International Journal of Cardiology 182 (2015) 494–499

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Myocardial viability for decision-making concerning revascularization in patients with left ventricular dysfunction and coronary artery disease: A meta-analysis of non-randomized and randomized studies

Andrés Orlandini *[,1], Noelia Castellana [1], Andrea Pascual [1], Fernando Botto [1], M. Cecilia Bahit [1], Carolina Chacon [1], M. Luz Diaz [1], Rafael Diaz [1]

ECLA (Estudios Clínicos Latino América), Argentina

ARTICLE INFO

Article history:
Received 14 November 2014
Received in revised form 31 December 2014
Accepted 5 January 2015
Available online 7 January 2015

Keywords:
Coronary artery disease
Revascularization
Myocardial viability

ABSTRACT

Background: Myocardial viability tests have been proposed as a key factor in the decision-making process concerning coronary revascularization procedures in patients with left ventricular dysfunction and coronary artery disease (LVD–CAD).

Methods: We performed a systematic review and meta-analysis of studies that compared medical treatment with revascularization in patients with viable and non-viable myocardium and recorded mortality as outcome.

Results: Thirty-two non-randomized (4328 patients) and 4 randomized (1079 patients) studies were analyzed. In non-randomized studies, revascularization provided a significant mortality benefit compared with medical treatment ($p < 0.05$). Since the heterogeneity was significant ($p < 0.05$) a viability subgroup analysis was performed, showing that revascularization provided a significant mortality benefit compared with medical treatment in patients with viable myocardium ($p < 0.05$) but not in patients without ($p = 0.34$). There was a significant subgroup effect ($p < 0.05$) related to the intensity of the effect, but not to the direction. In randomized studies, revascularization did not provide a significant mortality benefit compared with medical treatment in either patients with viable myocardium or those without ($p = 0.21$). There was no significant subgroup effect ($p = 0.72$). Neither non-randomized nor randomized studies demonstrated any significant difference in outcomes between patients with and without viable myocardium.

Conclusions: The available data are inconclusive regarding the usefulness of myocardial viability tests for the decision-making process concerning revascularization in LVD–CAD patients.

Patients with viable myocardium appear to benefit from revascularization, but similar benefits were observed in patients without viable myocardium. Moreover, a neutral or adverse effect of revascularization cannot be excluded in either group of patients.

1. Introduction

Since 1982, when Rahimtoola [1] first described the recovery of ventricular function after revascularization in patients with left ventricular dysfunction and coronary artery disease (LVD–CAD), our interest in myocardial viability has progressed from determining its pathophysiology, to its diagnostic potential, and finally to its usefulness in the clinical setting.

After the concept of hibernating myocardium was introduced [2], numerous techniques were developed for evaluating its presence or absence in patients with LVD–CAD or previous myocardial infarction (MI).

Once myocardial viability could be diagnosed with acceptable accuracy [3], the next step was to establish whether its presence or absence could guide clinical practice. The prognosis of patients with LVD–CAD is strongly related to the ejection fraction (EF) [4]. Consequently, the hypothesis was that if patients have viable myocardium, revascularization can improve heart function and therefore survival; otherwise, patients will do better with medical therapy alone.

The cardiovascular community adopted this premise as true, and myocardial viability tests gained a key place in the decision-making process concerning myocardial revascularization in patients with LVD–CAD. However, the published literature on this matter remains unclear and controversial. Accordingly, we performed a systematic review and meta-analysis of studies that compared medical treatment with revascularization in patients with viable and non-viable myocardium.

* Corresponding author at: Madres de plaza de 25 mayo 3020, Floor 10, S2013SWJ Rosario, Argentina.
E-mail address: aorlandinimd@eclainternational.org (A. Orlandini).

[1] All the authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2015.01.025
0167-5273/

2. Materials and methods

2.1. Literature search

The MEDLINE database was searched using PubMed to retrieve publications from between January 1960 and July 2013. Studies were selected if they: (1) included patients with LVD–CAD and/or previous MI, (2) tested myocardial viability, (3) compared medical treatment and revascularization in patients with viable myocardium and/or in patients without viable myocardium, and (4) recorded cardiac death or all-cause mortality as outcomes. Previous meta-analyses and systematic reviews were also analyzed [5–8]. Appendix 1 shows the detailed search strategy and search terms.

For each study, data relating to patient characteristics, study designs, viability criteria, imaging techniques, and outcome events were systematically extracted.

2.2. Statistical methods

We calculated risk ratios (RR) and 95% confidence intervals (CIs) for the primary outcome (cardiac death or all-cause mortality) for each study/viability subgroup separately. Overall estimates of effect were calculated using random-effect models, in which the effect of every study/viability subgroup was weighted by the inverse of its variance.

Publication bias was tested by visual inspection of the funnel plot and, more formally, using the Begg–Mazumdar test. In the absence of publication bias, the test result is not significant, and in the funnel plot, studies are distributed symmetrically about the mean effect size. To assess heterogeneity, the chi-square Q statistic was used. The null hypothesis evaluated by this test is that all the study subgroups share a common effect size. The proportion of the observed variance that reflects real differences in effect size was evaluated through the I^2 statistic. The chi-square Q statistic was also evaluated to compare subgroup effects. The p-value threshold for statistical significance was set at 0.05. Calculations were performed using Comprehensive Meta-Analysis Software (version 2.0; Biostat Inc., USA).

3. Results

3.1. Studies and patients

The database search identified 389 potentially relevant citations; 30 additional articles were included from references (Fig. 1). On the basis of their title and abstract, 101 studies were retrieved as complete reports, of which 36 met the eligibility criteria.

We included 32 non-randomized studies [9–40] (4328 patients) and 4 randomized studies [41–44] (1079 patients) in the analyses (Table 1). The mean duration of follow-up was 28.4 months for non-randomized studies and 45.6 months for randomized studies. The mean age of the patients was similar in the non-randomized studies (60.7 years) and randomized studies (61.1 years). The mean left ventricular EF was 31.8% in non-randomized studies and 34.4% in randomized studies.

For this analysis, patients were divided into 4 groups based on the treatment strategy (medical or revascularization) and the presence or absence of viable myocardium.

Table 2 shows the primary outcome (cardiac death or all-cause mortality) according to the treatment strategy and viability status. In the non-randomized studies, 2050 patients underwent revascularization by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), and 2278 patients were treated medically. In the randomized studies, 534 patients underwent revascularization by PCI or CABG, and 545 patients were treated medically.

3.2. Publication bias

Fig. 2 shows the funnel plot of standard error by log (risk ratio) and the results of the Begg–Mazumdar test for non-randomized studies (A) and randomized studies (B). Publication bias was observed in the non-randomized studies ($Z = 2.52$, $p = 0.012$); in the randomized studies, there was no significant publication bias ($Z = 0.24$, $p = 0.8$).

3.3. Meta-analysis

Figs. 3 and 4 show the forest plots for non-randomized and randomized studies, respectively. Fig. 5 presents a summary of the results.

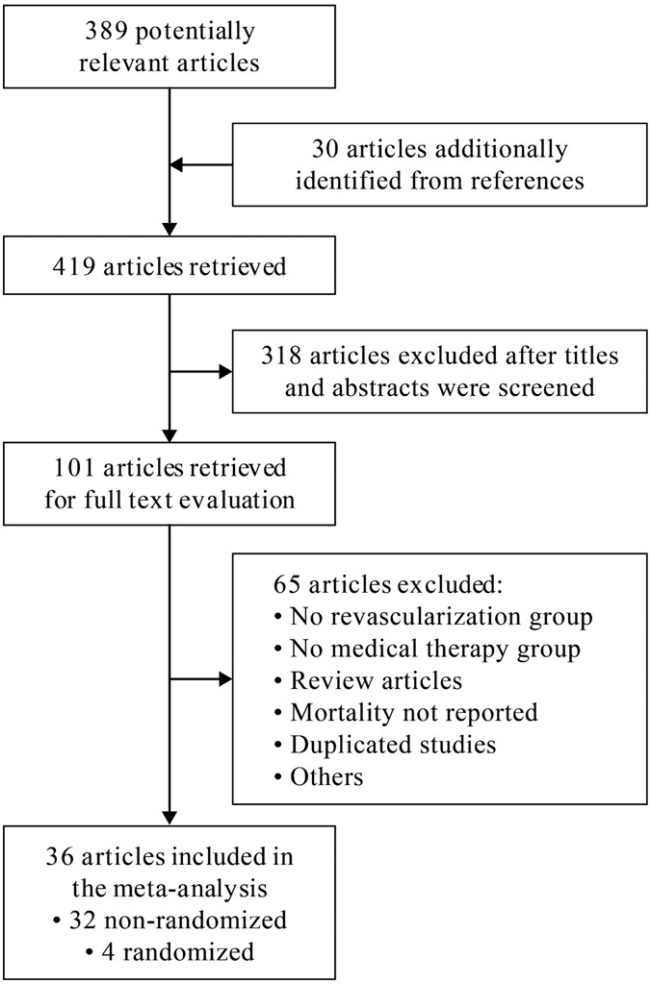

Fig. 1. Flow chart showing the process of study selection.

Overall estimates of the effect and estimations within each viability subgroup were calculated using random-effects models.

3.3.1. Non-randomized studies

Overall (Fig. 5), revascularization provided a significant mortality benefit compared with medical treatment (RR: 0.61, 95% CI: 0.53–0.69, $p < 0.05$). Since the heterogeneity was significant ($Q = 103.93$, $p < 0.05$, $I^2 = 46.12\%$), a viability subgroup analysis was performed. For patients with viable myocardium, revascularization also provided a significant mortality benefit compared with medical treatment (RR: 0.31, 95% CI: 0.25–0.39, $p < 0.05$); however, for patients without viable myocardium, this benefit was not statistically significant (RR: 0.92, 95% CI: 0.78–1.09, $p = 0.34$) (Fig. 3). There was a significant subgroup effect ($Q = 60.68$, $p < 0.05$) related to the intensity of the effect, but not to the direction (Fig. 5).

3.3.2. Randomized studies

Overall, revascularization did not provide a significant mortality benefit compared with medical treatment (RR: 0.89, 95% CI: 0.75–1.07, $p = 0.21$) (Fig. 5). Heterogeneity was not significant ($Q = 1.036$, $p = 0.90$). Revascularization did not provide a significant mortality benefit in either patients with viable myocardium or those without (Fig. 4). There was no significant subgroup effect ($Q = 0.13$, $p = 0.72$) (Fig. 5). Notably, the