Positive correlation of glucose to potassium ratio with the number of bypass vessels used in coronary artery bypass grafting

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Abstract: Objective: The focus of the current study was to identify and understand the efficiency of glucose to potassium ratio (Glu-K⁺) in bypass surgery, focusing on the findings of the Coronary Artery Bypass Grafting (CABG).

Methods: The study was performed as a retrospective single medical center and longitudinal-term research study, with a five years follow-up. Glucose and potassium levels were recorded at the closest preoperative time point on the day of surgery to calculate the Glu-K⁺. Following the patients’ data analysis, CABG outcomes (n: 3556) were grouped and compared according to the Glu-K⁺ levels, including value of < 20 (n: 496), 20-40 (n: 2345), 40-60 (n: 437), and > 60 (n: 278). Results: Number of bypass vessel (P < 0.0001), carotid (P = 0.008) and peripheral arterial disorder (P = 0.013), hypertension (P < 0.0001), diabetes (P < 0.0001), hyperlipidaemia (P < 0.0001) and myocardia infarct history (P = 0.012) showed significant difference in terms of the Glu-K⁺. In the multivariate logistic regression analyses, bypass vessels showed an increasing potential with an increasing Glu-K⁺ ratio. When compared to the CABG group that had Glu-K⁺ < 20, bypass vessels count showed a 10% increase in the group that had a 20-40 range of Glu-K⁺ (P < 0.012). 22% increase was seen in the 40-60 range of Glu-K⁺ (P < 0.0001), while there was a 34% increase in the group of > 60 (P < 0.0001). Conclusion: The results of the study indicated a significant and positive strong relationship between Glu-K⁺ and CABG operations. Thus, the Glu-K⁺ ratio before CABG surgery might be useful for cardiovascular surgeons to have beneficial information about the number of bypass vessels that would need.

Keywords: Glucose to potassium ratio, bypass grafting, cardiac surgery, CABG

Introduction

In any surgery or medical application, stress-induced hyperglycemia is one of the well-known phenomena elicited by temporary insulin-resistance from both increased psychological and physiological stress [1, 2]. Thus, the peroperatively performed insulin cure alters the overall clinical outcome positively in cases undergoing bypass surgery [3] and is commonly applied due to the harmful effects of hyperglycemia [4].

Primary cardiac surgery, called coronary artery bypass graft (CABG), is one of the most robust and long-lasting stress-loaded surgeries [5]. Today, the expected gains of glucose-insulin-potassium application are the subject of research among patients with a history of cardiac surgery and myocardial infarction [1, 6]. Recent evidence has shown that maintaining the regular insulin-signalling pathway during surgery stress can have significant effects on bypass surgery [7]. With hydration and insulin treatment, as acidosis improves, potassium returns to the cell, and serum levels decrease as expected [8]. Hypokalaemia may cause serious complications such as life-threatening arrhythmia [9, 10]. If urine output is sound, potassium replacement can be initiated at the beginning of fluid therapy [11, 12]. Serum potassium concentrations should be checked every hour [13]. Hence, electrocardiographic, clinical, and chemical parameters should also be monitored [14]. In this sense, glucose to potassium (Glu-K⁺) ratio can guide surgeons to follow both preoperative glucose and potassium levels together and help us to understand the course of the operation and to make inferences about possible surgical situations.
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Given in the flow chart (Figure 1), we analyzed and did not include the refused participation according to the exclusion criteria. Patients’ CABG data (n: 3556) were all grouped and analyzed according to the Glu-K’ levels, including value of < 20 (n: 496), 20-40 (n: 2345), 40-60 (n: 437), and > 60 (n: 278).

Exclusion criteria

We enrolled the patients in the study who received a CABG on-pump under general anesthesia. We excluded some of them who needed an open sternotomy again for surgery. Patients with chronic renal failure, acute renal failure, hepatic insufficiency, or primary conditions affecting results were excluded. The participants included in the study were limited to patients aged 18 years or older who underwent open-sternotomy for CABG and/or valve reconstruction for the first time. Besides, it was limited to cases without a history of neurocognitive disorder to reduce bias during bypass. This exclusion may lessen the discomfort for patient care approaches of clinicians.

Assessing comorbidities

Relevant comorbidities were assessed for all patients at the time of CABG, which were saved by physicians in the registry period of the bypass surgery. We accepted comorbidities like hypertension, cerebrovascular disease, immunosuppressive background, endocarditis, or peripheral vascular disease.

Laboratory analyse

As being in all tests, we measured glucose and potassium levels at the closest preoperative time point on the day of surgery. Biochemistry and hemogram tests were measured through patients’ serum samples by new system automatic-analysers manufactured by Beckman-Coulter Analyse in USA. We gained their laboratory findings via the hospital laboratory systems. The Glu-K’ ratio was calculated by divid-
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Table 1. Patients’ demographics and laboratory findings according to the groups of different glucose to potassium ratio

<table>
<thead>
<tr>
<th>Variables</th>
<th>&lt; 20 (n: 496)</th>
<th>20-40 (n: 2345)</th>
<th>40-60 (n: 437)</th>
<th>&gt; 60 (n: 278)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Stay*</td>
<td>5.4±1.9</td>
<td>5.2±1.6</td>
<td>5.3±1.8</td>
<td>5.3±1.5</td>
</tr>
<tr>
<td>Pomp PeriodΦ</td>
<td>73.5±51.5</td>
<td>69±25</td>
<td>69.4±22.8</td>
<td>69.3±21.6</td>
</tr>
<tr>
<td>Glu/K⁺ Ratio*</td>
<td>18.8±2.9</td>
<td>27.7±5</td>
<td>45.9±4.2</td>
<td>68.5±13.1</td>
</tr>
</tbody>
</table>

Variables showing significant difference (P < .05) are indicated by boldface. All data were given as mean+/−standard deviation, except gender that was given as frequency and percentage. *P < 0.05 - Φ P < 0.0001 Abbreviations. ALT: alanine aminotransferase, AST: aspartate amino transferase, BUN: blood urea nitrogen, eGFR: estimated glomerular filtration rate, INR: international normalized ratio, BMI: body mass index.

ing measured glucose to potassium levels manually in Microsoft Excel.

Operative techniques

In all patients undergoing CABG, standard anesthetic and operative techniques were performed. Anesthesia application was made with fentanyl (25-50 μg/kg) and rocuronium bromur (1 mg/kg). Cardiopulmonary bypass supported all cases, which covers arterial cannula on the ascendant aorta and venous cannula of right-atrium. We completed proximal anastomoses during the surgery with the heart-beating after distal anastomose construction during ischemic-arrest. We bypassed all blood vessels that had stenosis blocking the bloodstream. We used one or more internal-thoracic artery or saphenous vein for the patients. Multi-infusions of antegrade cardioplegic solution (pH: 7.6; Hct: 20%; potassium: 28 mEq/L) integrated with topical/systemic hypothermia was used to maintain myocardial protection.

Statistical method

Data assessment was done through SPSS software for the Mac-OS (IBM-Corp., USA). For categorical variables, we used the Chi-square test. Normally distributed continuous variables were compared using the ANOVA test. The relationship among four ranged values of Glu-K⁺ ratio as < 20 (n: 496), 20-40 (n: 2345), 40-60 (n: 437), and > 60 (n: 278) was investigated via ANOVA multi-group analyse. The Shapiro-Wilk test was used to analyze the normality of the data. The correlation between CABG related clinic conditions and serum Glu-K⁺ ratio was analyzed using the correlation coefficient or Spearman’s rank. Next, we evaluated the association of each variable with the Glu-K⁺ ratio, using correlation analysis. Results were shared as mean ± standard deviation, where appropriate, or frequency with percentage. Logistic regression analysis was used for comparing the extracted outcomes, including diabetes mellitus, bypass vessel count, ejection fraction, sex, myocardium infarct heart, cross-clamp count, and INR. Any comparison difference was accepted as statistically significant at a P value of < 0.05.

Results

Patients’ demographics

A total of 3556 patients (2565 male, 991 female) who underwent the CABG at our hospital were enrolled in the present study. There was no difference in terms of age and gender among the groups of Glu-K⁺ ratio (P > 0.05). Body mass index was found to be higher with increasing Glu-K⁺ ratios (P < 0.001). In all groups, the smoking habit was not observed as a significant factor (P = 0.287) (Table 1).

Patients’ clinic details

Cardiovascular findings according to the groups of glucose to potassium ratio were given in Figure 2. In patients’ clinical details, while blood supply and cross-clamp showed the difference, follow-up, drainage, intensive care period, ejection fraction, and hospital stay were similar among the subgroups (P > 0.05). In laboratory analysis, glucose, ALT, urea, BUN, potassium, leukocyte, neutrophil, and platelet were found to be significantly different among the groups, while INR, eGFR, creatine, natrium, lymphocyte, monocyte, basophil, and hemoglobin had no difference (P > 0.05).

In clinical assessment, number of bypass vessel (P < 0.0001), carotid arterial (P = 0.0078) and peripheral arterial disorder (P = 0.013) and hypertension (P < 0.0001), diabetes mellitus (P
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Figure 2. Comparison of glucose to potassium ratio with bypass vessel count.

Table 2. Correlations and regression summary for parameters on the variable of Glu-K+ ratio

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>Standard Error</th>
<th>Beta Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>28.5</td>
<td>1.68</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8.06</td>
<td>0.473</td>
<td>0.281</td>
</tr>
<tr>
<td>Bypass Vessels Count</td>
<td>1.05</td>
<td>0.191</td>
<td>0.093</td>
</tr>
</tbody>
</table>

Variables showing significant difference (P < 0.0001) are indicated by boldface. Abbreviations CI: confidence interval.

Discussion

In the study, we determined whether the Glu-K+ ratio has essential importance in bypass surgery and its outcomes. Our results showed a significant and positive strong relationship between CABG and Glu-K+ ratio, especially between the numbers of vessels used in CABG operation. This research is the first study to demonstrate the value of the Glu-K+ ratio for CABG surgery to the best of our knowledge. By recent studies, we acknowledged that increased glucose value has an association with worse outcomes following a bypass surgery [16-18]. Kubal et al. reported the efficiency of diabetes in patients undergoing bypass surgery [19]. Diabetes with insulin-dependence had an association with 1.6 times prolonged hospital stay after the surgery. According to the meta-analysis report of Capes et al., patients with diabetes showed 3.9 times higher adverse risk than patients who had no diabetes [20]. In their study, the risk of heart failure showed a strong relation with higher glucose concentrations. In another study, Gandhi et al. reported that a 20 mg/dL increase in glucose level was associated with increased adverse post-operative conditions for CABG [21]. According to the study of Doenst et al., cases of cardiac surgery showed that peak glucose was associated with many adverse events [22]. Considering these studies, they all revealed that morbidity and mortality increase with hyperglycemia in coronary syndrome after the bypass. In this sense, glucose levels have a critical position in terms of outcomes and mortality of CABG operations.

Many surgeons use glucose insulin and potassium (GIK) solution during the surgery to lessen lower than 20 to its intervals at 20-40, 40-60, and higher than 60. Bypass vessel count showed an increasing potential with an increasing Glu-K+ ratio. Comparing to lower than 20, bypass vessels count showed 10% increase in 20-40 range of Glu-K+ ratio (P < 0.012), 22% increase in 40-60 range of Glu-K+ ratio (P < 0.0001), and 34% increase in > 60 of Glu-K+ ratio (P < 0.0001).
perioperative mortality that can emerge due to increased glucose levels [23-25]. Some studies have reported that GIB decreases morbidity and mortality in acute infarct [26-28]. In CABG surgery, it can withstand myocardial, ischemia, and reperfusion periods, resulting in ischemic contractile dysfunction. It is recognized that morbidity and mortality are essential factors to the increase in the need for mechanical circulatory support [29]. Considering GIK, potassium levels gain different significance in these conditions and have to be followed with strong attention that should be assessed not only itself but also with glucose levels in a combination.

We know that potassium uptake via the cell surface and the pump of ATP-Na/K maintains its level. Both adrenergic hormones and insulin upregulate this pump and result in potassium decrease [30]. Precisely in this point, hypokalaemia, which is induced by epinephrine results from b-adrenoceptor stimulation linked to Na/K-ATPase in the cell membrane that causes potassium-influx [13]. In addition to that condition as mentioned above, CABG emerges higher glucose levels by catecholamines to be under stress; therefore, we see a medical outcome involving insulin secretion and K+ gathering in the cells. In a study by Matano et al. [31], the first report about the Glu-K+ index, there was a strong relationship between the serum Glu-K+ ratio and cerebral infarction, which elicited due to cerebral vasospasm. According to their report, the Glu-K+ ratio could be a potential indicator of catecholamine secretion and have benefits than glucose and potassium for their unique analysis.

In our study, we analyzed outcomes of CABG operation according to the Glu-K+ ratio and its four-stage ranges and found significance in terms of correlations and its different ranges. In patients’ clinical details, while blood supply and cross-clamp showed the difference, follow-up, ejection fraction, drainage, intensive care, and hospital stay were similar among different Glu-K+ ratio range subgroups. In clinical assessment, bypass vessel count, carotid arterial disorder, peripheral arterial disorder and hypertension, diabetes mellitus, hyperlipidemia, and myocardial infarct history showed a significant difference in terms of Glu-K+ ratios. In univariate correlation analysis, diabetes mellitus, bypass vessel count, ejection fraction, sex, myocardia infarct history, cross-clamp, and INR showed a significant relationship with Glu-K+ Ratio. Bypass vessel count was the most striking finding at this point because the high number of GLU-K in CABG operations showed that the number of vessels increased by increasing ranges of Glu-K+. In a way, this situation leads to the opinion that in patient with high Glu-K+ index, it may indirectly indicate that the patient has more vascular damage and needs more vessels to bypass surgery.

This study had some limitations. First, we performed a retrospective cohort study, and we could not follow the morbidity and mortality in the patients. Second, we did not have insulin and haemoglobinA1c values for these patients to be able to evaluate the detailed statistical comparisons of diabetic outcomes with the index. Therefore, we could not analyze the relation of those to the Glu-K+ index in the current study. Despite these limitations, our study is the first to show that the Glu-K+ index is essential and should be evaluated in CABG patients, and it is a valuable study in terms of shedding light on further prospective studies.

Disclosure of conflict of interest

None.

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