

Best Practice

Best Practice Protocol for the Blue Cross Blue Shield of Michigan Cardiovascular Consortium

Post-Discharge Management

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I. Antiplatelet and Anticoagulant Therapy

- For patients not taking an oral anticoagulant
 - Aspirin 81 mg daily PLUS ONE OF THE FOLLOWING P2Y12 inhibitors:
 - Clopidogrel (Plavix) 75 mg orally daily or,
 - Prasugrel (Effient) 10 mg orally daily or,
 - Ticagrelor (Brilinta) 90 mg orally twice a day
 - The duration of DAPT to be determined by presentation (SIHD vs ACS) as well as a discussion around bleeding/ischemic risk.
 - Interventional MD should make and document an initial minimum duration of antithrombotic therapy (i.e. specify DAPT plan).



Master treatment algorithm for duration of P2Y₁₂ inhibitor therapy in patients with CAD treated with DAPT. Reprinted from "2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease" by G.N. Levine, 2016, *Circulation*, *134*(10):e123-e155. (1)

- For patients taking an oral anticoagulant (trials were performed among patients taking an oral anticoagulant for atrial fibrillation).
 - General consensus is to minimize the duration of triple antithrombotic therapy (TAT) (2)
 - Recommend aspirin 81 mg daily use in the peri-PCI or in-hospital period; early discontinuation of aspirin 1-7 days post-PCI.



 Continue P2Y12 inhibitor for 12 months (shorter or longer duration can be considered based on thrombotic and bleeding risks) and oral anticoagulant (DOAC or VKA) indefinitely for atrial fibrillation stroke prophylaxis. (3)





Patient with AF on OAC Who Now Needs PCI: Post-Procedure and Long-Term Management of Antithrombotic Therapy. Reprinted from "2020 ACC Expert Consensus Decision Pathway for Anticoagulant and Antiplatelet Therapy in Patients With Atrial Fibrillation or Venous Thromboembolism Undergoing Percutaneous Coronary Intervention or With Atherosclerotic Cardiovascular Disease" by D.J. Kumbhani, 2020, *J Am Coll Cardiol, S0735-1097*(20), 36615-8.



- o Additional strategies to mitigate bleeding risk
 - PPIs should be used in patients with a history of prior GI bleeding who require DAPT.
 - Use of PPIs is reasonable in patients with an increased risk of GI bleeding (eg, advanced age, concomitant use of warfarin, steroids, NSAIDs, Helicobacter pylori infection) who require DAPT. (4)
 - For patients on ≥2 antithrombotic agents, recommend starting PPI (or H2-receptor antagonists in selected cases) along with avoidance of NSAIDs to reduce the risk of GIB. These medications should be discontinued when the regimen returns to OAC alone, unless there are other indications for continued use. (3)



II. Lipid Management

- o Statin
 - All patients <75 years old or those at very high-risk ASCVD (see table 4 below) should receive high-intensity or maximal statin therapy. (5)
 - If on maximally-tolerated statin and LDL-C ≥70 mg/dL, adding ezetimibe (Zetia) is reasonable.
 - If on maximal LDL-C lowering therapy (statin and ezetimibe) and LDL-C ≥70 mg/dL or non-HDL-C ≥100 mg/dL, adding a PCSK9-inhibitor is reasonable. (6)
 - Goal LDL <70 mg/dL; goal non-HDL <100 mg/dL.
- Icosapent ethyl (Vascepa)
 - Approved in patients with a known history of established cardiovascular disease or diabetes plus ≥2 more additional cardiovascular risk factors who have triglycerides >150 mg/dL on statin therapy.
 - 25% lower risk of the primary end point of CV death, nonfatal MI, nonfatal stroke, coronary revascularization, or unstable angina. (7)



Secondary prevention in patients with clinical ASCVD. Reprinted from "AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary" by S.M. Grundy, 2018, J Am Coll Cardiol, 73(24):3168-3209.



III. Hypertension Management

Categorize HTN (8)

Table 6. Categories of BP in Adults* (Table view)

BP Category	SBP		DBP			
Normal	<120 mm Hg	and	<80 mm Hg			
Elevated	120–129 mm Hg	and	<80 mm Hg			
Hypertension						
Stage 1	130–139 mm Hg	or	80–89 mm Hg			
Stage 2	≥140 mm Hg	or	≥90 mm Hg			

* Individuals with SBP and DBP in 2 categories should be designated to the higher BP category.

BP indicates blood pressure (based on an average of ≥2 careful readings obtained on ≥2 occasions, as detailed in Section 4); DBP, diastolic blood pressure; and SBP, systolic blood pressure.

Reprinted from "ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary", P.K. Whelton, 2018, *Hypertension*, 71(6), 1269-1324.

- Discuss the importance of non-pharmacologic interventions including weight loss, hearthealthy diet (DASH diet), sodium reduction, aerobic exercise, and advisement around alcohol consumption. Consider referral to behavior modification services after a discussion with the patient.
- Treat to a goal <130/80 with the selection of beta-blockers, ACE-I, ARB, aldosterone antagonists, diuretics, and dihydropyridine calcium channel blockers based on patient comorbid conditions (i.e. HF, CKD with proteinuria, stable ischemic heart disease).



Figure 5. Management of hypertension in patients with SIHD. Colors correspond to Class of Recommendation in Table 1. *GDMT beta blockers for BP control or relief of angina include carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol. Avoid beta blockers with intrinsic sympathomimetic activity. The beta blocker atenolol should not be used because it is less effective than placebo in reducing cardiovascular events. †If needed for BP control. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; GDMT, guideline-directed management and therapy; and SIHD, stable ischemic heart disease.



Reprinted from "ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary", P.K. Whelton, 2018, *Hypertension*, 71(6), 1269-1324.

IV. Heart Failure management

- o Randomized controlled trials have primarily enrolled patients with HFrEF (EF≤40%). (9,10)
- Patients should be on ACE-I/ARB and evidence-based beta-blockers (metoprolol succinate, carvedilol, or bisoprolol), and diuretics as needed.
- If they have NYHA class II-IV symptoms and CrCl >30 ml/min and K+ < 5.0 mEq/L, they should be on an aldosterone antagonist (spironolactone or eplerenone).
- If they have NYHA class II-III HF with adequate BP on ACEI or ARB and no contraindication to ARB or sacubitril, consider transition from ACE-I/ARB to ARNI (Entresto).

V. Diabetes management in patients with Atherosclerotic Cardiovascular Disease - Novel medications for CAD

GLP-1 agonists and SGLT-2 inhibitors (11)

- Recently, newer antidiabetic agents have demonstrated significant cardiovascular benefit among patients with cardiovascular disease. As such, we believe it is imperative that these medications be considered among our patients with CAD and T2DM so that a discussion with the patient and their outpatient providers may occur in the peri-PCI setting. Patients should already be taking metformin.
- These drugs should be administered in patients with T2DM already on metformin with A1C >7.0%. Increased vigilance for hypoglycemia is required in patients on insulin, sulfonylurea, or glinide therapy.
- At a minimum, consider communicating with outpatient providers the following: <u>"Recommend</u> <u>consideration of SGLT2 inhibitor or GLP-1 agonist if felt to be appropriate. Recent data has</u> <u>demonstrated improved cardiovascular outcomes in patients with diabetes mellitus and</u> <u>concomitant established or at a high risk for developing ASCVD."</u>





Summary of the Expert Consensus Decision Pathway. Reprinted from "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee", S.R. Das, 2020, *J Am Coll Cardiol, 76*(9), 111-1145.

o SGLT-2 inhibitors (11)

		Canagliflozin	Dapagliflozin	Empagliflozin
Recommended doses for CV benefit*	100 mg P	0 daily	10 mg PO daily	 10 mg PO daily
Indications	 Improve g adjunct to Reduce ris and CV di Reduce th serum cre patients v albuminum 	lycemic control in adults with T2D as an diet and exercise k of MI, stroke, or CV death in adults with T2D sease e risk of end-stage kidney disease, doubling of atinine, CV death, and hospitalization for HF in rith T2D and diabetic nephropathy with ia	 Improve glycemic control in adults with T2D as an adjunct to diet and exercise Reduce the risk of hospitalization for HF in adults with T2D and established CV disease or multiple CV risk factors Reduce the risk of CV death and hospitali- zation for HF in adults with HFrEF 	 Improve glycemic control in adults with T2D as an adjunc to diet and exercise Reduce risk of CV death in adults with T2D and estab- lished CV disease
Dose modifications	 eGFR 30 f eGFR <30 glycemic 	o 59 ml/min/1.73 m ² : max dose 100 mg daily ml/min/1.73 m ² : use is not recommended for control	 eGFR <45 ml/min/1.73 m²: use is not recommended for glycemic control eGFR <30 mL/min/1.73 m²: use is contraindicated. 	 eGFR <45 mL/min/1.73 m²: use is not recommended.
Contraindication	 History of Pregnancy On dialysi eGFR <30 ESRD (dag Severe res 	serious hypersensitivity reaction to drug or breastfeeding s mL/min/1.73 m ² (dapagliflozin) aggliflozin and empagliflozin) al impairment (empagliflozin)		
Cautions	 Discontinue at least 3 days before a planned surgery to prevent postoperative ketoacidosis. If HbA1c well-controlled at baseline, or known history of frequent hypoglycemic events, wean or stop sulfonylurea or glinide and consider reducing total daily insulin dose by ~20% when starting therapy. May contribute to intravascular volume contraction; consider stopping or reducing diuretic dose if applicable. Use with caution in patients with prior amputation, severe peripheral neuropathy, severe peripheral vascular disease, or active diabetic foot ulcers or soft tissue infections. Possible increased risk of bone fractures (canagliflozin) 			
Adverse effects to monitor	Genital fungal infections Urinary tract infections Euglycemic diabetic ketoacidosis Lower limb ulcerations and soft tissue infections			

outcomes trials. Those doses are listed here. No further dose titration is needed for CV or renal risk reduction. However, dose increases may provide further glucose reduction benefits if indicated. CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; HbA1c = hemoglobin A1c; HF= heart failure; PO = "per os," by mouth; SGLT2 =

CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; HbATc = hemoglobin A1c; HF= heart failure; PD = "per os," by mouth; SGLT2 = sodium-glucose cotransporter-2; T2D = type 2 diabetes.

Doses, Indications, Dose Modifications, Contraindications, Cautions, and Adverse Effects of SGLT2 Inhibitors With Demonstrated CV Benefit. Reprinted from "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients



With Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee", S.R. Das, 2020, J Am Coll Cardiol, 76(9), 111-1145.



Stepwise Approach to Prescription of SGLT2 Inhibitors by Cardiologists. Reprinted from "Practical Guide to Prescribing Sodium-Glucose Cotransporter 2 Inhibitors for Cardiologists", O. Vardeny, 2019, JACC Heart Fail, 7(2),169-172. (12)



o GLP-1 agonists (11)

Doses, Indications, Dose Modifications, Contraindications, Cautions, and Adverse Effects of GLP-1RAs With Demon-TABLE 4 strated CV Benefit Dulaglutide Exenatide OW Liraglutide Lixisenatide Semaglutide SC Semaglutide PO Recommended Initiate 0.75 mg SC 2 mg SC per week Initiate 0.6 mg . 10 mcg SC daily . Initiate 0.25 mg . Initiate 3 mg PO doses for CV SC daily. Titrate as toler-SC per week. per day for the first per week 30 days. benefit Titrate slowly to Titrate slowly to ated to 20 mcg . Titrate slowly to 1.5 mg or maximally 1.8 mg or maxidaily based on 1 mg once weekly Titrate slowly to 14 tolerated dose based mally tolerated prescribing or maximally mg daily or maxion prescribing dose based on information. tolerated dose mally tolerated information. prescribing based on predose based on preinformation. scribing scribing information. information. Indications Improve alycemic con-Improve alycemic Improve glycemic Improve alvcernic Improve alycemic Improve glycemic trol in adults with T2D. control in adults Reduce MACE for peowith T2D. with T2D. with T2D. with T2D. with T2D. ple with T2D with and Reduce risk of MI, Reduce risk of MI, without established CV CVA, or CV death CVA, or CV death disease. in adults with T2D in adults with T2D and CV disease. and CV disease Up-titrate slowly to Discontinue if Up-titrate slowly Up-titrate slowly Up-titrate slowly Dose . . . Up-titrate slowly modifications reduce nausea and pancreatitis is to reduce nausea to reduce nausea to reduce nausea to reduce nausea vomiting. suspected and do and vomiting. and vomiting. and vomiting. and vomiting. Discontinue if pancreanot restart if . Discontinue if Discontinue if . Discontinue if Discontinue if titis is suspected and pancreatitis is pancreatitis is pancreatitis is pancreatitis is pancreatitis is susdo not restart if confirmed. suspected and do suspected, and do suspected and do pected and do not pancreatitis is eGFR <45 mL/ not restart if not restart if not restart if restart if pancreaconfirmed. min/1.73 m2: pancreatitis is pancreatitis is pancreatitis is titis is confirmed. confirmed . eGFR ≥30 mL/ No dose adjustment Use is not confirmed. confirmed. No dose adjust-. No dose adjust-No dose adjustnecessary with renal or recommended. . ment is necessary min/1.73 m2: hepatic impairment; ment is necessary with renal or hement is necessary data in end-stage renal with renal or he-No dosage with renal or hepatic impairment. disease are limited. adjustment is patic impairment patic impairment required. eGER 15 to 29 ml / min/1.73 m2: Use caution and monitor renal function. eGFR <15 mL/</p> min/1.73 m² Use is not recommended. Contraindications History of serious hypersensitivity reaction to drug Pregnancy or breast feeding . Severe renal impairment or end-stage renal failure (exenatide, lixisenatide) . Personal or family history of medullary thyroid cancer . Personal or family history of MEN2 Cautions . Hypoglycemia risk increased with insulin, sulfonylureas, or glinides. May delay gastric emptying; not recommended in patients with clinically meaningful gastroparesis. This effect is usually transient with . longer-acting GLP-1Ras. Care should be taken in patients with prior gastric surgery, including bariatric surgery. Diabetic retinopathy complications were reported with semaglutide (injectable), although it is unclear if this is a direct effect of the drug or due to other factors such as rapid improvement in blood glucose control. Adverse effects . Nausea, vomiting, diarrhea, headache, weakness, or dizziness Hypoglycemia when given with insulin, sulfonylureas, or glinides. to monitor Weight loss . Injection site reactions

Doses, Indications, Dose Modifications, Contraindications, Cautions, and Adverse Effects of GLP-1RAs With Demonstrated CV Benefit. Reprinted from "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee", S.R. Das, 2020, *J Am Coll Cardiol, 76*(9), 111-1145.



TABLE 5 Opportunities to Initiate an SGLT2 inhibitor or a GLP-1RA With Demonstrated CV or Renal Benefit in Patients With T2D*

In a patient with T2D and ASCVD (SGLT2 inhibitor or GLP-1RA)

- At the time of diagnosis of clinical ASCVD (SGLT2 inhibitor or GLP-1RA), DKD, and/or HF (SGLT2 inhibitor)† in a patient with T2D on a drug regimen that does not include an SGLT2 inhibitor or GLP-1RA with CV benefit
- At the time of diagnosis of T2D in a patient with clinical ASCVD (SGLT2 inhibitor or GLP-1RA), DKD, and/or HF (SGLT2 inhibitor)^{†‡}
- At hospital discharge (with close outpatient follow-up) after admission for an ASCVD (SGLT2 inhibitor or GLP-1RA) or HF (SGLT2 inhibitor) events
- In a patient with T2D and diabetic kidney disease (SGLT2 inhibitor, alternatively GLP-1RA for eGFR <30 ml/min/1.73 m²)
- In patients determined to be at high risk of ASCVD (SGLT2 inhibitor or GLP-1RA) or HF (SGLT2 inhibitor)⁺⁺

Opportunities to Initiate an SGLT2 Inhibitor or a GLP-1RA With Demonstrated CV Benefit or Renal Impairment in Patients With T2D. Reprinted from "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee", S.R. Das, 2020, *J Am Coll Cardiol, 76*(9), 111-1145.

TABLE 6 Patient and Clinician Preferences and Priorities for Considering SGLT2 Inhibitors With Demonstrated CV Benefit Versus GLP-1RAs With Demonstrated CV Benefit

Preference or Priority	Consider Using an SGLT2 Inhibitor First When Patient and Clinician Priorities Include:	Consider Using a GLP-1RA First When Patient and Clinician Priorities Include: ++++	
MACE prevention	+++		
HF prevention	+++		
Weight loss	+	+++	
Renal disease progression prevention	+++	+	
Mode of administration	Oral	Subcutaneous	
Considerations that may prompt use of an alternative class	 Severely reduced kidney function*,† History of prior amputation, severe peripheral arterial disease, or active diabetic foot ulcers (caution with canagliflozin) History of recurrent genital candidiasis History of diabetic ketoacidosis History of fracture (caution with canagliflozin) The patient is considering pregnancy The patient is breast feeding 	 Persistent nausea, despite appropriate di- etary education and low doses History of gastroparesis Active gallbladder disease History of MEN2 or medullary thyroid cancer History of proliferative retinopathy (caution with semaglutide or dulaglutide) The patient is considering pregnancy The patient is breast feeding 	

*eGFR <45 ml/min/1.73 m² is currently a caution due to a decrease in glycemic efficacy (not due to safety), but ongoing studies are testing whether SGLT2 inhibitors offer renal benefits in these patients. The FDA label for canagliflozin allows use of canagliflozin to an eGFR of 30 ml/min/1.73m² specifically for patients with DKD.

†Use clinical judgement when initiating an SGLT2 inhibitor in a patient who will be starting or up-titrating an ACE inhibitor or ARB if the patient's renal function is impaired ACE – angiotensin-converting enzyme; ARB – angiotensin reception blocker; CV – cardiovascular; DKD – diabetic kidney disease; eGFR – estimated glomerular filtration rate; FDA – Food and Drug Administration; GLP-IRA – glucagon-like peptide-1 receptor agonist; HF – heart failure; MACE – major adverse cardiovascular event; MEN2 – multiple endocrine neoplasia type 2; SGLT2 – sodium-glucose cotransporter-2.

Patient and Clinician Preferences and Priorities for Considering SGLT2 Inhibitors With Demonstrated CV Benefit Versus GLP-1RAs With Demonstrated CV Benefit. Reprinted from "2020 Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes: A Report of the American College of Cardiology Solution Set Oversight Committee", S.R. Das, 2020, *J Am Coll Cardiol, 76*(9), 111-1145.



VI. Smoking cessation

- o Discussion around the importance of smoking cessation
- o Referral to smoking cessation program
- Nicotine replacement therapy discussed.
- Can also discuss smoking cessation treatments such as varenicline or bupropion with appropriate counseling, follow-up, and monitoring if these medications are prescribed.

VII. Cardiac rehabilitation

- Referral to cardiac rehabilitation. If not placed, indicate reason why. Attempt to schedule the patient for the first cardiac rehabilitation visit prior to discharge.
- Cardiac rehabilitation is associated with reductions in readmissions and mortality and improvements in exercise capacity and symptoms. (4)
- Research has demonstrated that clear physician endorsement of the benefits of cardiac rehabilitation significant increase patient participation in CR.
- Face-to-face discussion, recommendation, and prescription that documents the following:
 - Endorsement of cardiac rehabilitation noting that cardiac rehabilitation is an important next step in the patient's care.
 - An overview of what cardiac rehabilitation is and its associated benefits was discussed.
 - The patient's questions were answered.



VIII. REFERENCES

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