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Commentary
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Latest Standard Management for Heart Failure with Guideline-Directed Medical Therapy (GDMT)

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Abstract

Sodium–glucose cotransporter 2 inhibitor (SGLT2i) has been attracting attention for novel agent for patients with diabetes and also heart failure (HF), in which the left ventricular ejection fraction (LVEF) has decreased. For standard cardiovascular treatment, 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure is recently presented. Some important perspectives were found, which are HF with mildly reduced EF (HFmrEF), HF with improved EF (HFimpEF) and HF with preserved EF (HFpEF). For patients with HFmrEF, SGLT2i can contribute reducing HF hospitalizations and cardiovascular death. From now, the guideline-directed medical therapy (GDMT) will contribute the standard and beneficial therapy.

Keywords

Sodium–Glucose Cotransporter 2 Inhibitor, Left Ventricular Ejection Fraction, Heart Failure with Mildly Reduced EF, Guideline-Directed Medical Therapy, 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Abbreviations

ACEi: Angiotensin-Converting Enzyme Inhibitor; ARB: Angiotensin Receptor Blocker; ARNi: Angiotensin Receptor-Neprilysin Inhibitor; COR: Class of Recommendation; GDMT: Guideline-Directed Medical Therapy; HF: Heart Failure; HFmrEF: Heart Failure with Mildly Reduced Ejection Fraction; HFimpEF: Heart Failure with Improved Ejection Fraction; HFrEF: Heart Failure with Reduced Ejection Fraction; HFpEF: Heart Failure with Preserved Ejection Fraction; LVEF: Left Ventricular Ejection Fraction; MRA: Mineralocorticoid Receptor Antagonist; SGLT2i: Sodium-Glucose Cotransporter 2 Inhibitor; CANVAS: Choice of ANesthesia for EndoVAScular Treatment of Acute Ischemic Stroke; DECLARE-TIMI 58 trial: Dapagliflozin Effect on Cardiovascular Events – Thrombolysis in Myocardial Infarction 58; EMPEROR-Reduced: Empagliflozin in Patients with Chronic Heart Failure and a Reduced Ejection Fraction; DAPA-HF: The Dapagliflozin and Prevention of Adverse-Outcomes in Heart Failure (DAPA-HF) Trial; EMPA-REG OUTCOME: (Empagliflozin) Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) study

Commentary

Sodium–glucose cotransporter 2 inhibitor (SGLT2i) was originally developed as a drug for blood glucose control [1,2]. Data from clinical trials have shown that it is also useful for controlling heart failure events in diabetic patients [3,4]. For these trials, three representative studies were observed including EMPA-REG OUTCOME, CANVAS and DECLARE-TIMI 58. From clinical trials in patients with heart failure, major adverse cardiovascular events (MACE) and heart failure events were suppressed by SGLT2i regardless of the presence of diabetes. For the related studies, EMPEROR-Reduced and DAPA-HF were included. SGLT2i is now attracting attention as a new therapeutic agent for patients with heart failure (HF), in which the left ventricular ejection fraction (LVEF) has decreased.

From a historical point of view, the standard therapy for heart failure has been changed for decades. In 2013, ACCF/AHA Guideline for the Management of Heart Failure was observed and used at that time [5]. Successively, in 2017, ACC/AHA/HFSA focused update of the 2013 edition was found [6]. The latest topic would be the presentation of the latest announcement of revision, that is the "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure". Its characteristic points mean the intention for providing patient-centered recommendations of clinicians in the actual medical practice [7]. They include prevention, diagnosis and management for many patients with heart failure.

For the preparation of the standard guideline, lots of literature were searched from the period May-Dec 2020 [7]. The fields included reviews, various studies and other reports of English language which were from EMBASE, PubMed (MEDLINE), the Agency for Healthcare Research and Quality, Cochrane Collaboration and other databases. Furthermore, other relevant clinical and research investigations during Jan-Sept 2021 have been considered for analysis. The current standard guideline has been harmonized and collaborated with other main medical associations, including American College of Cardiology (ACC) and American Heart Association (AHA) for the period until Dec 2021.

For long years, heart failure has been the most prevalent cause of mortality and morbidity across the world. Current 2022 edition of the guideline for heart failure can provide adequate recommendations which are contemporary evidence-based aspects for actual treatment of HF patients [7]. These recommendations in the guideline can show some evidence-based approach method for applicable managing cases with heart failure. It includes the direction for improving the quality of care and cure along with each interest of the case. Former recommendations in the previous edition were updated and changed based on new evidence. Furthermore, recent recommendations have been announced that were strengthened by published evidence. With reported economic analysis, value statements were also included for several methods of treatment.

This guideline was proposed by the combination of ACC/AHA/HFSA, and its executive summary includes several crucial points [8]. There are four class of recommendation (COR) for the patients, where COR A: At-risk for heart failure (HF), B: pre-HF, C: symptomatic HF and D: advanced HF. COR A means the patients with hypertension, diabetes and others with possible arteriosclerosis without current or previous symptoms/signs of HF. The progress is found from COR A, B, C and D in this order.

In actual clinical practice, the following perspectives are beneficial from medical, cardiovascular points of view. They are i) there are Guideline-directed medical therapy (GDMT) for heart failure (HF) with reduced ejection fraction (HFrEF), ii) it has 4 categories of medications including SGLT2i, iii) The four groups reveal a) RAS inhibition with ARNi, ACEi, ARB, b) beta-blockers, c) MRAs, d) new group that is SGLT2i. iv) SGLT2i shows a class of recommendation 2a for HFmrEF, and weaker recommendation 2b are revealed for beta-blocker, ACEi, ARB, MRA and ARNi, v) New recommendations for HFpEF are for SGLT2i (2a), MRAs and ARNi (2b), vi) Improved LVEF has been used to refer to HF patient with previous HFrEF who shows now > 40% of LFEF, and such case has to continue HFrEF treatment, vii) When diagnosing HF with > 40% of LVEF, supporting the evidence of elevated filling pressure is important, viii) for

obtaining the evidence, invasive or noninvasive biomarkers can be beneficial such as hemodynamic exam, diastolic function with imaging or natriuretic peptide measurement [8].

In the current AHA/ACC/HFSA guideline for the management of heart failure, the most impressive point would be the following judgment. Treatment of HFmrEF (LVEF 41-49%) and HFpEF (LVEF > 50%) showed common evidence levels, which are diuretics as needed (1), SGLT2i (2a)[9] and ARNi[10] /MRA[11] / ARB (2b)[12,13]. The former only showed ACEi (2b)[14] and evidence-based beta blockers for HFrEF (2b)[15]. SGLT2i has been highly evaluated for HF, and it shows 1 for COR and A for Level of Evidence (LOE). In the case of symptomatic chronic HFrEF, SGLT2i agent has been recommended to decrease the hospitalization for HF and cardiovascular mortality, that is with or without T2D presence from DAPA-HF and EMPEROR-Reduced [9,16].

In the latest guideline, some important perspectives were found, which are a) Heart Failure with mildly reduced EF (HFmrEF), b) HF with improved EF (HFimpEF) and c) HF with preserved EF (HFpEF). For patients with HFmrEF, SGLT2i can contribute to reducing HF hospitalizations and cardiovascular death [17]. In the case of 41-49% of LVEF, HF hospitalizations/CV death can be decreased by ACEi, ARB, MRA, ARNi, beta-blocker [18,19]. Cases with HFmrEF would have repeated LVEF evaluation for clinical progress. For patients with HFimpEF after treatment, GDMT would be followed up for preventing LV dysfunction and HF relapse, even if the case keeps the condition without any symptoms [19].

The condition of HFpEF (LFEF 50%) has been rather prevalent, that seems to be at most 50% of all HF patients and shows significant association of mortality and morbidity [20]. HFpEF reveals a heterogenous situation associated with comorbidities such as diabetes, hypertension, obesity, CKD and others [21]. The definition of HFpEF has been variable in lots of clinical trials [22]. For recent trials, beneficial HFpEF results were not found for HF hospitalizations [23,24].

In summary, "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure" has been recently presented, in which SGLT2i shows novel therapeutic agents for HF. HF patients can be categorized as HFmrEF, HFimpEF and HFpEF, where SGLT2i may contribute to decreasing HF hospitalizations and cardiovascular death. This article hopefully becomes a useful reference for cardiovascular and diabetic practice and research.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

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