Optimizing Care of Patients With Coronary Artery Disease

(Modified May 2024)

The toolbox below provides practical tips and resources to help you maximize pharmacotherapy and improve lifestyle in your CAD patients.

Goal	Suggested Strategies or Resources

Ensure appropriate **beta-blocker** use.	• Initiate a beta-blocker for patients with LVEF ≤40%, and post-MI patients (based on older data), to reduce CV events.[6]
	  ○ In patients post-MI with LVEF ≥50%, beta-blockers have not been proven to reduce CV events.[6,22]
	  ▪ In the modern era (i.e., with stenting, statins, dual antiplatelet therapy, etc), beta-blockers might not benefit post-MI patients with preserved ejection fraction. In an open-label study in post-MI patients with LVEF ≥50%, beta-blocker use for about 3.5 years did not reduce the risk of death, MI, or heart failure hospitalization; however, 14% of patients randomized to "no beta-blocker" ended up on a beta-blocker by the end of the first year.[22]
	  ○ For LVEF <50%, choose sustained-release metoprolol succinate, carvedilol, or bisoprolol titrated to target doses.[6]
	• Other indications for beta-blockers may include angina, arrhythmia, or hypertension; however, the strongest evidence of benefit is in patients with reduced LVEF.[6]
	  ○ For patients with hypertension, beta-blocker options (in addition to those listed above) include metoprolol tartrate, nadolol, propranolol, and timolol.[7] Avoid atenolol; it does not reduce CV events.[6,7]
	• In post-MI patients, consider discontinuing the beta-blocker after a year in the absence of another indication (e.g., LVEF ≤50% [current or prior], angina, arrhythmia, resistant hypertension).[6] (Note that this is a shift from previous guidelines, and that evidence is still evolving.)
	• Titrate to **target** dose:
	  ○ For HF*r*EF patients, see our chart, *Target Doses of Medications for Heart Failure.*
	  ○ For post-MI dosing, see our charts *Comparison of Oral Beta-Blockers* (US)(Canada).
	• For more help with dosing and choosing a BB based on **comorbidities**, **side effects**, **drug interactions**, and **cost**, see our charts *Comparison of Oral Beta-Blockers* (US)(Canada).

Select appropriate first-line **antianginal** therapy.	• Choose antianginal therapy that effectively relieves symptoms, keeping in mind comorbidities, adverse effects, and drug interactions.[6] • Most patients will not achieve complete relief.[6] **Calcium channel blockers** • For patients who do not have an indication for a beta-blocker (see above), an appropriate calcium channel blocker can be used first-line for angina.[6,21]

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Goal	Suggested Strategies or Resources
Continued… Antianginal therapy, continued	• Strong evidence that beta-blockers are superior to calcium channel blockers in regard to exercise tolerance, nitroglycerin use, or reduced chest pain is lacking.[6] • Generally, avoid verapamil or diltiazem in addition to a beta-blocker, and in patients with HF*r*EF.[2,6,7] Consider amlodipine as a beta-blocker add-on instead.[6,7] • For help choosing and dosing CCBs, and for information on side effects and drug interactions, see our chart, *Comparison of Calcium Channel Blockers*. **Nitrates** • Long-acting nitrates improve exercise tolerance, reduce chest pain, and reduce need for short-acting nitrate use.[6] • Consider the addition or substitution of a **long-acting nitrate** when a beta-blocker or calcium channel blocker does not relieve symptoms sufficiently or cannot be used.[6] • Ensure patients have **sublingual nitroglycerin** on hand for quick relief of chest pain, or to prevent angina during exertion.[6] Nitroglycerin spray may be more effective with less headache than sublingual tablets.[6] • Educate patients on correct use with information from the American Heart Association (Managing Your Angina Symptoms with Nitroglycerin) at https://www.ahajournals.org/doi/epub/10.1161/CIRCULATIONAHA.113.000821.

Use **ranolazine** appropriately.
 	
Continued…
	• Reserve for patients who don't get adequate relief from the angina meds above.[6]
	  o Can combine with other angina meds.[6] Does not reduce blood pressure or heart rate.[5]
	  o Not more effective than other angina meds.[11] Reduces angina frequency by about two episodes per week and improves exercise tolerance by less than a minute.[3] Does not seem to reduce risk of MI or death.[10]
	o Check liver and kidney function.
	  o Contraindicated in liver cirrhosis (Canada: moderate or severe hepatic impairment).[4,9]
	  o Monitor kidney function periodically if CrCl<60 mL/min. Stop in the event of acute kidney failure.[4] (Canada: contraindicated if eGFR ≤30 mL/min/1.73m^2.[9]
	o Screen for drug interactions:
	  o CYP3A4
	  o Ranolazine is contraindicated with strong CYP3A4 inhibitors or inducers.[4,9]
	  o Avoid exceeding ranolazine 500 mg twice daily with moderate CYP3A4 inhibitors (e.g., diltiazem, verapamil).[4,9]
	  o Ranolazone inhibits CYP3A4.[4] Limit simvastatin dose to 20 mg.[4,9]
	  o CYP2D6
	  o Ranolazine side effects may be more common with CYP2D6 inhibitors or in CYP2D6 poor metabolizers.[9]
	  o Drugs metabolized by CYP2D6 may need dose reduction.[4,9]
	  o P-glycoprotein
	  o Ranolazine levels can be increased by p-glycoprotein inhibitors (e.g., cyclosporine).[4,9]

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Goal	Suggested Strategies or Resources
Use **ranolazine** appropriately, continued	○ Ranolazine can increase digoxin levels via p-glycoprotein inhibition.[4,9] ○ Limit total daily **metformin** dose to 1,700 mg when used with ranolazine 1,000 mg twice daily.[4,9] ○ Ranolazine can prolong QT interval.[4,9] Baseline electrocardiogram is recommended by Canadian labeling.[9] ○ Advise patients about common side effects: constipation, dizziness (may be dose-dependent), nausea, headaches.[4,9]
Ensure that CAD patients are on the correct **antithrombotic** regimen.	• For patients post-ACS, post-CABG, or with a stent, see our chart, *Dual Antiplatelet Therapy for Coronary Artery Disease.* • Patients with no indication for an oral anticoagulant should take aspirin 81 mg daily (75 to 100 mg) indefinitely to reduce CV events.[6] ○ Clopidogrel 75 mg once daily is an alternative for aspirin-intolerant patients.[6] ○ After completion of DAPT post-ACS and/or PCI, mounting evidence suggests that clopidogrel 75 mg once daily may be more effective for reducing CV events without causing more bleeding than aspirin.[18-20] • For patients with no indication for anticoagulation or dual antiplatelet therapy, consider adding rivaroxaban (*Xarelto*) to low-dose aspirin for patients with high cardiovascular risk and low-to-moderate bleeding risk.[6,13] For dosing and more, see our chart, *Comparison of Oral Anticoagulants*. • For patients with a history of MI, but without a history of stroke, transient ischemic attack, or intracerebral hemorrhage, vorapaxar can be added to aspirin to reduce the CV events.[6]
Ensure that CAD patients are on an evidence-based **ACEI or ARB**.	• For patients with HFrEF, see our chart, *Target Doses of Medications for Heart Failure*. • An ACEI (or ARB) is recommended for CAD patients with hypertension, diabetes, LVEF ≤40%, or chronic kidney disease. They can also be considered for other CAD patients to reduce CV events.[6] ○ The net benefit of ACEI or ARB treatment in CAD patients likely depends on comorbidities, CAD severity, and concomitant use of other CV risk-reducing medications.[6]
Ensure patients are taking a **statin** per guidelines.	• Get our FAQs, *Cholesterol Guidelines (United States)* or Canadian Dyslipidemia Recommendations, for recommendations on statin dosing and monitoring. • Save non-statins for statin-intolerant patients or those who don't get the expected LDL-lowering from their statin.[6] Among non-statins, evidence for CV risk reduction is best for ezetimibe or PCSK9 inhibitors.[6] • Educate patients about statins and other cholesterol medications with resources from the American Heart Association at https://www.heart.org/en/health-topics/cholesterol/prevention-and-treatment-of-high-cholesterol-hyperlipidemia/cholesterol-medications.

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Reduce coronary event risk with **diabetes medications**.	• An ACEI or ARB is recommended for patients with CAD and diabetes.[6] • Use an SGLT2 inhibitor or GLP-1 agonist to reduce CV events in patients with diabetes. See our chart, *Diabetes Medications: Cardiovascular and Kidney Impact* to see which agents have the best evidence. o Choose an SGLT2 inhibitor for patients with heart failure, regardless of whether they have diabetes.
Ensure CAD patients with **hypertension** have their blood pressure under control using appropriate therapy.	• Aim for a blood pressure goal of <130/80 mm Hg.[6-8] International Society of Hypertension guidelines recommend a goal of <140/80 mmHg for the elderly.[1] o Diastolic ≤60 mmHg could worsen myocardial ischemia, especially in patients with left ventricular hypertrophy.[2,8] • First-line antihypertensives for CAD include ACEIs (or ARBs) and beta-blockers (e.g., for angina or recent MI).[2,6-8] Use an ACEI (or ARB) plus a beta-blocker post-MI.[2] Diltiazem or verapamil can be substituted for a beta-blocker for angina in patients without a compelling beta-blocker indication, and can be used for recent MI if a beta-blocker cannot be used.[2,6-8] • Second-line antihypertensives might include a dihydropyridine calcium channel blocker (especially for angina despite a beta-blocker), long-acting thiazide (i.e., chlorthalidone or indapamide), and/or mineralocorticoid receptor blocker.[6,7] o For high-risk patients, give preference to an ACEI plus dihydropyridine calcium channel blocker over an ACEI plus thiazide/thiazide-like diuretic.[2,8]
Consider colchicine for appropriate patients, continued *Continued…*	• Consider colchicine 0.5 mg once daily as an add-on to optimized CAD pharmacotherapy (e.g., aspirin, statin, beta-blocker), without contraindications, to reduce cardiovascular events.[12,14-17] • Colchicine 0.5 mg (*Lodoco* [US]) reduces the composite end point of cardiovascular death, angina requiring acute revascularization, stroke, or MI in 1 in 35 patients with **stable** CAD receiving standard CV preventive meds (e.g., aspirin, statin, ACEI, beta-blocker) over about 29 months (LoDoCo2 trial).[16] This benefit derives mostly from MI and angina; it does not reduce cardiovascular death alone.[16] • Colchicine 0.5 mg **extended-release** (*Myinfla* [Canada]) reduces the composite end point of cardiovascular death, resuscitated cardiac arrest, angina requiring acute revascularization, stroke, or MI in 1 in 63 **post-MI** patients receiving standard CV preventive meds (e.g., aspirin, statin, beta-blocker), over about 23 months (COLCOT trial).[15] This benefit derives mostly from strokes and angina requiring acute revascularization; it does not reduce cardiovascular death alone.[15] • Patients with severe kidney or heart failure were excluded from LoDoCo2 and COLCOT.[15,16] Both trials were of short duration.[15,16] COLCOT recruited patients within 30 days of an MI, and excluded patients with recent stroke.[15] LoDoCo2 included only patients with CAD who had been stable for at least six months.[16] Colchicine 0.6 mg has not been studied for secondary cardiovascular prevention. • Colchicine 0.5 mg (*Lodoco* [US], *Myinfla* extended-release [Canada]) once daily is indicated, as an addition to standard treatment (e.g., statin, aspirin), to reduce cardiovascular events.[12,14]

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Goal	Suggested Strategies or Resources
Consider colchicine for appropriate patients.	○ Contraindicated in severe liver or kidney impairment (*Myinfla*: eGFR <30 mL/min/1.73m^2; *Lodoco*: CrCl <15 mL/min)[12,14] ○ Contraindicated with strong CYP3A4 (e.g., clarithromycin) or P-glycoprotein inhibitors (e.g., cyclosporine, ranolazine).[12,14] Avoid with grapefruit juice, and with other moderate CYP3A4 inhibitors in the elderly (*Myinfla*) or in patients with moderate kidney or liver impairment.[12,14] ○ Gastrointestinal symptoms (e.g., abdominal pain, diarrhea, nausea) are the most common side effects.[12,14]
Educate patients about diet, exercise, and other lifestyle interventions.	• Patient information on the American Heart Association diet and lifestyle recommendations is available at https://www.heart.org/en/healthy-living/healthy-eating/eat-smart/nutrition-basics/aha-diet-and-lifestyle-recommendations. **Diet** • Suggest a diet consistent with the DASH (Dietary Approaches to Stop Hypertension) or Mediterranean diet to lower cardiac risk.[6] • Have patients aim for **more** fruits and vegetables, low-fat dairy, whole grains, lean protein (e.g., fish), and beans, and **less** red meat and sugary drinks.[6] • Recommend limiting saturated **fats** to ≤6% of calories, and avoiding trans fats.[6] Recommend healthier oils (e.g., olive).[6] • Recommend limiting **sodium** to <2,300 mg/day (ideally <1,500 mg/day), or reduce sodium by 1,000 mg/day.[6] **Weight loss** • Patients with BMI ≥30 kg/m^2 or 27 to 29.9 kg/m^2 with weight-related comorbidities may be candidates for pharmacotherapy, failing lifestyle modification.[6] For information about use of approved weight-loss products, including dosing, expected weight loss, cost, and considerations for use, see our chart, *Weight Loss Products*. **Activity** • Encourage at least 150 to 300 minutes per week of moderate-intensity aerobic activity.[6] **Vaccines** • Recommend COVID-19 vaccination, and a yearly **flu vaccine**.[6] • Pneumococcal vaccination is also reasonable. For guidance on which adult should get which pneumococcal vaccine see: https://www.cdc.gov/vaccines/vpd/pneumo/downloads/pneumo-vaccine-timing.pdf (US) or https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html#a6 (Canada). **Smoking cessation** • To choose the most appropriate options for helping your patients stop smoking, see our chart, *Smoking Cessation Drug Therapy*.

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Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; AHA/ACC = American Heart Association/American College of Cardiology; ARB = angiotensin receptor blocker; CABG = coronary artery bypass graft; CAD = coronary artery disease; CV = cardiovascular; HF*r*EF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MI = myocardial infarction; SBP = systolic blood pressure.

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Cite this document as follows: **Clinical Resource,** ***Optimizing Care of Patients With Coronary Artery Disease. Pharmacist's Letter/Pharmacy Technician's Letter/Prescriber Insights.*** **September 2023. [390916]**

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