Effectiveness of tight glycaemic control on mortality and morbidity in patients undergoing cardiac surgery in hospital: a systematic review

Submitted by

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Declaration

I, Ali Morshed, certify that this work contains no material that has been accepted for the award of any other degree or diploma in any university or any other tertiary institution, and, to the best of my knowledge and belief, contains no material previously published or written by any other person, except where due reference has been made in the text.

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Ali Azam Mohammad Morshed

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Abstract

Background

Hyperglycaemia is a well-documented and common response to critical illness and metabolic stress during the perioperative period of cardiac surgery; however, there remains considerable controversy regarding the role of tight glycaemic control during and/or after cardiac surgery. The objective of this review was to identify the effectiveness of tight glycaemic control compared to conventional glycaemic control on the mortality and morbidity in diabetic and nondiabetic patients undergoing cardiac surgery.

Methods

A three-step search strategy was employed that aimed to locate both published and unpublished studies in the English language between 1990 until March 2014. An initial search in PubMed and CINAHL was followed by a second search using all identified keywords and index terms across multiple databases and grey literature sites. Critical appraisal was undertaken by two independent reviewers using the standard critical appraisal instrument from the Joanna Briggs Institute Meta-Analysis of Statistical Assessment and Review Instrument (JBI-MAStARI). Results from randomized controlled trials were pooled in statistical meta-analysis using RevMan V 5.3 software where appropriate. Effect sizes were calculated using a fixed effects model. Where the findings could not be pooled using meta-analysis, results are presented in a narrative form.

Results

Twelve studies including 2713 participants were identified that met the inclusion criteria and were considered to be of adequate methodological quality. The included randomised controlled trials were generally of good quality with a clear description of study design and statistical analysis methods employed. Meta-analysis was conducted on comparisons between very tight glycaemic control (80-150mg/dl), tight glycaemic control (100-200mg/dl) and conventional glycaemic control (160-250mg/dl).

For all patients (both diabetic and/or nondiabetic) undergoing cardiac surgery, very tight glycaemic control as compared to conventional glycaemic control significantly reduced all-cause mortality (odds ratio [OR] 0.59, 95% confidence interval [CI] of 0.37 to 0.96), length of stay in hospital (mean difference [MD] -0.21,95% CI of -0.28 to -0.14); and tight glycaemic control compared to conventional glycaemic control significantly reduced all-cause mortality (OR 0.25, 95% CI of 0.09 to 0.68), length of stay in intensive care units (MD -0.65, 95% CI of -0.68 to -0.62), length of stay in hospital (MD -2.70, 95% CI of -2.77 to 2.63), atrial fibrillation (OR 0.42, 95% CI 0.26 to 0.66) and renal failure (OR 0.09, 95% CI 0.02 to 0.51). In diabetic patients undergoing cardiac surgery, very tight glycaemic control in comparison with conventional glycaemic control showed significant reduction in length of stay in hospital (MD -0.21, 95% CI -0.28 to -0.14), and tight glycaemic control compared to conventional

glycaemic control showed significant reduction in length of stay in hospital (MD -2.71, 95% CI -2.78 to -2.63), length of stay in ICU (MD -0.65, 95% CI -0.68 to -0.62) and atrial fibrillation (OR 0.36, 95% CI 0.22 to 0.59).

Conclusions

The findings of this review indicate that very tight and/or tight glycaemic control compared to conventional glycaemic control during the periopertive period in patients undergoing cardiac surgery may have some positive effects in reducing mortality and morbidity following surgery.

Keywords

Tight glycaemic control, strict glycaemic control, aggressive glycaemic control, cardiac surgery, cardiovascular surgery, insulin therapy, intensive insulin therapy, mortality, morbidity, deep sternal infection, atrial fibrillation, mechanical ventilation, epicardial pacing.

Table 1: Summary of findings

Very tight glycaemic control versus conventional glycaemic control in all patients (diabetic and/or nondiabetic patients) undergoing cardiac surgery

Patient or population: All patients (Diabetic and/or nondiabetic patients) undergoing cardiac surgery
Settings: Inpatient
Intervention: Very tight glycaemic control(80-150mg/dl)
Comparison: Conventional glycaemic control(160-250mg/dl)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Conventional glycaemic control**	Corresponding risk **Very tight glycaemic control**				
All-cause mortality	**52 per 1000**	**32 per 1000** (20 to 50)	**OR 0.59** (0.37 to 0.96)	1729 (4 studies)	⊕⊕⊖⊖ **low**[1,2]	
Length of stay in hospital(in days)	The mean length of stay in hospital (in days) in the control groups ranged from **3-17 days**	The mean length of stay in hospital (in days) in the intervention groups was **0.21 days lower** (0.28 to 0.14 lower)		861 (5 studies)	⊕⊕⊖⊖ **low**[3,4]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Downgraded as I2 is 38% and heterogeneity is present.
[2] Downgraded as confidence intervals are imprecise and sample size is not large enough.
[3] Downgraded as wide variance of point estimate.
[4] Downgraded as small sample size.

Tight glycaemic control versus conventional glycaemic control in all patients (diabetic and/or nondiabetic patients) undergoing cardiac surgery

Patient or population: All patients (diabetic and/or nondiabetic patients) undergoing cardiac surgery
Settings: Inpatient
Intervention: Tight glycaemic control (100-200mg/dl)
Comparison: Conventional glycaemic control (160-250mg/dl)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Conventional glycaemic control**	Corresponding risk **Tight glycaemic control**				
All cause mortality	**72 per 1000**	**19 per 1000** (7 to 50)	**OR 0.25** (0.09 to 0.68)	529 (3 studies)	⊕⊕⊕⊖ **moderate**[1]	
Length of stay in hospital(in days)	The mean length of stay in hospital (in days) in the control groups ranged from **9-10 days**	The mean length of stay in hospital (in days) in the intervention groups was **2.7days lower** (2.77 to 2.63 lower)		553 (3 studies)	⊕⊕⊖⊖ **low**[2]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Downgraded as wide confidence intervals and small sample size
[2] Downgraded two levels as I2 is 87% indicates substantial to considerable heterogeneity

Very tight glycaemic control versus conventional glycaemic control in diabetic patients undergoing cardiac surgery

Patient or population: Diabetic patients undergoing cardiac surgery
Settings: Inpatient
Intervention: Very tight glycaemic control(80-150mg/dl)
Comparison: Conventional glycaemic control(160-250mg/dl)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Conventional glycaemic control	**Very tight glycaemic control**				
Length of stay in hospital (in days)	The mean length of stay in hospital (in days) in the control groups ranged from **3-11 days**	The mean length of stay in hospital (in days) in the intervention groups was **0.21 days lower** (0.28 to 0.14 lower)		182 (2 studies)	⊕⊕⊖⊖ **low**[1]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **OR:** Odds ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Downgraded as small sample size.

Tight glycaemic control versus conventional glycaemic control in diabetic patients undergoing cardiac surgery

Patient or population: Diabetic patients undergoing cardiac surgery
Settings: Inpatients
Intervention: Tight glycaemic control (100-200mg/dl)
Comparison: Conventional glycaemic control (160-250mg/dl)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Conventional glycaemic control**	Corresponding risk **Tight glycaemic control**				
All-cause mortality	See comment[1]	See comment[1]	Not estimable	341 (2 studies)	See comment	
Length of stay in hospital (in days)	The mean length of stay in hospital (in days) in the control groups ranged from **9-10 days**	The mean length of stay in hospital (in days) in the intervention groups was **2.71 days lower** (2.78 to 2.63 lower)		341 (2 studies)	⊕⊕⊕⊖ **moderate**[2]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] One study reported no event whereas another study was statistically significant.
[2] Small sample size.