chest* 2012;141:e637S; *Circulation* 2011;124:2574)
ACS w/o PCI: ASA (75–100 mg QD) indefinitely + clopidogrel (75 mg QD) for 1 y
After CABG: ASA (75–100 mg QD) indefinitely + clopidogrel (75 mg QD) or ASA (325 mg QD) for 9–12 mos depending on surgeon preference
Balloon angioplasty w/o stenting: ASA indefinitely (75–100 mg QD) + clopidogrel (75 mg QD) for 1 mo (*Chest* 2012;141:e637S)
BMS (elective PCI): ASA (75–100 mg QD) indefinitely + clopidogrel (75 mg QD) for a minimum of 1 mo & preferably for 12 mos*; Ticagrelor or prasurgrel may be substituted for clopidogrel if PCI was assoc w/ ACS
DES (elective PCI): ASA indefinitely (75–100 mg QD) + clopidogrel (75 mg QD) for a minimum of 3 mos (-limus stents) to 6 mos (-taxel stents) & preferably for 12 mos; Ticagrelor or prasurgrel may be substituted for clopidogrel if PCI was assoc w/ ACS
***Indefinite clopidogrel:** Consider shared decision-making for indefinite clopidogrel in pts w/o bleeding risk factors w/ complex PCI or who are at risk for catastrophic consequences for stent thrombosis (i.e., left main or proximal LAD stent); cardiology consultation advised
Warfarin + dual antiplatelet Rx (i.e., ASA + clopidogrel): If warfarin is needed for AF, mechanical valves, hx DVT, etc., aim for INR on the low side of target range (i.e., 2–2.5 if the goal is 2–3), & use ASA 81 mg QD (*JACC* 2008;51:172); for stented pts, consider discontinuation of clopidogrel after the minimum duration of dual antiplatelet Rx to minimize bleeding risk; use a PPI as below
Mgmt of bleeding risk for dual antiplatelet Rx: *Pts w/ hx GI bleeding:* Use PPI; *Pts at risk for GIB:* Consider PPI in elderly, pts on warfarin, steroids, NSAIDs, or *H. pylori* infection

- **Percutaneous coronary intervention (PCI):** Includes stenting & balloon angioplasty (w/o stenting); Morbidity/mortality 2/2 stent restenosis/thrombosis (*AFP* 2009;80:1245)
  - **BMS:** ↑ restenosis compared to DES; requires a *minimum* of 2–4 wks of dual antiplatelet Rx compared to 3–6 mos for DES, ∴ BMS preferable in pts at ↑ risk for bleeding, noncompliance, or antiplatelet interruptions for procedures, or who are on warfarin (*NEJM* 2007;356:984)
  - **DES:** Drug impregnated in stent is slowly released, ↓ neointimal growth & restenosis → less susceptible to restenosis in 1st y compared to BMS, but requires compliance w/ 1 y of dual antiplatelet Rx due to ↑ risk of stent thrombosis 2/2 to delayed endothelialization compared to BMS (*NEJM* 2013;368:254)
- **Platelet receptor blockers:** Clopidogrel & ticlopidine evaluated in stable CAD (i.e., elective PCI); ticlopidine rarely used (↑ risk of TTP & neutropenia) (*JAMA* 1999;281:806)
  - **Clopidogrel–PPI interaction:** Observational studies suggested PPIs ↓ the efficacy of clopidogrel (*JAMA* 2009;301:937), however a RCT of clopidogrel + omeprazole showed the combination ↓ the rate of GI events (i.e., bleeds) (2.9% vs. 1.1%) compared to placebo with **no difference in CV events** (COGENT, *NEJM* 2010;363:1909)

ANGINA (*NEJM* 2005;352:2524; 2007;357:1762)

- **Pathophysiology:** Myocardial oxygen demand >> supply → chest discomfort
- **Definition:** Chest discomfort reproduced by exertion/stress, relieved by rest/NTG
- **Diagnosis:** Clinical; typical angina + CV risk factors
- **History:** Squeezing, heaviness, pressure, burning, tightness in chest that radiates to shoulder/neck/jaw/arm; ♀ may report breast pain, palpitations, sharp/stabbing pain
- **Workup:** ECG, stress test for risk stratification, assessment of LV function
  - **Angiography:** Indicated for sx that interfere w/ pt's life, even w/ optimal medical Rx, abnl stress test, or for dx of recurrent atypical chest discomfort

Treatment (*Circulation* 2012;126:3097)

- **Medical management:**
  - **βB:** First-line Rx, titrate to resting HR of 55–60 bpm as BP allows; metoprolol & atenolol most commonly used; meta-analysis shows βB have similar rates of MI & cardiac death compared to CCB, but fewer s/e & an improvement in the number of weekly anginal episodes (*JAMA* 1999;281:1927); improved survival in CHF (see *"Heart Failure"*) & after MI; survival benefit in pts w/ angina less clear

Pathophysiology: βB compete w/ catecholamines for binding to β receptors; ↓ O_2 demand by ↓ HR & ↓ contractility, resulting in ↑ exercise tolerance, ↓ sx

Toxicity: HoTN, bronchoconstriction, fatigue, ED, nightmares, insomnia, worsening depression/PAD/Raynaud's (less so w/ β1-selective agents); taper rather than abrupt d/c due to w/d effects; antacids ↓ bioavailability of atenolol

CCB: Vasodilate & reduce contractility (*NEJM* 1982;307:1618); diltiazem, verapamil, & amlodipine typically used; may be used alone if βB contraindicated (e.g., in pts w/ resting bradycardia) or in combination w/ βB if sx poorly controlled by βB alone (combination of amlodipine & βB preferred due to ↓ s/e)

Toxicity: Edema; verapamil & diltiazem may worsen CHF & should be used cautiously in pts w/ sinus or AV node dysfunction; verapamil s/e incl constipation

Nitrates: Long-acting used as 2°-line Rx in combo w/ βB if sx poorly controlled on βB alone; may be used as monotherapy if βB contraindicated; ↑ arterial & venous dilatation, ↓ preload, ↓ myocardial O_2 demand (*NEJM* 1998;338:520)

Rapid-acting (SL tablet or spray): Rx acute anginal sx & in Ppx (i.e., before activities that trigger attacks); pts should be instructed on when to seek medical attention (i.e., call 911 if pain does not improve after 1 SL NTG)

Long-acting: 12–14 h nitrate-free interval (usually at night when there is less activity) & eccentric dosing (e.g., q8am, q1pm, q6pm for isosorbide dinitrate, or q8am, q4pm for isosorbide mononitrate) may ↓ tolerance; isosorbide dinitrate lasts 3–6 h; isosorbide mononitrate available in BID or extended release (QD) dosing; NTG patches may ↓ tolerance if used 12 h on, 12 h off

Toxicity: Flushing, HoTN, HA, syncope, nausea; tolerance; contraindicated in pts on sildenafil or w/ HOCM

Ranolazine: ↓ angina in pts w/ continued sx on βB, CCB, or nitrates; works by ↓ Ca overload in ischemic myocytes; ↑ QTc (*Circulation* 2006;113:2462)

ASA: 75–150 mg QD or 325 mg QOD ↓ CV morbidity & mortality by 20–25% (*NEJM* 2005;352:2524); clopidogrel may be substituted in pts intolerant of ASA

ACEI: Pts w/ angina & CHF, DM2, CKD, HTN; meta-analysis of ACEI or ARB in pts w/ stable angina & a nl EF shows ↓ risk of overall mortality, nonfatal MI, stroke, & revascularization compared to standard medical Rx (*AFP* 2012;86:21)

Statin: See *"Dyslipidemia"*

Risk factor modification & exercise: See secondary prevention above

Revascularization (*Circulation* 2011;124:2610; e574)
Indications: (1) Sx limit activities despite optimal medical Rx; (2) Pts do not tolerate medical Rx; (3) Revascularization may ↑ survival (i.e., >50% left main disease, large area of myocardium at risk for ischemia)
PCI: Preferred for 1 or 2 vessel disease w/o left anterior involvement, or in pts who are not surgical candidates; consider for *highly select* & stable pts w/ left main disease
CABG: >50% stenosis in LM (survival benefit seen), diffuse 3 vessel disease (>70% stenosis) w/ large area of myocardium at risk or EF < 40%, proximal LAD + another major coronary artery, or pts who are not PCI candidates

- **Ischemic cardiomyopathy:** See *"Heart Failure"* for more details; pts should avoid diltiazem, verapamil, & NSAIDs other than ASA; pts w/ hibernating myocardium or ongoing angina despite optimal medical Rx may benefit from revascularization
- **Cardiac rehabilitation:** Provides comprehensive eval of risk factors, psychosocial factors, & 2° prevention (*AFP* 2009;80:955); state index of cardiac rehab programs: www.aacvpr.org/Resources/SearchableCertifiedProgramDirectory/tabid/113/Default.aspx
- **Sexual activity:** Requires 4–5 METs (walking ~4 mph on flat ground); Sex ↑ HR & ↑ BP, causing pts to worry about triggering MI (*Am J Cardiol* 2000;86:27F; 51F); exercise training & medical Rx (ASA & βB) help mitigate risk; pts should wait 3–4 wks after MI & have a ⊖ ETT before resuming sexual activity (*Am J Cardiol* 2005;96:313)

  Treatment of impotence: Reassurance in low-risk pts; PDE-5 inhibitors (sildenafil, vardenafil, tadalafil) *contraindicated* in pts on nitrates & αB & should be used cautiously in pts w/ active ischemia, HF, low baseline BP, or on multiple BP meds (*JACC* 1999;33:273); yohimbine may cause ↑ HR & ↑ BP (see *"Male Sexual Dysfunction"*)
- **Patient information:** *JAMA* 2012;308:1824

Second Princeton Panel Recommendations for Risk Assessment for Sex
Low risk: Sex is safe & impotence may be treated if pt is: Asx w/ < 3 CV risk factors (excluding gender), controlled HTN, mild, stable angina, has undergone successful revascularization, >6–8 wks s/p uncomplicated MI w/ ⊖ ETT, has mild valvular disease, or asx LV dysfunction
Intermed risk: Cards consult and/or ETT advised if pt has: ≥3 CV risk factors (excluding gender, including sedentary lifestyle), mod, stable angina, recent MI (<6 wks) w/o revascularization or ⊖ ETT, EF < 40%, NYHA II HF, PAD, or hx stroke/TIA
High risk: Cards consult for mgmt: UA, poorly controlled HTN, NYHA III/IV HF, MI <2 wks, HOCM, mod–severe AS, high-risk arrhythmias

AORTIC DISEASE

Background (*Lancet* 2005;365:1577; *Circ* 2006;113:e463; *Circ* 2005;111:816; *AFP* 2006;73:1198)

- **Definition:** Abdominal aorta >30 mm *or* any section w/ >1.5× nl diameter
- **Location:** Abdominal (AAA), thoracic (TAA), thoracoabdominal aorta or aortic root
- **Prevalence:** AAA: 1.3–8.9% prevalence in men & 1–2.2% in women, ↑ w/ age; 15,000 deaths/y from AAA-related problems in US (13th leading cause of death)
- **Risk factors:** Age, ♂, smoking, HTN, HLD bicuspid AV, CAD or PAD, FHx

Types (*Lancet* 2005;365:1577; *Circ* 2006;113:e463; *Circ* 2008;117:242; *JAMA* 2007;297:395)

- **Atherosclerotic:** Most common, assoc w/ typical atherosclerotic risk factors (smoking, age >65, HTN, as well as HLD, CAD/PVD, & FHx); also assoc w/ COPD & PCKD
- **Congenital:** Marfan, Ehlers–Danlos, association of TAA w/ bicuspid AoV
- **Infectious:** Bacterial inflammation of aortic wall caused mainly by staph & salmonella
- **Inflammatory abdominal aortic aneurysm (5–10% cases):** Pts typically p/w back/abdominal pain; CT/MRI notable for periaortic inflammation & fibrosis; ESR/CRP ↑ (*JAMA* 2007;297:395)
- **Dissection:** Surgical emergency; risk factors: HTN, bicuspid AoV or AVR, coarctation, connective tissue d/o (e.g., Marfan), cocaine, trauma, recent cath (*JAMA* 2002;287:2262)

Evaluation and Screening (*Lancet* 2005;365:1577; *Circ* 2005;111:816; *JAMA* 2009;302:2015)

- **History:** Often asx; vague, chronic abdominal/CP radiating to back/flank
- **Exam:** Often unremarkable; sensitivity of palpation for AAA 4–4.9 cm = 50%, >5 cm 76%; Limited by body habitus (*JAMA* 1999;281:77)
- **Red flags:** Suspect dissection in pts w/ risk factors (above) & abrupt onset of severe, "tearing or ripping pain," mediastinal or aortic widening on CXR, or >20 mmHg BP difference between arms; **If suspected → ED** (*Arch Int Med* 2000;160:2977)
- **Thoracic aortic aneurysm:** No routine screening recommendations; pts w/ known TAA should be imaged at 6 mos & then annually if stable; also screen for coexisting AAA
- **Abdominal aortic aneurysm:** U/S × 1 men 65–75 who smoked >100 lifetime cigarettes (may be covered by Welcome to Medicare Physical Exam), & men >55 or women >65 w/ an affected 1st-degree relative; consider screening women >65 who smoked >100 lifetime cigarettes based on clinical hx
- **Rupture risk:** ↑ w/ larger diameter, ↑ rate of expansion, HTN, smoking; some studies suggest for small AAA (<5.5 cm), longer surveillance intervals may be used (*JAMA* 2013;309:806)

Abdominal Aortic Aneurysm Screening (*Circ* 2004;110:16; *NEJM* 2003;348:1895)	
AAA Diameter	**Screening Interval**
>4.5 cm	q3–6mos
4–4.5 cm	q6–12mos
<4 cm	q1–2y
AAA Diameter	**Annual Rupture Risk**
4–4.9 cm	0.5–5%
5–5.9 cm	3–15%
6–6.9 cm	10–20%
7–7.9 cm	20–40%
≥8 cm	30–50%