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The effect of off-pump coronary artery bypass on mortality after acute coronary syndrome: A meta-analysis

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ABSTRACT

Background: Patients requiring surgical revascularisation for acute coronary syndrome (ACS) form a clinically heterogeneous group ranging from haemodynamic stability to cardiogenic shock. Whilst 'off-pump' revascularisation (OPCAB) is often considered, patient selection and operative timing remain controversial. This study aims to identify whether OPCAB may confer a mortality benefit over ONCAB in revascularisation for ACS. Secondly, we review the impact of OPCAB on completeness of revascularisation (CR) and long-term re-intervention.
Methods: A systematic literature review identified 9 studies (1 randomised controlled trial) of which 8 fulfilled criteria for meta-analysis. Outcomes for a total of 3001 patients (n = 817 OPCAB, 2184 'on-pump' (ONCAB)) were meta-analysed using random effects modelling. Heterogeneity, subgroup analysis and quality scoring were assessed. Primary endpoints were 30-day and mid-term mortality. Secondary endpoints were CR, revascularisation index and re-intervention.
Results: OPCAB conferred comparable mortality to ONCAB at both 30-days and mid-term follow up ($p = 0.08$ and $p = 0.46$ respectively). OPCAB was also associated with less CR (WMD −0.60, 95% CI [−0.82, −0.38], $p < 0.00001$) and a lower revascularisation index (WMD −0.25, 95% CI [−0.30, −0.19], $p < 0.00001$), although no difference was observed in re-intervention rate (OR 1.33; 95% CI [0.99, 2.07], $p = 0.99$).
Conclusions: We conclude that OPCAB may be a safe and comparable alternative to ONCAB in clinically stable ACS patients requiring urgent/emergent revascularisation. However, in order to finally determine whether OPCAB may provide any more than just comparability to ONCAB in the setting of ACS, further research must clearly define selection criteria, better characterize this heterogeneous patient group and assess the effects of incomplete revascularisation on long-term outcomes.

1. Introduction

Acute coronary syndrome (ACS), defined as the spectrum of STEMI, NSTEMI and unstable angina, presents in a heterogeneous fashion with a clinical signs ranging from haemodynamic stability to cardiogenic shock. It is becoming an increasing clinical problem with an incidence reaching 785,000 per year in the United States alone, and accounting for approximately 150,000 hospital admissions per year in the UK [1,2]. Primary percutaneous coronary intervention (PCI) at the level of the culprit coronary vessel or intravenous thrombolytic therapy in institutions where PCI is not available is often the first line intervention in patients presenting with ACS. Coronary artery bypass grafting (CABG) in this setting is associated with high mortality and consequently its role and timing are still controversial. Nevertheless, several circumstances may necessitate emergency CABG in these patients including failure or unsuitability for primary PCI, haemodynamic instability, cardiogenic shock, severe three vessel disease or left main stem stenosis with significant area of 'at risk' myocardium. Although recent randomised trials have not demonstrated significant advantages in avoiding cardiopulmonary bypass in high-risk patients [2], there is on-going speculation over the benefits of OPCAB in 'high risk' patients and the role of off-pump surgery in the setting of ACS is yet to be determined.

Theoretically, off pump coronary artery bypass grafting (OPCAB) seems to be an ideal procedure for patients with ACS because the use of intra-luminal shunts may allow preservation of coronary flow during surgery, thus avoiding global myocardial ischaemia during cardioplegic arrest and myocardial damage caused by ischaemia–reperfusion. The main disadvantage of OPCAB is the necessity for extreme upward retraction of the heart during revascularisation of circumflex or obtuse marginal branches, which may be technically difficult or not tolerated in compromised patients with acutely ischaemic myocardium.

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The aims of this study are to identify whether OPCAB may achieve a mortality benefit in patients presenting with ACS requiring immediate or urgent surgical intervention [3] both in the immediate and mid-term post-operative period. Secondarily, we recognise the importance of addressing the issue of incomplete revascularisation (IR), and will assess the impact of OPCAB on revascularisation index and re-intervention (PCI or CABG) for graft stenosis or incomplete revascularisation.

2. Materials and methods

2.1. Literature search

A literature search was performed using PubMed, Ovid, Embase, Medline, and Cochrane databases using the MeSH terms "off-pump", "on-pump", "coronary artery bypass grafting" and "acute coronary syndrome". In addition, our search was extended to include the clinicaltirals.gov database and 'grey' literature for further rigour. The 'related articles' function in PubMed was also used to ensure completeness. The last date for this search was 19th July 2013. A summary of our search strategy is outlined in Fig. 1.

2.2. Inclusion and exclusion criteria

All articles reporting outcomes for urgent or emergency OPCAB and ONCAB in patients with a history of ACS (as defined by the ACC/AHA, 2007 [4]) on the same admission were included. Studies were excluded from the review if: (1) Inconsistency of data did not allow valid extraction; (2) Data was duplicated; (3) The trial was carried out on animal models.

Based on these criteria, two assessors (MM, LH) independently selected studies for further examination by title and abstract review. All potentially eligible studies were retrieved in full for further evaluation. Any disagreement was resolved by discussion with the senior author (TA). Statistical concordance testing was performed using Cohen's kappa coefficient to measure of inter-rater agreement.

2.3. Data analysis

Two authors (MM, LH) independently extracted the following data from each paper using a standardised spreadsheet including: First author; year of publication; study type; number of subjects and study population demographics. Specific outcome data was retrieved where possible for the following: (i) Primary endpoints: 30-day and mid-term mortality (defined as >1 year but <5 years). (ii) Secondary endpoints: (a) Morbidity outcomes including post-operative inotropic support, IABP use, atrial fibrillation, sepsis, respiratory failure, renal failure, blood transfusion and re-operation for bleeding. (b) Length of stay outcomes: ICU-stay and hospital stay. (c) Completeness of revascularisation (or revascularisation index = total number of distal anastomoses/number of diseased vessels on coronary angiogram) and re-intervention (defined as either de novo CABG or PCI for graft failure or incomplete revascularisation).

Meta-analysis was performed in line with recommendations from the Cochrane Collaboration and in accordance with both PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines [5,6]. Analysis was conducted by use of Review Manager® Version 5.1.7 for Windows (The Cochrane Collaboration, Software Update, Oxford, UK) and STATA v.11 statistical analysis software.

Data was analysed using a weighted DerSimonian–Laird random effects model. Continuous data were investigated using weighted mean difference (WMD) as the summary statistic, reported with 95% confidence intervals (CI). The point estimate of the WMD was considered statistically significant at $p < 0.05$, if the 95% confidence interval did not include the value zero. Categorical variables were analysed using the odds ratio (OR). An OR of <1 favoured the treatment group and the point estimate of the OR is considered statistically significant at the $p < 0.05$ level, if the 95% confidence interval does not include the value 1.

2.4. Heterogeneity

Inter-study heterogeneity was explored using the Chi^2-statistic, but the I^2 value was calculated to quantify the degree of heterogeneity across trials that could not be attributable to chance alone. When I^2 was more than 50%, significant statistical heterogeneity was considered to be present.

Three strategies were used to assess data validity and heterogeneity: (1) Subgroup analysis of higher quality studies (quality score > 7); (2) Funnel plots to evaluate publication bias; (3) Further assessment of publication bias using Egger's and Begg and Mazumdar's test for small-study effects.

2.5. Quality scoring

Quality assessment of each study was performed by attributing a quality assessment score using a modification of the Newcastle–Ottawa scale [6]. Studies attaining greater

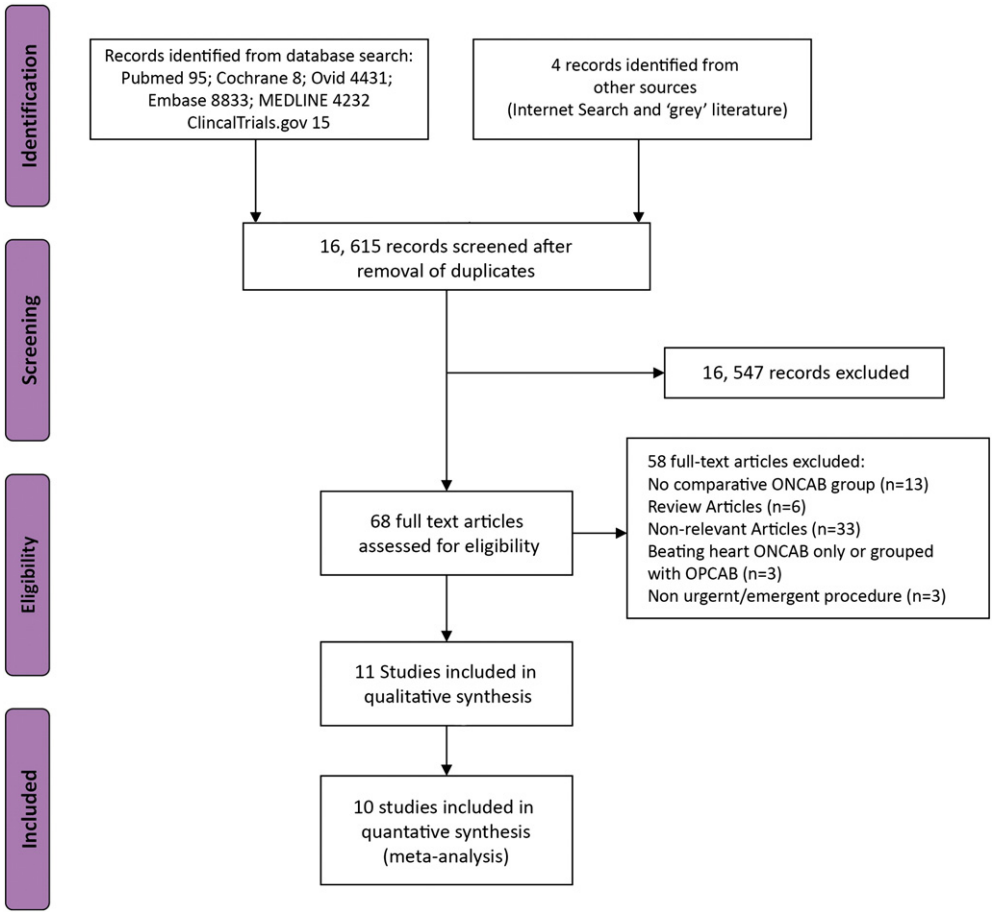

Fig. 1. Search strategy.