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Fragmented QRS complex and responsiveness to cardiac resynchronization therapy: a meta-analysis

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Review question / Objective: To assess whether fragmented QRS (fQRS) is an predictor of nonresponse to cardiac resynchronization therapy (CRT) in patients with heart failure with reduced ejection fraction.

Condition being studied: Heart failure is the end stage of various cardiac diseases and the main cause of death in cardiovascular diseases, and CRT is one of the effective strategies for its treatment, which can restore electro-mechanical synchronization of the right and left ventricles and effectively improve the clinical outcome of patients with heart failure. However, even in patients selected for CRT indications in strict accordance with the guideline recommendation criteria, there are still 30-40% of patients who do not respond to CRT treatment. Therefore, if markers exist to predict CRT responsiveness, the best suitable patients can be screened for such treatment, which will ultimately be of great significance in terms of improving treatment efficiency and reducing unnecessary financial burden on patients. Translated with <http://www.DeepL.com/Translator> (free version).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 October 2022 and was last updated on 25 October 2022 (registration number INPLASY2022100101).

INTRODUCTION

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METHODS

Search strategy: A systematic search was conducted from PubMed, The Cochrane Library, Web of science, EMBASE, China Knowledge Network, Wanfang, Wipu.com and China Biomedical Literature Service (CBDS) databases, and the search period was from the establishment of the database to May 2022, and all Chinese and English literature on fQRS and its relevance to CRT reactivity were included.

Participant or population: New York Heart Classification II-IV heart failure, who did not show significant improvement in cardiac function after at least 3 months of drug therapy for heart failure, and who were enrolled in CRT implantation for Class I-II indications according to strict guideline criteria.

Intervention: Presence of fQRS on ECG before CRT implantation.

Comparator: absence of fQRS on ECG before CRT implantation.

Study designs to be included: We will use RevMan version 5.4 software (Cochrane

Collaboration) and STATA/MP 14 (StataCorp LLC) for the meta-analysis.

Eligibility criteria: The inclusion criteria for this study were all clinical studies related to the assessment of fQRS and CRT responsiveness. Detailed data on the primary endpoint were required for inclusion. Literature with no reported follow-up time or follow-up time less than 6 months, literature with low quality ratings, case reports, conference abstracts, guidelines, expert consensus, reviews, review articles, and animal studies were excluded.

Information sources: Electronic databases.

Main outcome(s): CRT responsiveness, i.e. $\geq 15\%$ reduction in LVESV or $>5\%$ increase in LVEF compared with preimplantation.

Additional outcome(s): Cardiac ultrasound inverse remodeling-related index values (mean \pm standard deviation), including: (1) LVEF; (2) LVEDV; (3) LVESV..

Data management: We will use RevMan version 5.4 software (Cochrane Collaboration) and STATA/MP 14 (StataCorp LLC) for the meta-analysis.

Quality assessment / Risk of bias analysis: We used the Odd ratio (OR) and 95% confidence interval (CI) as pooled effect sizes for the dichotomous data. We used Mean difference (MD) as the summary effect size for continuous data. Heterogeneity tests and Q-tests were used to assess heterogeneity between studies, with $I^2 > 50\%$ and Q-test $p < 0.1$ indicating that heterogeneity was statistically significant. If there was no statistical heterogeneity among the studies included studies were tested for bias by Begg's test and Egger's test.

Strategy of data synthesis: a fixed-effects model was used for meta-analysis; if there was statistical heterogeneity, a random-effects model was used for meta-analysis. Sensitivity analysis was performed to determine whether the results were robust

by excluding low-quality studies. The test level of meta-analysis was set at $\alpha=0.05$.

Subgroup analysis: LVESV, LVEDV, and LVEF were used as quantitative outcome indicators, and a subgroup analysis of QRS on the degree of ventricular inverse remodeling after CRT implantation was performed on 3 cohort studies from the included literature.

Sensitivity analysis: Heterogeneity between included studies in the analysis of the degree of improvement of fQRS and LVEF was analyzed with a random-effects model for meta-analysis and a sensitivity analysis of the studies.

Country(ies) involved: China.

Keywords: fragmented QRS; cardiac resynchronization therapy; Meta analysis.

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