β-blocker therapy may be particularly effective in slowing the progression of HF in asymptomatic individuals with significantly reduced LVEF (92). With effective treatment, individuals in stage B HF may remain stable for many years (92).

Management of Hypertension in Individuals With Diabetes in Stage A or B HF

Although optimal control of BP remains a primary goal for all individuals at risk for HF, there are some particularities in the intersection of hypertension with diabetes. For instance, in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), treatment with doxazosin was associated with increased rate of HF, compared with chlorthalidone, in individuals with diabetes despite a similar reduction in BP (93). Findings of the Swedish Trial in Old Patients with Hypertension-2 (STOP-2) showed that ACEi were superior to calcium channel blockers in preventing HF in the subgroup of elderly individuals with diabetes (94).

ACEi or ARB are preferred agents in the management of individuals with either T1D or T2D and hypertension, especially in the presence of albuminuria, to reduce the risk of progressive kidney disease, and their dose should be optimized (95). Treatment with a thiazide-type diuretic or an ACEi has been shown to be more effective than treatment with a calcium channel blocker in improving HF outcomes (96). Thiazide diuretic use occasionally results in worsening glycemic control and/or raising serum triglycerides in individuals with diabetes.

Despite treatment with what is considered to be optimal doses of ACEi or ARB, there remains overactivation of the mineralocorticoid receptor in hypertension. Mineralocorticoid receptor antagonists (MRA) such as spironolactone or eplerenone are thus important adjuncts for management of hypertension. Recent studies determined that finerenone, a nonsteroidal selective MRA with more potent anti-inflammatory and antifibrotic effects than steroidal MRA, has superior benefits in diabetic kidney disease (DKD). In the Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease (FIDELIO-DKD) trial, in 5,734 individuals with CKD and T2D, it was determined that treatment with finerenone resulted in lower risks of DKD progression and cardiovascular events, myocardial infarction, and hospitalization for HF (97,98), while Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease (FIGARO-DKD) showed that finerenone significantly reduced cardiovascular death and nonfatal cardiovascular disease endpoints including hospitalization for HF in 7,400 individuals with T2D and DKD (99,100). Thus, finerenone is now approved by the U.S. Food and Drug Administration for reducing progression of DKD and reducing risk for cardiovascular complications including HF.

These agents are associated with risk for hyperkalemia and require careful serum potassium monitoring when used (as detailed in Supplementary Table 3).

Key Points

- ACEi and ARB are preferred agents in the management of stage A or B patients with either T1D or T2D and hypertension, especially in the presence of albuminuria and/or CAD.
- Treatment with a thiazide-type diuretic or an ACEi has been shown to be more effective than treatment with a calcium channel blocker in preventing progression to symptomatic HF, and their use is recommended for treatment of individuals with diabetes and hypertension.
- Among patients with diabetes and DKD without symptomatic HF, the use of finerenone, a nonsteroidal MRA, may reduce progression of DKD and lower risk for incident HF.
- Careful monitoring of serum potassium levels is needed with the use of MRA and other RAAS blockers.

Pharmacologic Therapy for Stages C and D HF: Guideline-Directed Medical Therapy

Recent clinical practice guidelines and expert consensus statements are available for detailed guidance regarding rationale for use, initiation and titration, and monitoring of the standard guideline-directed medical therapy (GDMT) for HFrEF treatment (67,101); clinicians are directed to these useful documents for specific advice regarding selection of agents, doses, and titration strategies. Here, we will only review the expected components of care, referring mainly to diabetes-specific topics related to use of GDMT in the presence of HFrEF or HFpEF.

For those individuals with diabetes with symptomatic HFrEF, barring contraindication, the expected components of GDMT include the following: *1*) angiotensin receptor/neprilysin inhibitor (ARNI) or ACEi/ARB, *2*) evidenced-based β-blocker, *3*) MRA, and *4*) SGLT2i. While the GDMT options for HFpEF are less well-defined, SGLT2i are now also recommended in HFpEF, as discussed below (1).

RAAS Inhibitors for Treatment of HFrEF. Inhibitors of the RAAS represent foundational therapy for the management of HFrEF, increasing LVEF even in those previously taking ACEi or ARB (102), reducing risk for hospitalization or death, and improving health status. Agents in this class include the ARNI sacubitril/valsartan, ACEi, ARB, and MRA.

ACEi have been a mainstay of treatment for such patients (with ARB reserved for those with intolerance to ACEi). With the development of the prototype ARNI sacubitril/valsartan, ACEi and ARB are no longer considered the gold standard renin-angiotensin inhibitors for care of HFrEF. Sacubitril/valsartan contains a neprilysin inhibitor plus an ARB, and there is evidence of benefits in HFrEF being superior to those with ACEi. In the landmark Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) trial (103), treatment with sacubitril/valsartan was associated with a 20% reduction in cardiovascular death or HF hospitalization compared with enalapril, a benefit that was observed also in participants with diabetes (104). These results and others led to embedding of sacubitril/valsartan as class I in clinical practice guidelines (67) and as the preferred frontline treatment for HFrEF (101). ARNI therapy is associated with higher rates of hypotension compared with ACEi or ARB, and individuals should be monitored for hyperkalemia or worsening kidney function and the drug should not be used in individuals with a history of angioedema.

The steroidal MRA spironolactone and eplerenone have been shown in large-scale prospective double-blind trials to reduce cardiovascular mortality and hospitalizations for HF in individuals with HFrEF. These drugs are critically important components of the GDMT for HFrEF; however, among individuals with