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Cardiac Resynchronization Therapy in Inotrope-Dependent Heart Failure Patients

A Systematic Review and Meta-Analysis

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ABSTRACT

OBJECTIVES The purpose of this study was to evaluate outcomes after cardiac resynchronization therapy (CRT) in inotrope-dependent patients with heart failure (HF) to ascertain the viability of CRT in these patients.

BACKGROUND During the last decade, significant numbers of trials have demonstrated the beneficial effect of CRT in the treatment of patients with HF and systolic dysfunction, prolonged QRS complex duration, and New York Heart Association functional class III or IV. However, it is currently undetermined whether CRT may benefit patients who require inotropic support.

METHODS The authors systematically searched Medline, Embase, Scopus, and the Cochrane Library through March 2017 for studies evaluating outcomes after CRT in inotrope-dependent patients with HF. The study analyzed 8 studies including 151 patients. Most of the patients were in New York Heart Association functional class IV (80.1%), and all had severe systolic HF, with left ventricular ejection fraction less than 30% and a significant intraventricular conduction delay in their surface electrocardiogram (QRS complex duration >130 ms).

RESULTS The pooled analysis demonstrated that 93% of the reported patients (95% confidence interval: 86% to 100%) were weaned from inotropic support after CRT, and the overall 12-month survival rate was 69% (95% confidence interval: 56% to 83%).

CONCLUSIONS This study suggests that rescue CRT may be considered a viable therapeutic option in inotrope-dependent patients with HF. In these patients, rescue CRT may allow them to be weaned from inotropic therapy, improve their quality of life, and decrease the rate of mortality; furthermore, rescue CRT may serve as a possible bridge to cardiac transplantation or left ventricular assist device therapy. (J Am Coll Cardiol HF 2018;■:■–■)

Despite multiple advances in the field of heart failure (HF), the mortality rate of patients with advanced disease continues to be exceptionally high (1,2). Among these patients, those with end-stage HF requiring inotropic support likely have the worse prognosis with medical management (3,4).

Heart transplantation remains the gold standard therapy for patients with end-stage disease; however, this option is constrained by limited donor supply.

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CRT = cardiac resynchronization therapy

INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support

HF = heart failure

LVAD = left ventricular assist device

NYHA = New York Heart Association

During the past decade, left ventricular assist devices (LVADs) have emerged as treatment options for those patients waiting for transplant, as destination therapy, and, in a smaller group, as a bridge to recovery (5). LVAD technology offers survival benefit and improved quality of life when compared with medical therapy alone (6–8), but it does come at the risk of well-described complications, financial cost, and some contraindications (9–14).

Along with this, significant numbers of trials have demonstrated the beneficial effect of cardiac resynchronization therapy (CRT) in the treatment of patients with HF by reducing morbidity and mortality in those patients with systolic dysfunction, prolonged QRS complex duration, and New York Heart Association (NYHA) functional class III or IV symptoms, when combined with optimal pharmacotherapy (15). However, during initial trials, NYHA functional class IV patients not only were underrepresented but also were considered not to be CRT candidates because of their poor estimated survival (16). Hence, it is currently undetermined whether CRT may benefit these patients. On the basis of a review of published reports, we sought to identify the possible benefits of this therapy in end-stage inotrope-dependent patients.

METHODS

We undertook this systematic review according to recommendations of the Cochrane Collaboration and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (17).

SEARCH STRATEGY FOR IDENTIFICATION OF RELEVANT STUDIES. We systematically searched Medline, Embase, Scopus, and the Cochrane Library through March 2017 for full papers that evaluated outcomes after CRT in inotrope-dependent patients with HF. No language limits were used. Databases were searched with the following terms: “end-stage heart failure,” “catecholamine-dependent overt heart failure,” “inotrope-dependent heart failure,” “advanced heart failure,” “New York Heart Association class IV,” “NYHA class IV.” These terms were searched individually with “cardiac resynchronization therapy” OR “CRT” OR “biventricular device,” combined by the boolean term “AND.” This strategy was used both as Medical Subject Headings (MeSH) terms if available and as free text. Reference lists from all included studies were manually searched for additional studies.

SELECTION CRITERIA AND DATA EXTRACTION. To be eligible, studies were required to meet the following inclusion criteria: 1) patients had to be dependent on inotropic support at the time of CRT implantation; 2) if the study included other patients, outcomes had to be specifically reported on the inotrope-dependent patients; 3) patients included had to be more than 18 years of age; and 4) papers included had to state a clear definition of “inotrope-dependence” or “inability to wean.” In most of the included studies, inotrope dependence was defined as the inability to wean or withdraw inotropic support without noting clinical or biochemical parameters suggestive of low cardiac output. Alternatively, in some studies, “inotrope-dependence” was endorsed by the treating cardiologist who considered that inotropic therapy could not be safely withdrawn. Both definitions were acceptable for inclusion in our analysis. If the paper did not include a specific definition, the corresponding authors were contacted to further query the selection criteria used We excluded studies containing patients with advanced HF that were not clearly dependent on inotropic support, and if the outcomes were not evidently distinguished in the inotrope-dependent population.

Three investigators independently reviewed the study titles, abstracts, and full-length articles to determine study inclusion and exclusion. These reviewers also independently abstracted the study design, patients’ baseline characteristics, and relevant outcomes. An electronic data form was used to compile abstracted information. Differences were adjudicated by consensus and by the senior author, when necessary.

DATA ANALYSIS. A random-effects meta-analysis was performed using pooled proportions, and heterogeneity was examined using I^2 statistics to determine the overall mortality rate of patients on inotropic support after CRT implantation. In secondary analysis, specific outcomes associated with CRT were studied in a similar manner. Outcomes of interest included proportion of patients off inotropic support and proportion of patients who improved their NYHA functional class after CRT. When available, we analyzed survival estimates at 1 year, in which possible endpoints were all-cause mortality, LVAD implantation, or heart transplantation. A Kaplan-Meier curve was generated to describe overall survival and survival free of LVAD. For the statistical analyses, we used Stata software version 13 (StataCorp., College Station, Texas).