mg per day for metoprolol succinate, and 25 mg twice daily for carvedilol (or 50 mg twice daily for patients weighing >84 kg).

3. Although previous iterations of the ACC/AHA guidelines on patients with stable ischemic heart disease recommended the use of beta-blocker therapy in patients with previous MI and preserved LV systolic function, this recommendation was based on data gathered from the noncontemporary era.[33] In the contemporary era of timely reperfusion/revascularization and progressive pharmacotherapy (including antithrombotic and lipid-lowering therapy) among patients with MI, the recommendation for long-term use (>1 year) of beta-blocker therapy in the absence of LV systolic dysfunction has been challenged.[13,14] Observational studies from the current era evaluating post-MI patients with preserved LV systolic function showed discrepant results with some studies suggesting clinical benefit while others showed lack of clinical benefit with long-term use of beta-blocker therapy.[9-15,34] Long-term use of beta-blocker therapy may also confer potential clinical risks including fatigue, depression, and drug-drug interactions, thereby necessitating future high-quality data to ascertain the need for and duration of beta-blocker use among this population. Several ongoing large randomized controlled clinical trials including REBOOT-CNIC (Treatment with Beta-blockers after MI without Reduced Ejection Fraction), REDUCE-SWEDEHEART (Evaluation of Decreased Usage of Beta-blockers After MI in the Swedeheart Registry), BETAMI (Beta-blocker Treatment after Acute MI in Revascularized Patients without Reduced LVEF), and DANBLOCK (Danish Trial of Beta-blocker Treatment after MI Without Reduced LVEF) aim to provide more clarity on the efficacy, safety, and QOL associated with beta-blocker therapy in patients with CCD, including post-MI patients with preserved LV systolic function.
4. Protective clinical benefits of beta-blocker therapy in reducing cardiovascular death have not been shown among CCD patients without previous MI or LV systolic dysfunction. The REACH (Reduction of Atherothrombosis for Continued Health) registry evaluated patients with CAD without history of MI and studied the effect of beta-blocker therapy on the primary endpoint of cardiovascular death, nonfatal MI, or nonfatal stroke.[18] Among patients with CAD without a history of MI, the use of beta-blocker therapy was not associated with a significant reduction in event rates for the primary endpoint. Similarly, a recent analysis from the National Cardiovascular Data Registry Cath-PCI registry evaluated the clinical benefit of beta blockers among patients with stable angina without a history of MI, LV systolic dysfunction, or systolic HF who were undergoing PCI.[19] The authors showed that the use of beta blockers was not associated with improvement in cardiovascular morbidity or mortality rates at 30 days or at 3-year follow-up. Similar results were seen in a post-hoc analysis from the CHARISMA (Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance) trial in which no reduction in cardiovascular events was observed with the use of beta blockers among patients without previous MI or HF.[17]

4.3.3. Renin-Angiotensin-Aldosterone Inhibitors

Recommendations for Renin-Angiotensin-Aldosterone Inhibitors
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD who also have hypertension, diabetes, LVEF ≤40%, or CKD, the use of ACE inhibitors, or ARBs if ACE inhibitor–intolerant, is recommended to reduce cardiovascular events.[1-5]
2b	B-R	2. In patients with CCD without hypertension, diabetes, or CKD and LVEF >40%, the use of ACE inhibitors or ARBs may be considered to reduce cardiovascular events.[6-10]

Synopsis

Patients at high risk for CCD who have structural abnormalities (LVEF ≤40%), comorbid conditions (eg, diabetes, CKD, hypertension), or both are at significantly elevated risk of developing symptomatic HF and recurrent cardiovascular events. In addition to lowering BP (see Section 4.2.6, "Lipid Management"), renin-angiotensin-aldosterone system inhibitors (RAASi) decrease MACE in high-risk patients with CCD.[1,3,5,8] In contrast, the efficacy of RAASi is less certain among populations with CCD with LVEF >40% and without comorbid hypertension, diabetes, or CKD.[6,8,9,11,12] RAASi trials (PEACE [Prevention of Events with Angiotensin Converting Enzyme Inhibition], QUIET [Quinapril Ischemic Event Trial], CAMELOT [Comparison of Amlodipine versus Enalapril to Limit Occurrences of Thrombosis], and IMAGINE [Clazakizumab for the Treatment of Chronic Active Antibody Mediated Rejection in Kidney Transplant Recipients]) in lower-risk