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Review

Impact of baseline renal function on all-cause mortality in patients who underwent cardiac resynchronization therapy: A systematic review and meta-analysis

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ABSTRACT

Background: Cardiac resynchronization therapy (CRT) improves both morbidity and mortality in selected patients with heart failure and increased QRS duration. However, chronic kidney disease (CKD) may have an adverse effect on patient outcome. The aim of this systematic review was to analyze the existing data regarding the impact of baseline renal function on all-cause mortality in patients who underwent CRT.
Methods: Medline database was searched systematically, and studies evaluating the effect of baseline renal function on all-cause mortality in patients who underwent CRT were retrieved. We performed three separate analyses according to the comparison groups included in each study. Data were analyzed using Review Manager software (RevMan version 5.3; Oxford, UK).
Results: We included 16 relevant studies in our analysis. Specifically, 13 studies showed a statistically significant higher risk of all-cause mortality in patients with impaired baseline renal function who underwent CRT. The remaining three studies did not show a statistically significant result. The quantitative synthesis of five studies showed a 19% decrease in all-cause mortality per 10-unit increment in estimated glomerular filtration rate (eGFR) [HR: 0.81, 95% CI (0.73–0.90), $p < 0.01$, 86% I^2]. Additionally, we demonstrated that patients with an eGFR < 60 mL/min/1.73 m^2 had an all-cause mortality rate of 66% [HR: 1.66, 95% CI (1.37–2.02), $p < 0.01$, 0% I^2], which was higher than in those with an eGFR ≥ 60 mL/min/1.73 m^2.
Conclusion: Baseline renal dysfunction has an adverse effect on-all cause mortality in patients who underwent CRT.

Contents

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1. Introduction

Chronic kidney disease (CKD) represents a prevalent comorbidity in patients with heart failure (HF). Accumulating evidence suggests that nearly one third of patients with HF have concomitant stage III or greater CKD [1–5]. In addition, the majority of individuals with advanced kidney disease who initiate renal replacement therapy will develop clinical HF or left ventricular dysfunction [6]. The combination of these two conditions results in a nearly three times greater mortality risk compared with patients without significant kidney disease [7]. Of note, landmark randomized trials including the COMPANION [8], CARE-HF [9], MADIT-CRT [5], and RAFT studies [10] clearly demonstrated that cardiac resynchronization therapy (CRT) improved morbidity and mortality in patients with HF who had a reduced left ventricular ejection fraction (LVEF $\leq$ 35%), left bundle branch block morphology, and QRS duration $\geq$ 150 msec on electrocardiogram (ECG). However, patients with an indication for CRT often have significant comorbidities such as atrial fibrillation, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, anemia, and/or kidney dysfunction, which may have a negative impact on patient outcomes. CKD is a common comorbidity in this setting [11]. The aim of this systematic review and meta-analysis was to investigate whether reduced renal function at baseline has an adverse effect on all-cause mortality in patients treated with biventricular pacing devices.

2. Materials and methods

2.1. Search strategy

The MEDLINE database was manually searched using PubMed web-based search engine without year or language restriction or any other limits until July 9, 2016. The following algorithm was used: "(cardiac resynchronization therapy OR CRT OR biventricular pacing) AND (renal failure OR kidney disease OR dialysis)". Further, the reference lists of all included studies as well as relevant review articles were searched.

2.2. Study selection

2.2.1. Inclusion/exclusion criteria

Randomized control trials and observational studies reporting original adjusted data about the impact of baseline renal function on all-cause mortality in patients who underwent CRT were included in our analysis. The exclusion criteria were: studies not reporting data on the study outcome, studies reporting only unadjusted data, review articles, letters to the editor, editorial comments, studies reporting data on mixed ICD/CRT populations, and studies reporting data on a combined endpoint only. Additionally, studies with potentially overlapping cohorts were excluded from the quantitative synthesis. In such cases, we included the cohort with the largest sample size.

2.3. Data extraction

The information extracted for each study was: i) publication details (first author's last name, journal, year of publication), ii) general characteristics of the study (country of origin, study design, single or multi-center, enrollment period, follow-up duration, number of patients included), iii) characteristics of the study population [age, gender, type of cardiomyopathy, LVEF, New York Heart Association (NYHA) HF classification, history of atrial fibrillation, QRS duration, type of CRT device, mean glomerular filtration rate (GFR), mean creatinine level], and iv) the results reported in the study [adjusted hazard ratio (HR), relative risk (RR), odds ratio (OR) with 95% confidence intervals (CI)] regarding the impact of baseline renal function on all-cause mortality.

2.4. Statistical analysis

Data were analyzed using Review Manager software (RevMan, version 5.3; Oxford, UK). Adjusted HR for the impact of baseline renal function on all-cause mortality, was used in the analysis. Moreover, we performed three separate analyses according to the comparison groups provided in the included studies.

The statistical heterogeneity of the study was assessed using the I^2 index. We considered low, medium, and high heterogeneity to have approximate values: 25% (I^2=25), 50% (I^2=50), and 75% (I^2=75), respectively [12]. Funnel plots were constructed using RevMan software to assess publication bias. Fixed effect models were utilized in the analysis because of the low heterogeneity of the included studies. Funnel plots showed no significant publication bias.

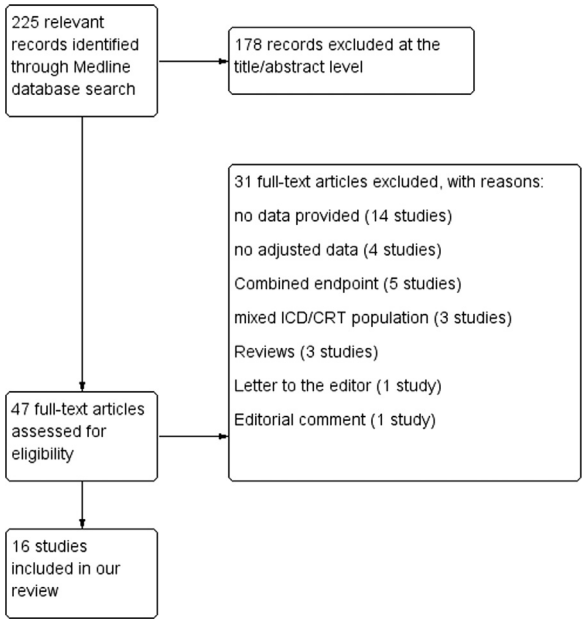

Fig. 1. Medline database search strategy.

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