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The association of concomitant serum potassium and glucose levels and in-hospital mortality in patients with acute myocardial infarction (AMI). Soroka acute myocardial infarction II (SAMI-II) project

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ABSTRACT

Background: Acute myocardial infarction (AMI) is associated with significant systemic metabolic changes. These changes include increased plasma concentrations of counter-regulatory hormones and changes in potassium (K, mEq/L) and glucose (mg/dL) levels. The latter are associated with outcomes and investigated as potential focus for intervention; glucose-insulin-potassium (GIK) solution.
Objectives: To evaluate the associations of concomitant K and glucose (K/glucose) levels with in-hospital mortality in AMI patients.
Methods: AMI patients hospitalized in a tertiary Medical Center through 2002–2012 were studied. K/glucose levels were divided into equally sized categories. The intermediate category (glucose 124–143 mg/dL, K 4–4.9 mEq/L) was the reference group. The associations of these tests with the outcome were assessed using Generalized Estimating Equations model which included the interaction of K and glucose levels, adjusted for the patient's baseline characteristics and other laboratory results.
Results: 17,670 AMI admissions (mean age 67.8 ± 4.0 years, 66.6% males, mortality rate 7.7%) were included; 112,531 results of K/glucose tests were recorded. Univariate and multivariate analyses showed that K/glucose levels were significantly associated with in-hospital mortality, with highest risk being in patients with concomitant low K (<3.7 mEq/L) and high glucose (≥217 mg/dL), adjOR = 2.53. It seems that low-normal glucose levels attenuate the increased risk associated with low K.
Conclusions: The highest independent risk for mortality is found with low K and concomitant high glucose levels. Additional studies evaluating mechanisms and therapeutic interventions in K/glucose levels in this setting are warranted.

1. Introduction

The setting of acute myocardial infarction (AMI) is associated with significant systemic metabolic changes. These changes include increased plasma concentrations of counter-regulatory hormones (e.g. adrenaline, cortisol and glucagon), increased insulin resistance and associated changes in potassium (K, mEq/L) and glucose (mg/dL) levels [1–6]. It has been consistently reported that low, high and fluctuations in K levels, as well as hyperglycemia are markers of poor prognosis in patients with AMI [5,7–18]. Furthermore, the degree of the observed potassium fluctuation (dip) in patients with acute coronary syndrome (ACS) was shown to be tightly correlated with glucose level, which also indicated the disease severity [4,6].

Attempts to improve the abovementioned metabolic perturbations were evaluated in experimental and clinical studies that used intravenous glucose-insulin-potassium (GIK) solution in the setting of AMI [19]. The rationale behind the latter treatment was to facilitate glucose and concomitantly potassium transportation into the cardiomyocyte in order to improve myocardial metabolism, lessen infarct size, reduce the risk for arrhythmia and thus to improve patient outcomes. However, meta-analysis of 8 randomized trials did not reveal mortality benefit with GIK therapy in STEMI [20]. The untoward effects of secondary hyperglycemia or K levels outside the optimal range might have offset the potential benefit [5,21].

The objective of the current study was to evaluate the association of concomitant K and glucose levels with in-hospital mortality in patients with AMI.

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2. Methods

2.1. Study population

In this retrospective study we reviewed the medical records of patients admitted to a tertiary medical center with the recorded diagnosis of AMI throughout 2002–2012, in consistency with previous description of the Soroka Acute Myocardial Infarction Project II (SAMI II) [5,22–24]. Exclusion criteria: cases in which synchronous K and glucose values were missing.

The local ethics committee approved the study, which was performed in accordance with the Helsinki declaration.

Table 1
Baseline characteristics and results of laboratory tests among hospital survivors and deceased patients.

	Number of admissions			p
	Total[a]	Survivors[a]	Deceased[a]	
	$n = 17{,}670$	$n = 16{,}316$	$n = 1354$	
Demographics				
Age, Years				
Mean (SD)	67.8 (14.0)	67.1 (14.0)	76.6 (11.4)	<0.001
Sex				
Male	11,764 (66.6)	11,035 (67.6)	729 (53.8)	<0.001
Cardiac diseases				
Cardiomegaly	2011 (11.4)	1879 (11.5)	132 (9.7)	0.049
Supraventricular arrhythmias	3304 (18.7)	2903 (17.8)	401 (29.6)	<0.001
CHF	4121 (23.3)	3580 (21.9)	541 (40.0)	<0.001
Pulmonary heart disease	2107 (11.9)	1930 (11.8)	177 (13.1)	0.175
CIHD	14,466 (81.9)	13,583 (83.2)	883 (65.2)	<0.001
AV block	721 (4.1)	620 (3.8)	101 (7.5)	<0.001
Cardiovascular risk factors				
Renal diseases	7910 (44.8)	6787 (41.6)	1123 (82.9)	<0.001
Diabetes mellitus	7596 (43.0)	6958 (42.6)	638 (47.1)	0.001
Dyslipidemia[b]	11,787 (66.7)	11,186 (68.6)	601 (44.4)	<0.001
Hypertension	9910 (56.1)	9173 (56.2)	737 (54.4)	0.202
Obesity	3569 (20.2)	3394 (20.8)	175 (12.9)	<0.001
Smoking	6729 (38.1)	6481 (39.7)	248 (18.3)	<0.001
PVD	2773 (15.7)	2455 (15.0)	318 (23.5)	<0.001
Family history of IHD	1073 (6.1)	1061 (6.5)	12 (0.9)	<0.001
Other disorders				
COPD	1824 (10.3)	1631 (10.0)	193 (14.3)	<0.001
Neurological disorders	3575 (20.2)	3128 (19.2)	447 (33.0)	<0.001
Malignancy	752 (4.3)	636 (3.9)	116 (8.6)	<0.001
Schizophrenia/Psychosis	318 (1.8)	282 (1.7)	36 (2.7)	0.013
Alcohol/drug addiction	379 (2.1)	353 (2.2)	26 (1.9)	0.553
Characteristics of the hospitalization				
Total hospital duration, days				
Mean (SD)	10.4 (10.7)	10.1 (9.4)	13.7 (20.2)	<0.001
Type of AMI				
STEMI	7964 (45.1)	7209 (44.2)	755 (55.8)	<0.001
Complications	780 (4.4)	694 (4.3)	86 (6.4)	<0.001
Results of echocardiography				
Echo performance, n (%)[c]	11,603 (69.8)	11,067 (71.0)	536 (51.8)	<0.001
Severe LV dysfunction	1539 (13.3)	1355 (12.2)	184 (34.3)	<0.001
LV hypertrophy	563 (4.9)	533 (4.8)	30 (5.6)	0.413
Mitral regurgitation	891 (7.7)	799 (7.2)	92 (17.2)	<0.001
Tricuspid regurgitation	544 (4.7)	471 (4.3)	73 (13.6)	<0.001
Pulmonary hypertension	1133 (9.8)	1019 (9.2)	114 (21.3)	<0.001
Results of angiography				
Angiography performance, n (%)[d]	11,884 (67.3)	11,266 (69.0)	618 (45.6)	<0.001
Measure of CAD				
No or non-significant	516 (5.1)	505 (5.2)	11 (2.5)	
One vessel	2425 (23.8)	2374 (24.3)	51 (11.5)	<0.001
Two vessels	2768 (27.1)	2680 (27.5)	88 (19.8)	
Three vessels/LM	4492 (44.0)	4197 (43.0)	295 (66.3)	
Type of treatment				
Noninvasive	6446 (36.5)	5596 (34.3)	850 (62.8)	
PCI	9185 (52.0)	8796 (53.9)	389 (28.7)	<0.001
CABG	2034 (11.5)	1919 (11.8)	115 (8.5)	
Results of laboratory data				
Serum potassium (mEq/L)				
Number of tests	113,253	95,847	17,406	
Mean (SD)	4.3 (0.62)	4.3 (0.58)	4.4 (0.80)	<0.001
Serum glucose (mg/dL)				
Number of tests	112,531	95,251	17,280	
Mean (SD)	152.9 (72.8)	150.2 (70.2)	167.9 (84.1)	<0.001
Serum sodium (mEq/L)				
Number of tests	113,123	95,736	17,387	
Mean (SD)	138.0 (4.4)	137.9 (4.0)	138.2 (6.0)	<0.001
Serum creatinine (mg/dL)				
Number of tests	112,939	95,595	17,344	
Mean (SD)	1.5 (1.3)	1.3 (1.2)	2.1 (1.6)	<0.001
Anemia[e]				
Number of tests	17,670	16,316	1354	
n (%)	10,839 (61.3)	9712 (59.5)	1127 (83.2)	<0.001

2.2. Data sources and classifications

Data were obtained from the patients' computerized medical records. The data comprised demographic and clinical characteristics, cardiovascular risk factors and co-morbidity, therapeutic interventions and routine clinical workup (e.g. blood tests, echocardiography and coronary angiography) [24]. Mortality data were obtained from the hospital's mortality database.

AMI diagnosis was identified based on the international Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes: ST-elevation AMI (STEMI): 410.0*–410.6* and Non-ST-elevation AMI (NSTEMI): 410.7*–410.9*. Grouping of diseases and interventions were based on ICD-9-CM discharge codes.

K and glucose (K/glucose) levels were divided into 7 equally sized categories, each. The intermediate categories (glucose 124–143 mg/dL) and (K 4–4.9 mEq/L) were used as the reference group.

Anemia was defined as hemoglobin (Hb) level < 14 g/dL or hematocrit (HTC) level < 42% for males and Hb level < 12 g/dL or HTC level < 37% for females during the hospitalization. Dyslipidemia was defined as recorded diagnosis of dyslipidemia and/or average low density lipoprotein (LDL) cholesterol level > 130 mg/dL during the hospitalization (mostly for corroboration, for potential cases of under-recording, the cut-off was chosen as this was throughout the study period the cut-off for lipid lowering treatment for patients with >2 major risk factors and a 10-year risk of 10% to 20%, even without coronary heart disease, i.e. before the index event) [25].

2.3. Outcome

The primary outcome was all-cause in-hospital mortality.

2.4. Statistical analysis

Statistical analysis was performed using SPSS Statistics 25 software. Patient characteristics were presented as mean and standard deviation (SD) for continuous variables and *n* and percent for the categorical data. The comparison of baseline characteristics and the laboratory data between the groups of hospital survivors and deceased was performed using Student's *t*-test and Chi-square test. The values of the laboratory data in this set of analysis were initially investigated in 7 equal-size categories and the third (middle) category served as the reference group. Subsequently several adjacent groups of parameters were merged according to the strength of the association with the outcome. The distributions (*n*, %) of K/glucose categories in hospital survivors and deceased patients were presented. The comparison of the risk of in-hospital mortality and K/glucose categories in univariate (unadjusted) and multivariate (adjusted) levels included generalized estimating equations (GEE) interactive models. The results of the models were presented as Odds Ratio (OR) with 95% Confidence Intervals (CI). The final interactive model (GEE) estimated the relationships between the investigated K/glucose parameters and the outcome adjusted for other laboratory data and the baseline characteristics. For each test, $p < 0.05$ was considered as statistically significant.

3. Results

Following exclusion of 110 admissions due to missing data, overall 17,670 admissions (12,535 patients), mean age 67.8 [SD = 4.0] years, 66.6% males, were included. In-hospital mortality occurred in 1354 patients that comprised 7.7% of all hospital admissions. Baseline characteristics, compared according to hospital survival or death, are presented in Table 1. Patients who died in hospital were older, higher rate of: males, cardiovascular risk factors and previous cardiovascular disease, STEMI, severity of coronary artery disease, incidence of in-hospital ventricular arrhythmias, conservative treatment and in-hospital stay. The included patients had a total of 112,531 laboratory K/glucose test results (95,251 for hospital survivors, 17,280 for deceased) throughout the hospital stay.

A significant yet relatively weak correlation between K and glucose level was found among study subjects ($r = 0.113$, $p < 0.001$). The distribution of paired K/glucose levels (by categories) among hospital survivors and deceased are displayed in Table 2. K/glucose levels in the more extreme ranges seemed to be more prevalent among deceased patients. Interestingly, a separate analysis of the distribution of K/glucose levels in patients with documented ventricular arrhythmias throughout the admission versus those without showed that low K (i.e. K < 3.7) was more prevalent among patients with ventricular arrhythmias (particularly the combination of low K and high glucose) vs. those without.

The association between baseline characteristics, laboratory tests and mortality (univariate association) is showed in Table 3. The following were associated with increased risk for mortality: increased age, females, previous cardiovascular morbidity and risk factors, non-cardiovascular co-morbidity, STEMI, three vessel coronary artery disease, severe left ventricular dysfunction (ejection fraction<35%), valvular disorders, and non-invasive treatment. Furthermore, both decreased and increased K levels were associated with increased risk for mortality, with K ≥ 4.9 mEq/L comprising the highest risk. Regarding glucose levels, the risk for mortality gradually increased with the increase in glucose level. Fig. 1a displays the unadjusted risk for mortality according to K/glucose levels (see appendix A for unadjusted interactive model). The graphs clearly show that the risk for mortality increases with the increase in glucose level, for every K category, and as K category is further from the reference category. More specifically, increased as well as decreased K levels are associated with increased mortality. In the lower glucose categories (i.e. <143 mg/dL), the combination with increased K comprises worse prognosis than with decreased K. However in the higher glucose categories the association is reversed and the combination with lower K, rather than higher K, is associated with increased risk for mortality. The combination of lowest K with highest glucose was found to associated with the highest risk for mortality.

Consistently, multivariate analysis (Fig. 1b) showed similar, yet somewhat attenuated OR, with highest risk for in-hospital mortality found in patients with combined low K (K < 3.7 mEq/L) and high glucose (≥217 mg/dL), adjOR = 2.53. Furthermore, it seems that the risk for mortality attenuated when K < 3.7 mEq/L was found in combination with lowest glucose levels. Moreover, at higher glucose levels low rather than high K levels were associated with higher risk for in-hospital mortality. Additional parameters included into the multivariate model were: age, sex, diabetes mellitus, chronic ischemic heart disease, alcohol and drug addiction, dyslipidemia, type of AMI and it's treatment, left ventricular dysfunction, anemia, levels of serum creatinine and serum sodium (see appendix B for full multivariate model). A subgroup analysis according to the AMI (STEMI/NSTEMI) and management type (Percutaneous Coronary Intervention [PCI]/conservative) has shown overall qualitatively similar associations between concomitant K/glucose levels and the outcome in these subgroups, yet a tendency towards more powerful associations were observed in the STEMI and the PCI subgroups. Furthermore, subgroup analysis according to diabetes mellitus status (see supplement Fig. 2a and b) has shown that the association of "extreme" K and glucose levels (and especially hyperglycemia, even in combination with normal K levels) and the outcome, is particularly high among the AMI patients with no recorded diabetes (e.g. hyperglycemia with normal K levels is associated with 3- fold increased mortality compared with the reference group).

4. Discussion

The current study evaluated the combined associations of K and glucose levels with in-hospital mortality in patients admitted with AMI.

Notes to Table 1:
Abbreviates: AMI – Acute myocardial infarction, AV – Atrioventricular, CABG - Coronary artery bypass surgery, CAD - Coronary artery disease, CHF - Congestive heart failure, CIHD –Chronic ischemic heart disease, COPD - Chronic obstructive pulmonary disease, IHD - Ischemic heart disease, LM – Left main (artery), LV – Left ventricular, PCI - Percutaneous coronary intervention, PVD - Peripheral vascular disease, SD – standard deviation, STEMI - ST segment elevation myocardial infarction, VF – Ventricular fibrillation, VT – Ventricular tachycardia.

[a] The data are presented as n (%) unless otherwise stated.
[b] Dyslipidemia is defined as recorded diagnosis of dyslipidemia and/or average LDL level > 130 mg/dL during the hospitalization.
[c] Among persons with the results of echocardiography.
[d] Among persons with the results of angiography.
[e] Anemia is defined as hemoglobin level < 14 g/dL or hematocrit level < 42% for males and hemoglobin level < 12 g/dL or hematocrit level < 37% for females.

Table 2
Distribution of K/glucose pair levels (by categories): a) among hospital survivors and b) among deceased.

a)

Potassium (mEq/L)	Glucose (mg/dL)						
	<94	94–109	109–124	124–143	143–170	170–217	≥217
<3.7	1426 (1.5%)	1475 (1.5%)	1425 (1.5%)	1648 (1.7%)	1484 (1.6%)	1284 (1.3%)	1044 (1.1%)
3.7–4.0	1931 (2.0%)	2179 (2.3%)	2167 (2.3%)	2376 (2.5%)	2051 (2.2%)	1725 (1.8%)	1429 (1.5%)
4.0–4.9	8612 (9.0%)	9795 (10.3%)	8593 (9.0%)	9096 (9.5%)	8466 (8.9%)	7957 (8.4%)	7730 (8.1%)
≥4.9	1434 (1.5%)	1492 (1.6%)	1280 (1.3%)	1417 (1.5%)	1509 (1.6%)	1721 (1.8%)	2505 (2.6%)

b)

Potassium (mEq/L)	Glucose (mg/dL)						
	<94	94–109	109–124	124–143	143–170	170–217	≥217
<3.7	361 (2.1%)	288 (1.7%)	370 (2.1%)	419 (2.4%)	494 (2.9%)	488 (2.8%)	431 (2.5%)
3.7–4.0	254 (1.5%)	219 (1.3%)	275 (1.6%)	406 (2.3%)	372 (2.2%)	451 (2.6%)	389 (2.3%)
4.0–4.9	896 (5.2%)	791 (4.6%)	939 (5.4%)	1216 (7.0%)	1427 (8.3%)	1575 (9.1%)	1603 (9.3%)
≥4.9	503 (1.5%)	323 (1.9%)	376 (2.2%)	457 (2.6%)	511 (3.0%)	572 (3.3%)	874 (5.1%)

The main findings of the current study are that both increased and decreased K levels as well as increased glucose levels are associated with increased mortality in patients with AMI. The highest independent risk for mortality is found with the combination of low K and high glucose levels. Furthermore increased risk for mortality found for low K levels seems to be significantly attenuated when it is found in combination with low glucose levels.

The setting of AMI is known to be associated with metabolic changes such as increased plasma concentrations of counter-regulatory hormones (e.g. catecholamines, glucocorticoids) and a state of increased insulin resistance supporting increased glucose levels as well [1–3,6]. Ito et al. [6] recently reported that changes in K during ACS (especially the early dip) were positively correlated with glucose and preserved even under insulin resistance condition. Furthermore, Sekiyama et al. [4] found that the plasma glucose level during ischemic attack was the sole factor which was positively correlated with changes in K. Thus the latter association between glucose and K levels in the setting of AMI could potentially be explained by insulin-dependent stimulation of intracellular K shift into the cardiac and skeletal muscles via sodium-proton exchanger (NHE) Na^+/K^+-ATPase activation [4,26,27]. Interestingly, diabetic patients with ACS did not exhibit the early dip in K levels seen in non-diabetics patients and were actually found to have higher serum potassium concentrations [28]. Possible explanation for the latter observation could be relative insulin deficiency and sympathetic nerve dysfunction in diabetic patients. These differences in the interaction of K/glucose between diabetics vs. non-diabetic ACS patients could also explain, at least partially, the stronger interaction of high glucose levels, with high or even normal concomitant K and the outcomes observed in non-diabetic patients in the current study. Nevertheless, "insulin-independent" glucose-coupled mechanisms for this interaction have been suggested as well, and include catecholamine stimulation of the Na^+/K^+-ATPase pump (primarily via β2-adrenergic receptor) resulting re-distributional decrease in K levels [13,26,28]. Furthermore the insulin independent sodium-glucose cotransporter (SGLT) 1, which is activated by Na^+/K^+-ATPase, works against the glucose concentration gradient by coupling glucose transport to the downhill Na^+ electrochemical gradient via Na^+/K^+-ATPase. Therefore, SGLT1 activation under ischemia, low-glucose conditions and in particular SGLT1 Na^+/K^+-ATPase coupling could explain glucose associated K decrease [6]. Additionally activation of renin-angiotensin-aldosterone system in response to the ischemic stress could also play a role [29]. Moreover, among patients presenting with AMI, a positive association between glucose levels and inflammatory markers, which are known prognostic markers, was reported [30]. Such an inflammatory state which is associated with multiple metabolic changes could be associated with changes in K levels [7–14,30].

Numerous previous reports showed that both increased and decreased K levels are associated with worse outcomes (i.e. higher risk for ventricular arrhythmias and mortality) in patients with AMI [5,7–14]. Similarly, hyperglycemia was reported to be a strong predictor of mortality in AMI patients with and without diabetes [15–18]. However, the current report investigated the combined association of the two important prognostic factors on in-hospital mortality.

Although multiple mechanisms have been suggested to explain the association between K levels and outcomes in AMI patients or alternatively between glucose levels and mortality in these patients, it is currently unclear whether this association is causative or circumstantial. Thus it is possible high/low K levels combined with increased glucose levels reflect a more severe presentation (as reflected metabolically of hormonally) with increased rate of complications (e.g. heart failure, renal failure, ventricular arrhythmias), hence K/glucose are serve as a marker of severity and therefore are associated with increased mortality. Since low K levels and increased glucose would be a more expected combination resulting from the metabolic effects of AMI [6], this could explain why this combination (rather than increased K and glucose levels) was found to be associated with higher risk for in-hospital mortality. Consistently, the combination of low K and high glucose was also found to be more prevalent among patients who developed ventricular arrhythmias versus those who did not develop such arrhythmias.

The findings of the current study could also hypothetically explain the reasons that routine administration of GIK in the setting of AMI was not consistently found to be beneficial. According to our findings the administration of GIK could result in shifting both glucose and K outside the ranges that are associated with best outcomes (e.g. further increase glucose levels and decrease/increase K) hence deleteriously effect outcomes. On the other hand the findings imply that selected patients, in which the effect of GIK would "normalize" K without significantly increasing glucose levels, could benefit from this intervention. Obviously these hypotheses need to be proven in a dedicated study.

4.1. Limitations

Several limitations of the current study should be mentioned. First the study is observational and shares the limitations of such a design. The results of the laboratory tests were obtained retrospectively based on available tests obtained routinely or as decided by the treating team decision rather than predesigned identical timing, thus tests like hormone levels (catecholamine, glucocorticoids) that could assist in further understanding of the mechanisms of our findings were not available. We did not collect information on medical treatment, especially treatments that potentially effect glucose or K levels (e.g. insulin therapy, beta blockers etc.).The cause of death is missing,

Table 3
Association between baseline characteristics, laboratory tests and mortality: univariate analysis.

Parameter	Values	B (SE)	OR (95% CI)	*p*
Age	One year increase	0.056 (0.002)	1.058 (1.053; 1.063)	<0.001
Sex	Male vs. female	−0.583 (0.057)	0.558 (0.499; 0.624)	<0.001
Cardiac diseases				
Cardiomegaly	Yes vs. no	−0.186 (0.095)	0.830 (0.689; 1.000)	0.049
Supraventricular arrhythmias	Yes vs. no	0.665 (0.063)	1.944 (1.719; 2.199)	<0.001
CHF	Yes vs. no	0.862 (0.059)	2.367 (2.110; 2.656)	<0.001
Pulmonary heart disease	Yes vs. no	0.114 (0.084)	1.121 (0.950; 1.322)	0.175
CIHD	Yes vs. no	−0.975 (0.061)	0.377 (0.335; 0.425)	<0.001
AV block	Yes vs. no	0.713 (0.111)	2.041 (1.641; 2.538)	<0.001
Cardiovascular risk factors				
Renal diseases	Yes vs. no	1.921 (0.074)	6.826 (5.904; 7.890)	<0.001
Diabetes Mellitus	Yes vs. no	0.181 (0.057)	1.198 (1.072; 1.339)	0.001
Dyslipidemia[a]	Yes vs. no	−1.005 (0.057)	0.366 (0.327; 0.409)	<0.001
Hypertension	Yes vs. no	−0.072 (0.057)	0.930 (0.832; 1.040)	0.202
Obesity	Yes vs. no	−0.571 (0.083)	0.565 (0.480; 0.665)	<0.001
Smoking	Yes vs. no	−1.078 (0.072)	0.340 (0.295; 0.392)	<0.001
PVD	Yes vs. no	0.550 (0.068)	1.733 (1.518; 1.979)	<0.001
Family history of IHD	Yes vs. no	−2.051 (0.292)	0.129 (0.073; 0.228)	<0.001
Other disorders				
COPD	Yes vs. no	0.403 (0.082)	1.497 (1.275; 1.758)	<0.001
Neurological disorders	Yes vs. no	0.731 (0.061)	2.078 (1.843; 2.342)	<0.001
Malignancy	Yes vs. no	0.837 (0.105)	2.310 (1.880; 2.839)	<0.001
Schizophrenia/psychosis	Yes vs. no	0.440 (0.179)	1.553 (1.093; 2.207)	0.014
Alcohol/drug addiction	Yes vs. no	−0.122 (0.205)	0.885 (0.592; 1.324)	0.553
Characteristics of the hospitalization				
Day after admission	One day increase	0.033 (0.005)	1.034 (1.024; 1.044)	<0.001
Type of AMI	STEMI vs. NSTEMI	0.465 (0.057)	1.592 (1.424; 1.780)	<0.001
Results of echocardiography				
LV dysfunction	Severe vs. less	1.467 (0.088)	4.338 (3.651; 5.154)	<0.001
LV hypertrophy	Yes vs. no	0.015 (0.192)	1.015 (0.697; 1.480)	0.937
Mitral regurgitation	Yes vs. no	1.011 (0.112)	2.748 (2.206; 3.423)	<0.001
Tricuspid regurgitation	Yes vs. no	1.289 (0.126)	3.631 (2.837; 4.647)	<0.001
Pulmonary hypertension	Yes vs. no	0.934 (0.105)	2.545 (2.071; 3.127)	<0.001
Results of angiography				
Measure of CAD	No or non-significant		1 (Ref)	
	One vessel	−0.014 (0.336)	0.986 (0.510; 1.906)	0.967
	Two vessels	0.410 (0.323)	1.507 (0.800; 2.842)	0.204
	Three vessels/LM	1.172 (0.311)	3.227 (1.755; 5.932)	<0.001
Type of treatment	Noninvasive		1 (Ref)	
	PCI	−1.234 (0.064)	0.291 (0.257; 0.330)	<0.001
	CABG	−0.930 (0.103)	0.395 (0.323; 0.483)	<0.001
Results of laboratory data				
Potassium (mEq/L)	<3.7	0.735 (0.060)	2.086 (1.856; 2.344)	<0.001
	3.7–4.0	0.195 (0.041)	1.216 (1.123; 1.316)	<0.001
	4.0–4.9		1 (Ref)	
	≥4.9	0.819 (0.045)	2.267 (2.077; 2.475)	<0.001
Glucose (mg/dL)	<94	−0.134 (0.055)	0.874 (0.785; 0.974)	0.015
	94–109	−0.460 (0.046)	0.631 (0.576; 0.691)	<0.001
	109–124	−0.166 (0.037)	0.847 (0.788; 0.910)	<0.001
	124–143		1 (Ref)	
	143–170	0.189 (0.034)	1.208 (1.129; 1.292)	<0.001
	170–217	0.348 (0.047)	1.416 (1.290; 1.553)	<0.001
	≥217	0.412 (0.064)	1.510 (1.333; 1.710)	<0.001
Anemia[b]	Yes vs.no	1.127 (0.063)	3.087 (2.726; 3.496)	<0.001
Serum creatinine (mg/dL)	<0.70	−0.023 (0.125)	0.977 (0.765; 1.248)	0.854
	0.70–0.83	−0.359 (0.071)	0.698 (0.608; 0.802)	<0.001
	0.83–0.96	−0.287 (0.054)	0.750 (0.675; 0.834)	<0.001
	0.96–1.13		1 (Ref)	
	1.13–1.42	0.436 (0.053)	1.547 (1.394; 1.717)	<0.001
	1.42–2.12	0.879 (0.075)	2.409 (2.078; 2.792)	<0.001
	≥2.12	1.695 (0.103)	5.445 (4.450; 6.663)	<0.001
Serum sodium (mEq/L)	<134	1.002 (0.071)	2.723 (2.371; 3.127)	<0.001
	134–136	0.477 (0.045)	1.611 (1.477; 1.758)	<0.001
	136–140		1 (Ref)	
	140–142	0.212 (0.046)	1.236 (1.130; 1.353)	<0.001
	≥142	1.280 (0.071)	3.596 (3.132; 4.129)	<0.001

Abbreviates: AMI – Acute myocardial infarction, AV – Atrioventricular, CABG - Coronary artery bypass surgery, CAD - Coronary artery disease, CHF - Congestive heart failure, CI – Confidence interval, CIHD –Chronic ischemic heart disease, COPD - Chronic obstructive pulmonary disease, IHD - Ischemic heart disease, LM – Left main (artery), LV – Left ventricular, NSTEMI - Non ST segment elevation myocardial infarction, OR – Odds ratio, PCI - Percutaneous coronary intervention, PVD - Peripheral vascular disease, SE – Standard error, STEMI - ST segment elevation myocardial infarction.

[a] Dyslipidemia is defined as recorded diagnosis of dyslipidemia and/or average LDL level > 130 mg/dL during the hospitalization.

[b] Anemia is defined as Hb level < 14 g/dL or HTC level < 42% for males and Hb level < 12 g/dL or HTC level < 37% for females during the hospitalization.

yet the study deals only with deaths occurring throughout the admission of AMI. The current study included consecutive real life AMI patients while the analyses were performed per-admission, and hence patients with re-infarction were included and analyzed as separate admissions with the use of an appropriate statistical model. Although it is possible that such an analysis might not accurately represent

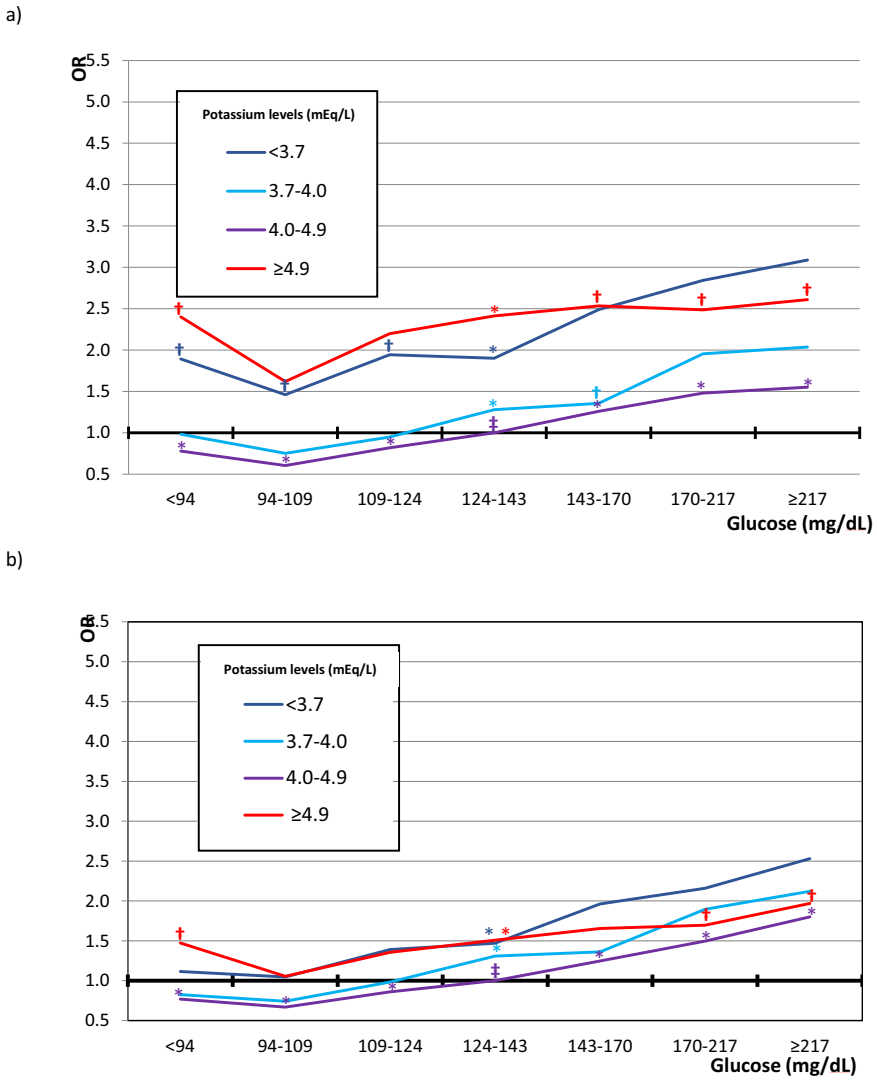

Fig. 1. Relative risk (Odds Ratio – OR) for in-hospital mortality by the categories of K/Glucose levels: a) unadjusted interactive analysis; b) multivariate interactive model. Legend: * $p < 0.05$, † p for interaction <0.05, ‡ Reference group.

per-patient outcomes, we believe that excluding patients with re-infarction could result in a significantly less externally-validated cohort.

5. Conclusions

Increased and decreased K levels as well as increased glucose levels throughout an admission with AMI are associated with increased risk for mortality in patients with AMI. The highest independent risk for mortality is found with the concomitant low K and high glucose. When low K levels are found concomitantly with low glucose levels the risk seems to be significantly attenuated. Additional studies evaluating mechanisms explaining current findings and therapeutic interventions effecting K/glucose levels in this setting and according to different initial K/glucose values are warranted.

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Declarations of interest

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