Clinical Radiology 70 (2015) 999–1008

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Prognostic value of late gadolinium enhancement in dilated cardiomyopathy patients: a meta-analysis

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ARTICLE INFORMATION

Article history:
Received 4 December 2014
Received in revised form
6 May 2015
Accepted 18 May 2015

AIM: To evaluate the association between late gadolinium enhancement (LGE) at cardiac magnetic resonance (CMR) and major adverse events in dilated cardiomyopathy (DCM) patients.

MATERIALS AND METHODS: Databases, including PubMed, Ovid, and EMBASE, were searched for studies evaluating LGE at CMR in DCM patient prognostication. Clinical outcomes were analysed using fixed-effects models or, in cases of significant heterogeneity, random-effects models.

RESULTS: In the meta-analysis of 13 studies on 1675 DCM patients with a mean follow-up of 3 years, LGE is associated with all-cause mortality (pooled odds ratio, 3.43 [95% confidence interval, 2.26–5.22], $p<0.00001$), cardiac death/transplantation (3.65 [1.80–7.40], $p=0.0003$), hospitalisation for heart failure (2.87 [1.53–5.39], $p=0.001$), major arrhythmia events (sudden cardiac death, sustained ventricular tachycardia or fibrillation, appropriate implantable cardioverter–defibrillator (ICD) discharge/pacing, and syncope: 4.24 [2.95–6.08], $p<0.00001$), and sudden cardiac death (3.33 [1.80–6.17], $p=0.0001$).

CONCLUSION: LGE in DCM patients appears to be associated with mortality and major cardiac events, underscoring its potential as an independent index for risk stratification and treatment guidance.

Introduction

Dilated cardiomyopathy (DCM) is characterised by systolic dysfunction and increased ventricular volume and myocardial mass. Regardless of aetiology, the hallmark of DCM is biopsy-confirmed myocardial remodelling with collagen fibre accumulation, i.e., myocardial fibrosis, which serves as a substrate for ventricular arrhythmia and sudden cardiac death.[1–6]

Implantable cardioverter–defibrillators (ICDs) use reduces mortality in non-ischaemic cardiomyopathy (ICM) patients in general, and the decision to use an ICD for primary prevention is mainly driven by the left ventricular ejection fraction (LVEF) ≤35%.[7,8] Over recent decades, annual insertion of ICDs has increased 20-fold,[9] however, 25–35% of all ICD therapy has been classified as

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http://dx.doi.org/10.1016/j.crad.2015.05.007
0009-9260/

inappropriate[10] and associated with high cost of sequential treatment and adverse psychological effects of ICD shocks,[11] stressing the need to identify parameters for better risk stratification of patients who would benefit from ICD implantation.[12]

Cardiac magnetic resonance (CMR) is an effective adjunct for cardiac function and structure assessment in cardiomyopathy diagnosis and evaluation.[13–15] In cohort studies limited by relatively low event rates, sample size, and/or single-centre design, late gadolinium enhancement (LGE) at CMR, which identifies myocardial fibrosis (predominantly mid-wall with endocardial sparing in DCM), appears associated with adverse cardiac events, rendering it potentially useful in long-term prognostication[15–17] and patient risk stratification.[18,19] This meta-analysis, therefore, further evaluates association between LGE at CMR and major adverse cardiac events in DCM patients.

Materials and methods

Data source

For inclusion in the meta-analysis, PubMed, Ovid, and EMBASE were searched to identify primary references up to 2 March 2014 using the following terms: (MRI or magnetic resonance or late-gadolinium or LGE or contrast-enhanced MRI) and (dilated cardiomyopathy or DCM or non-ischaemic) and (sudden cardiac death or arrhythmia or ICD or heart failure or mortality). Studies considered were limited to those published in English in peer-reviewed journals, i.e., abstracts or session presentations were excluded. This meta-analysis was approved by the ethics committee.

Study selection

Population, intervention, outcomes, and study design elements were assessed using the Population, Intervention, Comparison, Outcome, Setting (PICOS) system. During retrieval, 402 initial studies were collected, 376 of which were excluded by screening abstracts that were unrelated to the topic or unaccompanied by a published manuscript. Of the remaining 26 potentially appropriate studies, four did not contain specific outcomes, four did not present enough data for extraction, and five were reviews. Finally, 13 studies were included in the meta-analysis (Fig 1); among them, two, by Looi *et al.*[20] and Machii *et al.*[21] were retrospective, whereas the remaining 11 were all prospective cohort studies.

Data extraction

Adult patients diagnosed with DCM who had undergone LGE-CMR and completed follow-up were included. The endpoints in meta-analysis included (1) all-cause mortality; (2) cardiac death/transplantation; (3) hospitalisation for deteriorated heart failure; (4) major arrhythmia events (MAE), a composite of sudden cardiac death, sustained ventricular tachycardia (VT) or fibrillation (VF), appropriate ICD discharge/pacing (defined as electric shock for fast VT with R-R $<$320 ms) or VF, and syncope; and (5) sudden cardiac death. The cause of death was identified in all cases. Cardiac death was defined as death after a period of clinical deterioration in signs and symptoms of heart failure despite medical treatment.[22] SCD was defined as death with or without documented ventricular arrhythmia within 1 h of new symptoms, or nocturnal death with no antecedent history of worsening symptoms. VT was defined as ventricular extra-systoles at $>$120 beats/min lasting for $>$30 s on an electrocardiogram or 24 h tape.[15] These outcomes were chosen for the meta-analysis because they are the most clinically relevant hard endpoints in patients with DCM who are at increased risk of arrhythmias and sudden cardiac death, and are usually chosen by most studies.

Data extraction was performed independently by two physician investigators. When disagreements occurred, the final decision was made by the consensus of all authors.

Quality assessment

The Newcastle–Ottawa scale (NOS) for assessing quality of cohort studies in meta-analyses[23] was used in this review, and details are presented in Table 1. Common deficiencies included insufficient follow-up, defects in demographic baseline comparability, and patients lost during follow-up.

Statistical analysis

Data heterogeneity was assessed by Cochrane's q statistic and I^2 statistic with a p-value greater than 0.05 indicating homogeneity and I^2 -values of 25%, 50%, and 75% representing mild, moderate, and severe heterogeneity, respectively. A fixed-effects model was used to evaluate endpoints; those with significant heterogeneity were evaluated with a random-effects model to minimise bias and confounders, and sensitivity analysis was performed by excluding one study at a time and re-evaluating heterogeneity. Overall results are expressed as odds ratios (ORs) with 95% confidence intervals (CI), and the OR of each individual study was recalculated. A two tailed p-value less than 0.05 indicated significant difference.

Funnel plots were used to assess possible publication bias. A visually significant asymmetry in the funnel plots indicated a major publication bias.

Data analysis was performed using the review manager (Revman) computer program version 5.0 (The Cochrane Collaboration, 2008, Nordic Cochrane Centre, Copenhagen, Denmark).

Results

Study characteristics

The 13 studies enrolled 1933 patients, whereas only 1675 were included in this meta-analysis because in the studies by Gao *et al.*,[24] Leyva *et al.*[16] and Machii *et al.*[21] there were ICM patients and hypertrophic cardiomyopathy (HCM)