Long-Term Care Updates

April 2021

ACC 2021 Update on Optimizing Heart Failure Treatment

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Introduction

The American College of Cardiology (ACC) is a nonprofit medical society whose mission is to transform cardiovascular (CV) care and improve heart health. They develop numerous documents intended to provide guidance on topics relevant to CV care. Often, these documents complement clinical practice guidelines and inform clinicians about areas where evidence may be new and evolving. One example is expert consensus decision pathways, which are developed by a group of clinical experts to address key questions facing the ACC's members and provide guidance on applying clinical policy at the point of care.[1]

This newsletter will summarize the 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment.

Medication Management of Heart Failure

Initiating guideline-directed medical therapy

Guideline-directed medical therapy (GDMT) represents treatment options that are supported for use by clinical practice guidelines and is the mainstay of symptomatic heart failure (HF) management. The ACC's proposed treatment algorithm for GDMT includes angiotensin receptor-neprilysin inhibitors (ARNI)/angiotensin-converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARB), beta-blockers, diuretics, aldosterone antagonists, sodium-glucose cotransporter-2 (SGLT2) inhibitors, the combination of hydralazine and isosorbide dinitrate (HYD/ISDN), and ivabradine. With the exception of diuretics, all therapies have been shown to improve symptoms, reduce hospitalizations, and/or prolong survival in randomized clinical trials.[1]

In all patients diagnosed with symptomatic HF with reduced ejection fraction (HFrEF), treatment should start with an ARNI/ACEI/ARB and an evidence-based beta-blocker, with a diuretic agent as needed for volume overload. The three evidence-based beta-blockers are bisoprolol, carvedilol, and metoprolol succinate. Initiation of an ARNI/ACEI/ARB may be better tolerated when patients are still congested ("wet"), while beta-blockers may be better tolerated when patients are less congested ("dry"). In some cases, they may be started at the same time. An ARNI is the preferred renin-angiotensin inhibitor, while an ACEI/ARB is recommended for patients in whom ARNI administration is not possible. When switching from an ACEI to an ARNI, a 36-hour washout period is required to avoid angioedema; this delay is not necessary when switching from an ARB to an ARNI. Once GDMT has been established with an ARNI/ACEI/ARB and beta-blocker, an aldosterone antagonist should be added for all patients so long as their renal function and potassium levels meet certain criteria – estimated glomerular filtration rate (eGFR) ≥30mL/min/1.73m^2 or creatinine ≤2.5mg/dL in men or ≤2 mg/dL in women or K+ ≤5mEq/L. It is not necessary to achieve target or maximally tolerated doses of other therapies before adding an aldosterone antagonist. Next, for all patients receiving an ARNI/ACEI/ARB, beta-blocker, and aldosterone antagonist, an SGLT2 inhibitor should be added so long as they meet specific eGFR criteria – ≥30mL/min/1.73m^2 for dapagliflozin or ≥20mL/min/1.73m^2 for empagliflozin. It is not necessary to achieve target or maximally tolerated doses of other therapies before adding an SGLT2 inhibitor. HYD/ISDN should be added for persistently symptomatic African American patients despite optimal treatment with an ARNI/ACEI/ARB, beta-blocker, aldosterone antagonist, and SGLT2 inhibitor. Ivabradine should be added for patients with a resting heart rate (HR) ≥70 beats/minute in sinus rhythm despite optimal beta-blocker dose. It is an adjunctive means to reduce HR without lowering blood pressure (BP), since HR independently predicts outcomes in HFrEF.[1]

Vericiguat is the latest HF therapy to gain FDA approval in January 2021. It was approved on the basis of results from one phase III clinical trial that enrolled patients with symptomatic HFrEF <45% who were hospitalized within 6 months or required intravenous (IV) diuretics within 3 months prior to randomization. Researchers found it to be significantly better than placebo at reducing the composite risk of death from CV cause or first hospitalization for HF (hazard ratio 0.9; 95% CI 0.82-0.98; p=0.02). There was a 10% relative difference between groups which translated to an absolute event-rate reduction of 4.2 events per 100 patient-years. Based on this annualized absolute risk reduction of 4.2, the number needed to treat with vericiguat for 1 year to prevent CV death or first HF hospitalization would be 24 patients. While vericiguat is not included in the ACC's treatment algorithm for GDMT, it is reasonable to expect that it will not be a first-line treatment option for all patients but will instead be a potential add-on for patients with symptomatic HFrEF <45% following hospitalization for HF or the need for outpatient IV diuretics.[2,3]

Optimizing guideline-directed medical therapy

Optimal therapy delivers the best outcomes and is achieved when GDMT is provided at target or maximally tolerated doses. Target doses are based on doses targeted in clinical trials, and higher doses are not known to provide incremental benefits. Recommended starting and target doses of select GDMT are depicted in the table on the next page. Clinicians should aim to achieve optimal therapy within 3-6 months of initial diagnosis if possible.[1]

Table. Recommended starting and target doses of select GDMT.

Therapy	Starting Dose	Target Dose
Beta-blockers		
Bisoprolol	1.25mg daily	10mg daily
Carvedilol	3.125mg twice daily	25mg twice daily (<85kg) 50mg twice daily (>85kg)
Metoprolol succcinate	12.5-25mg daily	200mg daily
ARNIs		
Sacubitril/valsartan	24/26mg-49/51mg twice daily	97/103mg twice daily
ACEIs		
Captopril	6.25mg three times daily	50mg three times daily
Enalapril	2.5mg twice daily	10-20mg twice daily
Lisinopril	2.5-5mg daily	20-40mg daily
Ramipril	1.25mg daily	10mg daily
ARBs		
Candesartan	4-8mg daily	32mg daily
Losartan	25-50mg daily	150mg daily
Valsartan	40mg twice daily	160mg twice daily
Aldosterone antagonists		
Eplerenone	25mg daily	50mg daily
Spironolactone	12.5-25mg daily	25-50mg daily
SGLT2 inhibitors		
Dapagliflozin	10mg daily	10mg daily
Empagliflozin	10mg daily	10mg daily
Vasodilators		
Hydralazine	25mg three times daily	75mg three times daily
Isosorbide dinitrate	20mg three times daily	40mg three times daily
Fixed dose combination (HYD/ISDN)	20mg/37.5mg three times daily	40mg/75mg three times daily
Ivabradine		
Ivabradine	2.5-5mg twice daily	Titrate to HR 50-60 BPM Maximim dose 7.5mg twice daily

Doses of GDMT can be assessed and adjusted every 2 weeks, while monitoring for effects on BP, HR, electrolytes, renal function, and signs and symptoms of congestion. When titrating doses of an ARNI/ACEI/ARB and SGLT2 inhibitor, a lower dose of loop diuretic may be necessary to permit optimal titration.[1]

Potential barriers to titration may be clinical, social, or financial and include side effects, comorbidities, renal impairment, abnormal electrolytes, cost, and accessibility. GDMT should be optimized through team-based care and consider the significance of therapy benefits versus burdens to each patient as it relates to their values, goals, and preferences.[1]

Addressing Challenges

Care coordination

HF management is complex and typically requires the involvement of multiple clinicians across many care settings, which increases the risk of inefficiencies in care delivery, miscommunication, drug-drug and drug-disease interactions, and missed opportunities to achieve optimal outcomes. A team-based approach to HF management is recommended and has demonstrated superiority over usual care in randomized trials, resulting in less death and hospitalization, shorter lengths of stay, and better quality of life. Essential skills for care teams include proficiency in HF diagnosis and monitoring for progression, medication and lifestyle treatment, patient education, and care coordination. Infrastructure to support care teams includes electronic health records, patient monitoring devices, wearable activity monitors, and smartphones.[1]

Adherence

Estimates of nonadherence in patients with HFrEF range from 20-50%, and nonadherence is associated with worse outcomes. Adherence should be assessed regularly to guide appropriate interventions as needed. Potential interventions include patient education, medication regimen management, pharmacist consultation for disease co-management, cognitive behavioral therapy, medication-taking reminders, and incentives to promote adherence.[1]

Frail and elderly

The frail and elderly are patient populations that are not well-represented in randomized trials, so most data on them are observational. There is no evidence to withhold or modify doses pre-emptively in frail or elderly patients, so target doses should be attempted while closely monitoring for adverse drug reactions. Optimal doses may be lower than those studied in trials and tolerated in younger, healthier patients.[1]

Cost and accessibility

Medication cost and accessibility represents a potential barrier to optimal therapy. Strategies for cost reduction include considering limitations of insurance when prescribing, using generic equivalents, utilizing copay assistance programs, requesting price matching, and coordinating care to minimize duplication.[1]

Comorbidities

Comorbidities are particularly common in the elderly, and >50% of patients with HFrEF on Medicare have four or more non-cardiovascular comorbidities, while >25% have six or more. It is important to consider the diagnosis and treatment of relevant comorbidities alongside the use of GDMT for HF in order to optimally manage patients as a whole and improve their outcomes.[1]

Conclusion

HFrEF management is complex, and new evidence to guide recommendations is constantly emerging. The ACC's 2021 expert consensus decision pathway outlines current principles that clinicians can use to assist them in establishing HF treatment plans for their patients. The foundation of symptomatic HF management is GDMT, which recommends an ARNI/ACEI/ARB, beta-blocker, aldosterone antagonist, and SGLT2 inhibitor as first-line therapy in all patients, HYD/ISDN as first-line therapy in African Americans, and ivabradine as second-line therapy in select patients. GDMT should be started immediately upon diagnosis and up-titrated to target doses to achieve the best outcomes. In order to optimize patient care, it is also necessary to address and overcome potential challenges with clinical, social, and financial barriers, care coordination, nonadherence, and comorbidities. The ACC's 2021 expert consensus decision pathway can serve as interim guidance while awaiting development of a more robust, up-to-date HF clinical practice guideline.

References

1. Maddox TM, Januzzi JL Jr, Allen LA, et al. 2021 update to the 2017 ACC expert decision pathway for optimization of heart failure treatment: Answers to 10 pivotal issues about heart failure with reduced ejection fraction: A report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol.* 2021;77(6):772-810.
2. Verquvo [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; January 2021.
3. Armstrong PW, Pieske B, Anstrom K, et al. Vericiguat in patients with heart failure and reduced ejection fraction. *N Engl J Med.* 2020;382(20):1883-1893.

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