Effects and mechanisms of glucose-insulin-potassium on post-procedural myocardial injury after percutaneous coronary intervention

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Abstract

Objective To evaluate the effects and mechanisms of glucose-insulin-potassium (GIK) on post-procedural myocardial injury (PMI) after percutaneous coronary intervention (PCI).

Methods A total of 200 non-diabetic patients with documented coronary heart disease (CHD) were divided into the Group GIK and Group G, with 100 patients in each group. Patients in Group G were given intravenous infusion of glucose solution 2 hours before PCI. As compared, patients in Group GIK were given GIK.

Results Both post-procedural creatine phosphokinase isoenzyme MB (CK-MB; 62.1 ± 47.8 vs. 48.8 ± 52.6 U/L, P = 0.007) and cTnI (0.68 ± 0.83 vs. 0.19 ± 0.24 ng/mL, P < 0.001) in Group GIK were significantly higher than those in Group G. In Group G, 9.0% and 4.0% of patients had post-procedural increases in CK-MB 1-3 times and > 3 times, which were significantly lower than those in Group GIK (14.0% and 7.0%, respectively; all P values < 0.01); 13.0% and 7.0% of patients had post-procedural increases in cTnI 1-3 times and > 3 times, which were also significantly lower than those in Group GIK (21.0% and 13.0%, respectively; all P < 0.001). Pre-procedural (10.2 ± 4.5 vs. 5.1 ± 6.3, P < 0.001) and post-procedural rapid blood glucose (RBG) levels (8.9 ± 3.9 vs. 5.3 ± 5.6, P < 0.001) in Group G were higher than those in Group GIK. In adjusted logistic models, usage of GIK (compared with glucose solution) remained significantly and independently associated with higher risk of post-procedural increases in both CK-MB and cTnI levels. Pre-procedural RBG levels < 5.0mmol/L were significantly associated with higher risk of post-procedural increases in both CK-MB and cTnI levels.

Conclusions In non-diabetic patients with CHD, the administration of GIK may increase the risk of PMI due to hypoglycemia induced by GIK.

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Keywords: Glucose-insulin-potassium; Post-procedural myocardial injury; Percutaneous coronary intervention; Hypoglycemia

1 Introduction

Post-procedural myocardial injury (PMI) is one of the major complications of percutaneous coronary intervention (PCI), defined as creatine phosphokinase isoenzyme MB (CK-MB) and/or cardiac troponin (cTn) elevation above the 99th centile upper reference limit (URL).[1–3] Long-term follow-up studies revealed that elevated CK-MB and cTn significantly increased the risk of adverse cardiovascular events in patients underwent PCI.[1–6] How to reduce PMI is an ongoing topic of concern in the field of cardiovascular research in recent years. In 1962, Sodi-pallares, et al.[7] first proposed that the solution of glucose-insulin-potassium (GIK), namely the polarized fluid, could be used to treat myocardial ischemia/reperfusion injury (IRI). Opie, et al.[8–13] further explained the probable mechanisms of its cardioprotection and proposed the concept of metabolic therapy. However, with a large number of basic and clinical studies, the efficacy of GIK is still controversial and the exact mechanisms are unclear. GIK has been reported to cause hypoglycemic events.[14–29] We found that mild to
moderately decreased fasting plasma glucose levels (≤ 5 mmol/L) might be associated with a relative increase in risk of mortality, especially in patients with acute coronary syndrome (ACS).\[^{30–32}\] Also, we have reviewed the effects of hypoglycemia on cardiovascular events from the perspective of physiology and pathophysiology.\[^{33}\] This study aimed to evaluate the effects and mechanisms of GIK compared with the solution of glucose on PMI. We hypothesized that the administration of GIK might increase the risk of PMI due to hypoglycemia induced by GIK.

2 Methods

2.1 Study design and patient population

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the Ethics Review Boards of each participating institution. Written informed consent was obtained from each patient. A total of 200 patients with documented coronary heart disease (CHD) were selected from September 1, 2018 to December 31, 2019 in three tertiary medical centers. According to the random number table, all patients were divided into the experimental group (Group GIK) and the control group (Group G), with 100 patients in each group. Inclusion criteria were: (1) age at least 18 years; (2) patients with significant coronary artery obstruction in at least one major vessel (stenosis > 50% in left main or > 70% in any other epicardial artery); (3) all patients receiving successful PCI without significant residual stenosis in the target vessel; (4) without history of diabetes and/or hypoglycemic drugs usage; and (5) hemoglobin A1c (HbA1c) < 6.5% and fasting blood glucose < 7.0 mmol/L before PCI. Patients with hemodynamic or cardiac electrical instability, contraindications for PCI, significant comorbidities, or unable to give informed consent were excluded from the study. Note that inclusion in other clinical trials did not preclude enrollment in this study.

Patients in Group G were given intravenous infusion of 500 mL 10% glucose solution 2 h before PCI. As compared, patients in Group GIK were given intravenous infusion of GIK (10% glucose solution 500 mL + 10% potassium chloride 10 mL + insulin 12 U) 2 h before PCI. All procedures were performed by experienced senior physicians who were qualified for PCI. Rapid blood glucose (RBG) levels were measured immediately before and after PCI in all patients. Throughout this article, any reference to plasma myocardial injury biomarkers levels, including CK-MB and cTn, will pertain to that obtained at baseline (after an overnight fast of at least 8 h within 24 h of admission) and 24 h after PCI. During hospitalization, patients were treated with aspirin, clopidogrel, ticagrelor, low molecular weight heparin (LMWH), statins, beta-blockers, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and others according to practice guidelines. As is their routine, center staff abstracted demographic, clinical, and procedural data.

2.2 Statistical analysis

All case record form data were entered into Epidata 3.1 databases (Epidata Association) by different people. Analyses were conducted with SPSS statistical software, version 22.0 (IBM Inc.). Continuous variables will be recorded as mean ± SD. Categorical variables will be recorded as counts. The difference between groups will be analyzed using the student t-test to compare the mean values of biomarker abnormalities. Categorical variables will be compared between groups using the chi-square test. All statistical tests were two-sided and P-values of < 0.05 was considered to be statistically significant.

3 Results

3.1 Baseline demographic and clinical characteristics

Overall, the mean age of the cohort was 60.6 ± 10.8 years old, and 111 (55.5%) patients were males. There were 24 (12.0%), 11 (5.5%), 99 (44.5%) and 37 (18.5%) patients with the history of previous myocardial infarction, stroke, hypertension and hyperlipidemia, respectively. Among all patients, 8.5% were type A lesions, 52.0% type B lesions, and 39.5% type C lesions. As shown in Table 1, there were no significant differences in all baseline demographic and clinical characteristics between groups.

3.2 Comparison of fasting plasma glucose and rapid blood glucose levels between groups

As shown in Table 2, there were no significant differences in baseline fasting plasma glucose (FPG) levels between Group G (5.3 ± 0.6 mmol/L) and Group GIK (5.3 ± 0.5 mmol/L), P = 0.784. However, pre-procedural (10.2 ± 4.5 vs. 5.1 ± 6.3, P < 0.001) and post-procedural RBG levels (8.9 ± 3.9 vs. 5.3 ± 5.6, P < 0.001) in Group G were much higher than those in Group GIK. Compared with Group G, there were 4 (4.0% vs. 0, P < 0.001) and 3 (3.0% vs. 0, P < 0.001) patients in Group GIK with pre- and post-procedural RBG levels > 5.0 mmol/L, respectively. Furthermore, in Group GIK the minimum pre- and post-procedural RBG levels were 4.0 and 3.6 mmol/L, respectively.
Table 1. Baseline demographic and clinical characteristics.

| Characteristics                        | Group G (n = 100) | Group GIK (n = 100) | P-value |
|----------------------------------------|-------------------|---------------------|---------|
| Age, yrs                               | 61.0 ± 10.3       | 60.2 ± 10.2         | 0.306   |
| Male                                   | 55 (55.0%)        | 56 (56.0%)          | 0.724   |
| Hypertension                           | 48 (48.0%)        | 51 (51.0%)          | 0.117   |
| Hyperlipidemia                         | 19 (19.0%)        | 18 (18.0%)          | 0.562   |
| Prior myocardial infarction            | 11 (11.0%)        | 13 (13.0%)          | 0.193   |
| Prior stroke                           | 6 (6.0%)          | 5 (5.0%)            | 0.891   |
| HbA1c, %                               | 5.5 ± 1.1         | 5.6 ± 1.4           | 0.448   |
| Creatinine, μmol/L                     | 70.8 ± 20.3       | 72.4 ± 19.5         | 0.146   |
| LDL-C, mmol/L                          | 2.6 ± 0.8         | 2.6 ± 0.9           | 0.375   |
| HDL-C, mmol/L                          | 1.0 ± 0.4         | 1.0 ± 0.3           | 0.571   |
| K+, mmol/L                             | 4.3 ± 0.5         | 4.2 ± 0.6           | 0.490   |
| LVEF                                   | 58.2% ± 11.3%     | 56.7% ± 10.8%       | 0.104   |

Type of lesions in coronary artery disease
- Type-A lesion: 9 (9.0%) vs. 8 (8.0%)
- Type-B lesion: 51 (51.0%) vs. 53 (53.0%)
- Type-C lesion: 40 (40.0%) vs. 39 (39.0%)

Aspirin: 99 (99.0%) vs. 100 (100.0%)
Clopidogrel: 87 (87.0%) vs. 83 (83.0%)
Ticagrelor: 13 (13.0%) vs. 17 (17.0%)
LMWHs: 51 (51.0%) vs. 46 (46.0%)
Statins: 97 (97.0%) vs. 99 (99.0%)
β-blockers: 76 (76.0%) vs. 80 (80.0%)
ACEIs: 49 (49.0%) vs. 46 (46.0%)
ARBs: 30 (30.0%) vs. 28 (28.0%

Data are presented as mean ± SD or n (%). ACEIs: angiotensin-converting enzyme inhibitors; ARBs: angiotensin II receptor blockers; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; LMWHs: low molecular weight heparin; LVEF: left ventricular ejection fraction.

Table 2. Comparison of fasting plasma glucose and rapid blood glucose levels between groups.

| Characteristics                        | Group G, n = 100 | Group GIK, n = 100 | P-value |
|----------------------------------------|------------------|-------------------|---------|
| Baseline FPG, mmol/L                   | 5.3 ± 0.6        | 5.3 ± 0.5         | 0.784   |
| Pre-procedural RBG, mmol/L             | 10.2 ± 4.5       | 5.1 ± 6.3         | <0.001  |
| Post-procedural RBG, mmol/L            | 8.9 ± 3.9        | 5.3 ± 5.6         | <0.001  |
| Pre-procedural RBG < 5.0 mmol/L        | 0                | 4 (4.0%)          | <0.001  |
| Post-procedural RBG < 5.0 mmol/L       | 0                | 3 (3.0%)          | <0.001  |

Data are presented as mean ± SD or n (%). FPG: fasting plasma glucose; GIK: glucose-insulin-potassium; RBG: rapid blood glucose.

3.3 Comparison of myocardial injury biomarkers levels between groups

As shown in Table 3, there were no significant differences in pre-procedural myocardial injury biomarkers levels between Group G and Group GIK (CK-MB: 18.0 ± 11.2 vs. 17.9 ± 14.5 U/L, P = 0.336; cTnI: 0.01 ± 0.02 vs. 0.02 ± 0.02 ng/mL, P = 0.483). However, both post-procedural CK-MB (62.1 ± 47.8 vs. 48.8 ± 52.6 U/L, P = 0.007) and cTnI levels (0.68 ± 0.83 vs. 0.19 ± 0.24 ng/mL, P < 0.001) in Group GIK were significantly higher than those in Group G.

In Group G, 9.0% and 4.0% of patients had post-procedural increases in CK-MB 1 to 3 times and > 3 times above the URL (25U/L), which were significantly lower than those in Group GIK (14.0% and 7.0%, respectively; all P < 0.01); 13.0% and 7.0% of patients had post-procedural increases in cTnI 1 to 3 times and > 3 times above the URL (0.05 ng/mL), which were also significantly lower than those in Group GIK (21.0% and 13.0%, respectively; all P values < 0.001).

3.4 Association between usage of GIK or glucose solution with post-procedural increases in myocardial injury biomarkers levels

To evaluate the association between usage of GIK or
3.042, procedural increases in cTnI 1 to 3 times: 2.150, 95% CI: 1.539–1.548, 95% CI: 1.040–1.048.

Association between glucose levels with post-procedural increases in CK-MB levels. Increases in both CK-MB and cTnI levels above the URL (OR for post-procedural increases in CK-MB >3 times: 1.443, 95% CI: 1.260–1.629) were significantly associated with higher risk of post-procedural complications, pre-procedural RBG levels < 5.0 mmol/L were independently associated with higher risk of post-procedural complications.

After adjustment of baseline demographic and clinical characteristics (including age, gender, previous myocardial infarction, stroke, hypertension, fasting plasma glucose, HbA1c, creatinine, LDL-C, HDL-C, LVEF, type of lesions in coronary artery disease, and pharmacological treatment during hospitalization) in logistic models, usage of GIK (compared with glucose solution) remained significantly and independently associated with higher risk of post-procedural complications in both CK-MB and cTnI levels > 3 times above the URL (OR for post-procedural increases in CK-MB >3 times: 1.252, 95% CI: 1.097–1.869, P = 0.018; OR for post-procedural increases in cTnI >3 times: 1.443, 95% CI: 1.260–2.794, P = 0.014). Furthermore, usage of GIK tended to, but not significantly, be associated with higher risk of post-procedural complications in cTnI levels 1 to 3 times above the URL (OR: 1.175, 95% CI: 0.974–1.901, P = 0.062).

3.5 Association between glucose levels with post-procedural increases in myocardial injury biomarkers levels

Whether in unadjusted or adjusted models, baseline FPG level was not significantly associated with post-procedural increases in myocardial injury biomarkers levels. After adjustment of baseline demographic and clinical characteristics (including age, gender, previous myocardial infarction, stroke, hypertension, fasting plasma glucose, HbA1c, creatinine, LDL-C, HDL-C, LVEF, type of lesions in coronary artery disease, and pharmacological treatment during hospitalization), pre-procedural RBG levels < 5.0 mmol/L were significantly associated with higher risk of post-procedural increases in both CK-MB and cTnI levels above the URL (OR for post-procedural increases in CK-MB 1–3 times: 1.548, 95% CI: 1.040–3.553, P = 0.048; OR for post-procedural increases in cTnI 1–3 times: 1.705, 95% CI: 1.317–2.342, P = 0.009; OR for post-procedural increases in CK-MB > 3 times: 2.150, 95% CI: 1.539–3.728, P = 0.002; OR for post-procedural increases in cTnI > 3 times: 2.482, 95% CI: 1.881–4.563, P < 0.001).

### Table 3. Comparison of myocardial injury biomarkers levels between groups.

| Characteristics      | Group G (n = 100) | Group GIK (n = 100) | P-value |
|----------------------|-------------------|---------------------|---------|
| Pre-procedural CK-MB, U/L | 18.0 ± 11.2       | 17.9 ± 14.5         | 0.336   |
| Pre-procedural cTnI, ng/mL | 0.01 ± 0.02      | 0.02 ± 0.02         | 0.483   |
| Post-procedural CK-MB, U/L | 48.8 ± 52.6       | 62.1 ± 47.8         | 0.007   |
| Post-procedural cTnI, ng/mL | 0.19 ± 0.24       | 0.68 ± 0.83         | <0.001  |
| Post-procedural increase in CK-MB 1–3 times, % | 9 (9.0%)       | 13 (13.0%)          | 0.008   |
| Post-procedural increase in CK-MB >3 times, % | 4 (4.0%)       | 7 (7.0%)            | 0.002   |
| Post-procedural increase in cTnI 1–3 times, % | 14 (14.0%)      | 21 (21.0%)          | <0.001  |
| Post-procedural increase in cTnI >3 times, % | 7 (7.0%)        | 13 (13.0%)          | <0.001  |

Data are presented as mean ± SD or n (%). CK-MB: creatine kinase MB; cTnI: cardiac troponin I.

Discussion

PMI, which range from mild to extreme elevation of cardiac biomarkers, can result from the common complications of PCI such as distal embolisation, side-branch occlusion, coronary dissection and disruption of collateral flow, and IRI, etc.[1–3,34–36] The incidence of PMI varies from 5% to 40%, depending on which one biomarker is detected and the time point of sampling.[1–3,34,35] Compared with CK-MB, cTnI is the more sensitive biomarkers of PMI. Levels of cTnI and cTnT will reach the peak value at about 24-h after PCI.[37] Although the incidence of adverse cardiovascular events during hospitalization in patients with CK-MB elevation was the same as that in control group, the cardiovascular mortality was significantly increased in patients with elevated CK-MB level at a mean follow-up of four years.[38] Fuchs, et al.[39] found that cTnI level > 0.45 ng/mL after PCI and simultaneously elevated CK-MB and cTnI levels were both independent predictors for adverse cardiovascular events during hospitalization. The PMI-related higher risk of adverse cardiovascular events may be affected by the following mechanisms: (1) decreased left ventricular function; (2) ventricular arrhythmias via a small reentrant circuit in the ventricle as a result of scar formation; and (3) elevation in cardiac biomarkers indicating diffuse coronary atherosclerosis.[40, 41]

In 1962, Sodi-pallares, et al.[7] first proposed that GIK could be used to treat IRI. Opie, et al.[8–13] then further explained the mechanisms of its cardioprotective effects: (1) providing more energy substrate, and promoting the uptake and utilization of glucose by cardiomyocytes with insulin assistance, so as to eventually promote the functional recovery of ischemic myocardium; (2) activating cardiomyocyte Na⁺-K⁺-ATPase to promote the uptake of K⁺, thereby...
stabilizing the polarization state of cell membrane and reducing the occurrence of arrhythmia. However, the efficacy of GIK is still controversial and the exact mechanisms are not clear. In this study, we demonstrate for the first time an independent, highly significant, and positive correlation between the usage of GIK (compared with glucose solution) with higher risk of PMI, which may be due to hypoglycemia induced by GIK.

It has been known that intensive glycemic control may increase the risk of hypoglycemia threefold in patients with diabetes, which have been overlooked or dismissed for a long time.[42] As stated by American Diabetes Association (ADA), the barrier of hypoglycemia precludes maintenance of euglycemia over a lifetime of diabetes.[43] Furthermore, non-diabetic individuals can also experience hypoglycemic events due to iatrogenic or non-iatrogenic factors.[44–47] A large number of trials tend to suggest that hypoglycemia may in fact increase cardiovascular risks and mortality in either diabetic or non-diabetic patients with CHD.[48–51] Usually, hypoglycemia is defined as blood glucose level below 3.9 mmol/L (70 mg/dL) according to the ADA.[52] Whereas, blood glucose level below 3.3 mmol/L (60 mg/dL) was also used to define hypoglycemia in some studies.[33] We reported that mild to moderately decreasing FPG levels (≤ 5 mmol/L) were associated with a relative increase in risk of all-cause mortality in diabetic or non-diabetic patients with ACS.[30–32] Multiple mechanisms may be involved in the impact of hypoglycemia on cardiovascular prognosis, including but not limited to hemodynamic changes, electrophysiological effects, prothrombotic, proinflammatory and atherogenic effects.[33]

In the present study, no severe hypoglycemia, which met the general definitions of hypoglycemia as stated above, occurred in either group. However, both pre- and postprocedural RBG levels decreased significantly in patients infused with GIK compared with glucose solution. Furthermore, there were 4.0% and 3.0% patients in Group GIK with pre- and post-procedural RBG levels < 5.0 mmol/L, which were significantly and independently associated with higher risk of post-procedural increases in myocardial injury biomarkers levels. So far, we have proved the original hypothesis that the administration of GIK may increase the risk of PMI due to hypoglycemia induced by GIK. Because of the small size and open-label design of this study, the results may have some bias and other limitations. It is inconclusive and large randomized controlled trials are needed.

In conclusion, in non-diabetic patients with CHD, the administration of GIK may increase the risk of PMI due to hypoglycemia induced by GIK.

Competing interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors’ contributions

All authors contributed to the implementation of the research, discussing the results and giving comments on the manuscript. H.Y.D and H.P contributed to the analysis of the results and writing of the manuscript. Y.S.W, Z.Y.J and Z.Y.X contributed to the design, Y.S.W and Z.Y.J reviewed/edited/proved the manuscript.

References

1. Abu SH, Wohlleben D, Vafaie M, et al. Coronary angiographyrelated myocardial injury as detected by high-sensitivity cardiac troponin T assay. EuroIntervention 2016; 12: 337–344.
2. Malik SA, Brilakis ES, Pompili V, Chatzizisis YS. Lost and found: coronary stent retrieval and review of literature. Catheter Cardiovasc Interv 2018; 92; 50–53.
3. Zeitouni M, Silvain J, Guedeny P, et al. Periprocedural myocardial infarction and injury in elective coronary stenting. Eur Heart J 2018; 39: 1100–1109.
4. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/ AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. Circulation 2014; 130: 1749–1767.
5. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/ AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI Guideline for
Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. J Am Coll Cardiol 2016; 67: 1235–1250.

6 Lüscher TF. Optimizing percutaneous coronary interventions: Heart Team, SYNTAX II Score, physiology and imaging guidance, modern stents, and guideline-based medication. Eur Heart J 2017; 38: 3109–3113.

7 Sodi-Pallares D, Ma DE, Medrano G, et al. [Effect of glucose-insulin-potassium solutions on the electrocardiogram in acute and chronic coronary insufficiency]. Mal Cardiovasc 1962; 3: 41–79. [Article in French].

8 Opie LH. Proof that glucose-insulin-potassium provides metabolic protection of ischaemic myocardium. Lancet 1999; 353: 768–769.

9 Apstein CS, Opie LH. Glucose-insulin-potassium (GIK) for acute myocardial infarction: a negative study with a positive value. Cardiovase Drugs Ther 1999; 13: 185–189.

10 Opie LH. Glucose and the metabolism of ischaemic myocardium. Lancet 1995; 345: 1520–1521.

11 Oldfield GS, Commerford PJ, Opie LH. Effects of preoperative glucose-insulin-potassium on myocardial glycogen levels and on complications of mitral valve replacement. J Thorac Cardiovasc Surg 1986; 91: 874–878.

12 Dalby AJ, Bricknell OL, Opie LH. Effect of glucose-insulin-potassium infusions on epicardial ECG changes and on myocardial metabolic changes after coronary artery ligation in dogs. Cardiovasc Res 1981; 15: 588–598.

13 Opie LH, Owen P. Effect of glucose-insulin-potassium infusions on arteriovenous differences of glucose of free fatty acids and on tissue metabolic changes in dogs with developing myocardial infarction. Am J Cardiol 1976; 38: 310–321.

14 Avogaro A, Bonora E, Consoli A, et al. Glucose-lowering therapy and cardiovascular outcomes in patients with type 2 diabetes mellitus and acute coronary syndrome. Diab Vasc Dis Res 2019; 16: 399–414.

15 JAW P, van Steen SCJ, Thiel B, et al. Peri-operative management of patients with type 2 diabetes mellitus undergoing non-cardiac surgery using liraglutide, glucose-insulin-potassium infusion or intravenous insulin bolus regimens: a randomised controlled trial. Anaesthesia 2018; 73: 332–339.

16 EMA S, Shulman R, Singer M. Experience using high-dose glucose-insulin-potassium (GIK) in critically ill patients. J Crit Care 2017; 41: 72–77.

17 Polderman JA, Houweling PL, Hollmann MW, et al. Study protocol of a randomised controlled trial comparing perioperative intravenous insulin, GIK or GLP-1 treatment in diabetes-PILGRIM trial. BMC Anesthesiol 2014; 14: 91.

18 Shirakawa Y. [High-dose insulin therapy]. Chudoku Kenkyu 2012; 25: 201–204. [Article in Japanese].

19 Hirsch IB, O’Brien KD. How to best manage glycaemia and non-glycaemia during the time of acute myocardial infarction. Diabetes Technol Ther 2012; 14 (Suppl 1): S22–S32.

20 Lipton JA, Can A, Akoudad S, Simoons ML. The role of insulin therapy and glucose normalisation in patients with acute coronary syndrome. Neth Heart J 2011; 19: 79–84.

21 Goyal A, Mehta SR, Diaz R, et al. Differential clinical outcomes associated with hypoglycemia and hyperglycemia in acute myocardial infarction. Circulation 2009; 120: 2429–2437.

22 Pittas AG, Siegel RD, Lau J. Insulin therapy and in-hospital mortality in critically ill patients: systematic review and meta-analysis of randomized controlled trials. JPEN J Parenter Enter Nutr 2006; 30: 164–172.

23 van der Horst IC, Timmer JR, Ottervanger JP, et al. Glucose and potassium derangements by glucose-insulin-potassium infusion in acute myocardial infarction. Neth Heart J 2006; 14: 89–94.

24 Visser L, Zuurbier CJ, Hoek FJ, et al. Glucose, insulin and potassium applied as perioperative hyperinsulinaemic normoglycaemic clamp: effects on inflammatory response during coronary artery surgery. Br J Anaesth 2005; 95: 448–457.

25 Gu W, Pagel PS, Warthier DC, Kersten JR. Modifying cardiovascular risk in diabetes mellitus. Anesthesiology 2003; 98: 774–779.

26 Bonnier M, Lönnroth P, Gudbjörnsdottir S, et al. Validation of a glucose-insulin-potassium infusion algorithm in hospitalized diabetic patients. J Intern Med 2003; 253: 189–193.

27 Wistbacka JO, Nuutinen LS, Lepojärvi MV, et al. Perioperative glucose-insulin-potassium infusion in elective coronary surgery: minor benefit in connection with blood cardioplegia. Infusionsther Transfusionsmed 1994; 21: 160–166.

28 Girard C, Quentin P, Bouvier H, et al. Glucose and insulin supply before cardiopulmonary bypass in cardiac surgery: a double-blind study. Ann Thorac Surg 1992; 54: 259–263.

29 Husband DJ, Thai AC, Alberti KG. Management of diabetes during surgery with glucose-insulin-potassium infusion. Diabet Med 1986; 3: 69–74.

30 Yang SW, Zhou YJ, Liu YY, et al. Influence of abnormal fasting plasma glucose on left ventricular function in older patients with acute myocardial infarction. Angiology 2012; 63: 266–274.

31 Yang SW, Zhou YJ, Nie XM, et al. Effect of abnormal fasting plasma glucose level on all-cause mortality in older patients with acute myocardial infarction: results from the Beijing Elderly Acute Myocardial Infarction Study (BEAMIS). Mayo Clin Proc 2011; 86: 94–104.

32 Yang SW, Zhou YJ, Hu DY, et al. Association between admission hypoglycaemia and in-hospital and 3-year mortality in older patients with acute myocardial infarction. Heart 2010; 96: 1444–1450.

33 Yang SW, Park KH, Zhou YJ. The impact of hypoglycaemia on the cardiovascular system: physiology and pathophysiology. Angiology 2016; 67: 802–809.

34 Cuculi F, Lim CC, Banning AP. Periprocedural myocardial injury during elective percutaneous coronary intervention: is it important and how can it be prevented. Heart 2010; 96: 736–740.

35 Deng KW, Shi XB, Zhao YX, et al. The effect of exogenous creatine phosphate on myocardial injury after percutaneous coronary intervention. Angiology 2015; 66: 163–168.

http://www.jgc301.com; jgc@jgc301.com | Journal of Geriatric Cardiology
Bertinchant JP, Polge A, Juan JM, et al. Evaluation of cardiac troponin I and T levels as markers of myocardial damage in doxorubicin-induced cardiomyopathy rats, and their relationship with echocardiographic and histological findings. Clin Chim Acta 2003; 329: 39–51.

Bertinchant JP, Ledermann B, Schnurz L, et al. [Diagnostic and prognostic significance of CK-MB, troponins, CRP, BNP and/or NT-proBNP in coronary angioplasty. Elevation mechanisms and clinical implications]. Arch Mal Coeur Vaiss 2007; 100: 925–933. [Article in French].

Kong TQ, Davidson CJ, Meyers SN, et al. Prognostic implication of creatine kinase elevation following elective coronary artery interventions. JAMA 1997; 277: 461–466.

Fuchs S, Kornowski R, Mehran R, et al. Prognostic value of cardiac troponin-I levels following catheter-based coronary interventions. Am J Cardiol 2000; 85: 1077–1082.

Ishibashi Y, Muramatsu T, Nakatani S, et al. Incidence and potential mechanism(s) of post-procedural rise of cardiac biomarker in patients with coronary artery narrowing after implantation of an everolimus-eluting bioreabsorbable vascular Scaffold or Everolimus-eluting metallic stent. JACC Cardiovasc Interv 2015; 8: 1053–1063.

Golisash G, Winter MP, Ayoub M, et al. A contemporary definition of periprocedural myocardial injury after percutaneous coronary intervention of chronic total occlusions. JACC Cardiovasc Interv 2019; 12: 1915–1923.

Monami M, Dicembrini I, Kundisova L, et al. A meta-analysis of the hypoglycaemic risk in randomized controlled trials with sulphonylureas in patients with type 2 diabetes. Diabetes Obes Metab 2014; 16: 833–840.

Defining and reporting hypoglycemia in diabetes: a report from the American Diabetes Association Workgroup on Hypoglycemia. Diabetes Care 2005; 28: 1245–1249.

Tsumoto T, Yamamoto-Honda R, Kajio H, et al. High risk of abnormal QT prolongation in the early morning in diabetic and non-diabetic patients with severe hypoglycemia. Ann Med 2015: 1–7.

Lheureux O, Preiser JC. Year in review 2013: Critical Care—metabolism. Crit Care 2014; 18: 571.

Eckert-Norton M, Kirk S. Non-diabetic hypoglycemia. J Clin Endocrinol Metab 2013; 98: 39A–40A.

Nirantharakumar K, Marshall T, Hodson J, et al. Hypoglycemia in non-diabetic in-patients: clinical or criminal. PLoS One 2012; 7: e40384.

Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008; 358: 2545–2559.

Patel A, MacMahon S, Chalmers J, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med 2008; 358: 2560–2572.

Moritz T, Duckworth W, Abbraia C. Veterans Affairs diabetes trial—corrections. N Engl J Med 2009; 361: 1024–1025.

de Boer IH, Sun W, Cleary PA, et al. Intensive diabetes therapy and glomerular filtration rate in type 1 diabetes. N Engl J Med 2011; 365: 2366–2376.

Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998; 352: 837–853.

Holman RR, Paul SK, Bethel MA, et al. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008; 359: 1577–1589.

Bonds DE, Miller ME, Bergenstal RM, et al. The association between symptomatological, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. BMJ 2010; 340: b4909.

Riddle MC, Ambrosius WT, Brillon DJ, et al. Epidemiologic relationships between A1C and all-cause mortality during a median 3.4-year follow-up of glycemic treatment in the ACCORD trial. Diabetes Care 2010; 33: 983–990.

Duckworth W, Abbraia C, Moritz T, et al. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med 2009; 360: 129–139.

Gerstein HC, Bosch J, Dagenais GR, et al. Basal insulin and cardiovascular and other outcomes in dysglycemia. N Engl J Med 2012; 367: 319–328.

The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993; 329: 977–986.