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Cardioprotective Effects of Glucose-Insulin-Potassium Infusion in Patients Undergoing Cardiac Surgery: a Systematic Review and Meta-Analysis

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Running Head (Abbreviated Title)

Perioperative GIK cardioprotection: a meta-analysis

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Abbreviations (Glossary of Terms)

95%CI ς ninety-five percent confidence interval

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AF ς atrial fibrillation

AKI ς acute kidney injury

AXC ς aortic cross-clamping

CABG ς coronary artery bypass grafting

CPB ς cardiopulmonary bypass

GIK ς glucose-insulin-potassium

ICU ς intensive care unit

IQR ς interquartile range 25%-75%

k ς model sample count

MD ς mean difference

MI ς myocardial infarction (postoperative)

n ς count (events or participants)

OR ς odds ratio

RCT ς randomized controlled trial

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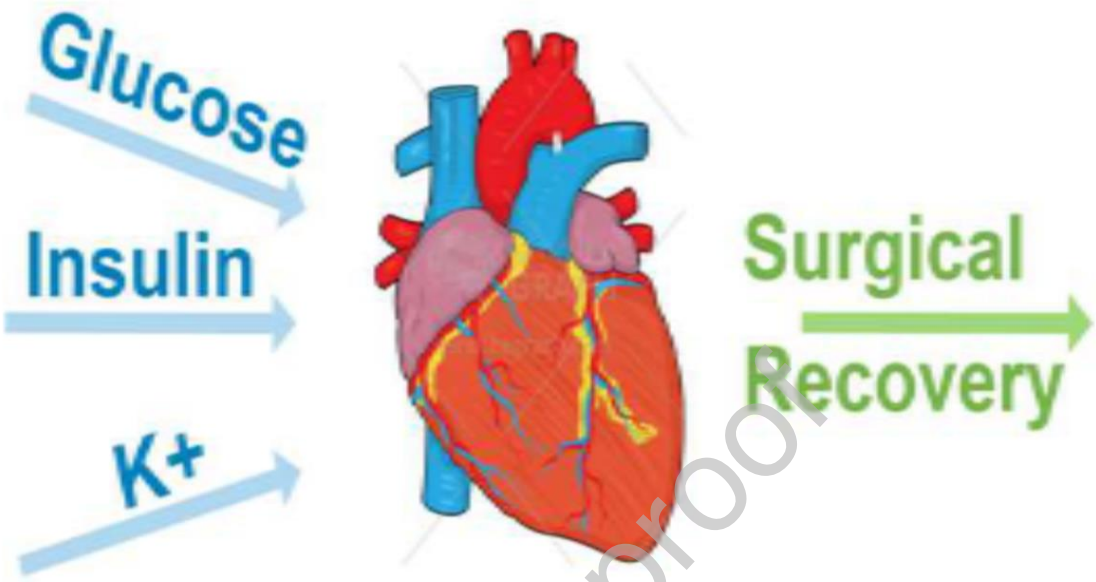

Central Picture Legend

GIK enhances recovery after cardiac surgery: a meta-analysis since inception

Central Message

The infusion of glucose-insulin-potassium lowers the risk of myocardial infarction while enhancing hemodynamics in patients undergoing on-pump cardiac surgery.

Perspective Statement

This updated meta-l·yl·fèăλă 2Ŧ po ăűdzŘλŜă λyŎftdzŘλyƎ 2ØŜℕ cΩллл LJI·ûλŜyűăΣ Ŧ2dzyŘ ûKI·ûΣ Ŏ2YLJI·ℕŜŘ with usual care, the infusion of GIK was associated with fewer postoperative myocardial infarctions and atrial fibrillation along with faster discharge from the ICU and the hospital.

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Therefore, perioperative GIK treatment could be recommended in association with current cardioprotective techniques to improve clinical outcome in cardiac surgical patients.

Keywords

glucose τ insulin τ potassium; cardiac surgery; myocardial injury; mortality; complications; CABG; valve

Abstract

Background

The infusion of glucose-insulin-potassium (GIK) has yielded conflicting results in terms of cardioprotective effects. We conducted a meta-analysis to examine the impact of perioperative GIK infusion in early outcome after cardiac surgery.

Methods

Randomized controlled trials (RCTs) were eligible if they examined the efficacy of GIK infusion in adults undergoing cardiac surgery. The main study endpoint was postoperative myocardial infarction (MI) and secondary outcomes were hemodynamics, any complications and hospital resources utilization. Subgroup analyses explored the impact of the type of surgery, GIK composition and timing of administration. Odds ratio (OR) or mean difference (MD) with 95% confidence interval (CI) were calculated with a random-effects model.

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Results

Fifty-three studies (n=6,129) met the inclusion criteria. Perioperative GIK infusion was effective in reducing MI (k=32 OR 0.66[0.48, 0.89] p=0.0069), acute kidney injury (k=7 OR 0.57[0.4, 0.82] p=0.0023) and hospital length of stay (k=19 MD -0.89[-1.63, -0.16] days p=0.0175). Postoperatively, the GIK-treated group presented higher cardiac index (k=14 MD 0.43[0.29, 0.57] L/min p<0.0001) and lesser hyperglycemia (k=20 MD -30[-47, -13] mg/dL p=0.0005) than in the usual care group. The GIK-associated protection for MI was effective when insulin infusion rate exceeded 2 mUI/kg/min and after coronary artery bypass surgery. Certainty of evidence was low given imprecision of the effect estimate, heterogeneity in outcome definition and risk of bias.

Conclusion

Perioperative GIK infusion is associated with improved early outcome and reduced hospital resource utilization after cardiac surgery. Supporting evidence is heterogenous and further research is needed to standardize the optimal timing and composition of GIK solutions.

Introduction

Each year, cardiac surgery is performed worldwide in ~1.5 million individuals with ischemic, congenital and valvular disorders.[1] Over time, outcomes after cardiac surgery have improved along with better preoperative patient preparation, progress in surgical and anesthetic management as well as cardioprotective protocols.[2ς5] Perioperative ischemia-reperfusion

injuries and the release of free radicals and inflammatory mediators are incriminated in causing ventricular dysfunction that either resolves spontaneously or requires cardiovascular drug support and occasionally circulatory assistance.[6–8] Importantly, cardiac complications such as postoperative myocardial infarction (MI) and heart failure are known predictors of increasing medical costs, poor survival and decreased quality of life.[9,10] Among various cardioprotective protocols, the infusion of glucose-insulin-potassium (GIK) has been studied extensively. In animal models, GIK has been shown effective in reducing the extent of MI and the occurrence of ventricular arrhythmias while preserving ventricular function.[11] These cardioprotective effects are mediated by pleiotropic glucose-dependent and -independent mechanisms of insulin involving preferential high-energy substrate production from glucose metabolism as well as upregulation of the reperfusion injury salvage kinase pathway.[12] Since its introduction in 1962[13], GIK has failed to show conclusive clinical cardioprotective effects following percutaneous coronary intervention whereas favorable results have been reported after cardiac surgery.[12,14] In previous systematic reviews,[15–18] the interactions between GIK therapy and confounding factors (*e.g.* diabetes mellitus, type of surgery, glycemia or timing and composition of GIK infusion) have not been examined. Hence, our meta-analysis addresses these issues and provides an up-to-date review of the impact of GIK on early postoperative outcome.

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Material and Methods

Search Strategy

This review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines and the Cochrane methodology as well as in agreement with a preregistered protocol (PROSPERO CRD42019117728).[19,20] Ethical review board approval was waived due to the absence of new data collection. Minor deviations from the protocol are reported in a Supplemental file (S1). Three investigators (R.S., A.H. and A.P.) independently searched MEDLINE, EMBASE and the Cochrane Central Register of Clinical Trials from inception to September 19th, 2022. The search strategy aimed to select RCTs with the following terms: glucose-insulin-potassium, GIK, cardiac surgery, cardiopulmonary bypass, CPB, coronary artery bypass surgery, CABG, valve (S2). Additional articles were identified by manual review of the references of included studies.

Study Selection

Search results were examined at the abstract level and the full-text version was retrieved if relevant. Eligibility criteria were defined following the PICOS approach: (P) adult patients scheduled for elective or emergent cardiac surgery with or without cardio-pulmonary bypass (CPB); (I) use of GIK in the perioperative period; (C) usual care or placebo, (O) MI and (S) RCT. Exclusion criteria were inclusion of pediatric cases, studies with overlapping population or irrelevant study endpoints. Four authors (A.H, R.S, A.P., and G.K-B.) independently made the final assessment for inclusion into the analysis and disagreements were resolved through

consensus or by third party adjudication (M.L.). If documents did not contain MI data or were unavailable as full-texts, the corresponding authors were contacted for further information. No language restriction was imposed.

Data Abstraction

The relevant information was extracted from each selected study by a single author (R.S.) and checked by two others (A.P. and G.K-B.), disagreements being resolved by a fourth author (A.H.). Sources of clinical heterogeneity were also extracted according to the same process (*i.e.* study design, clinical setting, inclusion/exclusion criteria. Study characteristics were collected regarding demographic data, the type of surgery, the duration of surgery as well as GIK composition (dose of insulin and glucose) and timing of administration (before, during or/and after CPB). The primary outcome was postoperative MI and secondary outcomes were in-hospital mortality, the postoperative occurrence of stroke, acute kidney injury (AKI), atrial fibrillation (AF), ventricular fibrillation (VF), any infections, postoperative gylcemia, cardiac index, the need for pharmacological or mechanical circulatory support as well as the duration of mechanical ventilation, intensive care unit (ICU) and hospital stay.

Quality Assessment

Two authors (R.S. and A.P.) independently assessed the internal validity of included trials according to the Cochrane Collaboration methodology (risk of bias 1 tool), namely: risk of bias associated to the random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data, selective

reporting and other biases.[20] Studies were rated as low, unclear, or high risk of bias. Included trials were rated as low risk of bias when five or more evaluation domains were judged as low risk of bias.[21] Studies that did not detail allocation concealment, blinding of participants and personnel or random sequence generation were graded as unclear.

The certainty of evidence was assessed using GRADE: the grading of recommendations assessment, development and evaluation framework.[22]

Statistical Analysis

Odds ratio (OR) or mean difference (MD) with 95% confidence intervals (95%CI) were reported. Random effects models were used in all cases. Between-study variance for binary analyses was assessed using the Paule-Mandel estimator since the DerSimonian-Laird estimator is known to be unreliable with sparse data.[23] Continuous models used the DerSimonian-Laird estimator. Prediction intervals were computed for all models. Heterogeneity was assessed using /2ŏKlI·yŜåă v I·yŘ ůKŜ Lч ØI·fdzŜ ! ft Y2ŘŜfă dzăŜŘ I· Ŏ2yűλyűzλúè correction of 0.5 at each step, except for Peto models. The analysis was performed using R 4.0.4 with package "meta".[24,25] Analysis of the primary outcome was stratified by GIK timing, composition, insulin infusion rate (cutoff 2 mUI/kg/min),[11,26,27] presence of diabetes mellitus and type of surgical procedure (coronary artery bypass, valve or combined surgery). Sensitivity assessments were performed using both fixed and random effects models for continuous meta-analyses, while Peto models were used for binary meta-analyses. Small-study effect for the primary outcome was investigated by the trim-and-fill method.[28]

Results

After removing 3,659 duplicates and adding 7 studies through manual search 2,647 citations were identified, of which 2,576 abstracts and 11 full-text articles were considered ineligible (S3).[6,29ç38] A total of 53 RCTs involving 6,129 participants were included in the meta-analysis (figure 1). Additional information was obtained from corresponding authors regarding 8 RCTs.[39ç46]

As reported in table 1, studies were published between 1977 and 2021, were conducted in 21 countries and included CABG surgery: (39 RCTs),[43ç81] valve surgery (4 RCTs)[82ç85] and combined procedures (10 RCTs).[39ç42,86ç91] The median of the mean times of CPB and aortic cross-clamping (AXC) were respectively 99 min (ranging from 47 to 167 min) and 59 min (ranging from 38 to 101 min). Patients with diabetes mellitus were enrolled in 31 RCTs. At the evaluation of risk of bias, 8 studies were rated at low risk,[41,42,57,58,68,88ç90] 5 with unclear risk [45,62,66,69,70] and 40 trials at high risk of bias.[39,40,43,44,46ç56,59ç61,63ç65,67,71ç87,91] The risks of bias assessment are summarized in figure 2 and detailed in a supplementary file (S4).

The proportion of participants with a MI was 5.3% and 8.2% in the GIK and control groups, respectively. As illustrated in figure 3, the GIK infusion was associated with a decrease in MI (k=32 OR 0.66[0.48, 0.89] p=0.0069 I^2=0%).[41,42,45,47,49,51,54ç58,61,63,65,67ç71,75ç81,83,88,90,91] The funnel plot for the primary analysis did not reveal a significant publication bias. A sensitivity cumulative meta-analysis with Peto OR yielded unchanged results (k=32 OR 0.58[0.42, 0.79] p=0.0007 I^2=11%). Adjustment for small-study effect left results unchanged (k=32 OR 0.66[0.48,

et al. 1993	ny	6)/ 63(7)			/64(7)	44(11)	CABG S	mUI/kg/min regular insulin, glucose, K 70 mEq/L	
Brodi n et al. 1993	Swede n	60(NA) / 57(NA)	(7/0) / (4/3)	Mixe d	NA	81(40)/ 55(21)	CABG S	22.5 mUI/kg/min insulin, 30% glucose, K 2000 mEq/L	preop
Brue mmer et al. 2002	UK	64(10)/ 66(10)	(19/ 0)/ (15/ 5)	No	NA	51(14)/ 45(12)	CABG S	2.5 mUI/kg/min insulin, 50% glucose, K 160 mEq/L	preop, cpb, posto p
Celka n et al. 2006	Turke y	58(11)/ 56(11)	NA	No	NA	70(15)/ 64(22)	CABG S	3.3 mUI/kg/min insulin, 30% dextrose, K 160 mEq/L	preop, posto p
Dunca n et al. 2015	USA	70(9)/ 70(11)	(36/ 13)/ (31/ 17)	mix ed	59(15)/ 64(9)	NA	Comb ined	5 mUI/kg/min insulin, 20% dextrose, K 40 mEq/L, PO 120 mEq/L	preop, cpb, posto p
Dunca n et al. 2018	USA	66(11)/ 66(11)	(520 /189 /(54 6/18 4)	mix ed	NA	80(33)/ 81(31)	Comb ined	5 mUI/kg/min insulin, 20% dextrose, K 40 mEq/L	NA
Ellenb erger et al. 2018	Switze rland	71(11)/ 72(11)	(73/ 80)/ (37/ 32)	mix ed	43(10)/ 47(9)	79(36)/ 76(33)	Comb ined	4.8 mUI/kg/min rapid insulin, 40% glucose, K 10 mEq/L	preop
Forou ghi et al.	Iran	61(1)/ 59(	(21/ 15)/ (17/	No	NA	62(19)/ 65(14	CABG S	1.3 mUI/kg/min regular insulin, 10% dextrose, K	preop, cpb

2012		1)	13)			)		80 mEq/L,	
Girard et al. 1992	France	58(9)/56(10)	(27/13)/(29/11)	mixed	NA	48(16)/45(16)	CABGS	insulin, 30% glucose, K 70 mEq/L	preop
Haider et al. 1984	Austria	58(NA)/52(NA)	NA	mixed	NA	35(NA)/39(NA)	Valve	16.7 mUI/kg/min rapid insulin, 33% glucose, K 70 mEq/L	preop
Hallhagen et al. 1992	Sweden	57(3)/56(4)	NA	No	NA	61(6)/66(8)	CABGS	22.7 mUI/kg/min rapid insulin, 40% glucose, K 100 mEq/L	postop
Howell et al. 2011	UK	70(10)/70(7)	(67/43)/(77/30)	No	NA	NA	Combined	NA	NA
Jovic et al. 2009	Serbia	NA	NA	mixed	NA	44(NA)/39(NA)	CABGS	1.1 mUI/kg/min insulin, 20% glucose, K 80 mEq/L	preop, postop
Jovic et al. 2009	Serbia	NA	NA	mixed	NA	47(NA)/39(NA)	CABGS	0.3 mUI/kg/min insulin, 10% glucose, K 80 mEq/L	preop, postop
Kjellman et al. 2000	Sweden	64(3)/63(2)	(14/0)/(14/0)	No	47(4)/42(6)	64(3)/64(3)	CABGS	66.7 mUI/kg/min insulin, 30% glucose, K 40 mEq/L	cpb
Koskenkari	Finland	67(8)/	(13/6)	No	NA	93(22)/	CABG	16.7 mUI/kg/min	cpb, posto

et al. 2006		67(8)	/(15/5)			84(13)	S	rapid insulin, 30% glucose, K 20 mEq/L	p
Laiq et al. 2015	Pakistan	NA	NA	Yes	NA	48(2)/45(1)	CABGS	1.5 mUI/kg/min regular insulin, 5% dextrose, K 80 mEq/L	preop, cpb, postop
Lazar et al. 1997	USA	60(NA)/65(NA)	(11/4)/(10/5)	No	NA	44(3)/41(2)	CABGS	regular insulin, 30% dextrose, K 80 mEq/L	preop, postop
Lazar et al. 2000	USA	65(9)/65(11)	(10/10)/(11/9)	Yes	41(10)/40(10)	47(12)/42(11)	CABGS	1.1 mUI/kg/min regular insulin, 5% dextrose, K 80 mEq/L	preop, postop
Lazar et al. 2004	USA	64(1)/64(2)	(42/46)/(30/23)	Yes	42(1)/41(2)	48(2)/44(1)	CABGS	1.1 mUI/kg/min regular insulin, 5% dextrose, K 80 mEq/L	preop, postop
Lell et al. 2002	USA	62(9)/57(10)	(11/10)/(13/7)	mixed	50(12)/41(16)	34(13)/31(14)	CABGS Off-pump	regular insulin, 25% glucose, K 80 mEq/L	preop, cpb, postop
Lindholm et al. 2001	Sweden	72(8)/74(7)	(8/8)/(5/9)	mixed	57(12)/57(15)	84(32)/114(45)	Combined	285.7 mUI/kg/min rapid insulin, 30% glucose, no K	postop
Lolley et al. 1978	USA	56(NA)/54(NA)	(84/30)/(126/31)	mixed	NA	48(16)/44(15)	CABGS	5.7 mUI/kg/min regular insulin, 5% dextrose, K 22.5 mEq/L	cpb

Lolley et al. 1985	USA	56(1)/54(1)	(40/13)/(40/9)	mixed	62(2)/64(2)	47(2)/42(2)	CABGS	4.8 mUI/kg/min regular insulin, 5% glucose, K 20 mEq/L	cpb
Nilsson et al. 1987	Sweden	52(NA)/64(NA)	(5/1)/(5/3)	No	NA	68(10)/78(7)	Combined	2.5 mUI/kg/min rapid insulin, 40% glucose, K 100 mEq/L, PO 120 mEq/L	postop
Nilsson et al. 1987	Sweden	56(NA)/64(NA)	(4/2)/(5/3)	No	NA	87(7)/78(7)	Combined	5 mUI/kg/min rapid insulin, 40% glucose, K 100 mEq/L, PO 120 mEq/L	postop
Nilsson et al. 1987	Sweden	60(NA)/64(NA)	(8/0)/(5/3)	No	NA	80(7)/78(7)	Combined	16.7 mUI/kg/min rapid insulin, 40% glucose, K 100 mEq/L, PO 120 mEq/L	postop
Oldfield et al. 1986	South Africa	38(27)/41(19)	(6/14)/(8/15)	mixed	NA	67(8)/63(6)	Valve	0.2 mUI/kg/min insulin, 20% glucose, K 45 mEq/L	preop
Quinn et al. 2006	UK	64(9)/64(9)	NA	No	NA	49(16)/48(18)	CABGS	2.1 mUI/kg/min rapid insulin, 40% dextrose, K 80 mEq/L	preop, cpb, postop
Ranasinghe et al. 2006	UK	64(9)/64(9)	(137/20)/(132/28)	No	NA	49(15)/47(18)	CABGS	0.9 mUI/kg/min rapid insulin, 40% dextrose, K 80 mEq/L	preop, cpb, postop

Ray et al. 1977	USA	NA	NA	mixed	NA	NA	CABGS	700 mUI/kg/min insulin, 10% glucose, K 120 mEq/L	cpb
Roh et al. 2015	Korea	61(11)/64(11)	(27/26)/(24/29)	mixed	62(10)/62(11)	96(41)/95(35)	Combined	1.7 mUI/kg/min insulin, 30% glucose, K 80 mEq/L	preop
Rujirojindakul et al.2014	Thailand	52(19)/55(15)	(55/44)/(57/43)	mixed	NA	62(24)/60(23)	Combined	5 mUI/kg/min insulin, 25% glucose, K 400 mEq/L	preop, cpb, postop
Salerno et al. 1980	Canada	NA	NA	No	NA	48(NA)/45(NA)	CABGS	0.3 mUI/kg/min insulin, 10% dextrose, K 40 mEq/L	preop
Sato et al. 2011	Canada	64(8)/65(11)	(14/6)/(15/5)	mixed	54(8)/55(8)	84(29)/82(30)	CABGS	5 mUI/kg/min insulin, 20% glucose, K NA, PO 120 mEq/L	NA
Seied et al. 2010	Iran	58(10)/61(8)	(9/16)/(14/6)	Yes	51(8)/50(12)	60(15)/61(17)	CABGS	1.1 mUI/kg/min regular insulin, 5% dextrose, K 80 mEq/L	preop, cpb, postop
Shim et al. 2006	Korea	64(9)/59(10)	(12/31)/(11/28)	Mixed	59(13)/62(12)	NA	CABGS	3.1 mUI/kg/min regular insulin, 50% dextrose, K 160 mEq/L	preop, cpb, postop
Shim et al. 2013	Korea	63(NA)/55(	(20/13)/(23/10)	Mixed	35(11)/39(9)	NA	CABGS Off-	3.3 mUI/kg/min regular insulin, 50% glucose, K 160 mEq/L	preop, cpb, postop

		NA)					pump		
Smith et al. 2002	UK	64(8)/68(8)	(9/2)/(10/2)	Mixed	NA	45(14)/40(16)	CABGS Off-pump	0.8 mUI/kg/min rapid insulin, 50% dextrose, K 250 mEq/L	preop, cpb, postop
Straus et al. 2013	Bosnia	62(8)/61(7)	(35/15)/(29/21)	Yes	50(NA)/45(NA)	42(NA)/39(NA)	CABGS	NA	cpb
Svensson et al. 1989	Sweden	61(4)/58(2)	NA	Mixed	50(7)/58(4)	65(7)/57(6)	CABGS	251.7 mUI/kg/min rapid insulin, 40% glucose, K 100 mEq/L, PO 120 mEq/L	cpb, postop
Szabo et al. 2001	Sweden	58(6)/56(9)	(9/1)/(7/3)	Yes	NA	45(22)/46(16)	CABGS	16.7 mUI/kg/min rapid insulin, 30% glucose, no K, PO 160 mEq/Lmmol/L	postop
Tsang et al. 2007	USA	64(9)/67(7)	(12/2)/(15/2)	Mixed	61(11)/58(14)	43(8)/42(9)	CABGS	0.8 mUI/kg/min regular insulin, 30% dextrose, K 80 mEq/L	preop, postop
Tuneir et al. 1998	Turkey	38(NA)/35(NA)	(4/11)/(3/12)	Mixed	55(NA)/52(NA)	76(NA)/73(NA)	Valve	0.2 mUI/kg/min insulin, 20% glucose, K 45 mEq/L	preop
Turkoz et al. 2000	Turkey	64(2)/60(	(10/5)/(13/	No	40(3)/41(1)	63(5)/63(6)	CABGS	2.3 mUI/kg/min insulin, 30% dextrose, K 160	preop

		2)	3)					mEq/L	
Visser et al. 2005	Netherlands	63(NA)/62(NA)	(8/2)/(10/1)	No	NA	57(34)/57(17)	CABGS	1.7 mUI/kg/min rapid insulin, 30% glucose, K 80 mEq/L, PO 240 mEq/L	preop, cpb, postop
Wallin et al. 2003	Sweden	66(9)/63(9)	(8/1)/(7/2)	No	NA	87(24)/87(24)	Combined	9.2 mUI/kg/min insulin, glucose, K 140 mEq/L	preop, cpb, postop
Wistbacka et al. 1992	Finland	56(7)/55(8)	(13/3)/(14/2)	No	56(5)/59(7)	104(31)/93(27)	CABGS	2 mUI/kg/min rapid insulin, 17% glucose, K 16.8 mEq/L	preop
Wistbacka et al. 1994	Finland	55(10)/57(9)	(16/4)/(16/4)	No	58(13)/57(11)	100(36)/102(23)	CABGS	1.2 mUI/kg/min rapid insulin, 20% glucose, K 147 mEq/L, PO 94 mEq/L	preop, cpb, postop
Zhao et al. 2020	China	42(14)/42(14)	(199/266)/(206/25)	No	NA	51(30)/52(31)	Combined + Congental	1.1 mUI/kg/min regular insulin, 20% glucose, K 80 mEq/L	preop, cpb, postop
Zuurbier et al. 2008	Netherlands	63(NA)/64(NA)	(18/5)/(18/3)	No	NA	62(29)/56(17)	CABGS	1.7 mUI/kg/min rapid insulin, 30% glucose, K 80 mEq/L, PO 240 mEq/L	preop, cpb, postop

AXC, aortic cross clamping; CABGS, coronary artery bypass graft surgery; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; M/F, male/female

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Table 2: Meta-Analyses of Secondary Endpoints.

	N RCTs (N participants)	Controls	GIK	TE (95\%CI)	I^2 (p-value)
In-hospital Mortality	38 (4,599)	58/2,338	36/2,261	OR=0.71 (0.49 to 1.04)	0% (0.08)
AKI	7 (2,939)	85/1,481	49/1,458	OR=0.57 (0.4 to 0.82)	0% (0.002)
Atrial Fibrillation	27 (4,664)	587/2,366	455/2,298	OR=0.68 (0.5 to 0.92)	52% (0.013)
Cardiac Index [L/min]	14 (707)	2.6(0.9)	3.1(0.9)	MD=0.43 (0.29 to 0.57)	79% (<0.001)
Glycemia [mg]	20 (2,024)	182.4(66.5)	152.5(46.8)	MD=-29.84 (-46.63 to -13.06)	99% (<0.001)
Hospital LOS [d]	19 (1,852)	9(3.3)	8.1(3.2)	MD=-0.89 (-1.63 to -0.16)	93% (0.018)
ICU LOS [h]	20 (4,023)	29.8(23.8)	24.6(24.4)	MD=-5.17 (-7.35 to -2.99)	99% (<0.001)
Infection	11 (3,201)	139/1,613	112/1,588	OR=0.78 (0.5 to 1.23)	41% (0.283)
Mechanical Ventilation	16 (2,247)	13.6(6.3)	11.9(4.8)	MD=-1.68 (-2.87 to -0.5)	97% (0.005)
Stroke	8 (1,743)	18/875	17/868	OR=0.96	0% (0.916)

				(0.48 to 1.92)	
Ventricular Fibrillation	11 (1,758)	210/903	159/855	OR=0.87 (0.56 to 1.35)	0% (0.527)

RCT, randomized control trial; N, participants count; GIK, insulin-glucose-potassium; TE, treatment effect (odds ratio [OR] or mean difference [MD]); 95%CI, 95% confidence interval; AKI, acute kidney injury; AF, atrial fibrillation; CI, cardiac index; LOS, length of stay; ICU, intensive care unit; MVT, mechanical ventilation time; VF, ventricular fibrillation.