Does fast-track treatment lead to a decrease of intensive care unit and hospital length of stay in coronary artery bypass patients: a meta-regression of randomized clinical trials

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CRD summary
The review assessed whether fast-track treatments for adults at low risk of complications after coronary artery bypass surgery reduce the length of stay in hospital. The authors concluded that a protocol for early tracheal extubation appears essential. The authors did not provide sufficient information about the included studies to justify their conclusions.

Authors’ objectives
To evaluate the effect of fast-track treatments on intensive care unit (ICU) and hospital stay among low-risk coronary artery bypass grafting (CABG) patients.

Searching
The authors searched MEDLINE, the Cochrane CENTRAL Register and reference lists for studies published between 1966 and 2004; the search strategy was reported. Abstracts and reviews were excluded from the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that evaluated fast-track treatments were eligible for inclusion. The aspects of fast-track treatment addressed in the review were anaesthetic dose, temperature management and tracheal extubation protocol. Interventions were categorised by:

- the type and dose of anaesthetics (high dose: >15 microg/kg fentanyl, >3 microg/kg sufentanil and >60 microg/kg alfentanil; low dose: <15 microg/kg fentanyl, <2 to 3 microg/kg sufentanil, <60 microg/kg alfentanil and remifentanil),
- temperature management during cardiopulmonary bypass (normothermia or hypothermia, defined as above or below 35 degrees C, respectively), and
- extubation protocol (the intention to extubate within or after 8 hours following surgery).

Participants included in the review
Studies in low-risk adults (at least 18 years old) who had undergone CABG were eligible for inclusion. Studies were excluded if the sample population comprised mainly non-CABG patients or patients at high risk of post-operative complications. High risk was defined in the report. The characteristics of the patients in the included studies were not reported.

Outcomes assessed in the review
The main outcome of interest was ICU stay (in hours). Other outcomes included in the review were hospital stay (in days), myocardial infarction (MI) as defined in the report, death and quality of life. The quality of life dimensions reported in the included studies were mostly pain and cognitive function.

How were decisions on the relevance of primary studies made?
Two of the authors discussed the eligibility of the studies.

Assessment of study quality
Three components of study quality were assessed: allocation concealment, blinding of the assessors of ICU stay, and intention-to-treat analysis of ICU stay. The assessment was done without concealing the name of the journal, authors or institution. Two of the authors discussed and resolved issues of uncertainty, although it was unclear if they assessed the articles independently.

**Data extraction**
Two reviewers independently classified the types of interventions used in the included studies. There were no further details of how the data were extracted for the review. The data extracted included the number of participants in each treatment group, the mean and standard deviation (SD) for continuous outcomes, and the number of events in each group for dichotomous outcomes.

Estimates of mean and SD were derived from reported median and ranges by assuming the mean to be equivalent to the median and the SD to be one quarter of the range. Data extracted in relation to quality of life were the dimension measured, instrument used, time points at which measurements were made, and the reported conclusions.

**Methods of synthesis**

**How were the studies combined?**
A meta-analysis was used to calculate the pooled standardised mean difference (SMD) in ICU stay between high- and low-dose anaesthetics, and between extubation within or after 8 hours following surgery. It was unclear if the pooled estimates were derived using a fixed-effect or random-effects analysis.

**How were differences between studies investigated?**
A meta-regression was used to investigate differences in treatment effects between the studies. The regression was weighted by the number of participants divided by the squared SD in each study.

The studies were categorised into two groups according to whether or not there was a major difference between the comparator groups in anaesthetic dose (i.e. low versus high) and/or extubation protocol (<8 hours versus >8 hours). The studies in each group were analysed together and in separate regression models with ICU stay and hospital stay as the dependent variables, such that six models in all were reported.

The study characteristics investigated as independent variables within each model were anaesthetic dose (low, unknown, high), temperature management (normothermia, unknown, hypothermia) and extubation protocol (<8 hours, unknown, >8 hours). The quality criteria of allocation concealment, blinding and intention-to-treat (adequate/yes or unclear/no) and the year of publication were included as covariables. Six additional regression models were used to explore the effect of fast-track treatments on MI and death.

**Results of the review**
Twenty-seven studies (2,821 participants) were included in the review.

The methodological quality of the included studies in general was described as moderate. One trial fulfilled all three quality criteria assessed, while 10 trials fulfilled none.

A meta-analysis of nine trials showed no statistically significant difference in ICU stay between low- and high-anaesthetic dose (SMD -0.11, 95% confidence interval, CI: -0.26, 0.03). In two of the trials the comparator groups also differed in extubation protocol (<8 hours versus >8 hours). A statistically significant difference was shown in favour of extubation within 8 hours compared with after 8 hours (SMD -0.32, 95% CI: -0.48, -0.17), based on five trials. No estimates of heterogeneity were reported.

Meta-regression using all studies showed that the use of an early extubation protocol had a statistically significant effect on decreasing ICU stay (p<0.0001) and hospital stay (p=0.002). Extubation protocol was shown to be a predictor of ICU and hospital stay in all but one of the other regression models reported. Study quality and year of publication explained some of the heterogeneity between the studies. The authors suggested that the significance of other variables which appeared to have an effect in some models, such as anaesthetic dose in one model and temperature management...
in two models, may have been due to multiple testing. Meta-regression did not find anaesthetic dose, temperature management or extubation protocol to be significant predictors for MI or death.

Quality of life was reported in 10 studies. Data could not be pooled due to differences in the instruments and time points used. One of four studies with a major difference in anaesthetic dose between treatment groups found a significant reduction in pain in the low-dose group after 1 to 2 days. Two studies with a major difference in extubation protocol and/or anaesthetic dose found no significant difference in cognitive function.

Cost information
Cost analysis and cost-minimisation analysis data were reported in seven of the included studies. The highest quality study reported a significant reduction in costs with fast-track treatment but most of the studies found no difference.

Authors’ conclusions
An early extubation protocol appears essential to decrease ICU and hospital stay in low-risk patients following CABG.

CRD commentary
The review defined the inclusion and exclusion criteria although the question was slightly unclear. The authors stated that they sought to investigate the combined effect of fast-track treatments, but they appeared to investigate the effect of the individual elements. The search was likely to be adequate for identifying most of the relevant published RCTs. Steps seemed to have been taken to minimise bias in the study selection process and reviewer errors in the data extraction. Adequate methods were used to assess the quality of the included trials using appropriate criteria. The authors' view of the general quality of the included trials was generous. Only three of the included trials reported adequate concealment of the allocation sequence, which is an important factor associated with bias.

There were insufficient details of the characteristics of the included studies to assess how appropriate it was to pool the data in a meta-analysis or to assess the potential for confounding in the meta-regression analysis. Estimates of statistical heterogeneity were not reported with the meta-analysis results. It was unclear why the SMD rather than hours was used to calculate pooled estimates of ICU stay, and the clinical significance of the difference was not elucidated. The authors appear to have conducted a fixed-effect meta-regression analysis, which did not allow for between-trial heterogeneity; hence, the CIs around the regression coefficients might be too narrow. There were few studies relative to the number of covariates, and to what degree the covariates were pre-specified was unclear. Overly strong conclusions should not be drawn from the results.

Implications of the review for practice and research
Practice: The authors stated that a protocol directed at early extubation seems essential to reduce ICU and hospital stay.

Research: The authors stated that further trials should evaluate the effect of adding ICU discharge criteria to fast-track protocols. Researchers investigating quality of life should use validated assessment tools and follow reporting guidelines.

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Bibliographic details

PubMedID
Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.