

Association between preoperative depression and long-term survival following coronary artery bypass surgery – A systematic review and meta-analysis



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ABSTRACT

Background: Depression is common in patients with cardiovascular disease. The importance of preoperative depression for long-term survival following coronary artery bypass grafting (CABG) is not well known. The aim was to provide a summary estimate of the association between preoperative depression and long-term survival in adults who underwent CABG.

Methods: We did a systematic search of MEDLINE, EMBASE, Cochrane Library, PsycINFO, Web of Science, and PubMed from inception to November, 2015, including cohort studies with at least one month of follow-up that reported hazard ratios (HR) and 95% confidence intervals (CI) for long-term all-cause mortality following CABG in patients with preoperative depression compared to non-depressed patients. Two reviewers independently extracted data on populations, exposure, outcome, risk of bias, and quality of evidence. We calculated HR and 95% CIs for all-cause mortality using random-effects meta-analyses and performed subgroup and sensitivity analyses.

Results: Seven studies were included with a combined study population of 89,490 patients (4002 depressed/85,488 non-depressed). All studies observed a positive association between preoperative depression and all-cause mortality, and in 4 studies the association was statistically significant. Patients with depression had a pooled hazard ratio of 1.46 (95% CI: 1.23–1.73, $p < 0.0001$) for all-cause mortality with moderate heterogeneity ($I^2 = 50.1\%$, $p = 0.061$).

Conclusions: This systematic review and meta-analysis indicates that patients with preoperative depression are at increased risk for long-term, all-cause mortality following CABG compared with those without depression. Systematic screening for depression prior to cardiac surgery could identify those at higher risk.

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1. Introduction

The rate of major depressive disorder is 2- to 3-fold higher in patients with cardiovascular disease (CVD) than among the general population [1]. Perioperative complications, risk for rehospitalization and mortality is also increased in patients with depression who undergo coronary artery bypass grafting (CABG) compared with patients without depression [2–5]. Depressive symptoms have been associated with the development and progression of coronary heart disease and a 2–2.5-fold increased risk of mortality [1]. In many patients depression has existed for months or years before a cardiac event rather than being a reaction to the event [6]. Previously published reviews have focused on the high rate of comorbid depression and CVD, and the effect

of depression on prognosis in patients with CVD [1]. [7] This is the first systematic review and meta-analysis that investigates the association between preoperative depression and long-term survival after CABG.

2. Methods

2.1. Study design

A systematic literature review and meta-analysis was performed following an a priori established study protocol.

2.2. Search strategy and selection criteria

References for this systematic review – depression and cardiac surgery – were searched without language or year restrictions in the following databases: OVID®, Embase® (Elsevier), Cochrane Library including CENTRAL (Wiley), PsycINFO® (OVID®), Web of Science™ Core Collection (Thomson Reuters), PubMed (complementary search of non-indexed material).

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Two librarians at the Karolinska Institutet University Library performed the searches in November 2015, starting with identifying Medical Subject Headings (MeSH-terms) in MEDLINE. The search strategy contained three concepts that were combined using the set operator AND. These three concepts were searched with the following MeSH-terms: "Myocardial Revascularization", "Percutaneous Coronary Intervention", "Cardiac Catheterization", "Cardiac Surgical Procedures", "Depressive Disorder", "Depression", "Survival Rate", "Survival", and "Mortality". Each search concept was also complemented with relevant free-text terms like: myocardial, coronary, revascularization, angioplasty, depression, depressive, mortality, and survival. The free-text terms were, if appropriate truncated and/or combined with proximity operators. The terms identified for searching MEDLINE were adapted in accordance to corresponding vocabularies of Embase and PsycINFO, as well as searched with free-text terms in Cochrane and Web of Science. A complementary search for the latest, non-indexed material in PubMed was conducted using free-text terms. Articles were also identified through searches of reference lists. The search strategy is available in the Supplemental material.

2.3. Selection criteria

All cohort studies investigating the association between depression prior to CABG and long-term survival were included. We excluded all studies that were not cohort studies, and studies focusing on postoperative depression. In the case of duplicate studies with accumulating numbers of patients or increased lengths of follow-up, we choose to include only the most complete study for quantitative assessment. We did not include animal studies, abstracts, case reports, conference presentations, editorials, reviews, and expert opinions.

2.4. Data extraction

Two investigators (M.S. and U.S.) independently extracted data and characteristics of included studies using separate spreadsheets. Any differences were resolved by dialogue until consensus was reached. Extracted characteristics included the first author's name, year, study period, country, study design, surgical procedure, definition of exposure, definition of outcome, adjustment for confounders, subgroup analysis, total number of patients, number of patients in the exposed and non-exposed groups, number of patients lost to follow-up, outcome measure, unadjusted and multivariable adjusted hazard ratios (HR) and 95% confidence intervals (CI).

2.5. Quality assessment

For quality assessment of observational studies in epidemiology we referenced the Newcastle Ottawa scale [8] and STROBE [9] guidelines. The Newcastle Ottawa scale [8] assesses 3 broad areas: the selection of non-exposed and exposed participants, comparability of the groups and assessment of outcome. A study can be awarded stars for high quality in each area, a maximum of 4 stars for the "selection" category, 2 stars for "comparability" and 3 stars for "outcome" (Supplemental material).

2.6. Exposure

Definition of exposure was preoperative depression. How depression was defined differed between the studies.

2.7. Outcome

The primary outcome was long-term all-cause mortality.

2.8. Data synthesis and statistical analysis

Adjusted HRs and CIs were extracted from the selected articles. Fixed and random effects models were used to compute the pooled HR and 95% CI. The random effects model was used to take into account the possible clinical diversity and methodological variation among studies. Additional tests included: Q-test to test heterogeneity between trials; and I^2 to estimate the percentage of total variation across studies due to heterogeneity rather than chance. I^2 can be calculated as follows: $I^2 = 100 \times (Q - df) / Q$ (where Q represents Cochran's measure of heterogeneity and the degrees of freedom), and can be categorised into low (<50%), moderate (51–75%), or high (>75%) according to predefined criteria [10]. Sources of heterogeneity were further investigated in a sensitivity analysis in which the pooled estimates were calculated omitting one study at a time using a random effects model. Data management and statistical analyses were performed using R version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

2.9. Publication bias

To detect funnel plot asymmetry both Begg and Mazumdar's [11] test and Egger's [12] test were used. Funnel plots can be useful to check whether effects from small studies differ from those in larger studies and therefore may distort the results of a meta-analysis [13].

2.10. Subgroup analysis

Due to different definitions of exposure, we performed separate analyses in patients with antidepressant use before CABG and in patients with self-assessed depression through questionnaires before CABG.

3. Results

The literature search was finalised on November 17 2015. A total of 1357 unique records were identified through the literature search. Of these, 1209 were excluded due to title or abstract content, 80 due to wrong population or outcome and 24 were review articles. The remaining 44 full-text articles were assessed for eligibility and 7 studies met the inclusion criteria [14–20] (Fig. 1). Studies included in the meta-analysis were published between 2003 and 2015, and included data for 89,490 patients from the USA, Sweden and Australia. Preoperative depression was present in 4215 patients. The number of patients in each study ranged from 309 to 56,064 with median or mean follow-up ranging from 3 to 9.3 years. Characteristics of the included studies are presented in Table 1.

3.1. Preoperative depression and mortality

As presented in Fig. 2, the overall pooled HR for preoperative depression and mortality was 1.46 (95% CI 1.23 to 1.73) according to a random effects model with moderate heterogeneity ($I^2 = 50.1\%$ $p = 0.061$).

3.2. Definition of depression

Three studies defined depression through self-assessment, three studies defined depression as anti-depressant use, and one study defined depression from diagnosis in the Swedish National Patient Registry. The study of Blumenthal et al. [14] defined depression according to the 20-item Center for Epidemiological Studies Depression (CES-D) questionnaire (non-depressed (CES-D < 16), mildly depressed (CES-D 16–26), and moderate to severely depressed (CES-D > 27)). Connerney

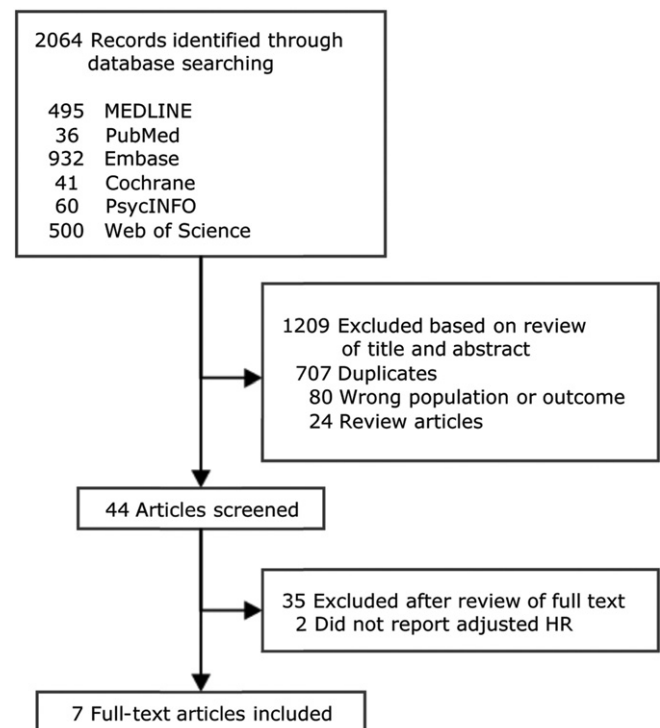


Fig. 1. PRISMA flow-chart for systematic review of preoperative depression and long-term survival following CABG.

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