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Novel Issues in the Treatment of Heart Failure, Based on the European Society of Cardiology (ESC) 2023 Congress

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Abstract

Context: Despite advances in the treatment of heart failure, mortality and morbidity remain high. Novel medical and surgical treatments have attempted to reduce the burden of disease.
Evidence Acquisition: In this review, we discussed newly proposed strategies for the treatment of heart failure based on the recent European Society of Cardiology (ESC) congress.
Results: Recent advances in heart failure treatment may play a pivotal role in prognosis and lead to significant changes in guideline-based recommendations.
Conclusions: Recent trials have demonstrated the effectiveness of several adjuvant treatments for heart failure.

Keywords: Heart Failure, CRT, Complementary Medicine

1. Cardiac resynchronization therapy (CRT) in patients with heart failure and high burden of right ventricular pacing

Pacing-induced cardiomyopathy (PIC) has been a real concern in patients with pacemakers or implantable cardioverter-defibrillators (ICD) with greater than 20 - 40 % right ventricular (RV) pacing (1-3). It has been defined as an absolute drop of 5 - 10% left ventricular ejection fraction (LVEF) or LVEF less than 50 % post-pacemaker implantation (4). Long-term observational and randomized trials have investigated various possible approaches to reduce RV pacing burden in patients with heart failure.

Recently, in the "Budapest upgrade CRT trial "recently presented in the ESC 2023 trial, 360 heart failure patients with left ventricular ejection fraction (LVEF) < 35% and pacing QRS equal to or greater than 150 ms who had previously been inserted into an ICD or pacemaker, were randomly divided into two groups in order to evaluate the role of RV pacing reduction in cardiovascular outcomes. The results of this study significantly support a reduction of primary endpoints: a composite of hospitalization for heart failure, all-cause mortality, or <15% reduction of LV end-systolic volume in patients with an RV pacing load of more than 20% (5).

HF hospitalization and all-cause mortality, LV morphology, and function were also affected by CRT implantation, and the results showed a significant improvement in these parameters (5).

ESC heart failure guideline 2021 states that "high RV pacing rates "should be treated by replacing the pacemaker or ICD with CRT. However, the exact threshold has not been mentioned (6). This threshold has varied in previous observational studies

and randomized controlled trials from 20 to 80 percent (7, 8).

It was also a curious issue at the time that left bundle branch pacing revealed favorable results, unlike traditional biventricular pacing (9).

In the recently published article, "Guideline on cardiac physiologic pacing for the avoidance and mitigation of heart failure", and another similar systematic review and meta-analysis, in the presence of an LVEF of 36 to 50 % and indications for pacemaker implantation, CRT, His bundle pacing (HBP) and left bundle branch area pacing (LBBAP) are recommended (class of recommendation:2a) (8, 10).

2. Natriuresis-Based Treatment vs Conventional GDMT

There are different parameters recognized to evaluate the severity of congestion in heart failure patients, such as:

Severity of edema, presence of orthopnea, elevated jugular venous pressure, etc (11). Successful decongestion plays an important prognostic role in patients with acute heart failure (12-14).

In recent years, natriuresis has been introduced as an additional parameter that can lead us to an effective decongestion strategy. Spot urine sodium as a marker of adequate natriuresis has been previously evaluated (15), and the relationship between inadequate natriuresis during acute heart failure treatment and long-term outcomes has been an issue (16, 17).

The ADVOR trial has played an important role in the field of acute heart failure management with a focus on natriuresis-based treatment. Intravenous acetazolamide has led to an increase in natriuresis and diuretic efficiency without a significant increase in side effects (18).

The PUSH-AHF trial, which focused on the impact of natriuresis-guided treatment on the major cardiovascular outcomes (rehospitalization for heart failure and all-cause mortality), was a negative trial without a significant impact on the mentioned primary outcomes (14).

3. Ferric carboxymaltose (FCM) in heart failure

Following previous studies on the impact of FCM (19, 20) in 2020, the results of AFFIRM-HF have been published in the journal Lancet. This trial concluded that a significant reduction in heart failure hospitalization was observed by intravenous FCM in patients with HFrEF and HFmREF (21) regardless of hemoglobin less than 12 or above (22).

At the recent ESC congress 2023, the results of a meta-analysis on "Effects of ferric carboxymaltose (FCM) on recurrent HF hospitalizations" were presented. They concluded that the use of intravenous FCM was associated with a significant reduction in the composite outcome of total cardiovascular hospitalization and mortality after a 52-week follow-up period (23).

Another pivotal study in this field, HEART-FID, was presented at a recent congress as a negative study. Ferric carboxymaltose did not make a significant improvement in the composite of death, heart failure hospitalization, or 6-minute walking in ambulatory patients with LVEF $\leq$ 40% (24).

4. Complementary Therapies in Heart Failure

Complementary and alternative medicine has been a field of interest in the accompanying modern medicine. A significant number of herbal medicines and complementary approaches have been evaluated in heart failure treatment. A comprehensive list of these complementary and alternative therapies has been presented in the related scientific statement for 2022 (25).

Previous studies have demonstrated that some methods or medications in this field can be useful, but a large number of known CAM therapies have not resulted in improvement.

Recently, in the QUEST trial, a well-known Chinese herbal medicine, qiliqiangxin, showed a significant reduction in HF hospitalization and CV death in patients with heart failure with reduced ejection fraction (HFrEF) (26).

Qliqiangxin has been evaluated before in post-myocardial infarction (MI), cardiac remodeling, and heart failure prevention with acceptable results (27, 28).

5. Novel Treatments of Transthyretin Amyloidosis

Transthyretin is a carrier protein that transports thyroxine (T4) and retinol-binding protein (RBP) (29). Transthyretin amyloidosis (ATTR) is a rare disease caused by abnormal deposition of transthyretin protein in various tissues such as the heart, kidney, liver, etc., which can lead to irreversible damage. More than 120 mutations have been reported to be the cause of cardiac ATTR, and the disease is more common in men over 60 years of age (29, 30).

ATTR amyloidosis is reported with significant prevalence in patients with heart failure preserved EF (HFpEF) and aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) (31).

Recent advances in the medical treatment of cardiac ATTR have been promising, and several medications with different mechanisms of action have been introduced in recent years.

In 2018, the results of the ATTR-ACT trial, which was published in the New England Journal of Medicine, revealed a significant reduction of all-cause mortality and cardiovascular-related hospitalizations in patients treated with tafamidis with a prohibitive effect in reducing functional capacity. Tafamidis is a transthyretin stabilizer that reduces the risk of transthyretin deposition in different tissues. The results led to FDA approval of this drug in 2019 (32).

Liver transplantation, diflunisal, tolcapone (TTR stabilizer), acoramidis (TTR stabilizer), a combination of doxycycline and tauroursodeoxycholic acid (TUDCA), monoclonal antibodies against TTR have also been considered as the treatment of TTR amyloidosis (33).

Recently, an ATTRibute-CM trial, a randomized, double-blind, placebo-controlled trial, revealed a significant effect of acoramidis (800 mg twice daily) on the prevention of cardiovascular events (absolute risk reduction (ARR) of 6.4% for all-cause mortality and about 50 % reduction in cardiovascular-related hospitalizations). Acoramidis also demonstrated benefits in NT-pro BNP levels and quality of life, providing new hope for the treatment of patients with wild-type or variant ATTR-amyloidosis (34).

6. Conclusions

A number of studies were presented at the 2023 ESC meeting that show promising prospects in the treatment of heart failure. Patients with heart failure and cardiomyopathy now have access to a variety of medical and surgical treatments that improve their prognosis and improve their quality of life. This process will continue based on the continued research in this area.

Footnotes

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