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REVIEW ARTICLES

Goal-directed therapy in cardiac surgery: a systematic review and meta-analysis

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Editor's key points

- The authors examined the effectiveness of goal-directed therapy (GDT) during cardiac surgery.
- For this meta-analysis, five studies met all inclusion criteria.
- Importantly, in a relatively small sample size for this meta-analysis, GDT was found to reduce morbidity and hospital stay.
- Further work will be required to determine the effects of GDT on mortality in this group of patients.

Background. Perioperative mortality after cardiac surgery has decreased in recent years although postoperative morbidity is still significant. Although there is evidence that perioperative goal-directed haemodynamic therapy (GDT) may reduce surgical mortality and morbidity in non-cardiac surgical patients, the data are less clear after cardiac surgery. The objective of this review is to perform a meta-analysis on the effects of perioperative GDT on mortality, morbidity, and length of hospital stay in cardiac surgical patients.

Methods. We conducted a systematic review using Medline, EMBASE, and the Cochrane Controlled Clinical Trials Register. Additional sources were sought from experts. The inclusion criteria were randomized controlled trials, mortality reported as an outcome, pre-emptive haemodynamic intervention, and cardiac surgical population. Included studies were examined in full and subjected to quantifiable analysis, subgroup analysis, and sensitivity analysis where possible. Data synthesis was obtained by using odds ratio (OR) and mean difference (MD) for continuous data with 95% confidence interval (CI) utilizing a random-effects model.

Results. From 4986 potential studies, 5 met all the inclusion criteria (699 patients). The quantitative analysis showed that the use of GDT reduced the postoperative complication rate (OR 0.33, 95% CI 0.15–0.73; P=0,006) and hospital length of stay (MD −2.44, 95% CI −4.03 to −0.84; P=0,003). There was no significant reduction in mortality.

Conclusion. The use of pre-emptive GDT in cardiac surgery reduces morbidity and hospital length of stay.

Keywords: cardiac output; cardiac surgical procedures; haemodynamics; intraoperative; monitoring

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Operative and postoperative mortality after cardiac surgery have decreased in recent years,[1–3] which highlights the progress in the care of these patients. The incidence of postoperative morbidity, however, is still significant.[2] As a result, up to 10% of patients require a prolonged postoperative care,[4] with longer intensive care unit (ICU) stays and worse long-term outcomes.[5 6] Patients with complications use a greater amount of resources,[7] and therefore these patients are associated with a higher healthcare cost.

The risk of adverse events increases in patients with certain co-morbidities, such as recent myocardial infarction, poor left ventricular ejection fraction, history of pulmonary disease, or renal dysfunction.[4 8] The impact of co-morbidities on postoperative morbidity and outcome has also been studied in non-cardiac surgery where the use of haemodynamic manipulations in the perioperative period has been associated with an improved outcome.[9–19] Fewer studies have been performed specifically for cardiac surgery, and even these are mostly on small sample sizes from single centres.[20–24]

This systematic review and meta-analysis investigates whether a goal-directed haemodynamic approach to therapy in the perioperative period is associated with improved postoperative outcomes in cardiac surgical patients.

Methods

Search strategy

Three electronic databases (Medline, EMBASE, and the Cochrane Controlled Clinical Trials register) were searched with the following keywords: haemodynamic monitoring, cardiac output, stroke volume, oxygen delivery, GDT, dobutamine, cardiac surgery, cardiac surgical procedures (full electronic search strategy is presented in Supplementary data).

The research strategy ran from 1985 to 31 December 2011. Articles were restricted to randomized clinical trials, English language, and adults and human studies only. In addition to electronic searching, industry representatives were contacted for additional material, and personal archives and communications were searched. All identified review articles and evidence-based guidelines were hand-searched for additional references, and reference lists for identified studies were snowballed for additional articles. The title and abstracts identified from the search strategy were then screened for potential articles by two investigators. After this primary exclusion, full articles were obtained and examined for suitability. When necessary, authors of the selected articles were contacted to obtain missing information for the quantitative analysis.

Study inclusion criteria

Studies were selected according to the following inclusion criteria:

(1) Randomized controlled clinical trials (RCTs) evaluating the effect of pre-emptive haemodynamic GDT. All studies had to be prospective, properly randomized to control for selection bias, and had to report hospital mortality as an outcome on an intention-to-treat basis. Only peer-reviewed papers were included. GDT was defined as perioperative monitoring and manipulation of haemodynamic parameters to reach either normal or supra-normal pre-determined values. Therapies could be classified as i.v. fluids, additional inotropic support or both. Haemodynamic intervention had to be pre-emptively started in the perioperative period, which was defined as 24 h before or after operation.
(2) Adult (age 18 years or over) patients as participants of the study design.
(3) Studies performed in cardiac surgical patients.

Methodological quality of included studies and risk of bias assessment

Eligible studies were graded using the systems described by Jadad and colleagues.[25] Non-randomized studies were excluded. This scale is used to describe the study quality by scoring five elements of randomization, implementation, and blinding with a score range of 1 to 5.

To assess risk of bias of selected studies, two reviewers working independently determined the adequacy of concealment of allocation, blinding of participants and healthcare providers, blinding of outcome assessors, extent of loss of follow-up (attrition bias), and risk of selective reporting bias using the Review Manager software (version 5.1, The Cochrane Collaboration, Oxford, UK). Risk was described for every item as 'low risk' if the information provided in the study was clear and complete, 'high risk' if there was no information about some of the items or the information provided reveal a clear risk of bias, and 'unclear risk' when the information provided is incomplete.

Outcome measures

The primary outcome was hospital mortality. The secondary outcome measures were postoperative morbidity and hospital length of stay.

A sensitivity analysis was performed on both the primary and secondary outcomes. This consisted of a correction for quality using the Jadad score, with a score >3 classified as a higher quality study.[25] Furthermore, a time-dependent analysis was performed to examine the influence of care evolution and underlying event rates in the last 20 years.

Statistical analysis

The meta-analysis was performed using the Review Manager, version 5.1.4 software (The Cocharane Collaboration, Oxford, UK), with a random-effects model. The results are presented as an odds ratio (OR) for dichotomous data with 95% confidence intervals (CIs) and as mean difference (MD) for continuous data. Significance was set at a *P*-value of <0.05. All results were checked for statistical heterogeneity presenting the among-study variance τ^2 and the chi-squared test. Statistical significance was set at a *P*-value of <0.1 for heterogeneity. Inconsistency was tested using the I^2 statistic and it was considered significant when it was $>40\%$.[26 27]

Results

Included trials

A total of 4986 titles were suitable for further review after database searching, snowballing of references, hand searching, and contacting experts and industry representatives. One hundred and three potential articles were selected after thorough examination of titles and abstracts. Further examination led to exclusion of 98 studies from the analysis, because they were not related to early goal-directed therapy, lacked randomization, had a non-prospective study design, or were not performed in cardiac surgical patients (Fig. 1). Five articles were finally included in the analysis.

Description of studies

The five identified studies are described in detail in Table 1. All of them reported mortality and morbidity. Definitions of complications were variable across the studies (reported in Supplementary Appendix 3). Although all the studies also reported ICU and hospital length of stay, these data were reported in different types of central tendency and dispersion measures (Table 2). Data regarding hospital length of stay were obtained from selected authors. None of these five studies used supra-normal targets of resuscitation.

Mortality

Mortality data were available for all five trials on 699 patients. There were no deaths reported in two trials; thus our estimate is based on three trials randomizing 632 patients, 15 of whom died. The overall effect when combining the studies was no reduction in mortality for the