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Cardiac resynchronization therapy in patients with postero-lateral scar by cardiac magnetic resonance: A systematic review and meta-analysis

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Abstract

Background: Cardiac resynchronization therapy (CRT) reduces morbidity and mortality in selected patients with heart failure, but up to one third of patients may not respond to CRT. A transmural postero-lateral (TMPL) wall scar in the left ventricle (LV) or over the LV pacing site may attenuate clinical and echocardiographic response to CRT.

Methods and results: We systematically searched PubMed, EMBASE, and Cochrane databases for studies examining the association between Cardiac magnetic resonance (CMR)-determined postero-lateral or LV pacing site scar and clinical and echocardiographic response to CRT. Eleven prospective studies were included. The presence of TMPL scar on pre-implant CMR was associated with a 75% lower chance of echocardiographic response to CRT, and a similarly lower chance of clinical response. Significant scar over LV pacing site on pre-implant CMR was also associated with a 46% lower chance of echocardiographic response to CRT, and a 67% lower chance of clinical response.

Conclusions: The presence of transmural postero-lateral scar or significant scar within the LV pacing site detected by pre-implant CMR is associated with a lower rate of clinical or echocardiographic response to CRT.

Keywords: Cardiac resynchronization therapy; Scar; Cardiac magnetic resonance

Introduction

Cardiac resynchronization therapy (CRT) improves symptoms of heart failure, quality of life and survival in selected patients [1]. Current practice guidelines recommend CRT in patients with reduced left ventricular (LV) ejection fraction, prolonged QRS duration, and symptoms of heart failure despite optimal medical therapy. Nonetheless, approximately one third of candidates who meet these criteria may not derive symptomatic benefit from CRT. Several reasons have been proposed to explain lack of response to CRT in such patients [2], one of which is the presence of extensive scarring in the postero-lateral site of the LV which is typically targeted for LV pacing. Various methods have been used for myocardial scar assessment. Cardiac magnetic resonance (CMR) imaging is a sensitive and widely studied modality for assessing LV scar burden and location, and was rated as appropriate for device planning [3].

The extent to which scarring in the postero-lateral or pacing site of the LV affects response to CRT is not well defined. We performed a systematic review and meta-analysis of studies examining the relationship between scarring in the LV postero-lateral or pacing site and echocardiographic or clinical response to CRT.

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Methods

Literature search and study inclusion

We searched Medline, EMBASE, and the Cochrane database to identify English-language publications examining the association between CMR-determined postero-lateral or LV pacing site scar and outcomes after CRT. We searched for studies published until June 2014 using the following terms: "resynchronization therapy," "biventricular pacemaker," "cardiac magnetic resonance" and "scar."

The literature search was complemented by reviewing the reference lists of eligible studies. Initial search was performed in July 2013 and updated in June 2014. Eligible studies had to include patients who received CRT and report both: 1) details of myocardial scar determined by a pre-CRT CMR that included the presence or absence of a scar in the postero-lateral or LV pacing site, and 2) response to CRT either in terms of clinical symptoms or echocardiographic parameters using a measure of LV remodeling. We included prospective observational studies. Studies published in abstract form only were excluded.

Data extraction

Three authors (A.D., A.A., A.L.) independently assessed eligibility at the abstract level and confirmed it at the full text manuscript level, and then extracted data in a standardized manner. Extracted data included patient baseline characteristics, findings on pre-CRT CMR and outcomes (clinical and/or echocardiographic stratified by CMR findings). Disagreements between reviewers were resolved by consensus. In cases of incomplete or unclear data on study design or clinical outcome, the investigators were contacted.

Statistical methods

We estimated pooled risk ratios (RR) and corresponding 95% confidence limits of response to CRT in patients with versus without transmural postero-lateral scar or significant versus non-significant scar at LV pacing site by CMR. Separate models were constructed for studies reporting echocardiographic and clinical response. Studies were pooled using the Mantel–Haenszel method which has been shown to be more reliable when there are few trials with small sample sizes. To ensure that our findings are not substantially altered by choice of pooling method, we performed a sensitivity analysis using random-effects models, which account for within- and between-study variability. The presence of between-study heterogeneity in risk ratios was assessed by the Q statistic ($P < 0.1$ considered statistically significant) and the degree of heterogeneity estimated by the I^2 index. All analyses were conducted using Stata version 11.0 (StataCorp, College Station, TX).

Results

Literature search outcome

Fig. 1 displays the flow of included studies from the literature search. Our search yielded 68 citations, of which 50 were excluded after screening at the abstract level. This resulted in 18 full-text manuscripts that were reviewed in detail. Of these, 7 were eventually excluded. Therefore, 11 studies formed the basis for this analysis.

Study and patient characteristics

The 11 included reports [7–17] were all prospective single center studies. These studies enrolled a total of 666 patients who underwent CMR before CRT (the number of patients per study ranged between 12 and 209 patients with the median being 45) (Table 1).

A total of 251 patients (204 with ischemic cardiomyopathy) were enrolled in studies reporting clinical and/or echocardiographic response to CRT stratified by scarring in the postero-lateral wall using pre-implant CMR. Additionally, 513 patients (234 with ischemic cardiomyopathy) were enrolled in studies reporting clinical and/or echocardiographic response to CRT stratified by scarring in the LV pacing site. Overall, more than half of the enrolled patients had ischemic heart disease with three of the studies enrolling only patients with ischemic cardiomyopathy. The age of enrolled patients ranged from 59 to 69 years (median 66 years) and 77.6% of the enrolled patients were male. The average follow-up ranged from 3 to 25 months (median 6 months).

Clinical response to CRT in the included studies was defined as one of the following: ≥1 NYHA class improvement, ≥25% increase in a 6-minute walked distance, improvement in quality of life score, or improvement in a composite clinical score (survival for one year following implantation; no hospitalizations for heart failure for one year following implantation, or improvement by ≥1 NYHA classes or by ≥25% in 6-min walking distance).

Echocardiographic response in the included studies was defined as ≥15% reduction in LV end-systolic volume.

Scar definition:

The definition below is consistent across the six included studies [7–9,12,13,16].

Transmural postero-lateral (PL) scar defined as >50% scar of the myocardial wall involving the PL segments.

Non-transmural PL scar defined as a scar of <50% of the myocardial wall involving the PL segments.

Non-PL scar defined as a scar involving non-PL segments of the left ventricle.

No scar (viable myocardium).

The definition below is inconsistent across the eight included studies [7,8,10,11,13–15,17].

Significant scar pacing defined as either:

- TM scar in distribution of LV pacing segment [13] or
- Non-TM scar in distribution of LV pacing segment [11] or
- TM and non-TM scar in distribution of LV pacing segment [7,8,10] or
- ≥25% scar at LV pacing region [14,17].

Non-significant scar pacing defined as either <25% scar at LV pacing region [14] or no scar at LV pacing site [7,8,10,11,13,15,17].