The effect of tight glycaemic control, during and after cardiac surgery, on patient mortality and morbidity: a systematic review and meta-analysis

Haga KK, McClymont KL, Clarke S, Grounds RS, Ng KY, Glyde DW, Loveless RJ, Carter GH, Alston RP

CRD summary
The authors concluded there may be some benefit in tight glycaemic control during and after cardiac surgery, but the available data were limited and variable; further research was required to give a definitive answer. The authors' cautious conclusions reflected the evidence presented, but the potential for language and publication bias, and the unknown quality of included trials should be considered.

Authors' objectives
To determine the effects of tight versus normal glycaemic control during and after cardiac surgery on patient morbidity and mortality.

Searching
MEDLINE, The Cochrane Library, EMBASE, NHS Scotland E-Library, SIGN (Scottish Intercollegiate Guidelines Network) and NICE were searched for relevant articles published in English; search terms were reported. Reference lists of relevant papers were handsearched for additional articles.

Study selection
Randomised controlled trials that evaluated the effect of tight versus normal glycaemic control during and/or after cardiac surgery were eligible for inclusion. Tight control was defined as patients whose blood glucose was controlled within a pre-defined upper limit. Normal control comparisons were of patients whose blood glucose levels were either not controlled or maintained below a higher limit. Trials that only evaluated the method of control or had no extractable data were excluded.

The outcomes of interest were early mortality (within the first 30 days after surgery or mortality in the coronary care unit), atrial fibrillation, time in intensive care unit, time on mechanical ventilation, and the need for epicardial pacing.

The definition of tight glycaemic control varied between included trials ranging from 80mg/dL to 200mg/dL. Normal control limits ranged from less than 180mg/dL to less than 250mg/dL, or no active glycaemic control. Two trials included both diabetic and non-diabetic patients, one trial included only diabetic patients, and the remaining trials included only non-diabetic patients. None of the trials reported the type of diabetes of participants. Most trials evaluated the control period as during surgery, two trials evaluated after surgery, and one trial evaluated during and after surgery.

Two reviewers independently selected studies for inclusion.

Assessment of study quality
The authors did not state that they conducted a quality assessment.

Data extraction
Data were extracted to calculate odds ratios (ORs) for dichotomous outcomes and mean differences (MDs) for continuous outcomes, with corresponding 95% confidence intervals (CIs).

Two reviewers appear to have independently extracted data.

Methods of synthesis
Pooled odds ratios and mean differences, with 95% confidence intervals, were calculated using the Mantel-Haenszel fixed-effect model. Heterogeneity was assessed using $X^2$ and $I^2$.

Results of the review
Seven RCTs (n=1,972 participants, range 20 to 970) were included in the review. Tight glycaemic control significantly reduced the incidence of early mortality following cardiac surgery (OR 0.52, 95% CI 0.30 to 0.91; three RCTs), post-surgical atrial fibrillation (OR 0.76, 95% CI 0.58 to 0.99; five RCTs), length of stay in the intensive care unit (MD -0.57 days, 95% CI -0.60 to -0.55; three RCTs), duration of mechanical ventilation (MD -3.69, 95% CI -3.85 to -3.54; four RCTs) and use of epicardial pacing (OR 0.28, 95% CI 0.15 to 0.54; three RCTs). There was significant statistical heterogeneity for early mortality ($I^2=71\%$), duration of mechanical ventilation ($I^2=94\%$), and time spent in the intensive care unit ($I^2=99\%$).

**Authors' conclusions**

Results suggested that there may be some benefit in tight glycaemic control during and after cardiac surgery, but they should be interpreted with caution due to the limited and variable data available. Further research was required to provide a definitive answer on the benefits of tight glycaemic control for cardiac surgery patients.

**CRD commentary**

The review question was clear with appropriate inclusion criteria. Several relevant sources were searched, but limiting inclusion to only studies published in English meant there was potential for language and publication bias. Appropriate methods were used to reduce reviewer error and bias in the selection of studies and extraction of data.

A quality assessment was not conducted on included trial, so the results from these trials and any synthesis may not be reliable. Some trial details were reported. Data were combined in a meta-analysis, but there was a high degree of heterogeneity reported, so the use of a fixed-effect model may not have been the most appropriate method to use. The authors discussed some of the limitations of the data.

The authors' cautious conclusions reflected the evidence presented, but the potential for language and publication bias and lack of quality assessment should be considered.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that further large-scale trials with double-blinding and definable outcome measures were needed to provide a definitive answer on the benefits of tight glycaemic control for cardiac surgery patients. Future studies should address the differences between diabetic and non-diabetic patients for tight control and outcomes, have a clearly defined and accepted glycaemic range for tight and normal control, and examine longer term outcomes as well as those immediately after surgery. In addition, timing of control and benefits, risks and underlying physiological mechanisms need further investigation.

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