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/Leschemia: Asx disruption in coronary circulation detectable by ambulatory ECG or stress testing (EKG, TTE, or nuclear imaging); new Q-wave on ECG (Ann Intern Med 2001;135:431); risk of silent schema ↑ in DM & hypothyroid pts.

Ischemic cardiomyopathy (CMP): EF ≤40% due to CAD.

Cardiac syndrome X/Microvascular angina: Angina + ST depression on ETT w/ or w/o angio (NEJM 2007:356:635); due to microvascular CAD or hypersensitivity to cardiac pain (Circulation 2004;109:618); treated w/ (ASA, 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 = internal dysfunction, cholesterol deposition, Ms foam cell accumulation → fatty streak → inflammation → atheroma → fibrous cap formation & remodeling → calcification & plaque formation → stenosis (angina) or plaque rupture → thrombosis (MI ± HF or SC). (Nahans 2015;473:317; NEJM 2013:368:2004).

Epidemiology: 1 in 2 & 1 in 3 will develop CAD (Carter 1999;353:879); 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 men to have typical angina, & typically present at a later age than men. (Ann Med 2006;151:673; Eur Heart 2008;29:927).

Risk factors: ↑ risk: Smoking (2.9 OR), HLD, HTN (1.9 OR), DM (2.4 OR), obesity (1.1 OR), ↑ age, rheumatoid arthritis (RA) (2.1 ↑ RR), SLE, FxH 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;107:183; Lancer 2004;364:937; NEJM 2012:366:321).

Genetics: Inheritance of CAD is complex & assoc w/ multiple genetic loci (Nat Genet 2012;45:35).

CAD risk equivalents: Carotid artery disease, PAD, AAA, DM, CKD. (Circulation 2011;124:20)

Definition of FxHx: MI or CAD death in 1st relative <50 y for ↓, <60 y for ↓ CKD.) ↓ GFR & ↑ proteinuria assoc w/ ↑ risk of CV events (Circulation 2013:108:2154; Lancer 2010;375:2073).

Estrogen supplementation in → USPSTF recommends against use of HRT to prevent CAD in postmenopausal ↓ & s/p hysterectomy (AP 2006:72:311).

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, FxHx, depression & ED (often comorbid w/ CAD). (Circulation 2008:118:716).


- Workup: Waist circumference, BMI, lipids, & DM2 screening (sex “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; Ann Intern Med 1997:177-179).

Prevention

<table>
<thead>
<tr>
<th>Goal</th>
<th>Primary (1)* Prevention</th>
<th>Secondary (2) Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise, healthy diet</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Quit tob, mod EtOH</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BMI 18.5–24.9, waist &lt;40”/35”</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Lipids at goal</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>DM well controlled</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>BP at goal (&lt;140/90)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>ASA</td>
<td>X (unless contraindicated)</td>
<td></td>
</tr>
<tr>
<td>ACEI/ARBs</td>
<td>DM2, HTN, MI, EF &lt;40%, CKD</td>
<td></td>
</tr>
<tr>
<td>He, MI or CHF</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

• 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 43–60% may 7% compliance (JVP 2009;79:571)

Mediterranean diet: ↓ CV events by ∼30% in pts at high CV risk (N Engl J Med 2013;368:1279)

• After STEMI:↓ CV events by ∼30% in pts at high CV risk (N Engl J Med 2013;368:1279)

• After NSTEMI:↓ CV events by ∼30% in pts at high CV risk (N Engl J Med 2013;368:1279)

All pts:

Aspirin:

Patient information:

CCB:

ACEI:

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:e26)

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

USPSTF recommendations:

In pts w/ hx vascular disease (i.e., MI, stroke, PAD), ASA ↓ risk of MI/stroke/vascular death by 25% w/o difference btw 75–325 mg QD dose (NEJM 2002;348:7)

In pts w/o 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 (NEJM 2002;348:7)

Bleeding risk:

While ASA for CV protection assoc w/ ↓ risk of CV death, MI, & stroke (JACC 2010;57:e26) vs no benefit w/ or without ASA (Lancet 2002;360:1339)

In pts w/ DM2 who have a 10 y CVD risk > 5%, & in pts w/ CKD (JAMA 2003;289:3810)

Established role in 2 dietary improvements: 1) Mediterranean diet & 2) enteric-coated ASA

Addition of ASA does not significantly ↓ risk of CV death, MI, & stroke (JACC 2003;41:425)

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) (Ann Intern Med 2013;158:204; benefit of ASA must be weighed against risk of bleeding & incorporate pt preference (Ann Intern Med 2009;150:394; 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 (Subhroso Cox 2010;3:195)

USPSTF recommendations:

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 (NEJM 2002;348:7)

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 (afedi 1.3 bleed/1000 ASA treated pts compared to placebo) (JAMA 2006;295:1942); 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 (N Engl J Med 2007;356:1253); ASA + esomprazole superior to clopidogrel as ↓ risk of rebleed (N Engl J Med 2006;354:1938)

Enteric-coated ASA: ↓ variable absorption may ↓ effectiveness (Circulation 2013;127:377)

• Patient information: AJP 2010;82:275 (MI risk); JAMA 2013;309:1645 (ASA use)

Medical Management

All pts: 1° & 2° prevention (see above); screening for depression

Cardiac rehab: Exercise-based tx programs ↓ risk of reinfection, cardiac, & all cause mortality (N Engl J Med 2011;365:1463; recommended by Medicare for pts w/ stable angina or who are s/p MI or CABG

After CABG: (N Engl J Med 2003;348:1486)

ACEI: Quinapril & ramipril evaluated in pts s/p CABG

βB: Atenolol or metoprolol validated

After STEMI: (Circulation 2013;127:129)

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:e26)

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
**Antplatelet Therapy** (Circulation 2011;124:2574; Circulation 2012;124:10377)  

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACS w/o PCI:</strong></td>
<td>ASA (75-100 mg QD) indefinitely + clopidogrel (75 mg QD) for 1 y</td>
</tr>
<tr>
<td><strong>After CABG:</strong></td>
<td>ASA (75-100 mg QD) indefinitely + clopidogrel (75 mg QD) or ASA (325 mg QD) for 9-12 mos depending on surgeon preference</td>
</tr>
<tr>
<td><strong>Balloon angioplasty w/o stenting:</strong></td>
<td>ASA indefinitely (75-100 mg QD) + clopidogrel (75 mg QD) for 1 mo (Circulation 2012;124:10377)</td>
</tr>
<tr>
<td><strong>BMS (elective PCI):</strong></td>
<td>ASA (75-100 mg QD) indefinitely + clopidogrel (75 mg QD) for a minimum of 1 mo &amp; preferably for 12 mos; Ticagrelor or prasugrel may be substituted for clopidogrel if PCI was assoc w/ ACS</td>
</tr>
<tr>
<td><strong>DES (elective PCI):</strong></td>
<td>ASA indefinitely (75-100 mg QD) + clopidogrel (75 mg QD) for a minimum of 3 mos (ilium stents) to 6 mos (radiopaque stents) &amp; preferably for 12 mos; Ticagrelor or prasugrel may be substituted for clopidogrel if PCI was assoc w/ ACS</td>
</tr>
<tr>
<td><strong>Indefinite clopidogrel:</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>Warfarin + dual antplatelet Rx (i.e., ASA + clopidogrel):</strong></td>
<td>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), &amp; use ASA 81 mg QD (JACC 2008;51:172); for stented pts, consider discontinuation of clopidogrel after the minimum duration of dual antplatelet Rx to minimize bleeding risk; use a PPI as below</td>
</tr>
</tbody>
</table>

**Mgmt of bleeding risk for dual antplatelet Rx:**  
**Pts w/ hx GIB:** 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 (JACC 2009;60:1246)
- BMS: ↑ restenosis compared to DES; requires a minimum of 2-4 wks of dual antplatelet Rx compared to 3-6 mos for DES; ✴. BMS preferable in pts at ↑ risk for bleeding, noncompliance, or antplatelet interruptions for procedures, or who are on warfarin (NEJM 2007;354:984)
- 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 antplatelet Rx due to ↑ risk of stent thrombosis 2/2 so delayed endothelialization compared to BMS (NEJM 2015;368:254)
- Platelet receptor blockers: Clopidogrel & ticlopidine evaluated in stable CAD (i.e., elective PCI); ticlopidine rarely used (↑ risk of TTP & neutropenia) (JAMA 1999;281:886)
- 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 (Circulation 2010;121:1909)

**ANGINA** (NEJM 2003;352:2324; 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
- Workups: 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, abl stress test, or for dx of recurrent anginal chest discomfort

**Treatment** (Circulation 2011;124:2574; Circulation 2012;124:10377)
- **BBs:** First-line Rx, titrate to resting HR of 55–60 bpm as BP allows; metoprolol & atenolol most commonly used; meta-analysis shows JBB 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
Indications: CABG: PCI: Sexual activity: Ischemic cardiomyopathy: Cardiac rehabilitation: Patient information:

Pathophysiology: β-blockers compete with catecholamines for binding to β receptors; ↓ β-adrenergic tone may limit activities despite optimal medical Rx; (3) Pts do not tolerate medical Rx; (2) Pts can tolerate medical Rx; (1) Survival may be improved in pts w/ left main disease; large area of myocardium at risk for ischemia

Toxicity: HoTN, bronchoconstriction, fatigue, ED, nightmares, insomnia, worsening depression/PAD/Raynaud’s; (less w/ β1-selective agents); taper rather than abrupt DisC due to w/d effects; antagonists; bioavailability of atenolol CCB: Vasodilator & reduce contractility (β-blockers reduce contractility, β1-selective agents); diltiazem, verapamil, & amiodidine typically used; may be used alone if β-blockers contraindicated (e.g., in pts w/ resting bradycardia) or in combination w/ β-blockers if too poorly controlled by β-blockers alone (combination of amiodidine & β-blockers preferred due to i. cap.)

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

Nitrites: Long-acting used as 24h line Rx in comb w/ β-blockers poorly controlled on β-blockers alone; may be used as monotherapy if β-blockers contraindicated; ↑ arterial & venous dilatation; i. preload; ↓ myocardin Q; demand (NEJM 1998:338:120)

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 h NTG)

Long-acting: 12–16 h nitrate-free interval (usually at night when there is less activity) & eccentric dosing (e.g., 1–2 tablets every 3–4 h; for s/o for isosorbide dinitrate, or q3h, q5h for isosorbide mononitrate) may ↑ tolerance; isosorbide dinitrate lasts 3–4 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, MA, syncope, nausea; tolerance; contraindicated in pts on sildenafill or w/ HECM

Ranolazine: ↓ angina in pts w/ continued sx on β-blockers, CCB, or nitrites; works by ↓ Ca overload in ischemic myocytes; QTc prolongation (Circulation 2006:113:2482)

ASA: 75–150 mg QD or 325 mg QOD ↓ CV morbidity & mortality by 20–25% (NEJM 2000:343:2534); 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 & nl EF shows 25% survival benefit seen), diffuse 3 vessel disease (≥70% stenosis) w/ large area of myocardium at risk for EF <0.40, proximal LAD & another major coronary artery, or pts who are not PCI candidates

Statin: See “Dyslipidemia”

Risk factor modification & exercise: See secondary prevention above

Revascularization (Circulation 2011;124:3610; e374)

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)

PCE: 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 for EF <0.40, 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, & NSAs except 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, & 24 h prevention (JACC 2008;51:1535); 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;86:275, 519); exercise training & medical Rx (ASA & β-blockers) help mitigate risk; pts should wait 3–4 wks after MI & have a negative ETT before resuming sexual activity (Am J Cardiol 2005:96:311)

Treatment of impotence: Reassurance in low-risk pts; PDE-5 inhibitors (sildenafil, vardenafil, tadalafil) contraindicated in pts on nitrates & β-blockers & 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

sex LV dysfunction

Intermediate risk: Cards consult and/or ETT advised if pt has: ≥ 3 CV risk factors (excluding gender) incl 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:e44; Circ 2005;111:816; JAMA 2007;297:395)

• 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


• 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)


• 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 aneurysms: 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 aneurysms: US ≤ 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)

<table>
<thead>
<tr>
<th>Abdominal Aortic Aneurysm Screening</th>
<th>(Circ 2004;110:16, NEJM 2003;348:1895)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAA Diameter</td>
<td>Screening Interval</td>
</tr>
<tr>
<td>&gt;4.5 cm</td>
<td>q3–6mos</td>
</tr>
<tr>
<td>4–4.5 cm</td>
<td>q6–12mos</td>
</tr>
<tr>
<td>&lt;4 cm</td>
<td>q1–2y</td>
</tr>
</tbody>
</table>

AAA Diameter Screening Interval

4.5 cm, >4.5 cm, <4 cm